

HIV Drug Resistance Early Warning Indicators Survey in Ethiopia, 2013/14



PREFACE

Ethiopia has been progressively expanding and intensifying her response to the epidemic since enactment of the National HIV/AIDS Policy in 1998. In 2003, the Government of Ethiopia introduced its ART programme with the goal of reducing HIV-related morbidity and mortality, improving the quality of life of people living with HIV and mitigating some of the impact of the epidemic.

Free ART was launched in 2005, since then both the numbers of sites providing the service and patients receiving treatment have rapidly increased. In June 2013, a total of 913 health facilities were providing HIV care and treatment services in all regions of the country while 308,860 of patients were on treatment. As the number of people on treatment increases, the emergence of HIV drug resistance (HIVDR) becomes a greater risk which has the potential to undermine the dramatic gains that ART programs have had in reducing the morbidity and mortality.

To respond to the problem of HIVDR and to attempt to minimize its occurrence, WHO has established several strategies for surveillance and monitoring of HIVDR. Among the activities proposed is monitoring the quality of care in ART programmes using “Early Warning Indicators” of HIVDR (EWI). The Ethiopian Ministry of Health (MoH) has been proactive in minimizing preventable HIVDR. A national HIVDR working group was established within the MoH to integrate the essential HIVDR strategy into the country’s ART and HIV prevention plans.

EWI pilot survey was conducted in December 2007 in 14 selected hospitals providing ART in 4 regions. Following the pilot study preparation was done to do the survey in different geographically representative ART sites, data was abstracted in 45 (2008), and 49 (2009&2010) health facilities. In 2014, following the 2012 update of WHO global strategy for HIVDR, EWIs survey was done in 81 different geographically representative sites of the country.

The report or result of this survey will be used to improve the performance of the ART site practice and quality of care and also be used to inform national decision-making on ART program development and other HIVDR prevention measures. As one of the major activities of the institute in supporting the HIV/AIDS control program, EPHI will continue to produce data

for decision making to improve programs. As a future plan effort will be done to integrate EWI collection in to the national ART program as routine practice.

CONTRIBUTORS

Dawit Assefa (EPHI)

Yimam Getaneh (EPHI)

Dr.Fekadu Adugna (WHO-E)

Dr.Yibeltal Assefa (EPHI)

Dr. Kussito Kursha (CDC-E)

Nigussie Gezahagn (EPHI)

Getnet Mesfin (EPHI)

Abebe H/Silasie (EPHI)

Zelalem yaregal (EPHI)

Tesfaye Tilahun (EPHI)

Atsbeha Gebrexier (EPHI)

Dr. Desta Kassa (EPHI)

ACRONYMS

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Therapy
ARV	Antiretroviral Therapy
AZT	Zidovudine (also known as ZDV)
EWI	Early Warning Indicator
HAART	Highly active anti-retroviral therapy
HIV	Human immunodeficiency virus
HIVDR	HIV drug resistance
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
PI	Protease Inhibitor
RNA	Ribonucleic Acid
RT	Reverse Transcriptase
TWG	Technical Working Group
UNAIDS	Joint United Nations Programme on HIV/AIDS
VL	Viral Load

OPERATIONAL DEFINITIONS

- **“Appropriate regimen”** Standard regimen listed in national ART guidelines and used according to those guidelines
- **“Baseline pill pick-up”**: The date of first drug pick-up during the selected study period using pharmacy records for data abstraction.
- **“Death”**: A report of confirmed death in the patient's medical record, for which a date (at least month/year) is recorded. This may be based on a formal death certification or on a report from a person/caregiver who knew the patient.
- **“First-line ART”**: The initial ARV regimen prescribed for a patient initiating ART.
- **“Initiating ART at the site”**: is defined as first prescription of ART at the site in an individual who has not previously received ART at the site, with the exception of ARV drugs for prevention of mother to child transmission (PMTCT), and who has not transferred in on ART. This definition includes: treatment naïve patients; patients who have received ARV prophylaxis for PMTCT; non-naïve patients who received ART from other sources and are not recorded as transferred in.
- **“Lost to follow-up at 12 months”**: A patient who missed a scheduled clinical consultation or ARV drug pick-up in the first 12 months of therapy and who did not return to the ART site or pharmacy within (that is, > 90 days after the last missed clinical consultation or missed drug pick-up, and for whom there is no information to classify the patient as "dead", "stop", or "transfer out". Patients who return during the 12-month period are not classified as LTFU.
 - For patients who cannot be classified as LTFU (using the above definition) at 12 months, the follow up period must be extended until the patient is seen at the site or to the 15 month date, whichever is earliest.
 - Patients whose transfer, ART or death status is unknown and who meet the ‘LTFU’ definition are considered 'LTFU' despite that some may have died or be attending another clinic.
- **“On-time pill pick-up of ARV drugs”**: A patient pick-up of ARV drugs on or before the date or "within seven days" of the previously dispensed drugs would have run out if they had been taken according to schedule.

- **“Retention in care”**: Percentage of adults and children known to be alive and on treatment 12 months after initiation of ART.
- **“Run-Out Date”**: The date on which ARV drugs dispensed at the last ARV drug pick-up would have been finished if taken as prescribed.
- **“Second-line ART”**: is defined as a regimen prescribed after clinical, immunological, or virologic failure of a first-line regimen as defined in the national guidelines. It does not include substitutions of one drug in the same class for another in a first-line regimen.
- **“Stock-out”**: Any occurrence of zero stock of a routinely-used ARV drug at the site at which the patient routinely picks up ARVs.
- **“Stop”** is a complete halt of the entire ART regimen, without a restart within the “12-month date” (i.e. one calendar year after the date of ART initiation).
- **“Switch”**: is defined as a change in an ART regimen after regimen failure. The change involves at least two new drugs; one of which is from a new ARV class.
- **“Transfer out”**: A patient whose ART is being provided at another identified ART delivery site, and who was still on first-line ART at the time of transfer. If the individual is known to be receiving ART at another site and this transfer has been recorded in the medical records, the participant meets the definition for transfer out.

Table of Contents

Page

PREFACE.....	i
CONTRIBUTORS.....	ii
ACRONYMS.....	iii
OPERATIONAL DEFINITIONS.....	iv
LIST OF TABLES.....	vii
LIST OF FIGURES.....	viii
EXECUTIVE SUMMARY.....	1
1. INTRODUCTION.....	2
1.1. RATIONALE.....	2
1.2. ETHIOPIA HIV SITUATION OVERVIEW.....	4
2. OBJECTIVE.....	7
3. METHODOLOGY.....	7
3.1 Study design.....	7
3.2 Site Selection and Data Abstraction.....	7
3.3 Sampling and sample size determination.....	8
3.4 Data Validation, Analysis and Interpretation.....	9
3.5 Data storage and disposition.....	10
3.6 Study variables.....	10
3.6.1. On-time pill pick-up (Cross-sectional).....	10
3.6.2. Retention in care (Longitudinal).....	11
3.6.3. Pharmacy stock-outs.....	11
3.6.4. Dispensing practices.....	11
3.6.5. Virological suppression.....	11
3.7 Ethics statements.....	12
4. RESULTS AND DISCUSSIONS.....	13
5. CONCLUSIONS AND RECCOMENDATIONS.....	24
6. LIMITATIONS.....	26
7. ACKNOWLEDGMENTS.....	27
8. ANNEXES.....	28

LIST OF TABLES

Table-1 WHO recommended sample size determination for each site.....	17
Table-2 Summary of EWIs as per health facilities in 2013/14.....	21
Table 3 Summarized result by the level of facilities.....	31

LIST OF FIGURES

Figure 1 <i>On-time pills pick up</i> achievement of health facilities by region (proportion).....	24
Figure-2 <i>Retention in care</i> of classification of health facilities by region (proportion).....	27
Figure- 3 Proportion of health facilities with ARV drug supply continuity by region.....	29

EXECUTIVE SUMMARY

Background: The rapid scale up of ART in Ethiopia may be associated with an increase in HIVDR in the population, if appropriate surveillance and prevention measures are not taken. To minimize the emergence of HIVDR and optimize the quality of patient care, World Health Organization (WHO) developed a set of HIVDR early warning indicators (EWIs) that assess antiretroviral therapy (ART), patient, clinic and program factors associated with HIVDR emergence and provide targets for optimal functioning of clinics and program.

Methods: The surveillance of HIVDR EWIs was done in 81 health facilities located in different region of the country. The four HIVDR EWIs were collected; (1) *on time pill pickup* (EWI-I), (2) *Retention in care* (EWI-II), (3) *ARV drug supply continuity* (EWI-III), (4) *ART dispensing practice practices* (EWI-IV).

Result: EWI-I; Twenty eight percent (23/81) of the facilities achieved “excellent” performance (> 90%), while 54% (44/81) and 17.3% (14/81) of them had “fair”, (80–90%), “poor” performance (<80%), respectively. **EWI-II;** Sixty two percent (50/81) of the sites achieved “excellent” performance (>85%) while 29.6% (24/81) had “fair” performance (75–85%), and 8.6% (7/81) had “poor” performance (<75%). **EWI-III;** only 36%(29/81) of the facilities reported that they did not have stock out of any of the ARV drugs over the 12 month preceding the survey. When stock out disaggregated by level of health facilities, 39 (66%) hospitals and 13 (59%) health centers had stock out of one or more ARV drugs. It was also understood that some of these health facilities tried to get supplies from neighboring health facilities to provide drugs to their patients. **EWI-IV;** The entire site achieved an excellent performance for EWI-IV had no case of dual -or mono ARV prescription.

Conclusion: Our results showed that good dispensing practices are performed in all the ART sites. However, the performance of some ART sites in other three EWIs was below the WHO targets, especially only 29(36%) of the sites reported that they did not have stock-out of any of the ARV drugs over the 12 months. All ART sites with suboptimal performance achievement are expected to identify appropriate program interventions to improve daily practices in order to reduce or minimize the expansion of HIV drug resistance and to provide the best care and treatment for their patients. Improvements in follow-up procedures, adherence support, and

continuous drug supply are some of aspects that need to be done to improve the performance of ART site to limit the risk of emergency of HIVDR.

1. INTRODUCTION

1.1.RATIONALE

The Human Immunodeficiency Virus (HIV) induced acquired immunodeficiency syndrome (AIDS) pandemic, has been a major medical and public health problem globally. At the end of 2013, an estimated 35 million people were living with HIV. According to the WHO, an estimated 39 million people have died since the first cases were reported in 1981 and 1.5 million HIV-related death and 2.1 million new infections has occurred only in 2013¹. Saharan Africa is the most affected region, with 24.7 million people living with HIV and 1.5 million new infections, accounts for almost 70% of the global new HIV infections in 2013¹.

The introduction of highly active antiretroviral therapy (HAART) was the significant breakthrough in the battle against HIV/AIDS. Although antiretroviral drugs cannot eradicate HIV from infected cells, the therapy has resulted dramatic decline in morbidity and mortality associated with HIV, prolong survival, improve quality of life, restore and preserve immunologic function. Furthermore potent and durable viral suppression decrease the number of viral copies and result in reduced probability of virus transmission, restricted viral evolution².

Following the recommendations of the United Nations General Assembly Special Session on HIV/AIDS (UNGASS) of 2011, rapid scale-up of antiretroviral therapy (ART) for HIV in resource-limited countries has been an international priority. Since then, incredible achievements were recorded in expanding the service particularly in countries with high burden of the disease³. At the end of 2013, 12.9 million people were receiving ART globally of which 11.7 million were in low- and middle-income countries, which represent 36% of the people living with HIV in low- and middle-income countries. ART has averted 7.6 million deaths between 1995 and 2013 including 4.8 million deaths in sub-Saharan Africa. Similarly, providing access to antiretroviral

¹The Gap Report Joint United Nations Program on HIV/AIDS (UNAIDS), 2014

² Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and heterosexual transmission of human immunodeficiency virus type Rakai Project Study Group. N Engl J Med. 2000;342(13):921-929

³World Health Organization Global Strategy for the Surveillance and Monitoring of Drug Resistance, 2012

medicines for pregnant women living with HIV has averted more than 900, 000 new HIV infections among children since 2009³.

Rapid scale-up of ART in resource-limited settings is accompanied with an increasing risk of emergency and transmission of HIVDR. Due to HIV's error-prone replication, high mutation rate and viral recombination, development of some HIVDR is inevitable, even with appropriate ART prescribing and adherence. HIVDR has significant human and financial implications. As the number of people on treatment increases, the emergence of meaningful population-level HIVDR becomes a greater risk which has the potential to undermine the dramatic gains that ART programs have had in reducing the morbidity and mortality of HIV-infected people in resource-limited settings⁴.

Monitoring of ART program factors known to be associated with the emergence of HIVDR for the purpose of improving programmatic functioning, may minimize the emergence of preventable HIVDR, especially at ART sites where viral load and HIVDR testing is not routinely available. In response to concerns regarding emergence and transmission of HIVDR, in 2004¹, the WHO and the United States Centers for Disease Control and Prevention (CDC), in collaboration with HIV Res Net, developed a global strategy for the assessment and prevention of HIV drug resistance, which was updated in 2012⁵. The updated strategy describes five components of a comprehensive package of HIVDR surveys that should be implemented in all countries scaling-up and maintaining populations on ART. These are 1) Monitoring of HIVDR early warning indicators (EWIs), 2) Surveillance of transmitted drug resistance (TDR) in recently infected populations, 3) Surveillance of HIVDR in populations initiating ART, 4) Surveillance of HIVDR in children <18 months of age, and 5) Surveillance of acquired HIVDR in populations on ART for >12 months and >24 months⁵.

HIVDR Early Warning Indicators

EWIs are quality of care indicators which specifically assess ART sites and program factors potentially associated with HIVDR at individual clinics. Utilizing data routinely collected in patients' medical and pharmacy records, EWI monitoring is a minimum-resource strategy designed to be integrated into national monitoring and evaluation programs. Monitoring EWIs

⁴Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med.* 2011;365(6):493-505

⁵WHO (2012) Report on assessment of World Health Organization HIV drug resistance early warning indicator advisory panel meeting.

annually at all or a large number of representative ART sites will provide countries with evidence to make programmatic adjustments at the level of an individual site or the country.

In the 2012 update of WHO global strategy for HIVDR, the number of EWIs was reduced from eight to five indicators that were believed to be closely associated with HIVDR. Definitions of indicators were also simplified and harmonized with indicator definitions used for reporting of Global AIDS Response Progress Report (GARPR) and the United States President's Emergency Plan for AIDS Relief (PEPFAR)⁵. The revised EWIs are 1) On-time pill pick up, 2) Retention in care, 3) Pharmacy stock-outs, 4) Dispensing practices, and 5) Viral load suppression at 12 month.

1.2.ETHIOPIA HIV SITUATION OVERVIEW

The HIV/AIDS epidemic remains one of the important public health challenges in Ethiopia since it was first recognized in the mid-1980s. Ethiopia has been one of the countries severely affected by the HIV/AIDS epidemic. In response to the epidemic, policies and implementation guidelines necessary to effectively guide the prevention, care and treatment efforts were issued by the government. The intensity and quality of interventions against HIV in the country have shown consistent and substantial improvements over time. The WHO ART guideline for public health approach strategy was adopted in 2003.

Recent data show that prevalence of HIV among pregnant women aged 15-49 has declined consistently from a peak of 5.8% in 2002 to 2.3% in 2012. Similarly, HIV prevalence among the same group has declined consistently in both urban and rural areas since 2003⁶. Estimated overall adult national HIV prevalence in 2013 was 1.3% with rural and urban prevalence of 0.5% and 3.5%, respectively⁷.

ART was made available freely in 2005 in Ethiopia and since then both the numbers of sites providing the service and patients receiving treatment have rapidly increased. In June 2013, a total of 913 health facilities were providing ART while 308,860 (75.4% of in need) of patients were on treatment⁸.

⁶Report on the 2009 Round Antenatal Care Sentinel HIV Surveillance in Ethiopia, Ethiopian Health and Nutrition Research Institute (EHNRI), Addis Ababa, August 2011

⁷HIV Related Estimates and Projections for Ethiopia, Ethiopian Health and Nutrition Research Institute Federal Ministry of Health, Addis Ababa, August 2012

⁸Federal HIV/AIDS Prevention and Control Office, 2005 EFY (July 2012 to June 2013) Multi-sectoral HIV/AIDS Response Annual Report, September 2013

With this rapid expansion of ART using the public health approach, emergence of HIVDR is an imminent threat for the national ART program. Cognizant of this fact, the national program adopted the WHO-recommended HIVDR prevention and monitoring strategy in 2007. A national advisory group was established under the leadership of the Ethiopian Public Health institute (EPHI) with the role of technical guidance for HIVDR activities. Since then, EWI surveys were conducted in 2007 (pilot in 14 health facilities). In the first round of EWI survey which was conducted in 2008 a total of 45 (28 hospitals and 17 health centers) health facilities were included in the survey. In the second round of EWI survey conducted in 2012 a total of 49 (33 hospitals and 16 health centers) health institutions were included in the survey. In these surveys 5 of the 8 EWI recommended were collected. These EWIs were: Percentage of adult patients initiating ART at the site who are initially prescribed, or who initially pick up from the pharmacy, an appropriate first-line ART regimen (**EWI-1**), Percentage of patients initiating ART at the site who are lost to follow-up 12 months after ART initiation (**EWI-2**), Percentage of adult patients initiating ART at the site who are taking an appropriate first-line ART regimen 12 months later (**EWI-3a**), Percentage of patients initiating ART at the site who attended all scheduled or expected clinical consultations on-time during the first 12 months of ART (**EWI-5b**) and Percentage of months in a designated year in which there were no ARV drug stock-outs (**EWI-6a**). Results of these surveys were disseminated in various ways and ART sites are believed to have taken the necessary programmatic correction based on the collected information during the survey.

In 2012, WHO updated the 2010 EWI guidance by conducting a critical review of the available medical literature and the multiple challenges observed with data collection and reporting. EWI definitions were simplified and harmonized with other monitoring and evaluation frameworks and processes, including those of the Global Aids Response Progress Reporting (GARPR) and the United States President's Emergency Plan for AIDS Relief (PEPFAR). The number of core indicators was reduced to five. Following this recommendation HIVDR technical working group (TWG) determined to abstract the four EWI indicators based on availability of data from existing pharmacy and medical record database.

These EWI indicators are, *On-time pill pick-up*(EWI-I), *Retention in care*(EWI-II), *Pharmacy stock-outs*(EWI-III), *Dispensing practices*(EWI-IV). The fifth indicator, *viral load suppression*(EWI-V) at 12 months, was recommended to be monitored only at sites where viral

load testing was routinely performed on all patients 12 months after therapy initiation. Since routine viral load testing is not done in most ART sites, EWI-V was not included in this survey. EWIs performance was rated according to WHO recommended scorecards. The scorecards utilize three classifications: red (poor performance, below desired level), amber (fair performance, not yet at desired level), and green (excellent performance, achieving desired level). Definitions (numerator/denominator) for these selected EWIs and their respective recommended targets are summarized in annex-1.

2. OBJECTIVE

General Objective

The main purpose of HIV drug resistance EWIs monitoring was to assess the extent to which ART programs are functioning to optimize prevention of HIVDR in selected geographically representative health facilities (hospital and health centers) in Ethiopia

3. METHODOLOGY

3.1 Study design

The study design of this survey was combination of cross-sectional and retrospective longitudinal.

3.2 Site Selection and Data Abstraction

The survey was conducted in all geographically representative areas of the country including all the regions. The source population was those HIV infected individuals who were enrolled for ART since January 1-2012 on wards and have at least 15 months complete data on the recommended EWI-II and all ART patients who were actively on ART in their respective health facilities in the year 2013 for EWI-I and IV.

Sites initiated ART and gave a service for at least three years (with 15 months of complete follow up data) plus minimum of 200 and 500 ART patients in follow up for health centers and hospitals, respectively, at the time of the sample start date were included in the survey. Considering all those parameters above mentioned, eighty one public ART delivery sites were selected for this survey (2013/14), which included the forty nine sites that participated in the second EWI survey in 2009/10.

Data abstraction was conducted from February to April 2014 by a data abstraction team organized by the EPHI and in collaboration with the WHO. The team consisted of four members (one of whom was a supervisor) who had been trained on data abstraction. Data were queried from individual sites' data base, patient follow up chart, pharmacy records and bin card for the respective EWIs taking hard copies as a priority data abstraction source to abstract into an Excel tool provided by the WHO.

3.3 Sampling and sample size determination

The sampling strategy was based on the number of eligible patients for each EWI and was according to the WHO recommendation for the minimum sample size determination as indicated on Table-1. For *On-time pill pick-up* and *Dispensing practices*, the number of eligible patients at each site to be sampled was those who were “actively” on ART at the time of the sample start date (1-January, 2013).

Though, WHO recommends data abstraction on a minimum number of consecutive patients following the sample size criteria (indicated on Table-1), data abstraction was oversampled by 20% to account for potential censoring of patients. All sites began abstraction from the sample start date and abstracted data until appropriate sample size for each site was reached; regardless of how many months it took to reach the appropriate sample size. Sample sizes for sites were based on the numbers of patients at each participating ART site meeting the eligibility definition of patients to be represented for each EWI according to WHO guidance⁹. For *Retention in care*, a census of all patients initiating ART in the 12 months of 2012 was taken (consistent with GARPR/PEPFAR).

According to the recommendation by WHO, all ART sites in the country or representative sentinel sites are recommended for such a survey. Due to logistic issue representative sites were selected from all regions of the country.

For this round of the survey, the plan was to address 70 geographically representative ART sites including all the 49 which were assessed during the second round survey. But at the end of this survey a total of 81 ART sites (59 hospitals and 22 health centers) were included in the survey.

⁹World Health Organization Global Strategy for the Surveillance and Monitoring of Drug Resistance, 2012

Table-1 WHO recommended sample size determination for each site

Annual number of eligible patients at the site	Number to be sampled at the site (Sample size)
1-75	All
76-110	75
111-199	100
200-250	110
251-299	120
300-350	130
351-400	135
401-450	140
451-550	145
551-700	155
701-850	160
851-1600	175
1601-2150	180
2151-4340	200
4341-5670	210
5671-10000	215
>10000	Consult WHO

3.4 Data Validation, Analysis and Interpretation

Structured formats for data collection adopted from WHO were used as a tool for data abstraction. Pre-data collection training was given for 11 data collectors and 5 supervisors. Soon after, data abstraction tools were piloted in selected health facilities in Addis Ababa and gaps identified from the pilot study were corrected before the field data collection. Moreover, survey sites were supervised and all the documentation related to the EWIs was revised.

The data were analyzed using excel with inbuilt analytic capacity developed by WHO for this purpose. Moreover, site profile assessment was included as recommended by WHO to see the

staffs, number of patients and quality of service in the site.

3.5 Data storage and disposition

Data were stored at the central data base of EPHI before and after analysis. The participated institutions were the part of the survey so that they can use the data for future actions. Moreover, the electronic form of data base generated was submitted to EPHI data base unit so that the confidentiality of data would not be breached. The collected data per site was based on Unique ART numbers which would not be linked in any form to the patients at a national level where data is stored. Since final data ownership is for EPHI, data retention and disposition is based on the rules and regulations of EPHI.

3.6 Study variables

According to the newly revised WHO guideline in 2012, there are five recommended set of indicators one of which (viral load suppression at 12 months), was considered conditional and designed to be implemented only at clinics where routine viral load monitoring is performed for all patients 12 months after ART initiation but none of the facilities had this practice of viral load monitoring and hence viral load suppression at 12 month was not calculated.

3.6.1. On-time pill pick-up (Cross-sectional)

Percentage of patients (adult or paediatric) that pick-up ART no more than seven days late at the first pick-up after the baseline pick-up

- **Numerator:** Number of patients picking up their ART no more than seven days later the first drug pick-up after baseline pick-up date.
- **Denominator:** number of patients who picked up ARV drugs on or after the designated EWI sample start date.

“**On time**” as it relates to pill pickup is defined as a patient picking up their ART within seven days of their previous prescription running out if taken according to schedule.

Target; Red <80%, Amber 80–90%, Green >90%

3.6.2. Retention in care (Longitudinal)

Percentage of adults and children known to be alive and on treatment 12 months after initiation of ART

- **Numerator:** Number of adults and children who are still alive and on ART 12 months after initiating treatment.
- **Denominator:** Total number of adults and children who initiated ART who were expected to achieve 12-month outcomes within the reporting period, including those who have died since starting therapy, those who have stopped therapy, and those recorded as lost to follow-up at month 12.

Target; Red <75%, Amber, 75–85%, Green >85%

3.6.3. Pharmacy stock-outs

Percentage of months in a designated year in which there were no ARV drug stock-outs

Numerator: number of months in the designated year in which there were no stock-out days of any ARV drug routinely used at the site.

Denominator: 12 months

Target; 100%

3.6.4. Dispensing practices

Percentage of adults and children prescribed or picking up mono or dual ARV therapy

- **Numerator:** number of patients who pick-up from the pharmacy, a regimen consisting of one or two ARVs
- **Denominator:** number of patients *picking up ART* on or after the designated EWI sample start date. Sampling continues until the full sample size is reached.

Target: 0%

3.6.5. Virological suppression

Percentage of patients receiving ART at the site after the first 12 months of ART whose viral load is <1000 copies/ml

- **Numerator:** number of patients receiving ART at the site after the first 12 months of ART whose viral load is <1000 copies/ml
- **Denominator:** number of patients at the site who by national policy should have had a viral load performed 12 months after ART initiation.

Target

Adult and pediatric >2 yrs; Red <70%, Amber 70–85%, Green >85%

3.7 Ethics statements

The project was ethically cleared and approved by EPHI Scientific and Ethical Review Office (SERO) and CDC Ethiopia. Only anonymised data were abstracted from the medical records for public health surveillance purposes. Names, dates of birth, addresses, and unique patient identifier numbers were not abstracted from records. Confidentiality was respected during abstraction of data by the use of specific identification code for each enrolled patient number. Since our study was conducted retrospectively, data were collected from medical/ART and pharmacy registers available at the ART sites. Thus, informed consent from the participants was not required.

4. RESULTS AND DISCUSSIONS

As finding of this survey result is summarized in table-2 below, the number of health facilities included in this survey were 81 (59 hospitals and 22 were health centers). All the hospitals had patients' ≥ 500 except two hospitals (Gelemso and Atat), while the health centers had ≥ 200 patients on ARV during the time of the survey.

Number of patients on ART

During the survey period in the selected health facilities 153,549 patients were on ART during the study period, of which, based on the WHO recommended sample size determination 16,370 data were collected and analyzed for the *On-time pill pick-up and dispensing practice*, and 10,649 data were collected and analyzed for the *retention in care*. The site specific finding of the four EWIs (*On-time pill pick-up, retention in care, pharmacy stock-outs and dispensing practices*) was presented in table-2, and the score or achievement is also indicated as WHO 2012 recommendations.

Table-2 Summary of EWIs as per health facilities in 2013/14

No	Facility name	Level	Region	EWI-1	EWI-2	EWI-3	EWI-4
1	Adama Hospital	Hospital	Oromia	92.38	74.74	83	0
2	Addis Zemen Health center	H/C	Amhara	86.02	76.92	83	0
3	Adigrat Hospital	Hospital	Tigray	77.14	88.07	75	0
4	Agaro Hospital	Hospital	Oromia	93.60	93.83	100	0
5	Akaki Health center	H/C	AA	74.09	70.43	100	0
6	Alamata Hospital	Hospital	Tigray	77.21	79.20	100	0
7	ALERT Hospital	Hospital	AA	81.25	95.65	67	0
8	Ambo Hospital	Hospital	Oromia	92.92	91.43	100	0
9	Arbamich Hospital	Hospital	SNNPR	86.12	98.26	58	0
10	Asella Hospital	Hospital	Oromia	88.75	100.00	92	0
11	Asossa Hospital	Hospital	BG	84.76	80.49	92	0
12	Attat Hospital	Hospital	SNNPR	64.88	95.12	67	0
13	Awash Health center	H/C	Afar	88.46	99.38	92	0
14	Axum Hospital	Hospital	Tigray	86.19	81.90	42	0
15	Babasi Health center	H/C	BG	82.50	90.00	83	0
16	Bedele Health center	H/C	Oromia	88.17	100.00	100	0
17	Betzata General Hospital	Hospital	AA	93.45	97.83	67	0
18	Bisidimo Hospital	Hospital	Harari	88.33	99.16	92	0
19	Bole Health center	H/C	AA	88.00	85.71	67	0
20	Bonga Hospital	Hospital	Oromia	78.16	83.13	100	0
21	Burie Health center	H/C	Amhara	78.57	85.22	42	0
22	Bushlo Health center	H/C	SNNPR	85.71	91.94	58	0

23	Butajira Hospital	Hospital	SNNPR	95.33	83.70	42	0
24	Chencha Hospital	Hospital	SNNPR	75.64	90.24	25	0
25	Chiro Hospital	Hospital	Oromia	77.62	100.00	100	0
26	Dangla Health center	H/C	Amhara	73.17	83.53	75	0
27	Debark Hospital	Hospital	Amhara	82.38	76.70	75	0
28	Debre Markos Hospital	Hospital	Amhara	89.17	84.83	42	0
29	Debre tabor Hospital	Hospital	Amhara	83.80	74.77	100	0
30	Debrebirhan Hospital	Hospital	Amhara	91.08	75.00	17	0
31	Dessie Hospital	Hospital	Amhara	96.08	86.30	100	0
32	Dilchora Hospital	Hospital	DD	94.17	100.00	75	0
33	Dilla Hospital	Hospital	SNNPR	87.50	100.00	25	0
34	Durit Hospital	Hospital	Oromia	80.48	100.00	75	0
35	Estie Health Center	H/C	Amhara	90.86	84.62	75	0
36	Felege Hiwot Hospital	Hospital	Amhara	85.66	76.65	33	0
37	Finote Selam Hospital	Hospital	Amhara	86.11	77.27	42	0
38	Gambella Hospital	Hospital	Gambella	95.24	79.70	100	0
39	Gandi Hospital	Hospital	AA	92.62	98.68	100	0
40	Gelemso Hospital	Hospital	Oromia	34.48	100.00	92	0
41	Gobba Hospital	Hospital	Oromia	92.92	100.00	83	0
42	Gonder Hospital	Hospital	Amhara	86.67	85.81	100	0
43	Hawassa Hospital	Hospital	SNNPR	82.45	92.75	42	0
44	Hirna Health center	H/C	Oromia	83.33	100.00	83	0
45	Hiwot Fana Hospital	Hospital	Harari	66.67	100.00	92	0
46	Hossana Hospital	Hospital	SNNPR	88.05	85.84	100	0
47	Jigel Hospital	Hospital	Oromia	81.90	100.00	92	0
48	Jimma Hospital	Hospital	Oromia	89.29	82.07	100	0
49	Karamara Hospital	Hospital	Somali	93.81	100.00	83	0
50	Kazanchis Health center	H/C	AA	94.39	60.71	100	0
51	Kemissie Health center	H/C	Amhara	84.62	86.08	42	0
52	Kombolcha Health center	H/C	Amhara	93.33	96.69	100	0
53	Kotebe Health Center	H/C	AA	90.61	95.49	83	0
54	Kuyu Hospital	Hospital	Oromia	88.17	66.25	50	0
55	Lalibela Hospital	Hospital	Amhara	83.65	85.02	58	0
56	Legehare Health center	H/C	Oromia	100.00	100.00	100	0
57	Mauchew Hospital	Hospital	Tigray	90.00	84.55	8	0
58	Mekele Health center	H/C	Tigray	84.29	84.72	50	0
59	Mekele Hospital	Hospital	Tigray	92.92	84.14	17	0
60	Meshualekia Health center	H/C	AA	92.31	92.13	83	0
61	Metema Hospital	Hospital	Amhara	86.02	61.34	75	0
62	Metukarl Hospital	Hospital	Oromia	85.71	90.09	83	0
63	Minilik Hospital	Hospital	AA	89.30	87.43	50	0
64	Mizan Aman Hospital	Hospital	Oromia	80.83	84.68	100	0
65	Moajo Hospital	Hospital	Oromia	87.96	92.43	92	0

66	Nekemte Hospital	Hospital	Oromia	94.91	83.72	100	0
67	Nifas Silk Health center	Hospital	AA	84.00	89.05	83	0
68	Police Hospital	Hospital	AA	91.76	86.92	92	0
69	Ras Desta Hospital	Hospital	AA	84.89	90.22	67	0
70	Sawla Health center	H/C	SNNPR	71.33	94.74	100	0
71	Shashemene Hospital	Hospital	SNNPR	84.72	97.33	67	0
72	Sheromeda Health cenetr	H/C	AA	82.22	74.14	100	0
73	Shewrobit Health center	H/C	Amhara	88.44	83.84	100	0
74	Shirie Hospital	Hospital	Tigray	82.38	78.13	25	0
75	St. Luk Hospital	Hospital	AA	96.19	91.87	8	0
76	St. Paulos Hospital	Hospital	AA	70.00	76.67	100	0
77	Teppi Health center	H/C	Oromia	63.81	93.33	100	0
78	Woldya Hospital	Hospital	Amhara	85.71	79.47	100	0
79	Yekatit 12	Hospital	AA	86.80	98.40	100	0
80	Yirgalem Hospital	Hospital	SNNPR	90.95	87.50	100	0
81	Zewditu Hospital	Hospital	AA	83.66	92.64	100	0

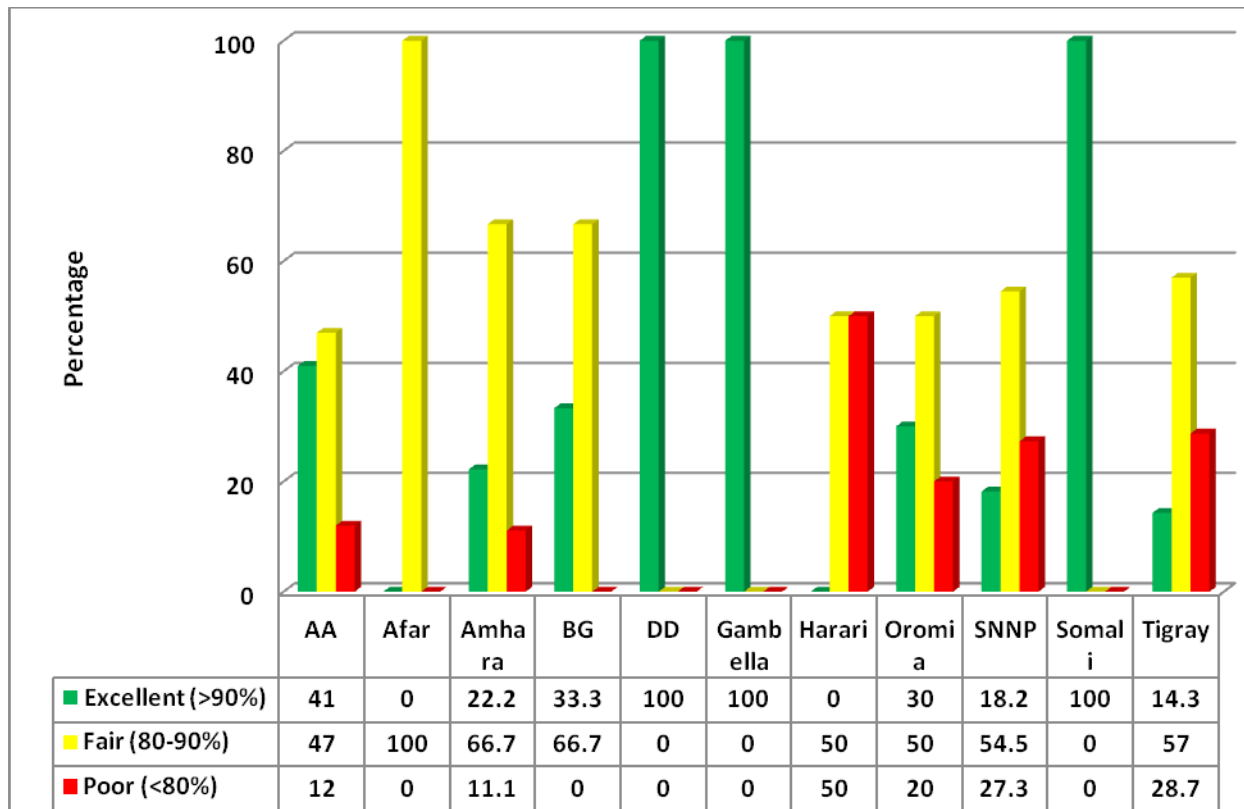
EWI-I: *On-time pill pick-up*

Twenty eight percent 28.4% (23/81) of sites achieved “excellent” performance (> 90%) on-time pill pick-up, while 54 % (44/81) and 17.3% (14/81) of sites had “fair” (80–90%), and poor” performance (<80%) respectively. The average on-time pill pick-up for the selected health facilities was 85.17% and ranges from 34.48% to 100% (34.48–100 %).

The comparison of health facilities by the level revealed that among the health centers, 27.3% (6/22) and 28.8% (17/59) of hospitals had "excellent" performance, 50% (11/22) of health centers and 56% (33/59) had "fair" performance and 22.7% (5/22) and 15.2% (9/59) of health centers and hospitals had the 'poor' performance respectively.

Regional comparison, as shown in figure-1, showed that, ART sites in Addis Ababa (AA), Amhara and Oromia region, 41.2% ,22.2 % and 30%, achieved “excellent” performance *on-time pill pick-up* respectively. Among the ART sites in Southern Nation and Nationality Peoples (SNNPR), and Tigray 18.2% and 14.3% of them achieved “excellent” performance *on-time pill pick-up* respectively. Interpretation of the performance of ART sites for region Afar, Beneshangul Gumz (BG), Harari , Somali, Dire Dawa (DD) and Gambella was difficult due to few ART sites were included in the survey.

Figure 1 *On-time pills pickup achievement of health facilities by region (proportion)*



A challenge to long-term ART programmatic success is maintaining populations of patients on ART without treatment interruptions. Treatment interruptions may arise due to poor patient adherence or may occur as an unintended consequence of ARV supply interruption at ART clinic dispensaries¹⁰. Non-adherence to ART causes the worsening of the immunological and clinical state and leads to treatment failure, emergence of drug resistant HIV strain and increases AIDS-related morbidity, mortality and hospitalization¹¹. Notably, ART interruptions of ≥ 48 hours in patients receiving NNRTI-based regimens are associated with the selection of drug-resistant HIV¹². Based on these facts, ensuring adequate and consistent adherence to ART is a high priority and critical element for the success of ART.

¹⁰Nachega JB, Knowlton AR, Deluca A, et al. Treatment supporter to improve adherence to antiretroviral therapy in HIV-infected South African adults. A qualitative study. *J Acquir Immune Defic Syndr*. 2006;43(Suppl 1):S127–33

¹¹Marcellin F, Boyer S, Protopopescu C, et al. Determinants of unplanned antiretroviral treatment interruptions among people living with HIV in Yaoundé, Cameroon (EVAL survey, ANRS 12-116) *Trop Med Int Health* 2008;13:1470–8

¹²Parienti JJ, Das-Douglas M, Massari V, et al. Not all missed doses are the same: sustained NNRTI treatment interruptions predict HIV rebound at low-to-moderate adherence levels. *PLoS One*. 2008;3:e2783

Studies have shown treatment pickup rate is a simple, inexpensive and a valid proxy measure of adherence to ART. It has also been shown that, treatment pickup rate was significantly higher among persons with suppressed viral load, while missed appointment rate was lower among persons with unsuppressed viral load¹³. Considering the importance of ensuring adequate and consistent adherence to ART is high priority for effective HIV management the national guidelines of Ethiopia recommends patients are required to attend a counseling sessions before ART initiation, in particular, education on the importance of adherence.

In most of ART facilities, routine pharmacy dispensing practice additional pills are dispensed to patient to support patient if they couldn't collect their drug on the expected date due to different reason, this means patient may have remnant pills (number of pills left over from the previous prescription). Since the number of remnant pills was not routinely recorded, thus it was not possible to calculate the actual pill run-out date necessary to monitor this EWI. For this survey patients who attended on or before the appointment date and those who picked up their ARVs up to 7 days later than the appointment date were considered to be *on-time pill pick up*.

Even though patient delay for drug pick-up could be explained by the availability of left over drugs from the previous appointments, the finding of this survey showed that the *on time pill pick up* is low in some of the study sites. Only 28.4 % (23/81) of health facilities sites achieved “excellent” performance *on-time pill pick-up*. This indicates a large proportion of patients was picking up medication late or is not returning at all after baseline pickup. Considering *on time pill-pick up* as a measure of adherence behavior, the overall delay in drug pick-up strongly suggests that more must be done at the clinics to strengthen rate of *on-time pill pick-up*.

The comparisons of health facilities achieved the “excellent” performance *on-time pill pick-up* showed, there is no significance difference between the hospitals and health center, which may show decentralization of the ART service has no impact on quality of the service and on the performance of *on-time pill pick-up*.

In general, it is essential that, the facilities with poor achievement of *on time pill pick up* require further evaluations to determine the underlying factors and implement targeted adherence improvement initiatives to improve adherence which include continuous adherence counseling,

¹³ Grossberg R & Gross R (2007) Use of pharmacy refill data as a measure of antiretroviral adherence. Current HIV/AIDS Reports, 4(4): 187-191

defaulter tracing, continuous health education, providing outreach services to remote sites, linking patients to community support organizations.

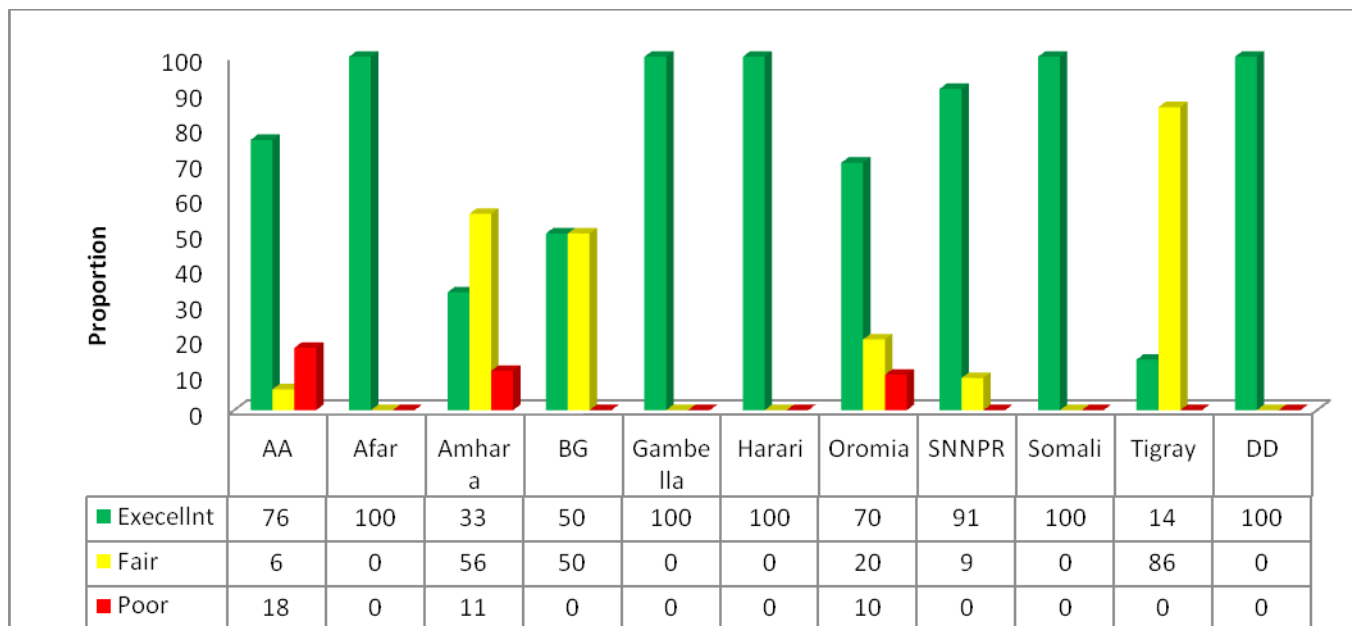
EWI-II: *Retention in Care*

The overall *retention in care* performance of the health facilities represented in this survey was 88% ranged from 60.7% to 100%. Specifically, 61.7% (50/81) of the sites achieved “excellent” performance (>85%) while 29.6% (24/81) had “fair” performance (75–85%) and 8.6% (7/81) achieved “poor” performance (<75%).

Regional comparison showed that; SNNPR, AA and Oromia regions score the maximum *retention in care* which accounted for 91% (10/11), 76.7% (13/17) and 70% (14/20) respectively while Tigray, Amhara and Benishangul Gumuz (BG) regions had the lowest with performance of 14.3% (1/7), 33% (6/18) and 50 % (1/2) respectively. Afar, Harari, Somali and Gambella regions score 100% that might be due to few facilities (one or two) from this region were included in the survey (Fig, 2).

With respect to the level health facility, 61% (36/59) and 64% (14/22) hospitals and health centers met the target excellent” performance (>85%) while 32% (19/59) and 23% (5/22) hospitals and health centers attain 'fair' score of WHO target. Only 7% (4/59) and 13% (3/22) hospitals and health centers had 'poor' performance during the study period.

Figure-2*Retention in care* of classification of health facilities by region (proportion)



ART provision can be effective only if patients are retained in care over time¹⁴. Studies showed that patients with low *retention in care* are at high risk of developing HIVDR¹⁵; this is also an important factor in the transmission of resistant viral strain in the community. Retention is also a critical issue for ART programs from a cost-effectiveness point of view. As programs are trying to maximize the impact of limited resources, a failure to ensure good *retention in care* is costly for both the program and the patient. Ensuring good *retention in care* remains one of the key challenges for ART programs while the treatment is still scaled up further¹⁶.

The average global *retention rate* in 2009 at 12 months was 82% and dropped to 77% at 24 months and remained stable at 75% and 74.5% at 36 and 48 months, respectively¹⁷. These figures were consistent with a meta-analysis of 39 cohorts from sub-Saharan Africa in 2011¹⁸ that assured *retention in care* remains to be a challenge for ART programs though it is improving over time^{19,20}. Many ART programs have therefore been striving hard to identify and implement

¹⁴WHO, Retention in HIV programmes: Defining the challenges and identifying solutions; Geneva: WHO; 2012.

¹⁵ WHO, UNAIDS, UNICEF: Towards universal access: scaling up priority HIV/AIDS interventions in the health sector. Progress report 2011

¹⁶ WHO, Retention in HIV programmes: Defining the challenges and identifying solutions; Geneva: WHO; 2012.

¹⁷ Assefa Y, Van Damme W, Haile Mariam D, Kloos H: Toward universal access to HIV counseling and testing and antiretroviral treatment in Ethiopia: looking beyond HIV testing and ART initiation.

¹⁸ Assefa Y, Van Damme W, Haile Mariam D, Kloos H: Toward universal access to HIV counseling and testing and antiretroviral treatment in Ethiopia: looking beyond HIV testing and ART initiation.

¹⁹ Tassie JM, Baijal P, Vitoria MA, Alisalad A, Crowley SP, Souteyrand Y: Trends in retention on antiretroviral therapy in National programmes in low and middle-income countries.

²⁰ Fox MP, Rosen S: Patient retention in antiretroviral therapy programs up to three years on treatment in sub-Saharan Africa: systematic review.

appropriate strategies to optimize their retention levels²¹. In addition, it has been identified that levels of retention vary widely across health facilities and programs²².

In Ethiopia, in spite of the achievements in scaling up ART in the country, lost to follow-up and early mortality of patients on ART has been challenges for the ART program. Only 65% of the patients were retained after two years on ART by 2008²³.

The overall *retention in care* performance of the health facilities represented in this survey was 88% ranged from 60.7% to 100%. This improvement might be due to the implementation of national programmatic intervention (like, programmatic, structural, socio-cultural and patient information) which has improved the retention rate significantly from 77% in 2004/5 to 92% in 2012/13²⁰.

The finding of this survey also indicates still a number of health facilities (38%) achieved below the expected excellent performance in *retention in care*. Therefore, a proportion of patients served by these health facilities may be at high risk for developing HIVDR or death.

As indicated in the result, there is also broad range of *retention in care* between ART sites (61-100%) which suggest there might be factors at site-level that are influencing this indicator. Literatures also suggest that adherence support and defaulter tracing has impact on improvement of ART programs²⁴. And hence, efforts should be made to investigate factors contributing to low patient *retention in care*. Moreover, for sites with migrant workers and daily laborers, additional strategies to retain patients either at the site or offsite of treatment needs to be devised.

Even though, there was no significant variation between the levels of health facilities in *retention in care*, there is variations among the regions which may intern suggest the need of programmatic support and intervention in some regions with poor performance.

²¹ WHO, UNAIDS, UNICEF: Towards universal access: scaling up priority HIV/AIDS interventions in the health sector. Progress report 2011

²² Assefa Y, Van Damme W, Haile Mariam D, Kloos H: Toward universal access to HIV counseling and testing and antiretroviral treatment in Ethiopia: looking beyond HIV testing and ART initiation.

²³ Federal HIV/AIDS Prevention and Control Office:2013, Monitoring and Evaluation Report, 2011/2012. Addis Ababa, Ethiopia:.

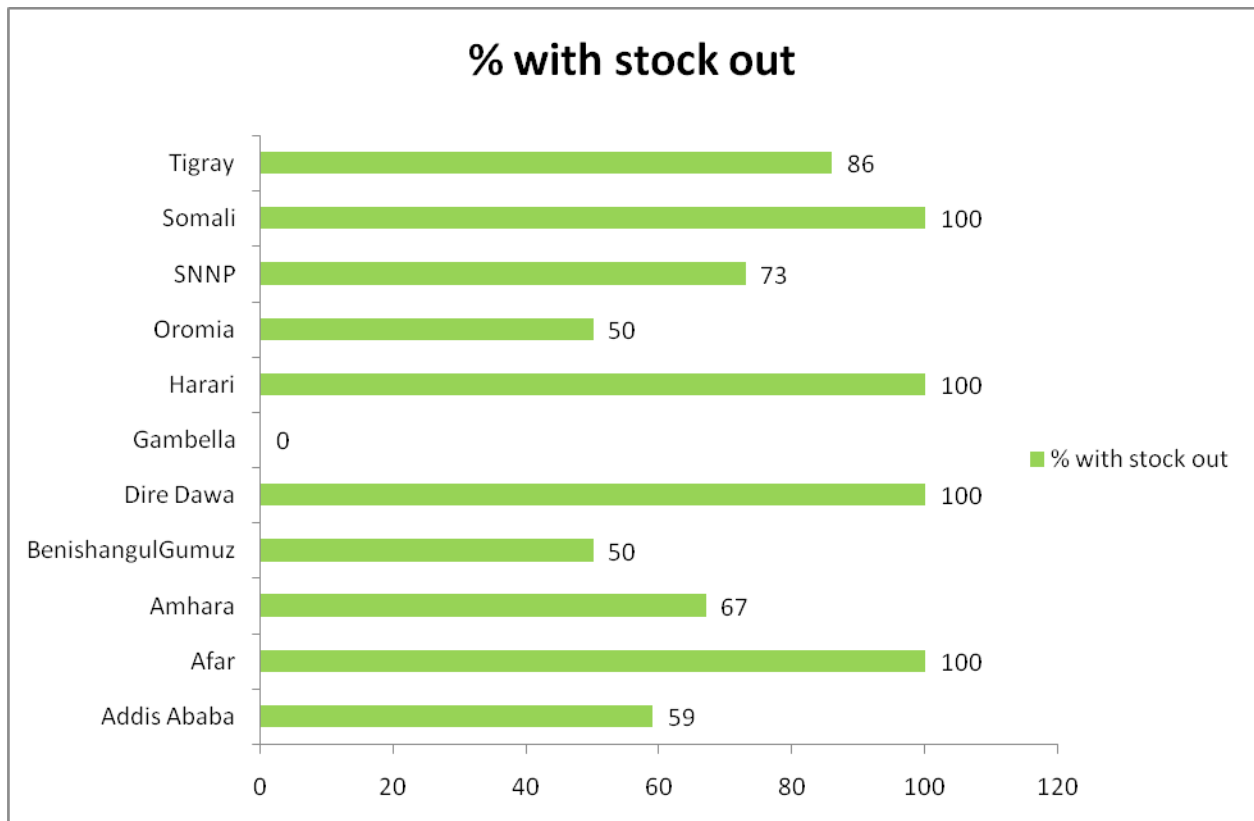
²⁴ UNAIDS (2013) Global Report

The finding of this survey generally showed, much has to be done to optimize the rate of *retention in care* to the level of WHO recommendation target (>85%) in the health facilities to minimize the emergency of preventable HIVDR and death.

EWI -III: Pharmacy stock-outs

Out of the 81 surveyed health facilities, only 29 (36%) reported that they did not have stock out of any of the ARV drugs over the 12 month preceding the survey and this is alarming. When stock out disaggregated by level of health facilities, 39 (66%) hospitals and 13 (59%) health centers had stock out of one or more ARV drugs. Except in Gambella, health facilities in all other regions had ARV stock out of various level (Table-2), precaution should be taken in interpreting this as some regions are represented by only one or two facilities.

Figure-3 Proportion of health facilities with ARV drug supply continuity by region



Uninterrupted and sustainable supply of ARV is one of the key elements of effective ART program. ARV stock-outs could directly affect treatment adherence and clinical outcomes. Obviously, ARV stock-out means patients may not get their refill and as a result miss treatment

doses. Several studies show that drug stock-outs are related to treatment interruption which in turn leads to development of drug resistance²⁵.

Various factors could contribute to stock-out of ARV drugs. Fragile drug procurement and supply management systems can result in drug stock-outs^{26,27}. In such situation the system cannot reliably forecast, procure and distribute ARVs leading to interruption of supply. Other factors like shortage of resources, lack of capacity of health facilities to submit reports and request for refill, and lack of buffer stock at the health facility level may result in ARV stock outs even in the presence of efficient supply management system.

EWI -IV: *Dispensing practices*

All sites, 100% achieved an “excellent” performance with 0% of patients dispensed mono- or dual therapy, and there was no facilities classified as “poor” performance. Irrespective of the level of health facilities at both hospitals and health centers patients were prescribed and dispensed the appropriate ARV based on the national ART guidelines.

Prescribing and dispensing practices are closely associated with the emergence of HIVDR. The prescribing of mono- and dual-ART and inappropriate dosing may lead to insufficient drug pressure to effect viral load suppression, leading to the selection of drug-resistant virus.

The rate of correct prescribing and dispensing was highest, all facilities has reached 100% dispensing practice according to the level of WHO recommendation and the National ART guideline of the country. This good performance would be likely being due to the ongoing efforts in training clinicians and pharmacist, which has greatly contributed to the conformity of prescribing habits with national guidelines. Thus continuous training of clinician and pharmacist need to be strengthened to maintain the good achievement ARV prescriptions and dispensing practice as it will support to minimize emergency of HIV drug resistance.

²⁵Claudia H, Robert M. *Adherence to antiretroviral therapy in resource-limited settings: everything matters.* *AIDS*, 2007, 21(8): 1041–1042.

²⁶Marcellin F et al. Determinants of unplanned antiretroviral treatment interruptions among people living with HIV in Yaounde, Cameroon (EVAL survey, ANRS 12-116). *Tropical Medicine and International Health*, 2008, 13:1470–1478.

²⁷Oyugi JH et al. Treatment interruptions predict resistance in HIV-positive individuals purchasing fixed-dose combination antiretroviral therapy in Kampala, Uganda. *AIDS*, 2007, 21:965–971.

Table-3 Summarized result by the level of facilities

		Performance		
Level of facilities	Level of facilities	Excellent	Fair	Poor
EWI-I	Hospital	19(32.2%)	31(52.54%)	9(15.25%)
	Health center	6(27.3%)	11(50%)	5(22.7%)
EWI-II	Hospital	36(61%)	19(32.3)	4(6.8%)
	Health center	14(63.6%)	5(22.7%)	3(13.6%)
EWI-III	Hospital	59(100%)	0	0(0%)
	Health center	22(100%)	0	0
EWI-IV	Hospital	21(35.6%)	0	38(64.4%)
	Health center	9(40.9%)	0	13(59.1%)

5. CONCLUSIONS AND RECCOMENDATIONS

Despite the undisputed benefits of ART in terms of reduced HIV-related morbidity and mortality, the long-term success of the treatment program is threatened by the emergence and spread of drug-resistant HIV. The development of HIVDR has significant public health implications, such as limiting the response to ART, restricting future treatment options, increasing treatment costs, and creating a reservoir for transmission of resistant virus to newly infected individuals.

As individual HIVDR testing is neither recommended nor feasible in most low and middle income countries, the monitoring of patient and clinic factors associated with the emergence of preventable HIVDR is comparatively inexpensive and can be used to identify these factors and reduce their harmful consequence. EWIs are ART site variables designed to be monitored in all (or are representative ART sites) ART sites within a country and permit countries to make evidence based recommendation about ART programme function and take an action to minimize the emergency of preventable HIVDR both at the national and ART site level without requiring laboratory testing. EWI monitoring also identifies successful clinics that could serve as best practice models to other clinics. EWI monitoring results in general can be used to improve patient and clinic management.

Ethiopia began to implement the WHO recommendations in the EWI collection activities in 2007 when it adopted the generic WHO developed tools for EWI collection as part of the global HIV Drug Resistance strategy. The overall objective was to integrate early warning indicator collection into the national ART program as a routine practice.

Following adaptation of the EWI protocol from the generic WHO protocol, an assessment on the feasibility of collecting EWI for Ethiopia was done together with a team from WHO-E and CDC-E. This assessment guided the TWG to select the EWIs that can be collected from ART medical records systems or ART cards at all sites used in the country.

Considering the *on time pill pick up* as indicator of population-level adherence to ART, an achievement of an excellent performance by only 28.4% of the facilities suggests that more must be done at the clinics to investigate reason for the drug pick up delays and to strengthen adherence education and support.

The overall *retention in care* of facilities is optimum (88%) compared to WHO recommendation (>85%) but a number of health facilities (38%) had below the expected excellent performance in *retention in care*, therefore efforts should be made to investigate and intervene on factors contributing for the low performance of patient retention in care.

Our results also showed that good dispensing practices are performed in the all the ART sites. This good performance would be likely be due to the ongoing efforts in training clinicians and pharmacist working in the facilities which has greatly contributed to the conformity of prescribing and dispensing habits with national guidelines and hence it should be maintained.

The extent to which stock outs of routinely used ARVs were reported is worrisome in most facilities. Only 29 (36%) of ART sites reported that they did not have stock out of any of the ARV drugs over the 12 month. The high rate of discontinuity in drug supply would have increased poor adherence to the ART programme, delay in drug pick-up and HIVDR emergency. This indicate strong effort must be done in strengthening drug supply management (forecasting, procurement, and supply distribution) systems as the availability of drug stock is one of the key factors in preventing HIVDR.

In general the finding of this survey thus can be seen as part of ongoing process to identify and solve problem within an existing program. ART site with suboptimal performance achievement are expected to identify appropriate program interventions to improve daily practices in order to reduce or minimize the expansion of HIV drug resistance and to provide the best care and treatment for their patients. Improvements in follow-up procedures, adherence support, continuous drug supply, are some of aspects that need to be done to improve the performance of ART site to limit the risk of emergency of HIVDR.

The number of sites covered by the survey is small compared to the total number of health facilities in the country. Further effort should be made to incorporate minor adjustments in existing databases (HMIS), which will facilitate abstraction of WHO recommended EWIs in the future and hence EWIs will be routinely monitored at all ART site and reported as an ongoing activity and can be used to make national statements about national and site-specific programmatic functioning in the context of HIVDR and related factors.

6. LIMITATIONS

- In this survey only one private hospital was included which will difficult to generalize the service delivery quality by the private sectors. Efforts need to be made to include the private sector in future EWI exercises.

7. ACKNOWLEDGMENTS

This survey was financially supported by WHO-E. Moreover, technical assistances were obtained from WHO-E and CDC-E country office. The regional health bureaus, hospitals and health centers participating in this survey are highly acknowledged for their unreserved support during the survey. Moreover the ART clinic staffs working in the selected site need to be acknowledged for their support in providing the necessary records, information and assistance during the data collection. Staffs involved in the survey from WHO-E, EHNRI, CDC-E and data collectors are highly appreciated for their for their dedication and hard work in the data collection process.

8. ANNEXES

Annex-1

DESCRIPTION OF EARLY WARNING INDICATORS (EWIS)

Indicator	Description	Status and target	Numerator/Denominator	Variables required to calculate EWI
Early Warning indicator 1: On time pill pick-up	Proportion of patients (adult or pediatric) that pick up ART no more than 7 days late at the first pick-up after the baseline pick-up “On time” as it relates to pill pick-up is defined as a patient picking up their ART within 7 days of their previous prescription running out if taken according to schedule	Red: <80% Amber: 80-90% Green: >90%	Numerator: Number of patients picking up their ART “on time” at the first drug pick-up after baseline pick-up date Denominator: Number of patients who picked up ARV drugs on or after the designated EWI sample start date	Date of first ARV drug pick-up (baseline) ARV drugs picked up at baseline Number of days of ART picked up at Baseline Date of first ARV drug pick-up after baseline pick-up date Date of death after baseline pick-up (if applicable) Date of transfer out after baseline pickup (if applicable) Date of ART stop without restart after baseline pick-up (if applicable)
Early Warning Indicator 2: Retention in care	Percentage of adults and children known to be alive and on treatment 12 months after initiation of ART	Red: <75% retained after 12 months of antiretroviral therapy Amber: 75-85% retained after 12 months of antiretroviral therapy Green: >85% retained after 12 months of treatment	Numerator: Number of adults and children who are still alive and on ART 12 months after initiating treatment Denominator: Total number of adults and children who initiated ART who expected to achieve 12-month outcomes within the reporting period The denominator excludes transfers out. The indicator includes children. There is now no separate pediatric EWI	UNGASS/PEPFAR/Global Fund numerator and denominator
Early Warning indicator 3: Pharmacy stock-out	Percentage of months in a designated year in which there were no ARV drug stock-outs	Red: <100 of a 12 months period with no stock-out Green: 100% of a 12 month period with no stock-out	Numerator: Number of months in the designated year in which there were no stock-out days of any ARV drug routinely used at the site Denominator: 12 months	All ARV drugs routinely used at the site Months in each year in which there was at least one stock-out of any ARV drug routinely used at this site
Early Warning Indicator 4: Dispensing practices	Percentage of adults or children being dispensed a mono or dual drug regimen	Red: >0% dispensing of mono-or dual therapy Green: 100% dispensing of mono-or dual therapy	Numerator: Number of patients who pick up from the pharmacy, a regimen consisting of 1 or 2 ARVs Denominator: Number of patients picking up ART on or after the designated EWI sample start date This new indicator assesses the percentage of adults and children being	ART regimen picked-up at baseline pickup Was it a Mono or Dual Therapy regimen (Yes or No)