



**FEDERAL DEMOCRATIC REPUBLIC
OF ETHIOPIA
MINISTRY OF HEALTH**

*Continuum of HIV services refers to a
comprehensive package of HIV
prevention, diagnostic, treatment, care
and support services provided for people
at risk of HIV infection or living with HIV
and their families*

NATIONAL GUIDELINES FOR COMPREHENSIVE HIV PREVENTION, CARE AND TREATMENT

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Antiretroviral treatment (ART) began in 2003 and free ART was launched in Ethiopia in 2005. According to the 2017 new spectrum estimate, 722,248 Ethiopians are currently living with human immunodeficiency virus (HIV) and all of them require ART. However, only 420,000 individuals are currently taking antiretroviral (ARV) drugs (2016 global AIDS monitoring report).

Recognizing the need for antiretroviral treatment, the Government of Ethiopia (GOE) issued the first ARV guidelines in 2003, which were revised in 2005, 2008 and 2014 to facilitate a rapid scale up of ART. With continued care and treatment updates, the Federal Ministry of Health has revised the national guideline to scale up and improve the quality of service at all levels.

Expansion and strengthening ART care and treatment activities at regional, zonal, woreda and kebele levels through targeted social mobilization and active community participation are expected to create an enabling environment to prevent and control the spread of the epidemic. The process of task shifting; training of nurses and community health agents in prevention, treatment, care and support activities will further strengthen community linkages and ensure availability of standard minimum packages of HIV/AIDS services at primary health care level. Currently there are more than 1,230 health facilities providing HIV care and treatment service.

This revised edition of the guidelines for use of ARV and opportunistic infection (OI) drugs in adults and children is based on recent national and global evidences and experiences. The Federal Ministry of Health believes that these guidelines, along with other national guidelines and training manuals, will be instrumental in maintaining the standard of care and ensuring quality of HIV service delivery.

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Acronyms and Abbreviations

3TC	Lamivudine
ABC	Abacavir
AFB	Acid fast bacilli
AIDS	Acquired Immune Deficiency Syndrome
ANC	Antenatal Care
ARV	Antiretroviral
ART	Antiretroviral Therapy
AZT/ZDV	Zidovudine
CBC	Complete Blood Count
CD4 cells	Type of T-lymphocyte, white blood cells
CMV	Cytomegalovirus
CPT	Cotrimoxazole Preventive Therapy
CrAg	Cryptococcal antigen
DBS	Dried Blood Spot
DTG	Dolutegravir
DRV	Darunavir
DHS	Demographic and Health Survey
DNA	Deoxyribonucleic acid
DOTS	Directly Observed Therapy Short Course
EFV	Efavirenz, also abbreviated as EFZ
FBO	Faith-based organization
FDC	Fixed dose combination
FHAPCO	Federal HIV/AIDS Prevention and Control Office
FMOH	Federal Ministry of Health
GAMR	Global AIDS Monitoring Report
HAART	Highly active antiretroviral therapy
HANS training	HIV/AIDS Nurse Specialist training
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus

HIV	Human Immunodeficiency Virus
HTS	HIV Testing Services
IDV	Indinavir
IP	Infection Prevention
IPT	INH Preventive Therapy
IPLS	Integrated Pharmaceuticals Logistics System
IRIS or IRS	Immune Reconstitution Inflammatory Syndrome also called Immune Reconstitution Syndrome (IRS)
INSTI	Integrase strand transfer inhibitor (also known as integrase inhibitor)
LFT	Liver Function Test
LPV	Lopinavir
MTCT	Mother-To-Child Transmission (of HIV)
MD	Medical Doctor
NFV	Nelfinavir
NGO	Non-governmental Organization
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside Analogue Reverse Transcriptase Inhibitor
NVP	Nevirapine
OIs	Opportunistic Infections
PCR	Polymerase chain reaction
PEP	Post-exposure prophylaxis
PI	Protease Inhibitor
PITC	Provider Initiative Testing and Counselling
PLHIV	People living with HIV
PMTCT	Prevention of mother-to-child transmission (of HIV)
PrEP	Pre-exposure prophylaxis using ARVs before HIV exposure
RMU	Rational medicine use
RNA	Ribonucleic acid
RTV, r	Ritonavir
PI/r	Ritonavir boosted Protease Inhibitor
RAL	Raltegravir

RFT	Renal function test
RT	Reverse transcriptase
STI	Sexually Transmitted Illnesses
TB	Tuberculosis
TDF	Tenofovir
U/A	Urine analysis
UNAIDS	The Joint United Nations Program on HIV/AIDS
UP	Universal Precautions
WHO	World Health Organization
ZDV	Zidovudine (also abbreviated as AZT)

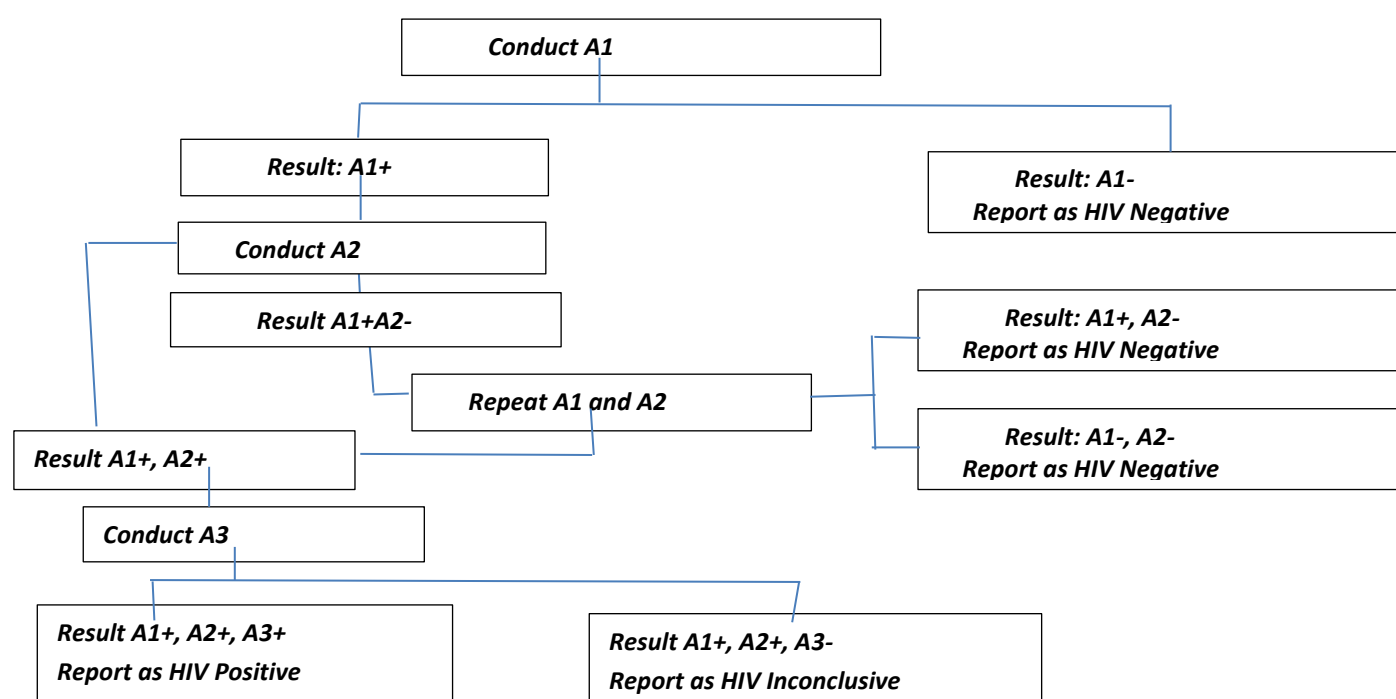
SUMMARY OF THE CHANGES MADE IN THIS GUIDELINE

The following list of recommendations consists of either brand-new or modifications of previous recommendations as adopted from the WHO 2016 consolidated guidelines and the July 2017 addendum.

Diagnosis of HIV

1. This guideline recommend targeted HIV testing and the list of eligible clients for targeted HIV testing has been refined to make the yield better. The revised list of eligible clients or groups is as follows:
 1. *All pregnant, laboring and postpartum women with unknown HIV status; and partners of HIV positive pregnant/postpartum women and partners of high risk HIV negative pregnant and post-partum women.*
 2. *Eligible family members (siblings under 15 years old and their parents) and sexual networks of index PLHIV.*
 3. *Commercial sex workers and their clients.*
 4. *All TB patients with unknown HIV status and presumptive TB cases.*
 5. *All sexually transmitted infections (STI) patients with unknown HIV status, their partners and sexual networks.*
 6. *Discordant couples.*
 7. *Children orphaned by AIDS and vulnerable children.*
 8. *Children with malnutrition.*
 9. *Patients with clinical signs and symptoms of HIV/AIDS visiting health facilities (outpatient and inpatient).*
 10. *Long distance truck drivers, mobile workers and daily laborers.*
 11. *Widowed, divorced & remarried.*
 12. *Vulnerable adolescents / youth clients (15-24 years).*
 13. *All under five children visiting health facilities.*
 14. *Refugees and inmates.*
 15. *Family planning clients with identified risk (history of having multiple sexual partner inconsistent condom use and their partners).*
2. The HIV testing strategy have been revised to incorporate the new WHO recommendation as described in the diagram below:
3. Retest all clients diagnosed as HIV-positive with a second specimen and a different provider using the same testing strategy and algorithm before enrolling the client in HIV care and/or initiating ART. Retesting people on ART is not recommended, as there are potential risks of incorrect diagnosis.

Recommended HIV testing strategy for Ethiopia



4. If the retesting result is negative (the previous test result is positive and the current test result is negative), sample should be sent to regional laboratories where HIV testing will be done using a more specific testing modality.
5. Testing at labor and delivery (L&D) unit for pregnant woman with unknown status will be done. If positive, provide ART for the mother and ARV prophylaxis for the infant. After delivery, perform retesting (different provider and different sample). If the positive test is verified, continue ART; if negative, refer the sample to the nearby regional laboratory to do the test using a more specific testing modality.
6. Other innovative HTS approaches to strengthen targeted HIV testing service have been highlighted for future consideration when applicable which includes:
 - a. Index case testing
 - b. HIV-self-testing for key populations.
 - c. Assisted partner notification services
 - d. *Respondent Driven HIV Testing*
 - e. Applying risk screening for high risk groups or individuals
7. HIV testing and counseling with other prevention services and linkage to treatment and care should be accessible to KEY POPULATIONS at health facilities and community service models.

8. Adolescent-friendly health services should be implemented in HIV services to ensure engagement and improved outcomes
9. Oral pre-exposure prophylaxis (PrEP) containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches.

Linkage to care and treatment

1. Linkage is defined as a process of actions and activities that support people testing for HIV and people diagnosed with HIV to engage with prevention, treatment and care services as appropriate for their HIV status. For people with HIV, it refers to the period beginning with HIV diagnosis and ending with enrolment in care or treatment
2. Following an HIV diagnosis, a package of support interventions should be offered to ensure timely linkage to care for all people living with HIV. The following interventions have demonstrated benefit in improving linkage to care following an HIV diagnosis:
 - Streamlined interventions to reduce time between diagnosis and engagement in care including (i) Enhanced linkage with case management; (ii) Support for HIV disclosure; (iii) Patient tracing; (iv) Training of staff to provide multiple services, and (v) Streamlined services
 - Peer support and navigation approaches for linkage; and
 - Quality improvement approaches using data to improve linkage

ART Initiation

1. It is critical for people living with HIV to initiate ART as early as possible and this enables to shorten the time between HIV diagnosis and ART initiation hence significantly reducing HIV related morbidity and mortality, and reducing forward transmission of HIV including MTCT.
2. All HIV positives are eligible for ART irrespective of their WHO clinical staging and/or CD4 count and the ideal time for ART initiation depends on the clinical condition and readiness of the client.
3. Rapid ART initiation should be offered to all people living with HIV following a confirmed HIV diagnosis, clinical assessment and assessment of client readiness. **Rapid ART initiation** is defined as initiation of ART within seven days of HIV diagnosis, provided that there are no contraindications.
4. ART initiation should be offered on the same day to people who are ready to start.

5. For women identified at labor and delivery, provide ART with in the same hour of HIV diagnosis with brief counseling and provide detailed counseling on ARV and adherence after delivery.
6. As a priority, ART should be initiated in all adolescents and adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with a CD4 count ≤ 350 cells/mm³.
7. Start ART as early as possible to all children living with HIV regardless of their WHO clinical stages and CD4 counts/percentage.
8. The preferred first-line regimen for adults and adolescents is TDF+3TC+DTG or TDF+3TC+EFV as a once-daily dose.
9. Fixed-dose combinations and once-daily regimens are preferred for antiretroviral therapy.
10. DTG containing regimens are not recommended for pregnant and breast feeding mothers. For HIV/TB co-infected adults and adolescents, the recommended dose of DTG is 50 mg twice daily.

Management of individuals with advanced disease

1. For adults and adolescents, and children older than five years, advanced HIV disease is defined as CD4 cell count < 200 cells/mm³ or WHO stage 3 or 4 event.
2. All children younger than five years old with HIV are considered as having advanced HIV disease.
3. A package of interventions including screening, treatment and/or prophylaxis for major opportunistic infections, rapid ART initiation and intensified adherence support interventions should be offered to everyone presenting with advanced HIV disease including those who are reengaging with care after a period of interruption.

Summary of Components of packages of care for people with advanced HIV disease.

Areas for the package	Intervention	CD4 cell count	Adults & adolescents	Children
Screening & diagnosis	Sputum Xpert® MTB/ RIF as the first test for TB diagnosis among symptomatic PLHIV	Any	Yes	Yes
	Cryptococcal antigen screening	≤100 cells/mm ³	Yes	No
Prophylaxis and pre-emptive treatment	Co-trimoxazole prophylaxis	≤350 cells/mm ³ or clinical stage 3 or 4	Yes	Yes For criteria, see chapter 4
	TB preventive treatment ^a	Any	Yes	Yes
	Fluconazole pre-emptive therapy for cryptococcal antigen– positive people without evidence of meningitis	<100 cells/mm ³	Yes	Not applicable (screening not advised)
ART initiation	Rapid ART initiation (as recommended in Chapter 3)	Any	Yes	Yes
	Defer initiation if clinical symptoms suggest TB or cryptococcal meningitis (see Chapter 3)	Any	Yes	Yes
Adapted adherence support	Tailored counselling to ensure optimal adherence to the advanced disease package, including home visits if feasible	<200 cells/mm ³	Yes	Yes

Re-engaging with care after ART interruption

1. Patients re-engaged into treatment after interruption should resume the same (previous) ART regimen they used before interruption after evaluation, assessment of adherence barriers and intensified adherence counseling. However, people interrupting treatment on NNRTI – containing regimen are at risk of drug resistance and should restart ART using a DTG-containing regimen. DTG has high genetic barrier to HIV drug resistance and can bring rapid viral suppression.
2. In addition, for re-engaged clients, the following essential elements should be part of the care:
 - Exhaust all possible adherence barriers and provide an ongoing Enhanced Adherence Counseling (EAC).
 - Maintain close or frequent follow-up schedule.
 - Monitor the viral load closely and determine the VL at 3 and 6 months after resuming ART. If the two consecutive viral load is >1000copies/ml, switch to second or third line regimen.

Care of HIV exposed infants

1. Infants born to mothers with HIV who are at high risk of acquiring HIV should receive dual Prophylaxis with AZT (twice daily) and NVP (once daily) for the first 6 weeks of life, whether they are breastfed or formula fed.

2. Breastfed infants who are at high risk of acquiring HIV, including those first identified as exposed to HIV during the postpartum period, should continue infant prophylaxis for an additional 6 weeks (total of 12 weeks of infant prophylaxis) using either AZT (twice daily) and NVP (once daily) or NVP alone.

Laboratory Monitoring

1. Baseline CD4 cell count testing for all people living with HIV remains clinically important in order to identify those who have advanced HIV disease and who should be offered the package of care required. CD4 cell count will be done every 6 months if indicated.
2. Routine viral load monitoring can be carried out at 6 months on ART, at 12 months and then every 12 months thereafter if the patient is stable on ART to synchronize with routine monitoring and evaluation reporting.
3. Viral load testing for pregnant mothers will be done as follows:
 - Newly diagnosed: after 3 months of ART initiation followed by every six months until the MTC risk ends or the routine at 6, 12 months and then every 12 months.
 - For those who are already on ART and their VL test done before 6 months, do the VL soon after pregnancy is known; then continue every six months until the MTC risk ends or routine VL testing should continue accordingly.
4. In settings where routine viral load monitoring is available, CD4 cell count monitoring can be stopped in individuals who are stable on ART and virally suppressed.
5. Dried blood spot specimens using venous or capillary whole blood can be used to determine the HIV viral load. A threshold of 1000 copies/mL can be used to determine virological failure when using dried blood spot samples, as defined for testing in plasma.
6. Aside from the routine viral load testing schedule, viral load testing should be used whenever there is clinical or immunologic suspicion of treatment failure.

Adherence monitoring and support

1. Adherence support interventions should be provided to people on ART .The following interventions have demonstrated benefit in improving adherence and viral suppression:
 - Peer counsellors
 - Mobile phone text messages
 - Reminder devices
 - Cognitive-behavioral therapy
 - Behavioral skills training/medication adherence training

- Fixed-dose combinations and once-daily regimens
2. When a client is found to have a viral load of >1000copies/ml on routine or need-based viral load test, providers should address adherence related issues by identifying adherence barriers and by providing enhanced adherence support (EAS) for three months.
 3. For those patients with identified significant adherence barriers, it is advisable to extend the provision of enhanced adherence support for 6 months before doing the second VL testing in order to properly address the barriers and give optimal time for viral suppression to happen.

Diagnosis and management of antiretroviral treatment failure

1. When a client is found to have a viral load of >1000copies/ml on routine or need-based viral load test, providers should address adherence related issues by identifying adherence barriers and by providing enhanced adherence support (EAS) for three months
2. If two consecutive viral load measurements within a 3-month interval with adherence support between measurements are greater than 1000 copies/ml, the results will confirm failure of the current treatment regimen and the client needs to be switched to appropriate second-line or third line regimen.

Summary of sequencing options for preferred first, second and third-line ART regimens in adults, adolescents, pregnant women and children

Population	1 st line regimens	2 nd line regimens	3 rd line regimens
Adults, adolescents, pregnant & breastfeeding women	AZT+3TC + EFV/NVP	TDF+3TC + ATV/r or LPV/r	DRV/r ^a + DTG + AZT+3TC
	TDF+3TC+EFV/NVP	AZT+3TC + ATV/r or LPV/r	DRV/r + DTG + TDF+3TC
	ABC+3TC+EFV/NVP	AZT+3TC + ATV/r or LPV/r	DRV/r + DTG + TDF + 3TC
Adults and adolescents 10 years & older with body weight $\geq 30\text{kg}$	TDF + 3TC + DTG ^f	AZT+3TC+ATV/r or LPV/r	DRV/r+ABC+3TC+EFV or NVP
Children younger than 3 years	ABC + 3TC + LPV/r	Maintain the 1 st line regimen	RAL ^b + AZT + 3TC
	AZT + 3TC + LPV/r		RAL + ABC + 3TC
Children older than 3 years, and adolescents 10 years & older with body weight < 30kg	AZT + 3TC + EFV	ABC + 3TC + LPV/r	DRV/r + RAL + ABC + 3TC
	ABC or TDF ^c + 3TC + EFV	AZT + 3TC + LPV/r	DRV/r + RAL + AZT + 3TC
All children (0 – 10)	AZT or ABC or TDF + 3TC + LPV/r ^d	AZT or ABC or TDF + 3TC + EFV or NVP	DRV/r ^{a,e} + RAL ^f + ABC + 3TC
			or RAL ^f + ABC + 3TC (for < 3yrs)
			DRV/r ^{a,e} + RAL + TDF + 3TC or RAL + TDF + 3TC (for < 3yrs)
			DRV/r + RAL ^f + AZT + 3TC RAL ^f + AZT + 3TC (for < 3yrs)

^a In PI-experienced patients, the recommended DRV/r dose should be 600mg/100 mg twice daily.

^b If RAL is not available, no change is recommended unless in the presence of advanced clinical disease progression or lack of adherence specifically because of poor palatability of LPV/r.

^c TDF may only be given to children >2 years.

^d ATV/r can be used as an alternative to LPV/r in children older than three months of age, however the limited availability of suitable formulations for children younger than six years of age, the lack of a fixed-dose formulation and the need for separate administration of RTV booster should be considered when choosing this regimen.

^e DRV/r should not be used in children younger than three years of age.

^f RAL can be used in children failing PI-based second-line treatment when DTG is not available and when RAL has not been used in a previous regimen. DTG is currently only approved for children 6 years and older (>30kg of weight), however studies are ongoing to determine dosing in younger children and approval to lower age groups is expected in the near future. DTG containing regimens are not approved for pregnant and breast feeding mothers. For HIV/TB co-infected adults & adolescents, the recommended dose of DTG is 50 mg twice daily.

Service delivery approaches and considerations

1. There will be scale up of the provision of second line ART to the health center level and the implementation will be in a phase-based approach using defined criteria as stated below for health centers to be included in the first phase of implementation.
2. Second line ART service will be made available at health centers that have a patient load of 200 or more.
3. The following criteria should be used to sort out treatment failure patients who will be switched to second line ART or will have follow up at the health centers:
 - a. Patients who fulfill the criteria of treatment failure and with no any signs of clinical failure
 - b. Patients who initiated on Second line ART at hospital, became stable with no signs of OI or drug toxicity, and transferred out to health centers while on second line ART.
4. Whenever patients develop toxicity or show any sign of deterioration upon switching to second line, the ART clinician should seek immediate advice from the clinical mentor or experienced physician and/or refer the patient immediately to the nearby hospital
5. The appointment spacing model (ASM) of care will be implemented at all treatment sites for stable adult individuals.
6. Stable individuals are defined as those who have received ART for at least one year and have no adverse drug reactions that require regular monitoring and have good understanding of lifelong adherence and evidence of treatment success.
7. In the ASM, stable clients will have follow up appointments every six months for clinical visit and medication refill.
8. Clients in the new care model should also get additional supports like arrangement of treatment supporter at home level among their family members and arrangement of adherence reminders like alarm and education on how to maintain the drug quality at home level.

CHAPTER ONE: INTRODUCTION

1.1. Background and Context

The first evidence of HIV epidemic in Ethiopia was detected in 1984. Since then, HIV/AIDS has claimed the lives of millions and has left behind hundreds of thousands of orphans. The government of Ethiopia took several steps in preventing further disease spread, and in increasing accessibility to HIV care, treatment and support for persons living with HIV.

According to the Ethiopian Demographic and Health Survey 2016 (EDHS 2016), the national HIV prevalence is 0.9%.; the urban prevalence was 2.9%, which is seven times higher than that of the rural (0.4%). The 2011 EDHS also show that the HIV prevalence varies from region to region ranging from less than 0.1% in Ethiopia Somali to 4.8% in Gambella. Furthermore, the 2017 spectrum HIV estimate indicate that the 2017 HIV prevalence in regions ranges from 0.16% to 4.34%.

In 2017, around 415,580 adults and 21,385 children under the age of 15 are taking ARV. Based on the spectrum estimate, the 2017 ART need is 551,630 for adults and 62,194 for children under 15 years of age. Free ARV service was launched in January 2005 and public hospitals start providing free ART in March 2005. Recently ART service is being available in more than 1,224 health facilities of which around 909 are health centers. Based on the new spectrum estimate for 2017, ART coverage for adults (age ≥ 15) has reached 75% but the coverage remains low (34%) for children (age < 15) living with HIV.

The national human resources development strategy focuses on training and upgrading of frontline, low and mid-level health workers that will staff primary health facilities. In line with this, appropriate HIV care and ART training, strong follow-up and effective clinical mentorship should continue to ensure the consistent application of the treatment guidelines and maintain the quality of HIV care and ART services at all levels. The National Guidelines for Comprehensive HIV Prevention, Care and Treatment was last revised in 2014. Since then, new information as well as evidence-based best practices has become available to make HIV treatment more effective and accessible, which create a need to revise the existing guidelines. Hence, this guideline is revised taking into consideration the current recommendations released by WHO in its 2016 and 2017 revised guidance for national programs.

1.2. Rationale for the Consolidated Guideline

The consolidated guidelines offer the following anticipated benefits:

- Guidance on using ARV drugs is presented within the context of the continuum of HIV-related prevention, treatment, and care. In addition to providing recommendations on the clinical use of ARV drugs for treatment, the guidelines address other major aspects of HIV-related care.
- The guidelines address the use of ARV drugs for all age groups and populations. Previously separate WHO guidelines on using ART among adults and adolescents have been combined with those for children and for prevention of mother to child transmission (PMTCT), harmonizing ARV regimens and treatment approaches to the extent possible across age groups and populations.
- New and existing guidance is harmonized. Consolidation has allowed for new recommendations to be harmonized with relevant, existing WHO guidance.
- Consolidation promotes the consistency of approaches and linkage between settings. Consolidated recommendations help to facilitate linkage and promote consistency of approaches across the various settings in which ARV drugs and related services may be provided, including specialized HIV care, primary care, community-based care, maternal and child health services, TB services and services for people who use drugs.
- Updates will be more timely and comprehensive. Consolidated guidelines enable key clinical, operational and programmatic implications of new science and emerging practice in the use of ARV drugs to be comprehensively reviewed every two years across populations, age groups and settings.

1.3. Objectives of the Guideline

This new version aims:

- To provide updated, evidence-based clinical recommendations outlining a public health approach to providing ARV drugs for HIV treatment and prevention in the context of the continuum of HIV care in the comprehensive HIV/AIDS service delivery setting.
- To provide guidance on key operational and service delivery issues that need to be addressed to increase access to HIV services, strengthen the continuum of HIV care and further integrate the provision of ARV drugs into health systems; and
- To serve as a reference material for health service providers and program managers.

1.4. Target Audience

The guideline is intended to be used by:

- Health care workers (physicians, health officers, nurses, pharmacy personnel, laboratory technicians) and case managers providing care to people infected and affected with HIV
- HIV/AIDS program managers, health planners and researchers
- Organizations involved in antiretroviral drug procurement, supply management, and ART service delivery.
- Community-based organizations and faith-based organizations working on HIV/AIDS programs.

1.5. Guiding Principles

- The guidelines should contribute to and expedite the achievement of key global and national HIV goals for 2016–2021 and to realizing the Sustainable Development Goals.
- The guidelines are based on a public health approach to scaling up the use of ARV drugs along the continuum of HIV prevention, treatment and care.
- Adapting and implementing the guidelines should realize the rights and responsibilities of people living with HIV and promote the greater involvement of people living with HIV (GIPA) and meaningful involvement of people living with HIV (MIPA) principles.
- In addition to strengthening the continuum of HIV services, the recommendations in the guidelines should be implemented with a view to strengthening broader health systems and provision of universal health care.
- Implementation of the guidelines needs to be accompanied by efforts to promote and protect the human rights of people who need HIV services, including ensuring informed consent, preventing stigma and discrimination in the provision of services and promoting gender equity.
- Implementation of the recommendations in these guidelines should be informed by local context, including HIV epidemiology, availability of resources and comorbidities, the organization and capacity of the health system and anticipated cost–effectiveness.

CHAPTER TWO: HIV DIAGNOSIS AND PREVENTION

2.1 HIV Testing Services

The term HIV testing services (HTS) is used in this guideline to embrace the full range of services that should be provided together with HIV testing including counselling (pre-test information and post-test counselling); linkage to appropriate HIV prevention, treatment and care services and other clinical services; and coordination with laboratory services to support quality assurance and the delivery of correct results.

HIV testing is the critical first step in identifying and linking people living with HIV (PLHIV) to the treatment cascade and it also provides an important opportunity to reinforce HIV prevention among the negatives.

Ensuring service quality is the area, which should not be compromised in HIV testing and counseling services provided by different models. National Guidelines, standard operating procedures, protocols and other necessary job aides must be followed and the HIV testing and counseling services must be regularly supervised.

One of the main objectives in HIV testing and counseling is to identify and link HIV positive persons to care and treatment services and HIV negative people to prevention services. Referral and linkage of clients must get necessary attentions to maximize the number of identified HIV infected persons that are linked to available care and treatment services in the country.

2.1.1 Guiding Principles

All forms of HIV testing and counseling should be voluntary and adhere to the five C's: consent, confidentiality, counseling, correct test results and connections to prevention, care and treatment services.

- **Consent:** People receiving HIV testing and counseling must give informed verbal consent to be tested and counseled. Written consent is not required. They should be informed of the process for HIV testing and counseling and their right to decline testing.
- **Confidentiality:** HIV testing and counseling services are confidential, meaning that what the HIV testing and counseling provider and the person discuss will not be disclosed to anyone else without the expressed consent of the person being tested. Counselors should raise, among other

issues, whom else the person may wish to inform and how they would like this to be done. Shared confidentiality with partner or family members and trusted others and with health care providers is often highly beneficial.

- **Counseling:** HIV testing and counseling services must be accompanied by appropriate and standardized pre-test information and post-test counseling.
- **Correct:** HIV testing and counseling providers should strive to provide standardized testing services to reach to correct diagnosis.
- **Connection:** Connections to prevention, care and treatment services should include the provision of effective referral to appropriate follow-up services as indicated, including long-term prevention care and treatment services.

2.1.2 Service Delivery Approaches

There are two major HIV testing and counseling service delivery models; and under these models there are different service delivery approaches. These models are health facility-based HIV testing and counseling model and community-based HIV testing and counseling model.

A. Facility-based HTS

Currently both Voluntary Counselling and Testing (VCT) and Provider Initiated Testing and Counselling (PITC) are the approaches being implemented in health facilities to deal with HIV testing and counseling services. Generally, the HIV testing and counseling approaches in health facilities are:

1. Client initiated HIV testing and counseling (VCT), which can be stand-alone or integrated with other health services.
2. Provider initiated HIV testing and counseling (PITC), which is provided by opt-out approach at clinical service points for eligible patients (who come to the facility for other medical reasons). All health facilities should provide PITC service for eligible clients at outpatient and inpatient departments, using the national testing algorithm.

Eligible clients for routine HIV testing and counseling by using PITC approach are:

- 1. All pregnant, laboring and postpartum women with unknown HIV status; and partners of HIV positive pregnant/postpartum women and partners of high risk* HIV negative pregnant and post-partum women.*
- 2. Eligible family members (siblings under 15 years old and their parents) and sexual networks of index PLHIV.*
- 3. Commercial sex workers and their clients.*
- 4. All TB patients with unknown HIV status and presumptive TB cases.*
- 5. All sexually transmitted infections (STI) patients with unknown HIV status, their partners and sexual networks.*
- 6. Discordant couples.*
- 7. Children orphaned by AIDS and vulnerable** children.*
- 8. Children with malnutrition.*
- 9. Patients with clinical signs and symptoms of HIV/AIDS visiting health facilities (outpatient and inpatient).*
- 10. Long distance truck drivers, mobile workers and daily laborers.*
- 11. Widowed, divorced & remarried.*
- 12. Vulnerable** adolescents / youth clients (15-24 years).*
- 13. All under five children visiting health facilities.*
- 14. Refugees and inmates.*
- 15. Family planning clients with identified risk (history of having multiple sexual partner, inconsistent condom use and their partners).*

**High risk includes having multiple partners, divorced and recently married, newly married, sex worker, waitress, daily laborer, mobile worker and age between 15-24 years.*

***Vulnerable children/adolescents/youth include those living in the street, orphans, adolescents in child headed household, girls engaged in sex with elder men or in multiple and concurrent sexual partnership, out of school youth, and adolescents who are sexually exploited.*

On public health grounds, mandatory and compulsory HIV testing and counseling are forbidden in Ethiopia. Therefore, health facilities and healthcare providers must refrain themselves from testing and counseling individuals without their will and consents. Mandatory testing is allowed in Ethiopia only

for screening purposes of blood and blood components for transfusion, in cases of organ transplantation and by order of court cases.

B. Community-based HTS

Community-based model is one mechanism of addressing eligible clients, who don't appear at health facilities for HIV testing and counseling for different reasons. This model builds public trust and also mitigates issues related to stigma and discrimination. Providing HIV testing and counselling (HTC) in the community relieves clients from transportation and other expenses. It has also importance in identifying HIV positive individuals earlier than facility-based HIV testing approach. Reaching populations through services provided at community level can break existing barriers to HIV testing and counseling. In Ethiopia community-based model of HIV testing and counseling is recommended in the following settings:

- Home-based testing targeting specific sub-population groups:
 - Families of index HIV cases.
 - Widow / widower, divorced and remarried.
 - AIDS orphans.
- Targeted outreach HIV testing and counseling services: Targeting specific geographic areas with high HIV prevalence (hot-spots). While planning outreach HTS, effective linkage of the identified HIV infected clients is very critical. Targeted outreach testing could be implemented to reach:
 - Commercial sex workers.
 - Long distance truck drivers.
 - Mobile workers.
 - Daily laborers.
 - Clients of sex workers.
 - Refugees.
 - Inmates.
- Work place HTS is recommended with high number of eligible persons for HIV testing and counseling. Some of the eligible work places where community-based model of HIV testing and counseling services are:
 - Big farms with huge number of regular and temporary workers.
 - Big construction sites (roads, dams for irrigation and hydro-electric etc.).
 - Big factories and mining sites.

Mixed service delivery approach will be used especially in cases of mobile populations and mega project sites.

2.1.3 Procedures of HTS delivery

VCT and PITC service providers should follow the national HTS guideline, protocol, cue-card and job-aids while providing HTS.

a. Client registration

At VCT service delivery points, clients will be registered using unique identifiers (code numbers) however at PITC service delivery points provider can use the patient's medical registration number (MRN).

b. Pre-test information

Pre-test information should be provided by VCT counselor using the cue-card. Couples should be encouraged to receive results together. Pre-test information for PITC can be provided in the form of individual or group information sessions. The relevant information that should be provided includes:

- The reasons why HIV testing and counseling is being recommended.
- The clinical and prevention benefits of individual and couple testing.
- The available services in the case of either negative or positive test result, including availability of ART.
- The confidentiality of result other than health care providers directly involved in providing services to the patient.
- The right to decline the offered test and declining an HIV test will not affect the patient's access to other medical services.
- The right of the client to ask the health care provider any concern or questions.

c. Informed consent

Informed consent should always be given as a verbal consent as individual or couple privately. For pediatric age group (less than 15 years of age) the parents or guardian of the child need to consent verbally. Mature minors (13-15 years old who are married, pregnant, commercial sex workers, street children, heads of families, or sexually active year age) can give verbal consent by themselves.

Unconscious or patient who is not in status of providing self-consent, should not be tested for HIV unless the clinician determines it necessary to establish diagnosis and make treatment decisions. The most senior clinician or counselor in the institution should be consulted before testing such patients. The patient's next of kin should be counseled and supported before HIV testing is carried out and

afterwards to understand the results and cope with the impact. Consent of kin should be obtained during counseling and service provider should act accordingly.

d. HIV Testing

To improve the acceptability, uptake & quality of service delivery for HTS $\neq$ all settings, rapid diagnostic tests (RDTs) should be used. These testing strategies have been developed assuming that all HIV assays used have a sensitivity of at least 99% and a specificity of at least 98%, resulting in an overall positive predictive value of 99%. The HIV testing must be done using nationally accepted RDTs following national HIV testing algorithm as shown below. Same day results should be respected at all times irrespective of the type of HTS delivery approach.

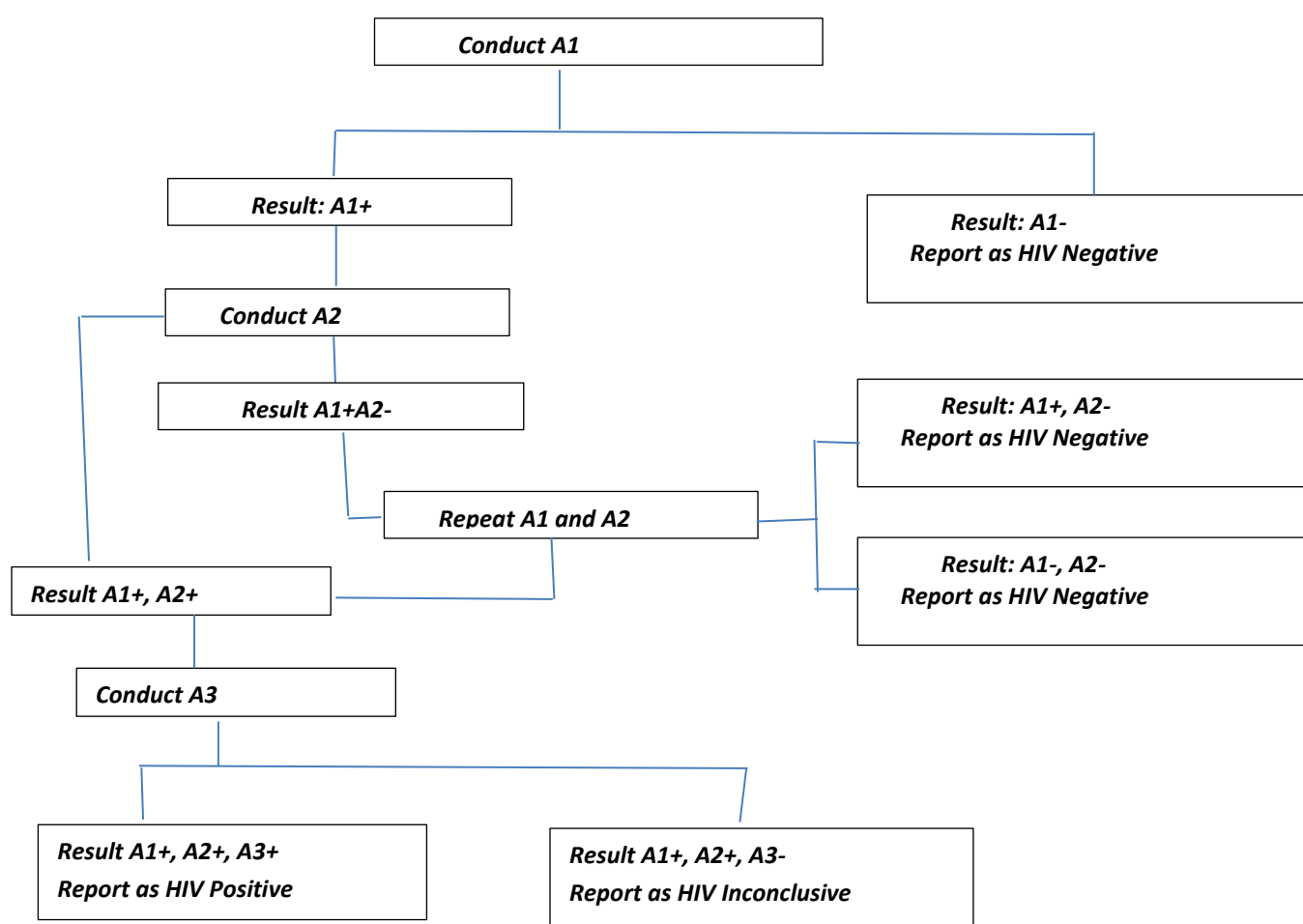


Figure 2.1: Recommended HIV testing strategy for Ethiopia.

e. Providing HIV test results

Test results should be declared in person (not by telephone, email or letter). HTS sites should not provide written HIV test results to clients to avoid misuse of results. Clients requesting or requiring referral to other facility should be referred to the appropriate institution with pertinent information.

f. Post-test counseling

All clients undergoing HIV testing should be provided with post-test counseling in person as individual or couple. The form of the post-test counseling session depends on the test result. For positives, sessions will focus on meaning of HIV positive result, coping with the test result, providing information on immediate treatment initiation, importance of medical care and treatment, disclosure and partner testing, prevention messages, positive living and referral for care and treatment. The post-test counseling session for negatives should include meaning of test result, risk-reduction plan to remain negative and importance of partner testing.

In situations where the counselor does not perform the test, results should be sent to the requesting counselor/service provider, and not disclosed to clients. All sites providing HTS (VCT or PITC) should ensure counselors follow the standardized protocol to provide post-test counseling.

g. Disclosure of HIV test results to other people

All clients, positive or negative, should be empowered to inform their sexual partner/s of their test result. When HIV-positive clients are reluctant or fearful to disclose their results, the counselor should provide additional counseling to help the client to disclose the test result and bring the partner for testing. If a client fails to disclose after repeated documented counseling sessions and the counselor feels that the partner is at risk of infection, he/she should consult the supervisor or immediate management staff for further action including revealing the result.

Disclosing HIV status to children is a process. Counselors should be encouraged to answer children's questions truthfully from early age. Information should be given in a way a child can understand at a pace s/he can cope with according to their cognitive and emotional maturity.

Refer: Pediatric disclosure section for more details.

h. Follow-up counseling

After counseling a client on test results, counselors should take the opportunity to review or share information that may not have been absorbed by clients within a week. Emphasis should be placed on prevention of further transmission, referrals to other services, involvement of partners and family members, coping mechanisms and identifying available support services and resources.

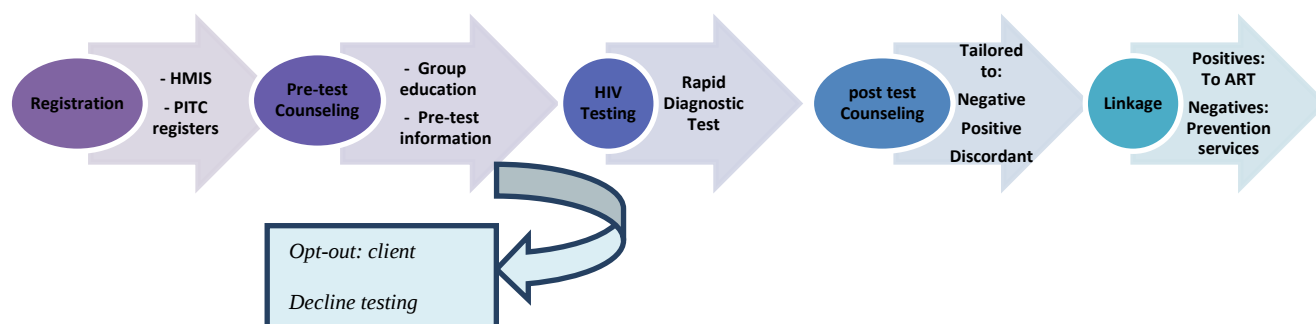


Figure 2.2: Provider initiated counseling and testing protocol with workforce

2.1.4 Retesting

There is a need to reduce unnecessary retesting among persons who have previously been tested and learnt their results. Most people do not require retesting to validate an HIV-negative result. However, it is important to accurately identify persons who do require retesting. Such persons include those whose initial test results were indeterminate, those who tested negative but are at ongoing risk for acquiring HIV (e.g. due to high-risk behaviors) and those who may be in the early stages of infection and have not yet developed a sufficient level of antibodies that can be detected by serological testing ('window period').

Repeat testing – Refers to a situation where additional testing is performed for an individual immediately following a first test during the same testing visit due to inconclusive or indeterminate test result; the same assays are used and, where possible, the same specimen.

Retesting – Refers to a situation where additional testing is performed for an individual after a defined period of time for explicit reasons, such as a specific incident of possible HIV exposure within the past three months, or ongoing risk of HIV exposure such as risky sexual exposure. Retesting is always

performed on a new specimen and may or may not use the same assays (tests) as the one at the initial test visit.

I. Retesting for individuals with ongoing risk

Retesting is recommended for persons who tested negative but have an ongoing risk:

1. Occupational exposure or sexually assaulted client who started post exposure prophylaxis (PEP): retest at 6 weeks, 3 months and 6 months.
2. Pregnant women, who have tested HIV negative in the first /second trimester of pregnancy: retest during third trimester or labor or postpartum.
3. People with STI: retest after 3 months.
4. People with continuing or ongoing risk of acquiring HIV (most-at-risk population- key populations): retest every 12 months but for female sex workers consider retesting every six months.
5. Have specific incidents of known HIV exposure within the past three months: retest after 3 months.
6. Discordant couple: retest after 6-12 month.

II. Retesting before initiation of ART

It is required that all HIV positive clients linked to care and treatment services need to be retested before treatment is initiated. Retesting aims to rule out possible technical or clerical errors; including specimen mix-up through mislabeling and transcription errors, as well as random error either due to the provider or the test device.

Retesting a person diagnosed to be HIV positive to verify the diagnosis should include:

- Taking a new specimen for each newly and previously diagnosed individual, preferably conducted by a different provider using the current testing algorithm, prior to initiation of ART.
- Retesting is preferably conducted at a different site/unit, ideally the site where the decision about ART initiation will be made. Retesting should be done in ART clinic or other unit designated and monitored by the ART clinic. For PMTCT, where there are providers other than those who did the first test, retesting could be done at the PMTCT unit; otherwise do the retest in the ART or in the unit designated by ART clinic or laboratory.

- If the retesting result is negative (the previous test result is positive and the current test result is negative), sample should be sent to regional laboratories where HIV testing will be done using a more specific testing modality.
- Testing at labor and delivery (L&D) unit for pregnant woman with unknown status will be done. If positive, provide ART for the mother and ARV prophylaxis for the infant. After delivery, perform retesting (different provider and different sample). If the positive test is verified, continue ART; if negative, refer the sample to the nearby regional laboratory to do the test using a more specific testing modality.

Retesting people on ART is not recommended. The effect of ART in suppressing viral replication may extend to suppression of the immune response and therefore reduction of antibody production will be there. Once a person is started on ART, low antibody titers make it challenging to discern whether an individual is indeed HIV positive and this will lead to potential risks of incorrect diagnosis.

2.1.5 HIV Testing Services in Specific Populations

a. Couples and partners

Testing the partners of people with HIV is an efficient and effective way of identifying additional people with HIV, who also can benefit from treatment. Providing couples and partner HTS has a number of benefits. These include adoption of prevention strategies by the couple (for example; condom use), immediate ART initiation, safer conception, improved uptake of and adherence to practices for PMTCT as well as to one's own ART (thus reducing transmission risk as well as morbidity and mortality). Couples and partner HTS help more people know their HIV status, particularly men, who in generalized epidemic settings are substantially less likely to test than women. Beyond the immediate partners of the index cases, the sexual networks of clients should be identified.

Couples and partner HTS can be conducted in various settings, including antenatal clinic (ANC), VCT or community-based testing settings. People attending ART services can be encouraged to bring their partners to be tested. As with all HTS approaches, couples and partner HTS should be voluntary. Informed consent should be obtained from all individuals receiving HIV testing. Providers must be aware of the potential for intimate partner violence and should support couples and partners to test with their partners. Currently, the prevalence of sero-discordance is estimated at one-half to two-thirds of cohabitating couples or partners where one partner has HIV. Nonetheless, many people do not know their partner's HIV status. Couples and partner HTS should be made available for partners of people

with HIV and people from key populations. To facilitate PLHIV partner testing, refer the section on disclosure in adults.

Recommendations

- Couples and partners in all settings should be offered HIV testing services with support for mutual disclosure.
- HIV testing services with support for mutual disclosure should be offered **to all individuals whose partners have HIV.**

b. Pregnant and postpartum women

Provider-initiated testing and counselling for pregnant women and linkage to prevention and care are needed to promote the mother's health and prevent new pediatric infections.

Recommendations

- Provider-initiated testing and counseling is recommended for women as a routine component of the package of care in all antenatal, childbirth, postpartum and pediatric care settings.
- Retesting is recommended in the third trimester, or during labor or shortly after delivery, because of the high risk of acquiring HIV infection during pregnancy.

c. Infants and children

Mortality is very high among untreated infants infected with HIV in the first year of life, making early HIV testing, prompt return of results and rapid initiation of treatment essential. Final diagnosis (or definitive diagnosis) at the end of the risk period for mother-to-child transmission (breastfeeding period) should be ensured. For children 18 months of age and older (who are not being breastfed or who stopped breastfeeding for at least six weeks), standard HIV serological tests such as rapid diagnostic tests can be used to reliably determine HIV infection status.

Recommendations

It is strongly recommended that:

- HIV testing and counseling should be offered to all under five children visiting health facilities.
- All HIV-exposed infants must have HIV virological testing at six weeks of age or at the earliest opportunity thereafter.
- For infants with an initial positive virological test result, it is strongly recommended that ART be started without delay and, at the same time, a second specimen be collected to confirm the initial positive virological test result.
- Children 18 months of age or older with suspected HIV infection or HIV exposure, have HIV serological testing performed according to the standard diagnostic HIV serological testing algorithm used in adults.

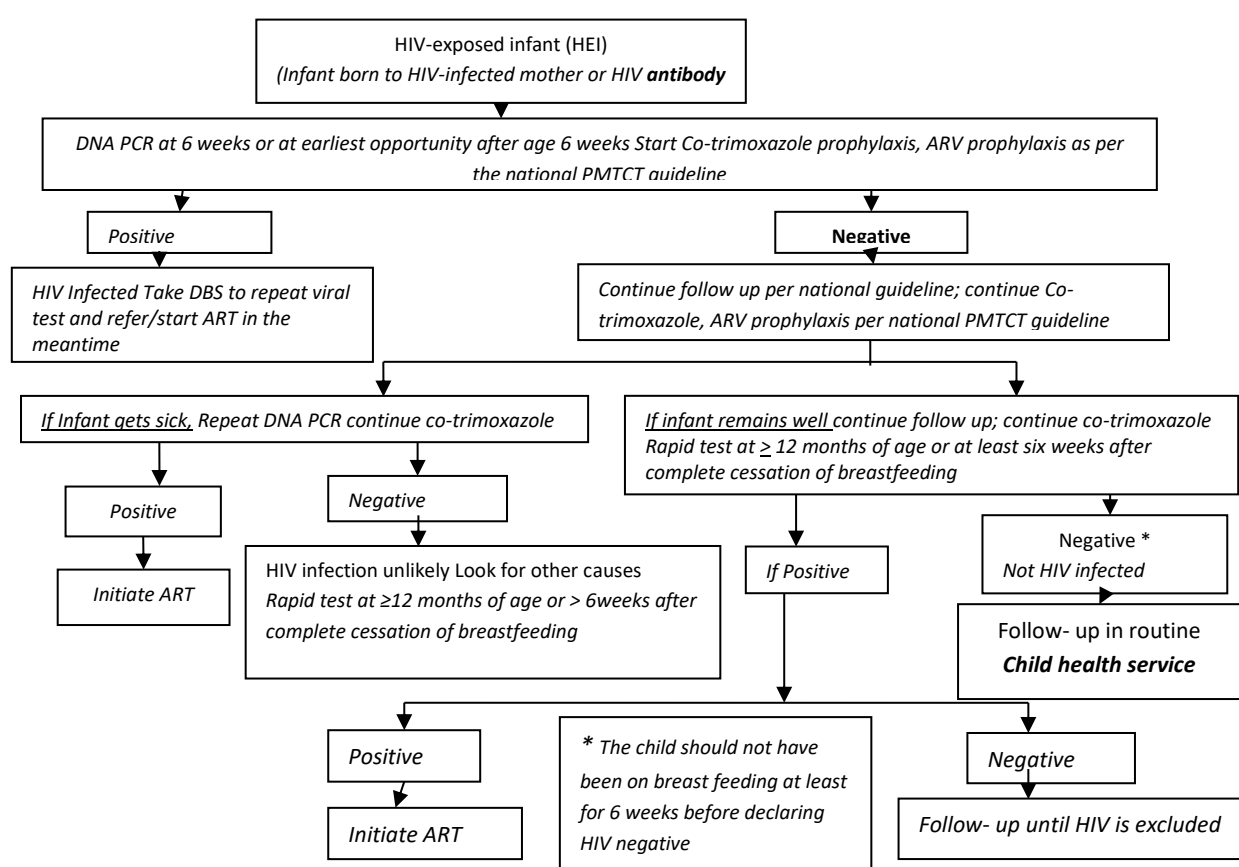


Figure 2.3: Algorithm for testing of HIV Exposed Infants < 18 months

NB: If the first test is positive and the confirmatory virological test is negative, a third test will be needed to resolve the discordance between the two earlier virological tests (WHO recommendations on the diagnosis of HIV infection in infants and children, 2010).

d. Vulnerable adolescents

Vulnerable adolescents are often underserved and given insufficient priority in many HIV programs, with poor access to and uptake of HIV testing and counseling and linkage to prevention and care. Adolescents with HIV include those surviving perinatal infection and those newly acquiring infection as they become sexually active or are exposed through sexual assault and blood transfusions. In generalized epidemic settings, many vertically infected infants are not diagnosed through program for PMTCT and would benefit from earlier HIV diagnosis and treatment. In many settings, adolescent girls and adolescents from key populations are also vulnerable to HIV infection and would benefit from access to acceptable and effective HIV services, including HIV testing and counseling. Mature minors and adolescents above 15 years can access HTS by giving self-consent.

Recommendations

- HIV testing and counseling with other prevention services and linkage to treatment and care is recommended for vulnerable adolescents and youth age 15-24 years.
- Vulnerable adolescents be counseled about the potential benefits and risks of disclosure of their HIV status and empowered and supported to determine if, when, how and to whom to disclose.

e. Key populations

HIV testing and counseling has been provided to key populations since HIV tests were first developed. Both existing and new recommendations for HIV testing and counseling for these most-at-risk and vulnerable groups should emphasize consent and confidentiality as well as ensuring that HIV testing and counseling is part of a comprehensive prevention, care and treatment program. Populations most-at-risk and vulnerable to HIV infections include but are not limited to: sex workers, truck drivers, mobile/daily workers, in and out-school youth, uniformed services and inmates.

Recommendations

HIV testing and counseling with other prevention services and linkage to treatment and care should be accessible to KEY POPULATIONS at health facilities and community service models.

2.2 Innovative HTS Approaches and Tools to Strengthen Targeted HIV Testing Service

2.2.1 Index Case Testing

The index case is the primary case, or patient zero who is the starting point (individual) in the population of an epidemiological investigation. The index case is defined as the individual who is found HIV positive on HIV Testing and Counselling (HTC) provided at the health facility. Counsellors provide HTS and identify HIV infected individuals and then provide HTS to their family members and partners.

Index case testing is also a high yield, targeted testing approach for identifying and linking new HIV-infected individuals to treatment services. This approach needs to be optimally utilized for case detection and to break the HIV transmission cycle. Some of the PLHIV might have not yet disclosed their HIV status to their partners while others have partners with ongoing risk, including none spouse partners. Clients concerns should be addressed to improve disclosure and testing service uptake among index partners (spouses and none spouse partners) and HIV exposed children.

2.2.2 Respondent Driven HIV Testing or Snow ball

Respondent Driven HIV testing is a network-based technique for reaching out the hard-to-reach populations through facilitating/addressing, such key populations, via a chain - referral procedure in which participants recruit one another.

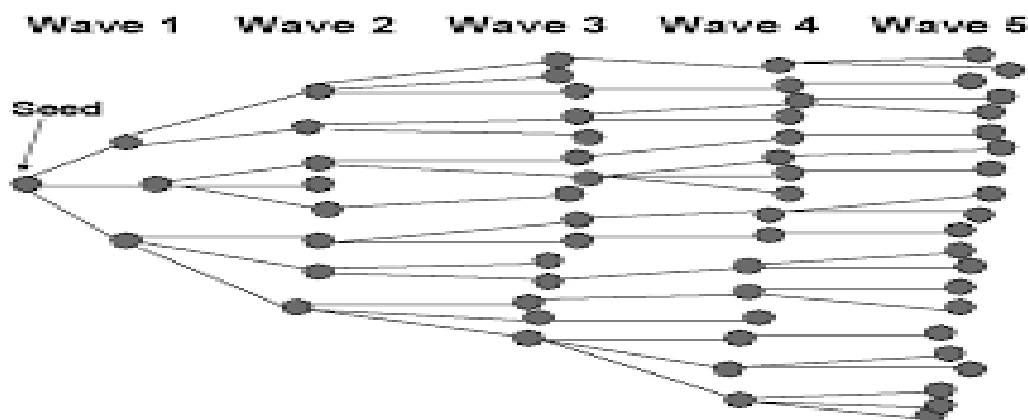


Figure 2.4: Respondent driven HIV testing or snow ball

2.2.3 HIV Self-Test

HIV Self-Test (HIVST) is an innovative approach to deliver HIV testing services and contribute more for the national testing targets goal of reaching 90-90-90 and specifically the first target of diagnosing

90% of all people with HIV. WHO recommends HIV self-testing should be offered as an additional approach to HIV testing services.

HIV self-testing (HIVST) refers to a process in which a person collects his or her own specimen (oral fluid or blood) and then performs an HIV test and interprets the result, often in a private setting, either alone or with someone he or she trusts. As with all approaches to HIV testing, HIVST should always be voluntary, not coercive or mandatory. The approaches of HIVST are:

Directly assisted HIVST refers to trained providers or peers giving individuals an in-person demonstration before or during HIVST of how to perform the test and interpret the test result.

Unassisted HIVST refers to when individuals self-test for HIV and only use an HIVST kit with manufacturer-provided instructions for use.

Both directly assisted HIVST and unassisted HIVST may supply additional support tools, such as telephone hotlines, mobile phone text messages, videos, social media and Internet-based applications, which provide technical support, counselling and referrals for further HIV testing services, HIV prevention, care and treatment and other services. For instance currently assisted self-testing has been piloted as one modality of testing on female sex workers in Ethiopia. The pilot finding will be used to scale up this initiative for different target groups in the future.

2.2.4 Applying risk screening for high risk groups or individuals, for more targeted PITC

A risk screening based HIV testing which enables service providers to identify risky groups during counseling & gives opportunity for being targeted HIV testing. HIV risk screening tool is a tool, having a set of questions, used to identify the clients with specific risks for HIV transmission. Risk screening tools have been utilized in other countries to identify who needs to be tested and maximize HIV case detection and increase efficient utilization of the limited RTKs. In our setup risk screening can be applied for vulnerable adolescents/Youth and HIV negative pregnant/lactating women to provide risk based HIV testing for their partners. The following questions can be considered as examples for risk assessment:

- Have you ever tested for HIV in the past 12 month?
- Have you had unprotected sex?
- Did you drink a lot during night time & have sex with clients?
- Have you ever experienced symptoms of sexually transmitted infections?

2.2.5 Partner Services

Partner services, sometimes also called Partner Notification Services (PNS) are a comprehensive array of services offered to persons diagnosed with HIV or other sexually transmitted infections (STI) and individuals they may have exposed to HIV infection (e.g. spouses, none spouse partners). A critical function of PNS is partner elicitation, a process through which index patients (i.e. an individual newly diagnosed as HIV-positive and/or an individual who is enrolled in HIV treatment services) are interviewed to elicit information about their partners, counseled and assisted on disclosure and continuously supported to bring their partner for HIV testing. Partner notification services are voluntary, based on the decision of the index patient, and are provided confidentially, at no cost, in a patient-centered framework. The role of the service providers here need to be providing counseling about the risk of HIV transmission and importance of disclosure, assisting on disclosure, educating on the benefits of early treatment and better outcome.

2.3 Quality Management

Quality HTS can be defined as accessible services that meet the need of clients and providers, in an equitable and acceptable manner, within the available resources and in line with national guidelines.

Quality assurance

Quality assurance (QA) for HIV testing and counseling refers to periodic assessments of factors that affect the quality of HTS. Issues that need to be addressed while assessing for QA:

- Have the counselors/service provider received basic HTS training packages approved by FMOH?
- Is there enough physical space to provide HTS that ensures privacy of the clients and point of care testing?
- Are basic supplies and provider support tools available to provide HTS?
- Is the service accessible and affordable to the clients?
- Are clients satisfied with the services?
- Are counseling and testing sessions conducted according to nationally approved protocols?

HTS should be supervised by well-trained program supervisors on regular basis to ensure HIV testing service qualities. The roles and responsibilities of the supervisors are:

- To determine if counselors/service providers received standard trainings and refresher courses.
- To monitor how well counselors/service providers follow the counseling and testing protocol.

- To monitor whether clients feel that their confidentiality is protected and satisfied with the services they are provided.
- To make sure that HIV test results are given in person during the post-test counseling session.

Supervision and quality assurance for HIV testing:

The supervisory visits for testing standards and bio-safety should assure that:

- The national testing protocol is consistently being followed.
- The laboratory operating procedures are being observed.
- Infection prevention practice is in place.
- Proficiency testing is in place including quality control testing in central laboratory.
- A standardized laboratory log book is available and being used.
- Technical support on the quality of HTS is in place.

Quality control (QC) is a procedure or set of procedures intended to ensure that a performed service adheres to a defined set of quality criteria or meets the requirements of the client. It is an important means of verifying for the test kit and the procedures used are performing according to the manufacturer's intended specifications.

Quality control of HIV testing

Only test kits validated by the Ethiopian Public Health Institute should be used by counseling and testing sites. Training and supervision of laboratory staff, accurate testing materials that are well stored and have not expired, and good maintenance of laboratory records are essential to quality HIV testing.

External quality assessment (EQA)

For EQA, proficiency testing samples (dried tube specimen), which was prepared by the higher laboratory tier, i.e. national reference laboratory (NRL), regional reference laboratory (RRL) or EQA centers must be done. This method evaluates individual's performance in testing procedure, results reporting, capabilities of laboratories and testing points on performing HIV rapid testing. Sites failing the proficiency tests need to receive additional technical supervision and support. In addition, onsite evaluation has to be done at least twice a year.

Internal quality control (IQC)

For IQC, trained laboratory technicians in the facility should regularly perform the IQC to verify the quality before the test kits are being used by the testing units.

2.4 Policy, Ethical and Legal Considerations for HIV Testing and Counseling

Policy and legal framework

The following policy, legal and ethical statements reflect existing Ethiopian HIV/AIDS policy.

General HTC services

Policy objectives

To promote and provide standard HTS to individuals, couples, and community groups of all ages regardless of gender, and especially to vulnerable and high-risk groups.

Policy statements

- HTS shall be integrated into existing health and social welfare services and promoted in all settings: government, non-governmental, private sector, cooperatives, workplace and faith-based organizations.
- HTS shall be strengthened through effective networking, consultation and collaboration among stakeholders.
- HTS shall be standardized nationwide and shall be authorized, supervised, supported and regulated by appropriate government health authorities.
- Informed consent for testing shall be obtained in all cases, except in mandatory testing.
- Adequate pre-test information, pre-test counseling and post-test counseling shall be offered to all clients.
- Test results, positive or negative, shall be declared to clients in person and must be provided with post-test counseling.
- HIV test results will not be provided in certificate form; however referral will be offered to access prevention, care and treatment.
- Clients' confidentiality will be maintained at all times. Results can be shared with other persons only at clients' request or agreement, and with those involved in clinical management of clients. Clients can be referred if required or upon request.
- Mandatory HIV testing is a violation of human rights, only permissible in exceptional cases by order of a court of law. Mandatory testing will be done on all voluntary blood, tissue and organ donors, who shall be informed about HIV testing and given opportunity to learn their test results.
- PITC shall be promoted to all eligible person as part of standard clinical management and care in all health facilities.

Couples

Policy statements

- Couples shall be encouraged to be counseled, tested and receive results together. Partner notification shall be encouraged in cases where one partner receives the results alone.
- The privacy and autonomy of the couple and individual must be respected. Informed decisions shall be encouraged among discordant couples to protect negatives and support positives.
- Pre-engagement, premarital and preconception counselling and testing will be promoted.

Women

Policy statements

- Women shall be routinely offered HTS during pregnancy, labour, post-natal and at family planning (FP) service points, with the right to refuse testing.

Children and youth

Policy statements

- HIV testing for children under the age of 15 shall only be done with the knowledge and consent of parents or guardians, and the testing must be done for the benefit of the child. However, children aged 13-15, who are married, pregnant, commercial sex workers, street children, heads of families, or sexually active are regarded as “mature minors” who can consent to HIV testing.
- Persons aged 15 years and above are considered mature enough to give informed consent for themselves.
- In some special cases, such as child adoption, a counselor may refuse a testing request when this is not in the best interest of the child.
- Children who have been sexually abused and put at risk of HIV infection shall receive counseling, be encouraged to test for HIV and helped to access appropriate services.
- The result of HIV testing is the property of the child tested and shall not be disclosed to third parties unless clearly in the best interest of the child
- Youth-friendly counseling and testing services shall be made widely available for youth population.

Physically disabled and mental impaired individuals

People with physical disabilities and mental impairment require special care when providing counselling and testing services, particularly regarding communication.

Policy statements

- HTS shall accommodate the special needs of people with visual and hearing impairments by adopting appropriate media of communication.
- Individuals under the immediate influence of alcohol or addictive drugs (substance use) shall not be offered HIV testing due to a mental inability to provide informed consent.
- HTS for a mentally impaired individual requires the knowledge and consent of his/her guardian, and should be for the benefit of the individual or patient.

Ethics in counseling

Policy statements

- All service providers shall abide by the rules, regulations and protocols contained in this document and other related national guidelines
- All service providers shall observe the ethical requirements of confidentiality, informed consent, proper counseling, anonymity and privacy.
- Shared confidentiality shall be promoted as an avenue to demystify and de-stigmatize HIV/AIDS

2.5 Linking People Diagnosed with HIV Infection

Linkage is defined as a process of actions and activities that support people testing for HIV and people diagnosed with HIV to engage with prevention, treatment and care services as appropriate for their HIV status. For people with HIV, it refers to the period beginning with HIV diagnosis and ending with enrolment in care or treatment. It is critical for people living with HIV to enroll in care as early as possible. This enables timely initiation of ART as well as access to interventions to prevent the further transmission of HIV, prevent other infections and co-morbidities and thereby to minimize loss to follow-up.

Good practices for linkage to care from HTS sites

The following are recommended good practices to improve linkage of HIV positive person to care and treatment services after the person is found positive at all HTS sites.

Implement standardized service delivery system that will improve referral and linkage between HTS and HIV chronic care through the following recommended priority interventions:

- Prepare standard operating procedure (SOP) for inter- and intra- facility service outlets referral linkage system.

- Establish site level support groups to improve escorting/accompanied referral and feedback practices for intra-facility referral.
- Conduct linkage audit to monitor clients' engagement to care and treatment service.
- Map and establish network between available HTS, chronic care, and other support services in the area (linkage service directory).

Standardize documentation, reporting system and feedback practice. The priority interventions are:

- Harmonize site level HTS and chronic care registers, reporting formats, referral and feedback formats (in line with health management information system, HMIS).
- Ensure the availability and sustainability of recording and reporting formats.
- Ensure a referral and linkage feedback mechanism in health facility.

Ensure standardization of HTS guidelines and training materials on referral and linkages issues. The priority intervention is:

- Ensure utilization of both VCT and PITC implementation manuals with referral and linkage issues.

Improve the involvement of Health Extension Workers (HEW), PLHIV in awareness creation activities as to improve referral and linkages through the following priority interventions.

- Support HEW in their day to day information education and communication (IEC) / behavioral change communication (BCC) activities in relation to HIV.
- Establish and strengthen PLHIV associations and support groups to be involved in the facilitation of referral and linkage through escorting and other mechanisms.

Reduce stigma and discrimination through community involvement, the Priority interventions are:

- Develop IEC/BCC material focusing on stigma and discrimination.
- Advocate gender inequality that predisposes to stigma and discrimination.
- Increase media utilization focusing on stigma and discrimination.
- Take a visible leadership role in community activities to address stigma and discrimination through contextual available values and norms of the community.
- Identify and analyze the root cause of stigma and discrimination.

- Involve PLHIV to reduce stigma and discrimination and to be part of prevention and care services.

Promote health seeking behavior and encourage HIV positive people for service utilization through the following priority interventions:

- Educate clients on benefits of chronic care and other misconception.
- Involve local officials, political leaders, community and faith-based organization leaders to advocate the advantage of standard referral and linkage.
- Involve HEW and other sectors such as agricultural extension workers, education workers, youth associations, women's associations, PLHIV, etc. and make them aware of the problem of referral and linkage and collaborate to resolve it.
- Adopt and implement innovative approaches using information technology to improve referral linkage.
 - eHealth/mHealth: call or text to the client and remind him/her on linkage
 - Strengthen Post-test counseling in such a way that the client understands the benefits of ART; develop trust and confidence on the provider and reaches to informed decision on linkage.
 - Establish facility and catchments area level regular referral linkage auditing system to ensure that all new HIV infected clients are linked to ART.

2.6 Post Exposure Management including Prophylaxis

2.6.1 Management of Occupational Exposure to HIV

- Health care workers and support staff have a low but measurable risk of HIV infection after accidental exposure to infected blood or body fluid.
- Compliance with infection prevention recommendations is the mainstay in prevention of occupational HIV infection. The priorities therefore must be to train health personnel in infection prevention and provide them with necessary materials and protective equipment.
- Risk of HIV infection after a needle stick or cut exposure to HIV-infected blood is estimated to be 0.3% (3 in 1000). Stated in another way, 99.7% of needle stick/cut exposures do not lead to infection. The risk of HIV infection after exposure of mucous membranes to HIV-infected blood

is estimated to be 0.1% (1 in 1000). However, risk could vary depending on severity of injury and viral load in the source patient.

- Antiretroviral treatment immediately after exposure to HIV can reduce risk of infection by about 80%.

Set up for post exposure management in health facilities

- Regular prevention education for employees (health workers, cleaners and other staff) involved in institutional care for PLHIV.
- Ensure availability of control mechanisms for effective observation of standard precaution.
- Establish system for post exposure management to ensure urgent attention for victims who have sustained accidental blood exposure

Minimum package for PEP sites/facilities

1. Assign one trained physician / Health Officer / nurse as PEP focal person for the facility.
2. The contact address of the facility PEP focal person and the facility ART nurse or any other second person assigned to coordinate PEP activities in the facility should be posted in all outpatient and inpatient departments within the health facility.
3. PEP starter packs including ARV drugs should be made available in designated sites inside the health facility which may be accessible to all staff, 24 hours and 7 days a week.
4. Provider support tools like algorithm for determination of the severity of exposure (Exposure Code) and PEP register should be available in the facility.

Steps to manage potential HIV exposed person

1. Treat the exposure site /Immediate measures
 - Percutaneous injury or injury to non-intact skin:
 - Wash the exposed site with soap and water as soon as possible, without scrubbing.
 - Avoid using antiseptics.
 - Allow free bleeding but do not squeeze the wound.
 - Exposed mucous membranes:
 - Irrigate copiously with clean water or saline.
2. Report the exposure :
 - To the PEP focal person or the ART physician or nurse in the facility immediately.
3. The PEP focal person or the ART physician /Health Officer /nurse who needs to do:

- a) Clinical evaluation, counseling and testing of the exposed person and complete the exposure reporting form.
- b) Do risk assessment and determine the exposure code (EC) and source HIV status code (HIV SC) using the PEP algorithm.
- c) Using the EC and HIV SC determine whether PEP is warranted for the exposed HCW.
- d) If the HCW is warranted to take PEP: Chose appropriate PEP regimen, counsel about the ARVs and prescribe according to PEP algorithm.
- e) Document properly on the PEP follow-up register.
- f) Appoint the exposed person and follow.
- g) Do all follow up HIV testing at 6 weeks, 12weeks and 24 weeks, and manage accordingly.

Assessment of exposure risk:

Low-risk exposure:

- Exposure to small volume of blood or blood contaminated fluids
- Following injury with a solid needle
- Asymptomatic source patient

High-risk exposure:

- Exposure to a large volume of blood or potentially infectious fluids.
- Exposure to blood or potentially infectious fluids from a patient with clinical AIDS or acute HIV infection.
- Injury with a hollow needle.
- Needle used in source patient's artery or vein.
- Visible blood on device.
- Deep and extensive injury.

Table 2.6.1: Interpretation of exposure code (severity of exposure).

	Exposure Code	Type of exposure
1	EC 1	Is a minor mucocutaneous exposure to small volume of blood for short period (few seconds to minutes).
2	EC 2	Is a major mucocutaneous exposure to large volume of blood for longer duration (several minutes), or Mild percutaneous exposure (with solid needle or superficial scratch or injury).
3	EC 3	Severe percutaneous exposure (large bore hollow needle, deep puncture, visible blood on device, needle used in patient artery/vein).

Table 2.6.11: Interpretation of the HIV status of the source patient.

	HIV Source Code (SC)	The HIV status and severity of the illness in the source patients
1	HIV SC 1	The source patient is HIV positive but is asymptomatic and has reasonably good immune status.
2	HIV SC 2	The source patient is HIV positive and is symptomatic, may have AIDS or has other evidence of advanced illness (low CD4 or high viral load).
3	HIV SC unknown	The HIV status of the source patients is unknown (either the patient has refused HIV testing or died or discharged before HIV testing) or the source patient is unknown (e.g. unlabeled blood sample in a laboratory).

Table 2.6.12: Recommended PEP based on risk assessment.

Status code	Exposure code		
	EC 1	EC 2	EC 3
SC 1	Basic 2 drug PEP	Basic 2 drug PEP	Expanded 3 drug PEP
SC 2	Basic 2 drug PEP	Expanded 3 drug PEP	Expanded 3 drug PEP
SC unknown	Consider basic 2-drugs PEP.		
HIV negative	No PEP warranted	No PEP warranted	No PEP warranted

Table 2.6.13: Recommended ARVs for PEP and administration guide.

ARV drug regimen	Dose	Frequency	Duration
2-Drug Regimen: Tenofovir (TDF) + Lamivudine (3TC) or Zidovudine (AZT) + Lamivudine (3TC)	TDF 300mg 3TC 300mg AZT 300mg 3TC 150mg	Once daily 12 hourly	28 days 28 days
3-Drug Regimen: Triple FDC Tenofovir (TDF) or Zidovudine (AZT) + Lamivudine (3TC) + Efavirenz(EFV) Or Lopinavir/ritonavir (LPV/r) Or Atazanavir/ritonavir (ATV/r) OR TDF+3TC+DTG, triple FDC	Triple FDC (TDF 300mg, 3TC 300mg, EFV600mg) AZT 300mg twice daily 3TC 150mg twice daily EFV 600mg once daily LPV/r400mg /100mg ATV/r300mg/100mg TDF300mg+3TC300mg+DTG 50mg	Once daily AZT&3TC 12 hourly; EFV600 once daily 12 hourly Once daily Once daily	 28 days

Timing of initiation of prophylaxis:

To be effective, PEP should commence as soon as possible (within 1-2 hours). The maximum delay for initiation of treatment which would prevent infection is not known in humans. Do not consider PEP beyond 72 hours post exposure. Prophylaxis is to be given for 28 days.

Testing and monitoring after occupational exposure:

- **Testing source:** rapid HIV test is done after counseling and consent has been secured. If the source patient is negative there is no need of further assessment of the exposed health care worker. If the result is positive the health care worker needs to be tested
- **Testing of health care worker:** HIV serology should be performed immediately after exposure. If result is positive there is no need for PEP, but if negative you should administer PEP as soon as possible as outlined above and then repeat serology at 6 weeks, 3 months, and 6 months.

Testing of Health Care Workers for possible Hepatitis B infections in line with national viral Hepatitis guideline is recommended.

- ✓ Remember to initiate PEP immediately after exposure until test result confirms the HIV status of the victim. Stop PEP if the health worker is positive for HIV antibodies.
- ✓ Following HIV exposure there is a need for psychosocial support.

2.6.2 Prevention of the Transmission of HIV after Sexual Assault

1. Any person presenting to a health facility after potential exposure to HIV during sexual assault should be counseled by the examining health care worker about the potential risk of HIV infection.
2. Parents/guardian of traumatized children should be counseled and informed on the risk of HIV infection after sexual assault.
3. The following points should be covered in the counselling:
 - a) The exact risk of transmission is not known, but it exists.
 - b) It is important to know the victim's HIV status prior to any antiretroviral treatment.
 - c) It is the patient's choice to have immediate HIV testing or, if s/he prefers, this can be delayed until 72 hours post examination visit (management guidelines on sexual assault provides for a 3-day starter pack for those who prefer not to test immediately, or those that are not ready to receive results immediately). However, encourage the patient to be tested.
 - d) PEP is not recommended after 72 hrs. following sexual assault. Patients should be counseled about risk of infection and the possibility of transmitting infection during sero-conversion. They should be instructed to return at 6 weeks and 3 months post sexual assault for voluntary counseling and HIV testing.
4. It is strongly recommended that the implementation of post-rape prophylaxis should be carefully monitored and evaluated for:

- ✓ Emergency contraceptives
- ✓ Psychosocial and legal support
- ✓ Screening for conventional STIs and follow-up management
- ✓ Drug side effects
- ✓ Sero-conversion

Recommended regimen AZT or TDF+3TC+EFV for 28 days. Alternatively, boosted Lopinavir OR boosted Atazanavir can substitute EFV.
PEP is not recommended a) If victim presents more than 72 hours after exposure. b) Following condom leak or tear.

Follow-up of client exposed to HIV

Post exposure testing

- A **client** who is taking PEP should be followed in the adult ART clinic

Monitoring and management of PEP toxicity

1. Exposed client should be reassessed within 3-5 days for medication tolerability and toxicity. If further details about the source become available, a risk assessment re-evaluation may also be appropriate.
- Clients taking PEP should be monitored for drug toxicity by testing at baseline and again 2 weeks after starting PEP. The scope of testing should be based on medical conditions in the exposed person and the toxicity of drugs included in the PEP regimen.
 - Minimally, lab monitoring for toxicity should include a complete blood count and liver function tests.
 - If toxicity is noted, modification of the regimen should be considered.

Pre-Exposure prophylaxis

Oral pre-exposure prophylaxis (PrEP) of HIV is the use of ARV drugs by people who are not infected with HIV but at a substantial risk to block the acquisition of HIV. Substantial risk of HIV infection is provisionally defined as an incidence of HIV higher than 3 per 100 person-years in the absence of pre-exposure prophylaxis (PrEP). Oral pre-exposure prophylaxis (PrEP) containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches.

Pre exposure prophylaxis (PrEP) is one of the new innovative approaches for prevention of HIV and will be piloted in selected target groups in Ethiopia for future considerations.

2.7 Combination Prevention

HIV prevention approach based solely on one element does not work and can hinder the HIV response. There is no single magic bullet for HIV prevention. However, a growing number of interventions have shown promise in partially protecting against HIV transmission and acquisition that includes knowledge of sero-status, behavioral risk reduction, condoms, male circumcision, treatment of curable sexually transmitted infections, and use of antiretroviral medications. We need to use a mix of behavioral, biomedical and structural HIV prevention actions and tactics which suit with our country's actual epidemic. HIV prevention strategies that combine partially effective interventions should be scaled up and evaluated.

Combination HIV prevention is likely to be most effective when different points in the “transmission cycle” are impeded; combining strategies to reduces infectiousness of HIV-positive persons with strategies that reduce HIV susceptibility in the uninfected person. Most early HIV prevention policies focused heavily on HIV- negative, at-risk persons (e.g. using behavior change communication campaigns). However, sero-negative persons represent a very large pool to target for high coverage. Strategies to reduce the infectiousness of HIV positive individuals by reducing secondary HIV transmission should be part of the prevention policy. Theoretically, if high proportions of people living with HIV (PLHIV) learned their HIV sero-status and adopt interventions such as ART coupled with behavioral risk reduction, this could have a significant impact on HIV transmission.

Core programmatic components

Combination approach to prevent HIV includes three types of mutually reinforcing interventions:

1. **Biomedical interventions** are those that directly influence the biological system through which the virus infects a new host, such as **male and female condoms and voluntary medical male circumcision**. Male condoms reduce heterosexual transmission by at least 80%, if used consistently and correctly. Voluntary medical male circumcision reduces acquisition of infection and the risk of acquisition for men by up to 66% and offers a significant lifelong protection.
2. **Behavioral interventions** include a range of sexual behavior change communication programs that use various communication channels (e.g. mass media, community level and inter personal) to disseminate behavioral messages designed to encourage people to reduce behaviors that increase risk of transmission.
3. **Structural interventions** address the critical social, legal, political, and environmental enablers that contribute to the spread of HIV including legal and policy reform, measures to reduce

stigma and discrimination, the promotion of gender equality and prevention of gender-based violence, economic empowerment, access to schooling and supportive interventions designed to enhance referrals, adherence, retention and community mobilization.

Recommendations

Behavioral interventions

- Peer education
- Outreach activities
- Condom distribution
- Risk reduction counseling
- Life skills training
- BCC materials distribution
- Promotion of health care seeking behaviors through existing services
- Strengthen community-based HIV prevention interventions to address the general population through
 - Scale-up of quality community conversation (CC) and integrate with existing community structures.
 - Develop and disseminate HIV prevention messages using print and electronic media.
- Strengthen workplace HIV prevention interventions.
 - Strengthen workplace HIV mainstreaming.
- Strengthen school-based HIV prevention interventions.
 - Conduct peer education programs in schools, higher education institutes and Technical, Vocational Education and Training (TVET).
 - Conduct life-skill education in schools, higher education institutes and TVET.
 - Conduct school-based CC in high schools, higher education institutes and TVET.
 - Integrate HIV/AIDS into school curriculum.
 - Train teachers on management of school HIV/AIDS programs.
 - Develop and disseminate targeted BCC message in schools, higher education institutes and TVET.
 - Strengthen youth leadership development programs.
 - Develop an HIV intervention strategy for school and higher education.

- Strengthen anti-AIDS clubs in schools, higher education institutes and TVETs.
- Ensure active participation/ membership of students in anti-AIDS clubs of schools in higher education institutes and TVET.
- Scale-up comprehensive prevention interventions addressing key populations.
- Strengthen out-of-school youth HIV prevention programs.
- Intensify HIV prevention in development schemes including new business opportunity locations.
 - Target business opportunity locations, industries and private development schemes.
 - Integrate HIV prevention in the project proposals of development schemes.
 - Develop and disseminate targeted HIV/AIDS messages.
 - Conduct peer education.
 - Referral and linkages with health facilities for VCT, STI and ART services.
 - Ensure HIV prevention among development schemes/projects areas communities.
- Scale-up HIV prevention among population groups with special needs.
 - Integrate BCC interventions in youth centers for people with disability.
 - Develop and disseminate BCC materials for people with special needs.

Biomedical interventions

- Ensure access and enhance uptake of HIV testing and counseling services to eligible patients.
- Ensure access and enhance uptake of PMTCT services.
 - Strengthen the integration of PMTCT with maternal, neonatal and children health (MNCH) in all health facilities.
 - Mobilize the community to be actively involved in PMTCT.
 - Promote PITC for all pregnant women attending antenatal/Postnatal clinic (ANC/PNC) and delivery services.
 - Ensure male involvement in PMTCT service.
 - Promote PMTCT by the health development armies.
 - Provide education to households on PMTCT by health development armies.
 - Expand PMTCT services to people with disability.
 - Provide PMTCT training for service providers.
 - Involve private health facilities to provide PMTCT services.
- Increase availability and utilization of STI services. STI services need to be revitalized in all health facilities through implementation of syndromic case management.

- Create strong leadership for STI programs.
- Expand STI services to all health facilities.
- Intensify health education to improve treatment seeking behavior and utilization of STI services.
- Promote and implement active STI partner notification system to identify and link those in the sexual network to STI management and HTS.
- Ensure availability of drugs and reagents in all public health facilities.
- Train health care workers on syndromic STI case diagnosis and management.
- Provide STI training for service providers to provide user-friendly services to people with disability.
- User Friendly health services for adolescents.
- Increase supply, distribution and utilization of male and female condoms.
 - Ensure adequate supplies of condoms.
 - Conduct targeted condom distribution, particularly for KEY POPULATIONS.
- Ensure infection prevention and safe blood supplies in health system.
- Avail PEP treatment.
- Accelerate voluntary medical male circumcision in areas needed.
- Intensifying positive prevention

Structural interventions

- Community mobilization and awareness through health development army.
- Access to health services.
- Address socio-cultural factors.
 - Address harmful traditional practices that fuel HIV/AIDS.
- Address stigma and discrimination.
- Reduce economic vulnerability.
 - Provide income generating activity (IGA) support to vulnerable women.
- Legal and policy environment (legal support system and partnership).
- Promote gender equality and prevention of gender-based violence including sexual violence.
- Supportive interventions designed to enhance referrals, adherence, retention and community mobilization.
- Mainstream HIV/AIDS prevention activities in to workplace.

2.8 Care of HIV Exposed Infants (HEI)

Introduction

Infants born to HIV positive pregnant women by definition are HIV exposed and these infants can be infected with HIV during pregnancy, labor or after birth through breast feeding. All HEI (infected and non-infected) will test antibody positive during the first few months of life. While the child with HIV infection can often be identified during the first months of life, HIV infection often cannot be excluded until after 1 year of age particularly in breast feeding babies.

Pediatric HIV disease can progress very rapidly and may require treatment before a positive diagnosis can be confirmed. HIV infected infants are susceptible to many opportunistic infections including pneumocystis pneumonia (PCP), TB and other bacterial infections that are associated with high rates of mortality. In the provision of care for these children, we use the national HIV exposed follow-up card.

Components of clinical care for the HEI

1. History
2. Physical examination
3. Growth assessment
 - Growth is the most sensitive clinical indicator of HIV infection in infants and young children.
 - Children with HIV infection are at high risk for poor growth.
 - Growth should be monitored closely for all HIV exposed and infected infants.
4. Developmental assessment: Use developmental check list to assess growth & development.
5. Infant feeding: Nutrition and feeding history should be assessed regularly.
6. Immunization: All HEI should be immunized according to expanded program on immunization (EPI) recommendations.

Table 2.6.2: Immunization schedule for HIV exposed infants

Immunization schedule for infants and children recommended by the WHO Expanded Program on Immunization					
Vaccine	Age				
	Birth	6 weeks	10 weeks	14 weeks	9 months
BCG	X				
Oral Polio	X	X	X	X	
DPT-HepB-Hib		X	X	X	
Pneumococcal vaccine (PCV)		X	X	X	
Rota		X	X		
Measles					X
Infants with symptomatic HIV should not receive BCG vaccine.					

7. ARV infant prophylaxis

- For infants born to HIV infected mothers and on breastfeeding
 - Initiate ART for the mother.
 - Infants of mothers who are receiving ART and are breastfeeding should receive 6 weeks of infant prophylaxis with daily NVP. If the infant is considered at high risk, provide enhanced AZT+NVP for the first 6 weeks followed by NVP alone for additional 6 weeks. If AZT is not available, provide extended NVP alone for 12 weeks. Refer Table 3.3.
 - Collect specimen for DNA PCR testing at 6 weeks of age.
- For infants born to HIV infected mothers but not breast feeding:
 - Initiate ART for the mother.
 - If the infant is brought within 72 hours of birth provide NVP prophylaxis for 6 weeks; otherwise there is no need to provide NVP syrup for the infant.
 - If the infant is considered at high risk, provide enhanced AZT+NVP for 6 weeks. Refer Table 2.8.2.
 - Collect specimen for DNA PCR testing at 6 weeks of age. Refer algorithm for testing of HEI less than 18 months (Fig. 2.3).
- High-risk infants are defined as those infants:
 - Born to women with established HIV infection who have received less than four weeks of ART at the time of delivery; OR
 - Born to women with established HIV infection with viral load >1000 copies/mL in the four weeks before delivery, if viral load measurement available; OR

- Born to women with incident HIV infection during pregnancy or breastfeeding (incident HIV infection is new HIV diagnosis in pregnancy or breastfeeding woman with a prior negative HIV test during pregnancy); OR
- Identified for the first time during the postpartum period, with or without a negative HIV test prenatally.

Table 2.6.2.: Dosage of AZT and NVP syrup for infant prophylaxis for different age groups.

Infant age	NVP daily dosing (10mg/ml)		AZT daily dose (10mg/ml)	
	Dose in mg	Dose in ml	Dose in mg	Dose in ml
<u>Birth to 6 weeks:</u>				
Birth weight <2000g	2mg/kg, once daily	0.2ml/kg, once daily	4mg/kg per dose, twice daily	0.4ml/kg per dose, twice daily
Birth weight 2000-2499 g	10mg, once daily	1 ml, once daily	10mg, twice daily	1ml, twice daily
Birth weight $\geq$ 2500 g	15mg, once daily	1.5 ml, once daily	15 mg twice daily	1.5ml twice daily
> 6 weeks to 12 weeks				
	20mg, once daily	2 ml, once daily or half a 50 mg tablet, once daily	No dose established for prophylaxis for this age group.	

Note:

- AZT and NVP concentration is 50mg/5ml.
- Follow the manufacturer's instruction for the duration of use following opening. The bottle should be labeled with the date on which it was 1st opened.
- Infant dosing: The oral syringe should not be placed directly into the bottle. Infant dose should be measured by pouring a small amount of NVP syrup into a cup, and then draw the actual dose with oral syringe. Discard the leftover suspension in the cup.

8. Co-trimoxazole preventive therapy (CPT)

Using pediatric co-trimoxazole in ALL HIV EXPOSED INFANTS significantly reduces the rate of PCP and other bacterial infections and in turn reduces infant morbidity and mortality rates. Start co-trimoxazole to all HEI from 6 weeks of age and continue until the child is confirmed not to have HIV infection using antibody test after 18 months of age.

9. TB risk assessment

At each visit the infant should be evaluated for Tuberculosis. We need to ask for household exposure with an adult who has tuberculosis and symptoms suggestive of the disease and chest radiograph if clinically indicated.

10. Determination and evaluation of infection status

One of the goals of follow-up of HEI is to identify and treat the HIV infected ones early. All HEI should have virologic testing at 6 weeks of age or at earliest opportunity thereafter.

11. Current assessment and plan

At each visit based on the findings on history, physical examination (that includes growth and development assessment) and/or laboratory investigations, we need to have the assessment of the infant and we should plan our next steps in their management and follow-up.

Follow-up visits and schedule

Follow-up of HEI is recommended to be done monthly for the first six months of life then every 3 months until infection status is determined. See table below for details of follow-up schedule and the care components that should be evaluated at each visit.

Table 2.6.23. Follow-up visit schedule for HIV exposed infants

Age in weeks /months	at birth	6 wk	10 wk	14 wk	5 m	6 m	9 m	12 m	15 m	18 m
History	x	x	x	x	x	x	X	x	X	x
Physical exam	x	x	x	x	x	x	X	x	X	x
Growth	x	x	x	x	x	x	X	x	X	x
Developmental assessment	x	x	x	x	x	x	X	x	X	x
Infant feeding counseling	x	x	x	x	x	x	X	x	X	x
Determination of HIV status		DNA PCR	Do DNA PCR if the test is not done at 6 weeks* Repeat DNA PCR if infant is sick or the first DNA PCR test is positive.					Perform rapid antibody test at least 6 weeks after cessation of breastfeeding.		
CPT		x	Continue until HIV is excluded and infant is no longer at risk from breastfeeding.							
TB Risk Assessment	At each visit									
Immunizations	x	x	x	x			x			
Adherence counseling	x	x	x	x	x	x	x	x	X	x
Note: This is the minimum; children should be seen more frequently if clinically indicated. * If the infant is between 9-12 months, first do antibody test and if positive do DBS for DNA.										

CHAPTER THREE: CARE AND TREATMENT OF PEOPLE LIVING WITH HIV INFECTION

It is critical for people living with HIV to initiate ART as early as possible. This enables to shorten the time between HIV diagnosis and ART initiation hence significantly reducing HIV related morbidity and mortality, and reducing forward transmission of HIV including MTCT. The chapter will discuss the general packages of care, when, what ARV regimen, monitoring of treatment response and diagnosis and management of failure cases for first line as well as second line regimens.

3.1. General care packages for PLHIV

As all PLHIV are eligible for ART, enrolment in care provides an opportunity for close clinical and laboratory monitoring, early assessment and timely management of opportunistic infections and other comorbidities. Many care interventions are relevant across the full continuum of care, including HIV-exposed individuals and people living with HIV before initiation and during ART. The following critical interventions need to be addressed at initial encounter:

- Confirm HIV status by retesting and enrolling into HIV care (including recording into pre-ART register).
- Ensure any OI and other clinical problems that may delay ART initiation are ruled out or addressed.
- Ensure that adherence barriers are assessed and addressed accordingly.
- Ensure client is committed and ready for early initiation.

Note: All confirmed HIV positive patients should be enrolled on the pre-ART register initially until they start ART and transferred to ART register as soon as they start the ART.

Package of care for PLHIV with advanced disease

Around 1 in 3 people living with HIV present to care with advanced HIV disease; this proportion is higher in low- and middle-income settings. Additionally, a growing number of PLHIV are returning to care with advanced disease following a period of treatment interruption.

People with advanced HIV disease are at high risk of death, even after starting ART, with this risk increasing with decreasing CD4 cell count. The most common causes of death are TB, severe bacterial infections and cryptococcal meningitis.

Definition of advanced HIV disease

For adults and adolescents, and children older than five years, advanced HIV disease is defined as CD4 cell count $<200\text{cells/mm}^3$ or WHO stage 3 or 4 event. All children younger than five years old with HIV are considered as having advanced HIV disease.

A package of interventions including screening, treatment and/or prophylaxis for major opportunistic infections, rapid ART initiation and intensified adherence support interventions should be offered to everyone presenting with advanced HIV disease including those who are re-engaging with care after a period of interruption. Baseline CD4 cell count testing for all people living with HIV remains clinically important in order to identify those who have advanced HIV disease and who should be offered the package of care as presented in table 3.1.

Table 3.1: Components of packages of care for people with advanced HIV disease.

Areas for the package	Intervention	CD4 cell count	Adults & adolescents	Children
Screening & diagnosis	Sputum Xpert® MTB/ RIF as the first test for TB diagnosis among symptomatic PLHIV	Any	Yes	Yes
	Cryptococcal antigen screening	$\leq 100\text{ cells/mm}^3$	Yes	No
Prophylaxis and pre-emptive treatment	Co-trimoxazole prophylaxis	$\leq 350\text{ cells/mm}^3$ or clinical stage 3 or 4	Yes	Yes For criteria, see chapter 4
	TB preventive treatment ^a	Any	Yes	Yes
	Fluconazole pre-emptive therapy for cryptococcal antigen– positive people without evidence of meningitis	$<100\text{ cells/mm}^3$	Yes	Not applicable (screening not advised)
ART initiation	Rapid ART initiation (as recommended in Chapter 3)	Any	Yes	Yes
	Defer initiation if clinical symptoms suggest TB or cryptococcal meningitis (see Chapter 3)	Any	Yes	Yes
Adapted adherence support	Tailored counselling to ensure optimal adherence to the advanced disease package, including home visits if feasible	$<200\text{ cells/mm}^3$	Yes	Yes

^a For children younger than 12 months, only those with a history of TB contact should receive TB preventive treatment if the evaluation shows no TB disease.

Key elements of chronic HIV care are:

1. Complete clinical assessment (history taking, complete physical examination and relevant lab tests).
2. WHO clinical staging.
3. Prevention, screening and management of opportunistic infections and co-morbidities (see chapter 4).
4. Support for disclosure and assisted partner notification.
5. Risk reduction counseling and combination HIV prevention approaches.
6. Screening for and managing of mental health problems and substance use.
7. Adherence and psychosocial counseling and support.
8. Nutritional assessment and counseling.
9. Screening for other STI.
10. Prevention and screening of cervical cancer.
11. Management of pain and symptoms.
12. Pregnancy status, family planning and contraception.

Screening and management of opportunistic infections is the most critical care that needs to be addressed on the first encounter with a patient before initiation of ART.

3.2. Preparing People Living with HIV for ART

Before initiating people on ART, conduct a detailed discussion with them about their willingness and assess their readiness to initiate ART, the ARV regimen, dosage and schedule, the likely benefits and possible adverse effects, and the required follow-up and monitoring visits. For children with HIV, this conversation should directly involve the parent/legal guardian and include discussion about disclosing their HIV status. Initiation of ART in children should consider nutritional status, any co-morbidities and potentially interacting medications for possible contraindications or dose adjustment.

After going through detailed discussion, assess the readiness and offer to initiate ART. Most clients will be ready at most on the second session. Check the following issues to assess readiness of the clients:

- Patient understands the benefits of ART, adherence and need for lifelong commitment and appointment schedules.
- Patient understands possible side effects of ARVs.
- Patient has accepted the importance of disclosure and family support.
- Patient demonstrated good adherence to other medications and appointments if applicable.

If clients or care taker defer initiating ART as early as possible, address the following issues in the subsequent visits:

- Identify and address barriers for starting ART.
- Consequences of delaying initiation.
- The implication of treatment for transmission, person's own health etc.
- ARV regimens and schedule of follow-up.
- Disclosure to partners/family.
- Family testing.
- Treatment planning.
- Importance and engaging in peer support.

NB: Clients who deferred initiation need to be seen repeatedly for continued counseling and support to initiate ART.

If there is mental health problem, substance use or other problems that are major barriers to adherence/initiation, appropriate support should be provided, and readiness to initiate ART should be reassessed at regular intervals. Utilize a range of patient information materials as well as community and peer support to help the person's readiness and decision to start therapy.

People starting treatment and care givers should understand that the first ART regimen offers the best opportunity for effective virological suppression and immune recovery, and that successful ART requires them to take the medications exactly as prescribed. They should be advised that many adverse effects are temporary or may be treated, or that substitutions can often be made for

problematic ARV drugs. People receiving ART and care givers should also be asked regularly about any other medications that are taken, including herbal remedies and nutritional supplements.

People receiving ART should understand that; while the ARV drugs reduce the risk of HIV transmission, they cannot be relied on to prevent other people from acquiring infection. They should be given advice on safer sex (including condom use) and avoidance of other high-risk activities, such as sharing of injecting equipment, to prevent transmitting HIV to other people.

In conclusion the following principles should be considered:

- Treatment should be started based on a person's informed decision to initiate ART.
- Interventions to remove barriers to ART initiation once an individual is diagnosed with HIV should be implemented.
- HIV programs should promote treatment literacy among all PLHIV, including information on the benefits of early treatment, the lifelong commitment required, the risks of delaying treatment and available adherence support.
- Care providers should support shared decision-making.

Efforts should be made to reduce the time between HIV diagnosis and ART initiation based on clinical conditions and an assessment of a person's readiness.

3.3. When to Start ART

All HIV positives are eligible for ART. The ideal time for ART initiation depends on the clinical condition and readiness of the client. Understanding of clients about HIV and the importance of life long treatment adherence need to be emphasized. All adherence barriers should be exhaustively assessed and addressed before considering ART initiation. For those HIV positive clients, who understand the importance and benefits of life long adherence and are ready for early initiation, start ART as early as possible including same day.

Rapid ART initiation is defined as initiation of ART within seven days of HIV diagnosis, provided that there are no contraindications. Rapid ART initiation should be offered to all people living with HIV following a confirmed HIV diagnosis, clinical assessment and assessment of client readiness. ART initiation should be offered on the same day for people who are ready to start. The offer of rapid ART initiation, including same-day (initiating ART on the date of confirmed HIV

diagnosis), increases the number of people starting ART, reduces mortality, and may further reduce both mother-to-child transmission and transmission to HIV-negative partners. This recommendation applies to all PLHIV at all age groups and is particularly important in people with very low CD4 cell counts who have an increased risk of death.

History and clinical examination to evaluate for opportunistic infections shall be carried out before rapid ART initiation. People with advanced HIV disease should be given priority for assessment and initiation.

3.3.1 When to Start ART in Adults and Adolescents

Early treatment initiation is associated with clinical and HIV prevention benefits, improving survival and reducing the incidence of HIV infection at the family and community level. Start ART as early as possible to all adults and adolescents with a confirmed HIV diagnosis who are ready and willing regardless of their WHO clinical stages and CD4 counts. As the level of maturity varies, some younger adolescents may need parental consent and support. Prenatally infected adolescents need special consideration and support.

3.3.2 When to Start ART in Pregnant and Breast-feeding Women

Start ART as early as possible to all pregnant and breastfeeding women living with HIV regardless of their WHO clinical stages and CD4 counts. For women identified at labor and delivery, provide ART within the same hour of HIV diagnosis with brief counseling and provide detailed counseling on ARV and adherence after delivery. Consequently, provide ARV prophylaxis for the infant. (Refer to table 3.3).

3.3.3 When to Start ART in Children

Start ART as early as possible to all children living with HIV regardless of their WHO clinical stages and CD4 counts/percentage. Infants and young children infected with HIV have exceptionally higher morbidity and mortality. Up to 52% and 75% of children die before the age of two and five years respectively in the absence of any intervention.

For HIV infected infants diagnosed with the first DNA PCR result, initiate ART and take DBS specimen for confirmatory DNA PCR. Continue ART if the second DNA PCR confirms; whereas

if the second DNA PCR turns negative, without holding the ART, make the 3rd DNA PCR test. (Refer the algorithm, Fig. 2.3).

For HIV infected infants and younger children, who need particular care and support from parents and care givers, ensure the readiness and understanding of their parents and care givers. HIV infected infants shall be started on ART and counseling on dosage and administration will be provided for parents.

3.3.4 When to start ART in adults, adolescents and children with TB

Start ART in all TB patients living with HIV as soon as possible within 8 weeks following initiation of anti-TB treatment regardless of their CD4 count. TB patients with profound immune suppression (e.g., CD4 < 50 cells/ml) should receive ART within the first 2 week of initiation of TB treatment. Initiating ART within 2 weeks in profoundly immune-compromised patients after initiation of anti-TB treatment significantly reduces mortality. Start CPT for TB/HIV co-infected patients. (Refer TB section under chapter 4). For patients taking DTG while they are on TB treatment, the dose of DTG need to be 50mg BID.

3.3.5 When to start ART in adults, adolescents and children with drug resistant TB

Antiretroviral therapy is recommended for all patients with HIV and drug- resistant TB (both MDR/XDR-TB) requiring second-line anti-tuberculosis treatment, irrespective of CD4 cell count, as early as possible (within the first eight weeks) following initiation of anti-tuberculosis treatment.

Unrecognized drug-resistant TB (DR-TB) is associated with very high mortality in people with HIV, hence, Xpert MTB/RIF is recommended as the initial diagnostic test in all PLHIV with presumptive TB. Patients with both HIV and DR-TB face complicated clinical management, fewer treatment options and poorer treatment outcomes. The complexity of ARV regimens and second-line TB treatment, each with its own toxicity profiles and some of which may be potentiated by concomitant therapy, demands rigorous clinical monitoring, and early recognition and management of adverse drug reactions. PLHIV with DR-TB should receive both second-line anti-TB and ART in DR-TB treatment initiating centers (TIC), and close collaboration between health facility MDR-TB TIC and HIV care clinic is strongly recommended for early initiation of ART and optimal management of these patients. It is also advisable to minimize the contact of MDR- TB and HIV co-infected patients with other PLHIV in the ART clinic through initiating

and refilling the ART in the MDR-TB clinic. (Refer the TB section under chapter 4 of this guideline).

3.3.6 When to start ART in HIV/HBV co-infected adults

Start ART in all HIV/HBV co-infected patients regardless of their CD4 count. The preferred regime for first line ART (TDF+3TC+EFV) is already the treatment for HBV. If TDF is contraindicated for first line regimen refer the client to specialist for consultation.

ART should be initiated for all individuals (children, adolescents and adults) living with HIV immediately after confirming HIV diagnosis, regardless of WHO clinical stage and CD4 cell count.

3.4 What ART regimen to start with (first-line ART)

Using simplified, less toxic, more effective and convenient regimens as fixed-dose combination is recommended for first-line ART. The preferred first-line regimen for adults and adolescents is TDF+3TC+DTG or TDF+3TC+EFV as a once-daily dose. Upon availability of the FDC DTG containing regimen, it will be the preferred first line regimen for adult and adolescent HIV patients. In case of TB-HIV coinfections in adults and adolescents, the dose of DTG should be 50mg BID. (Refer Table 3.2).

For pregnant and breast feeding mothers, the preferred first-line regimen is TDF+3TC+EFV as once daily dose. Although there is no clear pattern of abnormalities emerged with DTG during pregnancy, more data are needed on maternal safety and tolerability and adverse outcomes to the fetus exposed in utero and on the safety of infants exposed during breastfeeding. (Refer Table 3.2).

For children younger than three years a protease inhibitor (PI)-based regimen is the preferred approach. (Refer Table 3.2).

Table 3.2: Summary of first-line ART regimens for adults, pregnant & breastfeeding women, adolescents and children.

Population	Preferred first-line regimens	Alternative first-line regimens ^a
Adults (including those with TB/ HIV ^b -coinfection.)	TDF + 3TC + DTG (FDC)* OR TDF + 3TC + EFV (FDC)**	AZT + 3TC + EFV AZT + 3TC + NVP TDF + 3TC + NVP
Pregnant and breastfeeding women	TDF + 3TC + EFV (FDC)	AZT + 3TC + EFV AZT + 3TC + NVP TDF + 3TC + NVP
Adolescents (10 to 19 years) weight ≥30 kg (Including those with TB/HIV ^b -coinfection.)	TDF + 3TC + DTG (FDC)* OR TDF + 3TC + EFV (FDC)**	AZT + 3TC + EFV AZT + 3TC + NVP TDF + 3TC + NVP ABC + 3TC + EFV
Children 3 years to less than 10 years and adolescents weight <30 kg	AZT or ABC + 3TC + EFV	AZT + 3TC + NVP TDF + 3TC + EFV TDF + 3TC + NVP ABC + 3TC + NVP***
Children <3 years	ABC or AZT + 3TC + LPV/r	ABC + 3TC + NVP AZT + 3TC + NVP

^a ABC or boosted PIs (ATV/r, LPV/r) can be used in special circumstances.

^b In case of TB-HIV coinfection, the dose of DTG should be 50mg BID.

*If available as triple FDC, TDF+3TC+DTG is the preferred regimen for HIV positive adult and adolescent patients.

**TDF+3TC+EFV₄₀₀ (FDC) will replace the TDF+3TC+EFV₆₀₀ (FDC) for adults and adolescents (except for pregnant mothers and TB/HIV co-infected patients as there is no adequate data for this groups) up on availability.

*** Caution: co-administration of ABC with NVP in pediatric patients will increase the risk of hypersensitivity reaction and requires extreme precaution.

3.4.1 First-line ART for adults and adolescents

The preferred first-line regimen for adults and adolescents is TDF+3TC+DTG or TDF+3TC+EFV as a once-daily dose. When available, use TDF+3TC+DTG as the preferred first-line regimen for HIV positive adults and adolescents. In patients with depression, suicidal ideation and previous history of acute psychosis, use TDF+3TC+DTG or other alternative regimens to avoid EFV. In older patients with long-term diabetes, uncontrolled hypertension or renal failure, select appropriate drug from the alternative regimens.

3.4.2 First-line ART for pregnant and breastfeeding women and ARV prophylaxis for their infants

A once-daily fixed-dose combination of TDF + 3TC + EFV is recommended as first-line ART in pregnant and breastfeeding women, including pregnant women in the first trimester of pregnancy and women of child bearing age.

The infant prophylaxis duration bases on the total duration of maternal ART usage. For infants born to HIV infected women who took ART for more than 4 weeks at time of delivery, give NVP prophylaxis for 6 weeks. For infants born to mothers covered with ART for less than 4 weeks or those who are diagnosed at birth or postpartum and breast feeding, give NVP+AZT prophylaxis for the first 6 weeks and continue NVP prophylaxis for additional 6 weeks or extended NVP prophylaxis for 12 weeks starting at birth. If not breast feeding or formula fed, provide 6 weeks prophylaxis based on the level of risk of the infant to acquire HIV. Infant prophylaxis should begin within 1 hour at birth or when HIV exposure is recognized postpartum.

Table 3.3 Summary of maternal and infant ARV prophylaxis for different clinical scenarios

Scenario	Maternal ARV ^a	Infant ARV Prophylaxis ^b	Duration of infant ARV prophylaxis
Mother diagnosed with HIV during pregnancy	Initiate maternal ART	NVP Or AZT+NVP based on risk	NVP for 6 weeks. If mother took ART for <4 weeks, NVP+AZT for the first 6 weeks and continue NVP for additional 6 weeks OR extended NVP alone for 12 weeks.
Mother diagnosed with HIV during labor or immediately postpartum and plans to breastfeed	Initiate maternal ART	NVP+AZT OR NVP	NVP+AZT for the first 6 weeks and continue NVP for additional 6 weeks OR extended NVP alone for 12 weeks.
Mother diagnosed with HIV during labour or immediately postpartum and plans replacement feeding	Initiate maternal ART	NVP+AZT OR NVP	NVP+AZT for the first 6 weeks OR NVP alone for 6 weeks.
Infant identified as HIV exposed after birth (through infant or maternal HIV antibody testing) and is on breastfeeding	Initiate maternal ART	NVP+AZT OR NVP	NVP+AZT for the first 6 weeks and continue NVP for additional 6 weeks or extended NVP alone for 12 weeks. plus take DBS specimen for DNA PCR for EID same day if infant older than 4weeks

Infant identified as HIV exposed after birth (through infant or maternal HIV antibody testing) within 72 hours and is not breastfeeding	Initiate maternal ART	NVP+AZT OR NVP	NVP+AZT for the first 6 weeks OR NVP alone for 6 weeks.
Infant identified as HIV exposed after birth (through infant or maternal HIV antibody testing) after 72 hours and is not breastfeeding	Initiate maternal ART	No ARV prophylaxis	Take DBS, do DNA PCR test, initiate treatment if the infant is infected
Mother receiving ART but interrupts ART regimen while breastfeeding (such as toxicity, stock-outs or refusal to continue)	Determine an alternative ART regimen; counsel regarding continuing ART without interruption	NVP	Until 6 weeks after maternal ART is restarted or until 1-week after breastfeeding has ended

- a. If there is documented maternal viral suppression near delivery for a mother receiving ART and using replacement feeding, four weeks of infant ARV prophylaxis may be considered.
- b. If infant AZT or NVP cause toxicity or not available, 3TC can be substituted.

3.4.3 First-line ART for children

Pediatric ARV formulations should be easy to administer for children at different age groups. There are optimal pediatric ARV formulations including FDCs, dispersible tablets, scored tablets, pellets, etc. These formulations are appropriate for various age and weight bands (see dose in the annex). Dosage of ARV for children should be progressively changing as the weight of the children increase.

3.4.4 First line ART for infants and children younger than 3 years

Optimizing first-line ART in children younger than three years is critical to achieve effective and rapid control of viral replication in the context of high viral load and rapid infant growth. Considerations that may require alternative therapeutic approaches include the limited availability of drugs in appropriate formulations, the long-term toxicities of ARV drugs, difficulty with

adherence and the possibility of pre-existing viral resistance because of ARV drug exposure for PMTCT.

For infants and children infected with HIV younger than three years, the NRTI backbone for an ART regimen should be ABC or AZT + 3TC. A boosted PI (LPV/r) based regimen should be used as first-line ART for all children infected with HIV younger than three years (36 months) of age, regardless of NNRTI exposure. If LPV/r is not feasible, treatment should be initiated with a NVP-based regimen. For HIV infected infants and children younger than three years, ABC+3TC+AZT is recommended as an option for children who develop TB while on an ART regimen containing NVP or LPV/r. Once TB therapy has been completed, this regimen should be stopped and the initial regimen should be restarted. (Refer table 3.4).

3.4.5 First line ART for Children 3 years and older (including adolescents < 35 kg)

For children, infected with HIV three years and older (including adolescents), EFV is the preferred NNRTI for first-line treatment and NVP is the alternative. For children infected with HIV three years to less than 10 years old (or adolescents less than 35 kg), the NRTI backbone for an ART regimen should be one of the following, in preferential order ABC+3TC or AZT+3TC or TDF+3TC and for adolescents infected with HIV (10 to 19 years old) weighing 35 kg or more, the NRTI backbone for an ART regimen should align with that of adults and be one of the following, in preferential order TDF+3TC or AZT+3TC or ABC+3TC. At or above 35 kg, the dose of TDF in the adult dual and triple fixed-dose combinations and the dose of EFV in adult triple fixed-dose combinations are acceptable for use in adolescents. (Refer table 3.2).

3.4.6 First-line ART for TB co-treatment in children with HIV

TB is one of the most common opportunistic infections affecting children with HIV. Selecting regimens that are compatible with TB therapy is therefore essential. Interactions between rifampicin and LPV/r or NVP mean that co-treatment in children under three years is challenging, but recent evidences in children has generated preliminary evidence on the efficacy of triple nucleoside therapy which, despite limited data in the context of TB co-treatment, offers a suitable option for children who require TB treatment while already receiving ART. For children diagnosed with TB/HIV co-infection, ART should be started as soon as TB treatment is tolerated within 8 weeks of initiating anti-TB. (Refer table 3.4).

Table 3.4: Summary of recommended ART regimens for children and adolescents (<35kg) who need TB treatment.

Recommended regimens for children and adolescents (<35kg) initiating ART while on TB treatment ^{a b}		
Younger than 3 years		Two NRTIs + NVP or Triple NRTI (AZT+3TC+ABC) ^c
Three years and older		Two NRTIs + EFV or Triple NRTI (AZT+3TC+ABC) ^c
Recommended regimen for children and infants initiating TB treatment while receiving ART		
Child on standard NNRTI-based regimen (two NRTIs + EFV or NVP)	Younger than 3 years	Continue NVP or Triple NRTI (AZT + 3TC + ABC) ^c
	3 years and older	If the child is receiving EFV, continue the same regimen. If the child is receiving NVP, substitute with EFV or Triple NRTI (AZT + 3TC + ABC) ^c
Child on standard PI based regimen (two NRTIs + LPV/r)	Younger than 3 years	Triple NRTI (AZT + 3TC + ABC) ^c or substitute NVP for LPV/r
	3 years and older	If the child has no history of failure of an NNRTI-based regimen: Substitute with EFV ^d or Triple NRTI (AZT + 3TC + ABC) ^c or if the child has a history of failure of an NNRTI-based regimen: Triple NRTI (AZT + 3TC + ABC) ^c Consider consultation with experts for constructing a second-line regimen.

a. Ensure optimal dosing of rifampicin based on new dosing guidelines.

b. Substitute ARV drugs based on an age-appropriate ART regimen in line with nationally recommended first-line ART.

c. Triple NRTI is only recommended for the duration of TB treatment; an age-appropriate PI or NNRTI-based regimen should be restarted when rifampicin-based therapy ends. Triple NRTI should also be considered as the preferred regimen for children older than 3 years with a history of failure on a NNRTI-based regimen.

d. Substitution with EFV should be considered as the preferred option, and EFV could be maintained after TB treatment ends to enable simplification and harmonization with the ARV drug regimens used for older children.

3.5 Monitoring response to ART

Monitoring of patients on ART should start from the day of initiation. Although taking ART is a lifelong commitment, the first six months of therapy are especially important.

3.5.1 What to expect in the first months of ART and how to manage them

Clinical and immunological improvement and biological suppression are expected when individuals adhere to ART, but care providers need to be alert as opportunistic infections and/or immune reconstitution inflammatory syndrome (IRIS) may develop, as well as early adverse drug events, such as drug hypersensitivity, in the first three months of ART. ART significantly decreases mortality and HIV related illnesses, however mortality can be higher in the first three to six months of ART initiation among people who started ART with advanced HIV disease with existing co-infections and/or co-morbidities, severely low hemoglobin, low body mass index (severe malnutrition) and/or very low CD4 counts.

In most adults and children, when ART is initiated, immune recovery starts and CD4 cell counts rise. Generally, this increase occurs during the first year of treatment, and then continues to rise further during the second year. However, severe immune-suppression may persist in some individuals who do not experience a significant rise in CD4 cell count with treatment, especially those with a very low CD4 cell count when initiating ART. Hence, failure to achieve CD4 recovery or presence of CD4 decline should alert the health care provider to potential adherence problems or primary non-response to ART, and consideration should be given to continue prophylaxis for OI such as CPT till patients recover immunologically.

Immune reconstitution inflammatory syndrome

IRIS is a spectrum of clinical signs and symptoms thought to be associated with immune recovery brought about by a response to ART. It occurs among 10–30% of the people initiating ART, usually within the first 4–8 weeks after initiating therapy. It may present in two different ways: **paradoxical IRIS**, when an opportunistic infection or tumor diagnosed before ART initially responds to treatment but then deteriorates after ART starts; or **unmasking IRIS**, in which initiating ART triggers disease that is not clinically apparent before ART. It should be considered

only when the presentation cannot be explained by a new infection, expected course of a known infection or drug toxicity.

The clinical spectrum is diverse, and IRIS has been reported for many different infections, tumors and non-infectious conditions. The most serious and life-threatening forms of paradoxical IRIS are for TB, Cryptococcus's, Kaposi's sarcoma and hepatitis. BCG vaccine-associated IRIS (localized and systemic) may occur in some HIV infected infants. IRIS is generally self-limiting, and interruption of ART is rarely indicated, but people may need to be reassured in the face of protracted symptoms to prevent discontinuation of or poor adherence to ART.

Before initiating ARV, providers need to give due consideration for patients with low CD4 cell count (<50 cells/mm³) at ART initiation, disseminated opportunistic infections or tumors and a shorter duration of therapy for opportunistic infections before ART starts as they are the main risk factors for IRIS.

The most important steps to reduce the development of IRIS include:

- Earlier HIV diagnosis and initiation of ART before a decline to below 200 CD4 cells/mm³;
- Improved screening for opportunistic infections before ART, especially TB and Cryptococcus; and
- Optimal management of opportunistic infections before initiating ART.

Timing of ART in people with opportunistic infections requires balancing a greater risk of IRIS after early initiation against continuing high mortality if ART is delayed.

Most or all of the following features should be present in order to make the diagnosis of IRIS:

- A low pretreatment CD4 count (often less than 100 cells/ μ L) except in tuberculosis. IRIS secondary to preexisting M. tuberculosis infection may occur in individuals with CD4 counts >200;
- A positive immunological response to ART;
- The absence of evidence of drug-resistant infection, bacterial super infection, drug allergy or other adverse drug reactions, patient noncompliance, or reduced drug levels due to drug-

drug interactions or mal-absorption after appropriate evaluation for the clinical presentation;

- The presence of clinical manifestations consistent with an inflammatory condition; and
- A temporal association between highly active antiretroviral therapy (HAART) initiation and the onset of clinical features of illness- usually within the first 6 months.

Management of IRIS

- Patients should generally be treated for the underlying OI as soon as possible.
- Continuation of ART when IRIS occurs.

Role of anti-inflammatory agents:

Anti-inflammatory agents may be particularly helpful in the setting of obstructive mass lesions (e.g. expanding cervical lymph node). Use of anti-inflammatory agents, particularly corticosteroids, must be weighed against potential risks and side effects. When a decision is reached to treat with corticosteroids, initiate therapy with prednisone at a dose of 1 mg/kg/day (maximal dose 60 to 80 mg) followed by a rapid taper over a 10 to 14-day period. IRIS in closed spaces (e.g. CNS OI) should be managed promptly or referred to appropriate center to avert significant morbidity and mortality.

IRIS is not indicative of treatment failure or drug side effect. It is a transient phenomenon and is not a reason to stop ART or change regimen. The OI should be treated using standard guidelines and in critically sick patients short course of corticosteroid might be indicated to control severe symptoms.

NB: Actively watch for IRIS in patients starting with first-line regimens containing integrase-inhibitors such as DTG.

3.5.2 Clinical and laboratory monitoring

Standardized clinical assessment of patients and, when available baseline CD4 count, are important to determine the severity of immunosuppression and decide on initiation of prophylactic therapies. Before initiating antiretroviral therapy, patients shall be thoroughly evaluated at baseline and periodically for the rest of their lives to monitor toxicity, intolerance, poor response or failure to treatment. Before ART initiation patient readiness and thereafter adherence to therapy are always assessed and necessary supports need to be provided. Opportunistic infections including TB, Cryptococci infection and other co-morbidities are always need to be looked for and managed.

Table 3.5: Baseline and follow-up assessment

Baseline assessment, week 0	
Objective: to conduct initial assessment.	
Activities	Intervention
• Check confirmatory HIV test is done and documented. • Clinical assessment: socio-economic status, any HIV related illnesses in the past, symptom screen for TB, other OI, co-morbidities, pregnancy, past and current medication. • Determine WHO staging. • Register: fill intake form, follow up form and pre ART or ART (if applicable) registers. • Counselling and education: adherence, treatment readiness, disclosure, and address adherence barriers. • Lab assessment: ○ baseline CD4¹, ○ CBC, ALT, creatinine (if available). ○ If presumptive TB diagnosis do Gene Xpert. ○ Pregnancy* and other tests as necessary.	• Develop impression on treatment readiness. • Start CPT and IPT if clinically indicated • Treat OI. • Manage co-morbidities/refer if necessary. • Continue ART for transfer-ins. • Start ART for those who are ready and have no adherence barriers; and give appointment to return after two weeks. If not, give appointment to return within one week. • Refer if necessary.
2nd visit, Within 1 week after baseline visit	
Objective: To decide on initiation for those who did not start ART during the first visit.	

¹ ART initiation should not be delayed waiting for the CD4 test result; however do the test to assess the severity of immunosuppression.

• Review clinical and lab data. • Adherence counselling and ensure readiness. • Counseling and education on ART and preventive therapies. • Encourage disclosure and discuss on treatment support.	• Determine ART treatment readiness. • Start CPT (as indicated) and IPT if not started. • Treat OI, Initiate TB treatment if indicated. • Manage any drug toxicity and intolerance. • Decide on regimen and initiate ART if ready. • Provide adherence counselling and patient education • Appointment to return after 2 weeks if ART initiated. • Give appointment for those patients who defer early initiation after 1 week for 3rd session. <i>NB: Continue the same session and counseling until the patient is ready and initiated on ART.</i>
3rd visit: 2 weeks after initiation Objective: To determine toxicity/intolerance, adherence, and IRIS.	
• Clinical assessment for: IRIS, toxicity etc. • Assess and support adherence, addressing adherence barriers. • Provide counseling and education including prevention of HIV transmission. • Lab tests if necessary. • Support disclosure if not done.	• Increase/escalate dose of nevirapine if patient is on NVP containing regimen. • Manage toxicity as indicated. • Provide adherence support and patient education including HIV prevention. • Treat OI if diagnosed. • Give appointment to return in 2 weeks.
4th visit: 4 weeks after initiation Objective: Same as third visit	
• Same as 3rd visit. • Hg if patient is on AZT.	• Refill ART and other medicine as necessary for one month. • Treatment of OI if identified.

Assess and support adherence.	- Manage drug toxicity and intolerance. - Provide adherence support and patient education including HIV prevention. - Refer if necessary. - Appointment to return after 4 weeks.
5th visit 8 weeks after initiation Objective: same as 4th visit	
Same as 4th visit.	- Refill ART and other drugs as necessary for 1 month. - Treatment of OI and co-morbidities. - Manage toxicity and intolerance. - Provide adherence support and patient education including HIV prevention. - Refer if necessary. - Appointment to return after 4 weeks.
6th visit: 12 weeks after initiation Objective: Same as 5th visit.	
Same as 5th visit.	- Refill ART and other drugs as necessary for 1 month. - Treatment of OI and other co-morbidities. - Manage toxicity and intolerance. - Provide adherence support and patient education including HIV prevention. - Refer if necessary. - Appointment to return after 4 weeks.
7th visit: 16 weeks after initiation Objective: Same as 6th visit	
Same as 6th visit.	- Refill ART and other drugs as necessary for 2 months. - Treatment of OI and other co-morbidities. - Manage toxicity and intolerance. - Provide adherence support and patient education including HIV prevention.

	• Refer if necessary. • Appointment to return after 8 weeks.
8th visit: 24 weeks after initiation Objective: Same as 7 th visit	
• Same as 7th visit.	• Provide adherence support and patient education including HIV prevention. • Determine viral load. • Determine CD4 if viral load testing is not available or patient is on CPT. • Refill ART and other drugs as necessary for 3 months. • Treatment of OI and other co-morbidities. • Manage toxicity and intolerance. • Refer if necessary. • Appointment to return after 12 weeks.

Note:

- CD4 testing may be used to determine the need and discontinuation of OI prophylaxis.
 - Newly started patients will be appointed every two weeks during the first month of treatment and every 4weeks (every month) then after until 24 weeks of treatment. After the 24th week of initiation of antiretroviral therapy patients will be scheduled to return every twelve weeks. At each visit antiretroviral drugs and CPT for three months are given, counseling of positive living, safe sexual practice, adherence assessment and support will be done. Lab tests including ALT will be requested when indicated.
 - Patients should be encouraged to come at any time if they have concerns and can be seen out of the above schedule whenever necessary.
 - At every visit conduct screening for TB.
- * When a woman in reproductive age is taking DTG containing regimen, occurrence of pregnancy shall be prevented and monitored. If pregnancy happens while on DTG containing regimen, DTG shall be replaced with EFV.

Table 3.6 Recommended tests for HIV screening and monitoring and approaches to screening for confections and non-communicable diseases

Management	Recommended	Desirable (if feasible)
At HIV diagnosis or at baseline	• HIV testing (serology for adults and children 18 months or older; EID for children younger than 18 months). • Cryptococcus antigen if CD4 cell count ≤ 100 cells/mm³.^b • CD4 cell count. • TB symptom screening. • Screening for STI.	• HBV (HBsAg) serology.^a • HCV serology. • Pregnancy test. • Assessment for major non communicable chronic diseases and comorbidities.
Follow-up for clients who differed ART initiation	• CD4 cell count (every 6 months in circumstances where ART initiation is differed).	
ART initiation		• Hemoglobin test for starting AZT^d • Pregnancy test • Blood pressure measurement • Serum creatinine and estimated glomerular filtration rate (eGFR) for starting TDF^e • Alanine aminotransferase for NVP^f • Baseline CD4 cell count •

Receiving ART	• HIV viral load (at 6 and 12 months after initiating ART and every 12 months thereafter) • Viral load testing for pregnant mothers: ○ Newly diagnosed mother: after 3 months followed by every six months until the MTC risk ends or the routine at 6, 12 month and then every 12 months. ○ For those who are already on ART and their VL test done before 6 months, do the VL soon after pregnancy is known; then continue every six months until the MTC risk ends or routine VL testing should continue accordingly. • CD4 cell count every 6 months if indicated	• Serum creatinine and eGFR for TDF^c • Pregnancy test*, especially for women of child bearing age not receiving family planning.
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^a If feasible, HBsAg testing should be performed at baseline to identify people with HIV and HBV coinfection and who should therefore initiate TDF-containing ART.

^b Can be considered in settings with a high prevalence of *Cryptococci* antigenemia (>3%).

^c Consider assessing for the presence of chronic conditions that can influence ART management, such as hypertension and other cardiovascular diseases, diabetes and TB according to the WHO Package of Essential NCD interventions (PEN), mental health Gap Action Program (mhGAP) or national standard protocols (see section 5.3 “Prevention, screening and management of other comorbidities and chronic care for people living with HIV”). Monitoring may include a range of tests, including serum creatinine and estimated glomerular filtration rate (eGFR), serum phosphate and urine dipsticks for proteinuria and

glycosuria. $eGFR = 140 - \text{age (years)} \times \text{body weight (kg)} / (72 \times \text{serum Cr in mg/dL})$ for male and $eGFR = 140 - \text{age (years)} \times \text{body weight (kg)} \times 0.85 / (72 \times \text{serum Cr in mg/dL})$ for female.

^d Among children and adults with a high risk of adverse events associated with AZT (low CD4 or low BMI).

^e Among people with a high risk of adverse events associated with TDF: underlying renal disease, older age group, low body mass index (BMI), diabetes, hypertension and concomitant use of a boosted PI or potential nephrotoxic drugs.

^f Among people with a high risk of adverse events associated with NVP, such as being ART-naïve, women with HIV with a CD4 count $>250 \text{ cells/mm}^3$ and hepatitis C virus (HCV) coinfection. However, liver enzymes have low predictive value for monitoring NVP toxicity.

* For women in the reproductive age taking DTG based regimen, if pregnancy is detected, the DTG shall be substituted with EFV based regimen.

3.5.3 Monitoring drug toxicities and substitution of ARV

Guiding principles

- Establish whether the clinical condition is due to ARV toxicities, other drugs, or other illness including new OIs.
- Try to identify the responsible ARV drug.
- Assess the severity using toxicity grading matrix (Annex 5)

Major types of ARV toxicities

The major causes of drug discontinuation in the first 3-6 months after initiating ART are due to drug toxicities; and hence, they must be closely monitored. They occur from few weeks to months. The most frequent drug adverse reactions include:

- Toxicities of NNRTIs (NVP and EFV) occurring in the first few weeks, and may be life-threatening.
- ABC hypersensitivity reaction starting from first week following initiation.
- Anemia and neutropenia due to AZT occur in the first 3 months.

The clinical manifestations due to hypersensitivity reactions (ABC and NVP) may be confused with IRIS. Intolerance to certain drugs, in particular AZT induced gastrointestinal problems, are important barriers to adherence unless appropriate measures are taken.

Table 3.7 Types of toxicities associated with first, second and third-line ARV drugs

ARV Drug	Major types of toxicity	Risk factors	Suggested management	Remark
ABC	Hypersensitivity reaction.		Substitute with TDF or AZT for first line, substitute with TDF, for second line.	
ATV/r	Electrocardiographic abnormalities (PR and QRS interval prolongation).	Pre-existing conduction system disease; concomitant use of other drugs that may prolong the PR interval	This phenomenon is clinically benign but potentially stigmatizing. Substitute with LPV/r only if adherence is compromised.	
	Indirect hyperbilirubinaemia (clinical jaundice)	Underlying hepatic disease, HBV and HCV co-infection; Concomitant use of hepatotoxic drugs.	This phenomenon is clinically benign but potentially stigmatizing. Substitute with LPV/r only if adherence compromised.	
	Renal stone	History of renal stone.	Substitute with LPV/r.	
AZT	Anaemia, neutropenia	Baseline anaemia or neutropenia CD4 count ≤ 200 cells/mm ³ .	Substitute with TDF or ABC.	
DRV/r	Hepatotoxicity	Underlying hepatic disease, HBV and HCV coinfection; concomitant use of hepatotoxic drugs.	Substitute with ATV/r or LPV/r. When it is used in third-line ART, limited options are available.	Usual adult dose of DRV/r 600/100

				mg twice daily.
	Severe skin and hypersensitivity reactions.	Sulfonamide allergy.	For hypersensitivity reactions, substitute with another therapeutic class.	
DTG	Hepatotoxicity Hypersensitivity reactions.	Hepatitis B or C coinfection, Liver disease.	If DTG is used in first-line ART, and there are hypersensitivity reactions, substitute with another therapeutic class (EFV or boosted PIs).	Usual adult dose. DTG 50mg once daily. But in case of TB coinfection , the dose should be 50mg BID.
LPV/r	Electrocardiographic abnormalities (PR and QT interval prolongation, torsade's de pointes).	People with pre-existing conduction system disease; concomitant use of other drugs that may prolong the PR interval, Congenital long QT syndrome, Hypokalemia Concomitant use of drugs that may prolong the QT interval	Use with caution in people with pre-existing conduction disease or those on concomitant drugs that may prolong the PR or QRS intervals	
			If LPV/r is used in first-line ART for children, use an age-appropriate NNRTI	

	Hepatotoxicity	Underlying hepatic disease HBV and HCV co-infection Concomitant use of hepatotoxic drug	(NVP for children younger than 3 years and EFV for children 3 years and older). ATV can be used for children older than 6 years If LPV/r is used in second-line ART for adults, use ATV/r. If boosted PIs are contraindicated and the person has failed on treatment with NNRTI in first-line ART use DTG or consult specialist	
	Pancreatitis	Advanced HIV disease		
	severe diarrhea		Substitute with ATV/r	
	Risk of prematurity, Lipoatrophy or metabolic syndrome, dyslipidemia or pancreatitis	Risk factors unknown		
NVP	Hepatotoxicity	Underlying hepatic disease, HBV and HCV Co-infection, Concomitant use of hepatotoxic drugs, Baseline CD4 >250 cells/mm ³ in Women, Baseline CD4 >400 cells/mm ³ for men, First month of therapy (if lead-in dose is not used)	Use EFV, If the person cannot tolerate either NNRTI, use DTG or boosted PI	
	Severe skin rash and	Risk factors unknown	Use DTG or boosted PIs	

	hypersensitivity reaction including Stevens-Johnson syndrome			
EFV	Persistent central nervous system toxicity (such as abnormal dreams, depression or mental confusion) ²	Depression or other mental disorder (previous or at baseline) Daytime dosing	Use NVP. If the person cannot tolerate either NNRTI, use DTG or boosted PI	
	Hepatotoxicity	Underlying hepatic disease – HBV and HCV co-infection Concomitant use of hepatotoxic drug		
	Convulsions	History of seizure		
	Severe skin Hypersensitivity reaction.	Risk factors unknown.	Use DTG or boosted PI	
	Gynecomastia	Risk factor unknown.	Substitute with NVP.	
RAL	Rhabdomyolysis, myopathy, myalgia.	Concomitant use of other drugs that increase the risk of myopathy and rhabdomyolysis, including statins.	Substitute with another therapeutic class like boosted PIs.	
	Hepatitis and hepatic failure, Severe skin rash and	Risk factors unknown.		

² Most CNS side effects will improve within 2-4 weeks after initiation

	hypersensitivity reaction.			
TDF	Chronic kidney disease, acute renal injury, Fanconi syndrome.	Underlying renal disease; older age; BMI <18.5 (or body weight <50 kg); untreated diabetes mellitus; untreated hypertension; concomitant use of nephrotoxic drugs or a boosted PI.	Substitute with AZT or ABC. Do not initiate TDF at eGFR <50 mL/min, uncontrolled hypertension, untreated diabetes, or presence of renal failure.	
	Decreases in bone mineral Density.	History of osteomalacia and pathological fracture; risk factors for osteoporosis or bone loss.		
	Lactic acidosis or severe hepatomegaly with steatosis.	Prolonged exposure to nucleoside analogues; Obesity.		

NB: For those patients with HBV and HIV co-infection suffering from TDF toxicity, consult the national guideline on management of HBV infection-2016.

Monitoring TDF toxicity

It is advisable for high-risk people (those who are older or have underlying renal disease, long-term diabetes or uncontrolled hypertension concomitant use of boosted PIs or nephrotoxic drugs) to detect and limit further progression of renal impairment. A significant uncertainty remains around how best to monitor TDF-related bone toxicity among children, however it is recommended to monitor growth in children taking TDF containing regimen.

Clinical recommendations

- Laboratory monitoring is not mandatory to initiate treatment with TDF.
- Routine blood pressure monitoring may be used to assess for hypertension.
- Urine dipsticks may be used to detect glycosuria or severe TDF nephrotoxicity in individuals without diabetes using TDF-containing regimens.
- If the creatinine test is routinely available, use the estimated glomerular filtration rate at baseline before initiating TDF regimens.
- Do not initiate TDF when the estimated glomerular filtration rate is <50 ml/min, or in long-term diabetes, uncontrolled hypertension and renal failure.
- Monitor growth in children using TDF.

Toxicity monitoring for other ARV drugs

AZT

AZT is associated with a risk of hematological toxicity, and measuring hemoglobin is recommended before initiating ART and monthly at least for the next three months. Avoid use of AZT for people with HIV and severe anemia at baseline (hemoglobin <7.0 g/dl) as first-line therapy.

NVP

The laboratory measurement of liver enzymes has very low predictive value for NVP-containing regimens. However, monitoring hepatic enzymes is recommended, especially for women with HIV who have CD4 cell counts >250 cells/mm³ and men who have CD4 cell counts >400 cells/mm³ and individuals with HIV who are co-infected with HBV or HCV.

EFV

The main type of toxicity of EFV is central nervous system side effects, which typically resolve after a few weeks. However, in some cases, they can persist for months or not resolve at all.

DTG

The main type of toxicity is abnormal liver function, particularly in patients with HBV and HCV coinfection and potentially serious hypersensitivity reactions. There will be mild or moderate nausea, headache and diarrhea that do not limit treatment.

Drug substitutions for ARV drug toxicity

Drug regimen or single agent substitutions may be required for drug toxicity and to avoid drug interactions.

Clinical considerations

- Delaying substitutions or switches when there are severe adverse drug effects may cause harm and may affect adherence, leading to drug resistance and treatment failure.
- When drug interruptions are required, it is important to consider the various half-lives of ARV drugs. For example, when a NNRTI needs to be discontinued, a staggered approach should be used by prolonging the use of the NRTI backbone for two weeks except life threatening conditions (grade 4 conditions) where you have to discontinue all ARV drugs (see annex for details).

Strategies for managing adverse drug reactions:

Step 1: Establish whether the problem is due to antiretroviral drugs, other medications, OIs, non HIV related problems or clinical condition.

Step 2: Try to identify the responsible ARV drug.

Step 3: Assess the degree/severity of the Adverse Event using the ACTG/PACTG adverse events grading system.

Step 4: Manage the adverse event according to severity and also decide whether to substitute or discontinue ARV drug based on common adverse events clinical grading system in adults and adolescents –Annex 6 and Annex 8.

Drug interactions

Providers should be aware of all drugs that people with HIV are taking when ART is initiated and new drugs that are added during treatment maintenance.

Table 3.8: Key ARV drug interactions and suggested management

ARV drugs	Key interactions	Effect	Suggested management
AZT	Ribavirin and pegylated interferon alpha-2a		Substitute with TDF

NVP	Rifampicin		Substitute NVP with EFV
	Itraconazole and ketoconazole	Decrease concentration of anti-fungals to sub therapeutic level	Use an alternative antifungal agent (for example fluconazole)
	Methadone		Adjust the methadone dose as appropriate
	Astemizole and terfenadine		Use alternative antihistamine agent
EFV	Amodiaquine		Use an alternative antimalarial agent
	Methadone		Adjust the methadone dose as appropriate
	Estrogen-based hormonal contraception		Use alternative or additional contraceptive methods
	Astemizole and terfenadine		Use an alternative anti-histamine agent
Boosted PI (ATV/r, LPV/r)	Rifampicin		Substitute rifampicin with rifabutin, Adjust the PI dose or substitute with three NRTIs (for children)
	Lovastatin and simvastatin	Increase concentration	Use an alternative dyslipidemic agent (for example pravastatin)
	Halofantrine and lumefantrine		Use an alternative antimalarial agent
	Estrogen-based hormonal contraception		Use alternative or additional contraceptive methods

	Methadone and Buprenorphine		Adjust methadone and buprenorphine doses as appropriate
	Astemizole and terfenadine		Use alternative antihistamine agent
TDF	nephrotoxic drugs [e.g. aminoglycosides, amphotericin B, ganciclovir, pentamidine, vancomycin or interleukin-2]	Exacerbate nephrotoxicity	Avoid concurrent use
	ritonavir boosted PIs		Closely monitor renal function
DTG	Carbamazepine, Phenobarbital and phenytoin		Use alternative anticonvulsant agent
	Polyvalent Cation products containing Mg, Al, Fe, Ca, and Zn	Absorption of DTG is affected/reduced	Use DTG at least 2 hours before or at least 6 hours after supplements containing polyvalent cations, including but not limited to – Fe-, Ca-, Mg-, or Zn-multivitamin supplements; mineral supplements, cation containing laxatives and Al-, Ca- or Mg-containing antacids. Monitor for virological efficacy.
RAL	Polyvalent Cation products containing Mg, Al, Fe, Ca, and Zn	Absorption of RAL is affected/reduced	Use RAL at least 2 hours before or at least 6 hours after supplements containing polyvalent cations, including but not limited to – Fe-, Ca-, Mg-, or Zn-multivitamin

			supplements; mineral supplements, cation containing laxatives and Al-, Ca- or Mg-containing antacids. Monitor for virological efficacy.
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Table 3.9: Drug-drug interactions (ARVs and anti-TB drugs for treatment of DR-TB).

Clinical Condition	Responsible ARV drug/s	Responsible anti TB drug/s	Recommendations
Bone marrow suppression	AZT	Lzd, R, H	Monitor blood counts regularly. Replace AZT if bone marrow suppression occurs. Consider suspension of Lzd. Also consider cotrimoxazole, if patient is taking.
Hepatotoxicity	NVP, EFV, protease inhibitors, NRTIs	H, R, E, Z, Bdq, PAS, Eto/ Pto, FQ	When severe, stop both the ART and TB medications, and restart the TB medications first. Consider cotrimoxazole, if patient is taking. Also rule out viral hepatitis (Hepatitis A, B, C & Cytomegalovirus (CMV)).
Renal toxicity	TDF	Amino-glycosides, Cm	TDF may cause renal injury. If possible, avoid TDF in patients receiving aminoglycosides or Cm. If TDF is absolutely indicated, serum creatinine and electrolytes should be monitored (at least every two weeks). Even without the concurrent use of TDF, PLHIV have increased risk of renal toxicity secondary to aminoglycosides and Cm. In the presence of renal insufficiency, ARV and anti-TB medications need to have their doses adjusted.

Central nervous system (CNS) toxicity	EFV	Cs, H, Eto/Pto, FQ	EFV has a high rate of CNS side effects in the first 2–3 weeks of use, but typically self-limited and resolves. At present, there are limited data on the use of EFV with Cs; concurrent use is the accepted practice with frequent monitoring for central nervous system toxicity. Psychosis can occur with Cs, but is rare with EFV alone; other causes should always be ruled out.
QTc Prolongation	Protease inhibitors (PIs) LPV/r	Bdq, Dlm, Mfx, Gfx, Cfz, Lfx, Ofx	PIs may result QTc prolongation. The additive effects of combining ART with known second-line anti-TB drugs on QTc prolongation is not known. Close monitoring is indicated.
Dysglycaemia (disturbed blood sugar regulation)	Protease inhibitors (PIs)	Gfx, Eto/Pto	Protease inhibitors tend to cause insulin resistance and hyperglycemia. Eto/Pto tends to make insulin control in diabetics more difficult, and can result in hypoglycemia and poor glucose regulation.
For patients who are co-infected with HIV and MDR/XDR-TB, there is limited information on interactions of ARV drugs with new drugs such as bedaquiline and delamanid. Concomitant use of EFV and PIs with bedaquiline may interfere with drug concentrations and require close clinical monitoring; alternative ARV options should be considered, if possible.			

3.6 Re-engaging with care after ART interruption

People who interrupted their treatment need to be re-evaluated for possible adherence barriers and advanced clinical conditions. After evaluation, assessment of adherence barriers and intensified adherence counseling, Patients re-engaged into treatment after interruption should resume the same (previous) ART regimen they used before interruption. However, people interrupting treatment on NNRTI –containing regimen are at risk of drug resistance and should restart ART using a DTG-containing regimen. DTG has high genetic barrier to HIV drug resistance and can bring rapid viral suppression.

In addition, for re-engaged clients, the following essential elements should be part of the care:

- Exhaust all possible adherence barriers and provide an ongoing Enhanced Adherence Counseling (EAC).
- Maintain close or frequent follow-up schedule.
- Monitor the viral load closely and determine the VL at 3 and 6 months after resuming ART. If the two consecutive viral load is ≥ 1000 copies/ml, switch to second or third line regimen.

3.7 Diagnosis and management of antiretroviral treatment failure

Monitoring individuals receiving ART is important to ensure successful treatment, identify adherence problems and determine whether and which ART regimens should be switched in case of treatment failure. Routine viral load testing is a more sensitive and early indicator of treatment failure. Routine viral load testing should be done at 6 and 12 months of initiating ART and then every 12 months thereafter in order to detect treatment failure proactively. Aside from the routine viral load testing schedule, viral load testing should be used whenever there is clinical or immunologic suspicion of treatment failure.

Table 3.10 Definitions of clinical, immunological and virological failure for the decision to switch ART regimens

Failure	Definition	Remark
Clinical failure	Adults and adolescents New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 condition and certain WHO clinical stage 3 conditions (pulmonary TB and severe bacterial infections) may also indicate treatment failure) after 6 months of effective treatment. Children	The condition must be differentiated from immune reconstitution inflammatory syndrome occurring after initiating ART.

	New or recurrent clinical event indicating advanced or severe immunodeficiency (WHO clinical stage 3 and 4 clinical condition with exception of TB) after 6 months of effective treatment.	
Immunologic failure	Adults and adolescents • CD4 count at or below 250 cells/mm³ following clinical failure or • Persistent CD4 levels below 100 cells/mm³.	Without concomitant or recent infection to cause a transient decline in the CD4 cell count. Persistent is to mean at least 2 CD4 measurements below the threshold. Current WHO clinical and immunological criteria have low sensitivity and positive predictive value for identifying individuals with virological failure.
	Children Younger than 5 years Persistent CD4 level below 200 cells/mm³ or <10% Older than 5 years Persistent CD4 levels below 100 cells/mm³.	
Virologic failure	Viral load above 1000 copies/ml based on two consecutive viral load measurements in 3 months, with enhanced adherence support following the first viral load test.	An individual must be taking ART for at least 6 months before it can be determined that a regimen has failed. VL testing should not be done when there is an acute infection/fever.

When a client is found to have a viral load of >1000copies/ml on routine or need-based viral load test, providers should address adherence related issues by identifying adherence barriers and by providing enhanced adherence support (EAS) for three months. Viral load testing must be repeated

after three months of enhanced adherence support. If the second viral load test is ≤ 1000 copies/ml, the patient should be maintained on the first-line regimen with continued adherence support. However, if two consecutive viral load measurements within a 3-month interval with adherence support between measurements are greater than 1000 copies/ml, the results will confirm failure of the current treatment regimen and the client needs to be switched to appropriate second-line or third line regimen based on the first line combination. Patients with mental health problems and substance abuse may need extended periods of support before deciding regimen switch for treatment failure.

Enhanced Adherence support (EAS)

Enhanced Adherence support is important for patients that have unsuppressed VL, persisted or new immunosuppression, developing new OI or have multiple adherence barriers. It shall be systematic and with documenting the interventions provided during the EAS period.

Table 3.11: Summary of components of enhanced adherence counseling (EAC or EAS).

Enhanced adherence counselling sessions overview	
Session 1	• Review cognitive, behavioral, emotional and socio-economic barriers to adherence: - Treatment literacy - Medications: dosage, timing, storage - Side effects - Discuss risk reduction (e.g. for substance abuse) - Motivation - Mental health screening (screen for depression and other common mental problems using national mental health assessment tool (Annex 13) - Discuss patient's support systems • Referrals and networking. • Assist patient to develop adherence plan to address the identified issues.
Session 2	• Review adherence plan from the first session and discuss any challenges. • Identify other possible gaps and issues emerging. • Referrals and networking.

	• Assist patient to modify the adherence plan to address the identified issues.
Session 3	• Review adherence plan from the first and second session and discuss any challenges. • Identify other possible gaps and issues emerging. • Assist patient to modify the adherence plan to address the identified issues. • Decision on repeat VL based on current adherence: 1. If the adherence is good: plan repeat VL testing after three months of good adherence and explain possible ways forward, emphasizing role of the patient and the health facility. • If adherence challenges persist: plan further EAC sessions before repeating the VL.
Session to discuss on repeat viral load results	• Discuss result of the second VL test with the patient. • Plan the way forward: 1. If VL now $\leq 1,000$: continue current regimen with enhanced adherence 2. For those patients with identified significant adherence barriers, it is advisable to extend the provision of EAC for 6 months before doing the second VL testing in order to properly address the barriers and give optimal time for viral suppression to happen

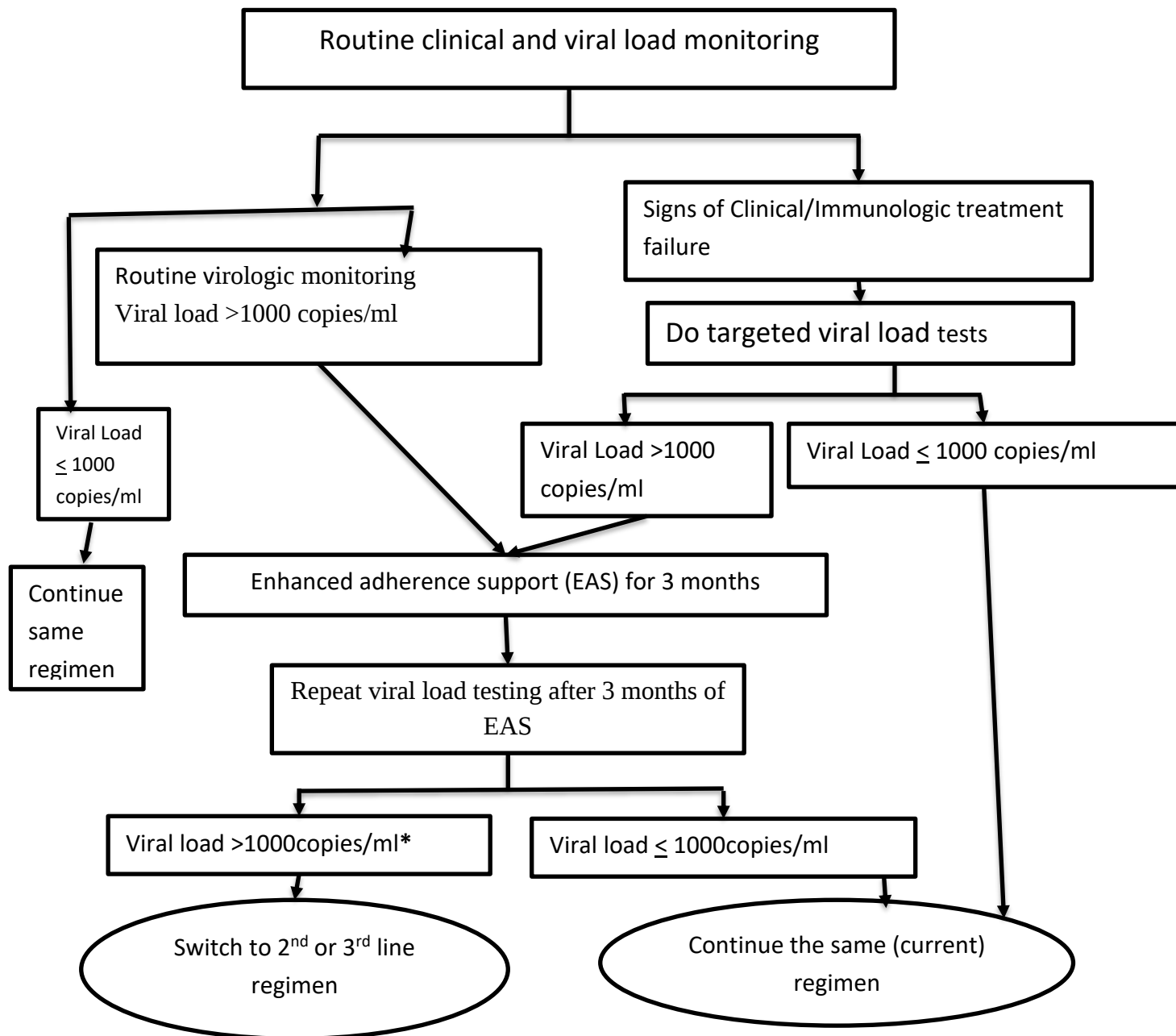


Figure 3.1. Algorithm for routine clinical and viral load monitoring

** For those patients with identified significant adherence barriers, it is advisable to extend the provision of EAC for 6 months before doing the second VL testing in order to properly address the barriers and give optimal time for viral suppression to happen.*

3.8 What ART regimen to switch to (second-line ART regimens)

Using a boosted PI + two NRTI combinations is recommended as the preferred strategy for second-line ART for adults, adolescents and also for children when NNRTI-containing regimens were used in first-line ART. In children using a PI-based regimen for first-line ART, switching to NNRTI or maintaining the PI regimen is recommended according to their age.

3.8.1 Second-line ART regimens for adults and adolescents

It is recommended that second-line adult and adolescent regimens include a boosted-PI plus two NRTIs (determined by the drug used in first-line therapy).

Guidance for changing ARV regimens for treatment failure

- Ensure diagnosis of treatment failure to avoid premature switching.
- Assess adherence and address barriers.
- Assess for and Address drug interaction issues.
- Do not add one drug to a failing regimen.
- Consider resistance and cross resistance patterns.
- Get advice from experienced clinicians.
- At least two new drugs.
- Preferably one new drug class.

Once it is decided and patients are switched to second-line regimen, strong adherence support should be continued and viral load monitoring should be started after 6 months of second-line treatment and then every 12 months.

Table 3.12: Summary of preferred second-line ART regimens for adults and adolescents.

Target population	Preferred second-line regimen	
Adults and adolescents (≥10 years)^a	If AZT was used in first-line ART	TDF + 3TC + LPV/r or ATV/r
	If TDF was used in first-line ART	AZT + 3TC + LPV/r or ATV/r
	If TDF+3TC+DTG ^b used in first-line	AZT + 3TC + ATV/r or LPV/r
HIV and TB co-infection	If rifabutin is not available	Same NRTI backbones as recommended for adults and adolescents plus double-dose LPV/r (that is, LPV/r 800 mg/200 mg twice daily) or standard LPV dose with an adjusted dose of RTV (that is, LPV/r 400 mg/400 mg twice daily).
HIV and HBV co-infection	AZT + TDF + 3TC + (ATV/r or LPV/r)	

^a Adult clients taking ABC can be shifted to AZT. For pregnant women same regimens recommended as for adults and adolescents.

^bDTG containing regimens are not recommended for pregnant and breast feeding mothers. For HIV/TB co-infected adults and adolescents, the recommended dose of DTG is 50 mg twice daily.

3.8.2 Second-line ART regimens for children

Recommending potent and effective second-line regimens for infants and children is especially difficult because of the current lack of experience in resource-limited settings and the limited formulations available. This highlights the importance of choosing potent and effective first-line regimens and ensuring their durability and effectiveness by optimizing adherence.

For children starting first-line ART with an NNRTI-based regimen, PI-based regimens remain the recommended choice for second-line therapy. LPV/r is the preferred boosted PI option, but ATV/r may be considered if more appropriate formulations become available. After failure of a first-line

LPV/r-based regimen, children younger than 3 years should remain on their first-line regimen, and measures to improve adherence should be undertaken. After failure of a first-line LPV/r-based regimen, children 3 years or older should be switched to a second-line regimen containing an NNRTI plus two NRTIs; EFV is the preferred NNRTI. After failure of a first-line regimen of ABC or TDF + 3TC, the preferred NRTI backbone option for second-line ART is AZT + 3TC and failure of a first-line regimen containing AZT + 3TC, the preferred NRTI backbone option for second-line ART is ABC or TDF + 3TC.

Table 3.13: Summary of recommended first- and second-line ART regimens for children.

ARV	Children	First line regimen	Second line regimen
LPV/r-based first-line regimen	Younger than 3 years	ABC + 3TC + LPV/r	No change ^a
		AZT + 3TC + LPV/r	
	3 years and Older	ABC + 3TC + LPV/r	AZT + 3TC + EFV
		AZT + 3TC + LPV/r	ABC or TDF ^b + 3TC + EFV
NNRTI-based first-line regimen	All ages	ABC + 3TC + EFV (or NVP)	AZT + 3TC + LPV/r ^c
		TDF ^b + 3TC + EFV (or NVP)	
		AZT + 3TC + EFV (or NVP)	ABC or TDF + 3TC + LPV/r ^c

^a No change is recommended unless in the presence of advanced clinical disease progression or lack of adherence specifically because of poor palatability of LPV/r. In this case, switching to a second-line NVP-based regimen should be considered.

^b TDF may only be given to children >2 years.

^c ATV/r can be used as an alternative to LPV/r in children older than 6 years.

3.9 Implementation of Second Line ART at Health Center Level

Rationale

The possibility of treatment failure and the need for second line ART will increase as more and more people enrolled in to treatment and the time on treatment advances. The capacity of diagnosing treatment failure cases has been also improving as a result of advances in diagnosis criteria and through implementation of routine viral load testing service at all treatment providing facilities. Previously diagnosis of treatment failure cases were made using immunologic and/or clinical failure criteria which required relatively a high level of clinical expertise to identify these conditions and make a clinical decision. Due to this and its relative limited demand, second line ART service has been available and provided only at hospitals level.

During the recent years, the demand for second line ART has been increased and patients at the health center level are also complaining for not getting the treatment at a reasonable distance and due to long waiting time while getting the service at hospital level. The follow up frequency is also more for patients on second line compared to patients on first line and stable. And hence, limiting the provision of second ART at hospital level only contributed to the high rate of lost to follow up, demotivation of the service users and increased transport cost of individual clients.

Decentralization of the provision of second line ART at health center level has been endorsed. The scale up will be implemented through a phase based approach and there will be a criteria as stated below for health centers to be included in the first phase of implementation.

The main objective of decentralization is to improve quality of service and retention to care through availing the service closer to those in need and assure program sustainability. It will also allow for continuity of care and treatment at the nearest health facility as well as ensure equitable distribution of services.

Eligible health centers to provide second line ART service

Second line ART service will be made available at health centers that have a patient load of 200 or more. That is a reasonably adequate patient load which could give rise to viable number of prospective clients who might need to be switched to a second line ART. It is an evidence based recommendation through analysis of available surveys and service records about the prevalence of first line ART treatment failure. The cut-off point will be revised in due time depending on the emerging evidence through time.

Eligible patients for second line ART service at health centers

The precise definition of treatment failure through a Viral load count and the availability routine viral load testing through specimen referral networking throughout ART facilities has created an opportunity to scale-up second line ART to health centers for a defined group of patients. The following criteria should be used to sort out treatment failure patients who will be switched to second line ART or will have follow up at the health centers:

- a) Patients who fulfill the criteria of treatment failure and with no any signs of clinical failure
- b) Patients who are initiated on Second line ART at hospital and became stable with no signs of OI or drug toxicity and transferred out to Health centers having second line ART.

Whenever patients develop toxicity or show any sign of deterioration upon switching to second line, the ART clinician should seek immediate advice from the clinical mentor or experienced physician and/or refer the patient immediately to the nearby hospital.

Follow-up and support system

The scale-up of ART to health centers in Ethiopia has been a success so far. We have learned that with a carefully designed support system in place, health centers could be very effective in the treatment of patients with HIV infection. The critical support systems put in place to maintain the service quality while scaling-up the ART service through a public health approach were clinical mentoring and supportive supervision. A regular, systematic, and focused clinical mentoring program will build the capacity of health professionals in the clinical management of HIV infection while supportive supervision ensures that the overall health system stays strong and responsive to the service needs of PLHIV. This very same system can be applied to scale-up second line ART services to health centers. The clinical mentors should focus and give emphasis to create competencies pertaining to second line ART during their mentoring visits. Much more attention is ought to be provided to the one to one mentoring as there is much knowledge and skill to be transferred in this case.

Follow-up schedule for patients on second line ART at health centers

Individuals on second line ART needs strong adherence support and relatively more frequent follow visits. The follow-up schedule for patients on second line ART at health center level will be similar to the recommendations made for patients at hospitals. Patient's switched to second line

ART have been in care for a long time .Consequently, they are expected to be experienced in the recognition of symptoms which could possibly indicate illness or toxicity. However these patients might not know the conditions related to second line ART regimens. Therefore, they should be instructed well on the possible symptoms of toxicities related to second line ARV drugs and when to seek care if they experience any. Generally a follow-up schedule of every one to three months suffices if the patients didn't experience any illness or complaint in between.

Monitoring and evaluation

Effective HIV prevention, care and treatment require standardized recording and reporting system. Recording and reporting is used to systematically monitor and evaluate progress of patient/s and treatment outcome as well as the overall program performance. Monitoring and evaluation will be done at the different levels of the health system. The standardized HIV program recording and reporting tools both at the health center and hospital levels are similar. The existing patient monitoring registers and formats will be used and there is no need to develop additional monitoring tools. The reporting will also be done using the existing HMIS tally sheets and reporting formats.

Supportive supervision helps to ensure and improve quality, effectiveness and efficiency of services provided. It will also enhance competence and satisfaction of the staff at all levels. Since it is an essential tool in the management of staff and facilities, it should be done on a regular basis. It will be conducted at all levels in an integrated manner using standardized checklist. The issue of scale up of second line ART at the health centre level will be clearly identified or included in the checklist. It will be conducted by each administrative level to the respective offices and health facility to assess the coordination efforts and implementation status.

Integrated review meeting will also be conducted on regular bases at every level. In this manner, activities taking place at all levels will then be brought forward to the respective review meeting sessions where the second line ART scale up performance will be reviewed as part of the overall review meeting.

Supply of second line ARVs to health centers

The overarching objective of pharmaceuticals supply management system is to support national policy with the adequate and continuous availability of the most safe, effective, quality-assured

ARV pharmaceuticals at service delivery sites, in the right quantity, at the lowest possible cost and in a timely manner. The second line ARV drugs supply and distribution will follow the existing delivery system that extends from the central level to health facilities. Central PFSA will have a major role of delivering the products to its Hubs; subsequently the hubs distribute the commodities to health facilities based on orders placed by health facilities to PFSA hubs every two months. The identified health centers for the scale up of second line ART will try to estimate their needs and place an order at the start up. The PFSA hubs will prepare and plan on how to address the startup orders from health centers very shortly and need to instruct the health center logistics team for continued action to avail second line ART at the health center as per the need.

3.10 Identification and management of second-line treatment failure

Even though there is limited data regarding second line treatment failure, the national routine viral load program data from EPHI showed that 40 out of 198 (20%) patients on second-line had virologic failure for second line regimens. i.e. viral load of >1000 copies/ml. Patients who are on second-line regimen and have high viral load level (>1000 copies/ml) after 6 months of treatment need to go through the algorithm as described for first line treatment failure with enhanced adherence support and repeat test after three months to decide second line treatment failure. Once patients are confirmed to have second line failure they should be referred to hospital with experienced physicians for initiation of third line regimens.

Management of second-line treatment failure

Treatment failure is indicated by biological non-suppression with or without immunologic and/or clinical deterioration. Before switching to third-line regimen, the issue should be discussed with experienced physician in HIV care and treatment. Treatment failure while on a second line PI regimen is often due to non-adherence. Doctors and nurses should participate directly in the adherence assessments, and do not delegate the assessment to the adherence counselor alone (see enhanced adherence counseling section for detailed steps of adherence counseling for patients with adherence problems). Before switching to third line regimen, health care providers should ensure the following.

- Two consecutive viral load measurements > 1000 copies/ml usually 3 months apart.
- First viral load measurement done at least 6 months after switching to second-line regimen.

- The repeat VL test should be done after 3 months of enhanced adherence support.

The approach in switching to third-line should follow the guiding principles listed out for switching to second line drugs. Table 3.14 shows the regimens to be selected for third line.

Table 3.14 Summary of sequencing options for preferred first, second and third-line ART regimens in adults, adolescents, pregnant women and children

Population	1 st line regimens	2 nd line regimens	3 rd line regimens
Adults, adolescents, pregnant & breastfeeding women	AZT+3TC + EFV/NVP	TDF+3TC + ATV/r or LPV/r	DRV/r ^a + DTG + AZT+3TC
	TDF+3TC+EFV/NVP	AZT+3TC + ATV/r or LPV/r	DRV/r + DTG + TDF+3TC
	ABC+3TC+EFV/NVP	AZT+3TC + ATV/r or LPV/r	DRV/r + DTG + TDF + 3TC
Adults and adolescents 10 years & older with body weight ≥35kg	TDF + 3TC + DTG ^f	AZT+3TC+ATV/r or LPV/r	DRV/r+ABC+3TC+EFV or NVP
Children younger than 3 years	ABC + 3TC + LPV/r	Maintain the 1 st line regimen	RAL ^b + AZT + 3TC
	AZT + 3TC + LPV/r		RAL + ABC + 3TC
Children older than 3 years, and adolescents 10 years & older with body weight < 35kg	AZT + 3TC + EFV	ABC + 3TC + LPV/r	DRV/r + RAL + ABC +3TC
	ABC or TDF ^c + 3TC + EFV	AZT + 3TC + LPV/r	DRV/r + RAL + AZT + 3TC
All children (0 – 10)	AZT or ABC or TDF + 3TC + LPV/r ^d	AZT or ABC or TDF + 3TC + EFV or NVP	DRV/r ^{a,e} + RAL ^f + ABC +3TC or RAL ^f + ABC + 3TC (for < 3yrs)
			DRV/r ^{a,e} + RAL + TDF +3TC or RAL + TDF + 3TC (for < 3yrs)
			DRV/r + RAL ^f + AZT + 3TC RAL ^f + AZT + 3TC (for < 3yrs)

^a In PI-experienced patients, the recommended DRV/r dose should be 600mg/100 mg twice daily.

^b If RAL is not available, no change is recommended unless in the presence of advanced clinical disease progression or lack of adherence specifically because of poor palatability of LPV/r.

^c TDF may only be given to children >2 years.

^d ATV/r can be used as an alternative to LPV/r in children older than three months of age, however the limited availability of suitable formulations for children younger than six years of age, the lack of a fixed-dose formulation and the need for separate administration of RTV booster should be considered when choosing this regimen.

^e DRV/r should not be used in children younger than three years of age.

^f RAL can be used in children failing PI-based second-line treatment when DTG is not available and when RAL has not been used in a previous regimen. DTG is currently only approved for children 6 years and older (>30kg of weight), however studies are ongoing to determine dosing in younger children and approval to lower age groups is expected in the near future. DTG containing regimens are not approved for pregnant and breast feeding mothers. For HIV/TB co-infected adults & adolescents, the recommended dose of DTG is 50 mg twice daily.

Table 3.15 Recommended doses of third-line ARV drugs for adults and adolescents.

Generic Name	Dose
Proteases inhibitors (PIs)	
Darunavir + ritonavir (DRV/r)	800 mg + 100 mg once daily ^a or 600 mg + 100 mg twice daily ^b
Integrase strand transfer inhibitors (INSTIs)	
Dolutegravir (DTG)	50 mg once daily
Raltegravir (RAL)	400 mg twice daily

^a For individuals with no previous use of protease inhibitors.

^b For individuals with previous use of protease inhibitors.

Table 3.16: Recommended doses of third line ARV drugs for children.

Drugs	Strength of tablets (mg) or oral liquid (mg/ml)	Number of tablets or ml by weight-band morning (AM) and evening (PM)										Stren gth of adult tablet (mg)	Number of tablets by weight band	
		3.0–5.9 kg		6.0–9.9kg		10.0–13.9kg		14.0–19.9kg		20.0–24.9 kg			25.0–34.9 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM
Solid formulations:														
DRV ^a	75 mg	-	-	-	-	3	3	5	5	5	5			
DRV/r	120mg/20mg	-	-	-	-	2	2	3	3	3	3		4	4
RAL	Chewable tablets 25 mg	-	-	-	-	3	3	4	4	6	6	400	1	1
	Chewable tablets 100 mg	-	-	-	-	-	-	1	1	1.5	1.5	400	1	1
	Granules ^b (100 mg/sachet)	0.25	0.25	5	5	-	-	-	-	-	-		-	-
Liquid formulations														
DRV ^a	100mg/ml	-	-	-	-	2.5ml	2.5ml	3.5ml	3.5ml	-	-			

^a DRV must be administered with 0.5 ml of RTV 80 mg/mL oral suspension if the child weighs less than 15 kg and with RTV 50 mg solid formulation for children weighing 15–30 kg.

^b RAL granules are approved for use for children as young as 4 weeks, but the feasibility and acceptability of such formulations has not been widely investigated, and concerns have been raised regarding administration in resource-limited settings. The bioequivalence of RAL chewable tablets dispersed in liquid is currently being explored, and more guidance will be provided as soon as additional evidence becomes available.

CHAPTER FOUR: PREVENTION, SCREENING, AND MANAGEMENT OF COMMON CO-INFECTIONS

Although ART is initiated for all HIV diagnosed patients as early as possible, most patients present for care and treatment at late clinical stages. Therefore, screening and management of OI is still critical. Opportunistic infections are the predominant causes of morbidity and mortality among HIV-infected patients. Frequently affected organ systems are the nervous, gastro-intestinal and respiratory systems, and the skin. The level of immunity determines the occurrence and type of opportunistic infections. In general, milder infections such as herpes zoster and other skin infections occur early whereas serious life-threatening infections such as CNS toxoplasmosis and Cryptococcal meningitis occur later with severe immune-suppression. Some life-threatening infections, such as pneumonia and TB, may occur early as well as later. When TB occurs later it is atypical, more disseminated and more extra pulmonary.

General strategies to prevent opportunistic infections are:

- Reduction of exposure
- Chemoprophylaxis (primary/secondary)
- Immunization and
- Starting HAART

4.1. *Co-trimoxazole preventive therapy*

Co-trimoxazole preventive therapy should be implemented as an integral component of a package of HIV-related services. Existing recommendations cover initiation of CPT among adults, adolescents, pregnant women and children for prevention of *Pneumocystis pneumonia*, toxoplasmosis, bacterial infections and diarrhea caused by *Isospora belli* or *Cyclospora* species, as well as benefits for malaria prophylaxis.

Table 4.1 CPT indication for primary prophylaxis

Age	Criteria for initiation	Criteria for discontinuation*	Monitoring approach
HIV exposed infants	In all, starting at 4–6 weeks after birth	Until the risk of HIV transmission ends or HIV infection is excluded	Clinical at 3-month Intervals
<5 years	In all	Discontinue for those older than 5 years of age who are clinically stable, with evidence of immune recovery and/or viral suppression on ART**	
≥5 years, including adults	Any WHO stage and CD4 count ≤350 cells/mm ³ Or WHO stage 3 or 4, irrespective of CD4 level	Discontinue in those who are clinically stable (those individuals on ART for at least one year without any new WHO clinical stage 2, 3 or 4 events) with; • Evidence of immune recovery and/or viral suppression (CD4 count >350 cells/mm³, with viral load suppression) or • Two consecutive CD4 count > 350 cells/mm³ if no VL result	

* Discontinue also if the person has Stevens-Johnson syndrome, severe liver disease, severe anemia, severe pancytopenia or negative HIV status. Contraindications to co-trimoxazole preventive therapy: severe allergy to sulfa drugs; severe liver disease, severe renal disease and glucose-6-phosphate dehydrogenase (G6PD) deficiency.

**Parameter for immune recovery in children when >5 years old: CD4 cell count >350 cells/mm³, with viral load suppression.

Table 4.2: Dosage of co-trimoxazole for adults, adolescents, children and infants.

Age (weight)	Suspension (240 mg/5 ml co-trimoxazole)	Single strength tab (480 mg of Co-trimoxazole)	Double strength tab (960 mg of co-trimoxazole)
Up to 6month (5kg)	2.5 ml/day	¼ tab/day	-
6 months to 5 yr (5-15 kg)	5 ml/day	1/2 tab/day	-
6-14 yr (15-30 kg)	10 ml/day	1 tab/day	½ tab/day
>14 yrs (>30 kg)		2 tab/day	1 tab/day

Table 4.3: Adverse effects of CPT and management.

Toxicity	Clinical description	Recommendation
Grade 1	Erythema, pruritis	Prescribe anti-histamine and continue CPT and close follow-up.
Grade 2	Diffuse maculopapular rash, dry desquamation	Prescribe Anti-histamine and continue CPT and close follow-up.
Grade 3	Vesiculation, minor mucosal ulceration	STOP CPT, manage and re-introduce after 2 weeks with observation (desensitize).
Grade 4	Exfoliative dermatitis Steven-Johnson syndrome or erythema multiforme, moist desquamation	STOP CPT NEVER RESTART CO-TRIMOXAZOL

4.2. Management of opportunistic diseases of the respiratory system

4.2.1. Tuberculosis

TB is the most frequent life-threatening OI and a leading cause of death among HIV infected people. TB increases HIV replication through the process of immune activation leading to increased viral load. This results in more rapid progression of HIV disease. On the other hand, HIV increases susceptibility to be infected with *M. tuberculosis*, the risk of progression to TB disease and the incidence and prevalence of TB. The life time risk of HIV positive individuals who develop TB is 20-37 times greater than HIV negative individuals. Thus, it is essential for both TB

and HIV control programs to synergize their joint efforts and intensify the implementation of TB/HIV collaborative activities to mitigate the dual burden of TB/HIV in populations at risk or affected by both diseases. The rationale for the integration is that tuberculosis and HIV prevention and control programs share mutual challenges of high impact of TB on HIV and vice versa. Therefore, the two programs must collaborate to provide better service for the co-infected patients.

Nationally recommended TB/HIV collaborative activities

A. Strengthen the mechanisms for integrated TB and HIV services delivery

- Strengthen the coordination mechanism for integrated TB/HIV services at all levels;
- Conduct surveillance to determine HIV burden among TB patients and TB burden among HIV patients;
- Carry out joint TB/HIV planning for integrated TB and HIV services delivery; and
- Conduct monitoring and evaluation of collaborative TB/HIV activities.

B. Reduce the burden of TB in HIV infected people and initiate early antiretroviral therapy (the three I's i.e. **Intensive case finding, **I**NH preventive therapy and **I**nfection control)**

- Intensify TB case finding and ensure quality TB treatment;
- Initiate TB prevention with earlier initiation of ART and isoniazid preventive therapy (IPT); and
- Ensure tuberculosis infection control in healthcare and congregate settings.

C. Reduce the burden of HIV in patients with presumptive and diagnosed TB.

- Provide HIV testing and counseling to presumptive and confirmed TB patients;
- Provide HIV prevention services for presumptive and confirmed TB patients;
- Provide co-trimoxazole preventive therapy for HIV positive TB patients;
- Ensure HIV/AIDS prevention, treatment and care for HIV positive TB patients; and
- Provide ART for HIV positive TB patients.

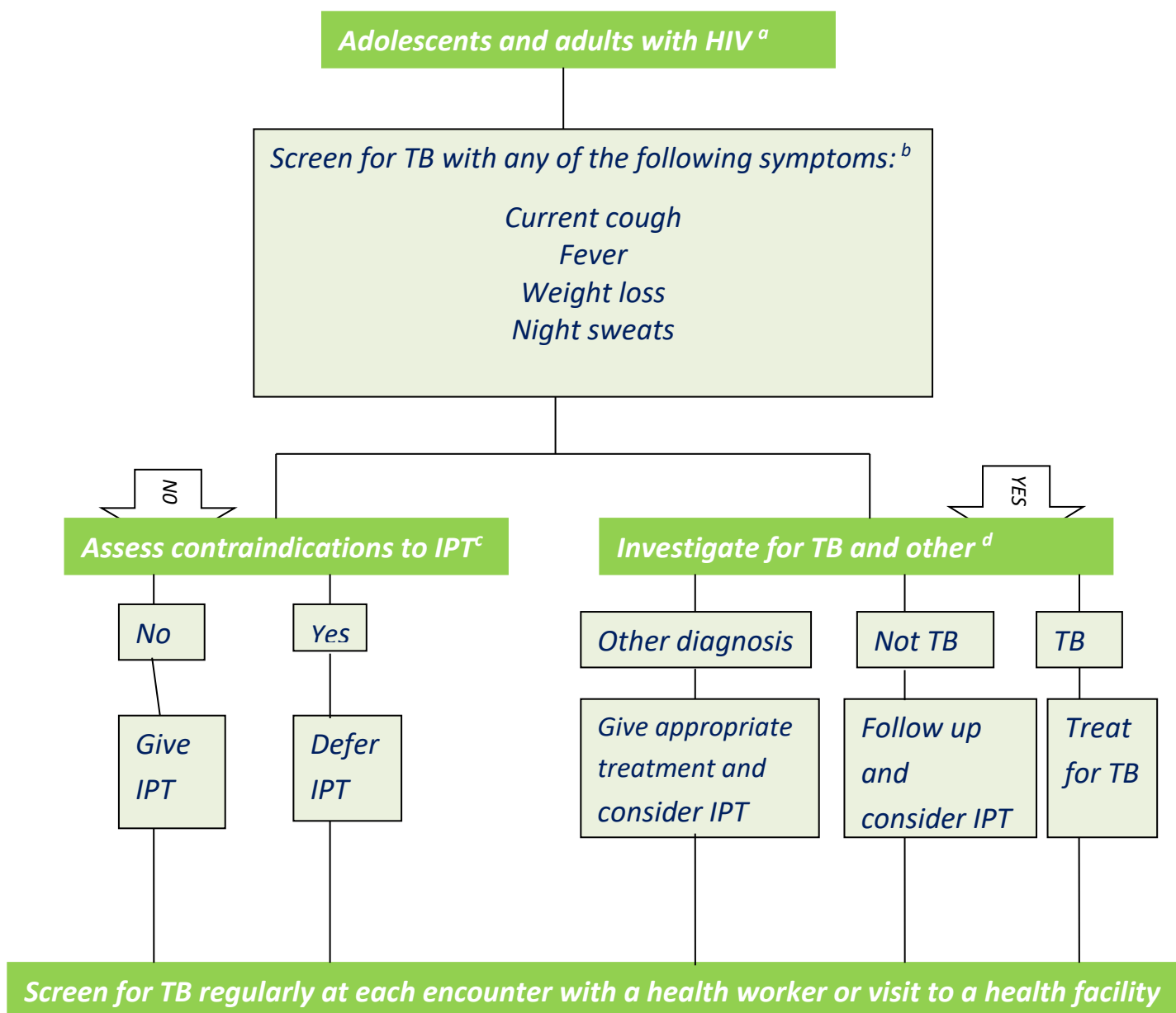
Table 4.4 Timing of ART for adults and children with TB

Patients with tuberculosis found to be HIV positive	HIV positive patients taking ART diagnosed with TB
• ART should be started in all TB patients, including those with drug-resistant TB, irrespective of the CD4 count. • Anti-tuberculosis treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment. The HIV-positive TB patients with profound immune-suppression (such as CD4 count less than 50 cells/mm³) should receive ART immediately within the first two weeks of initiating TB treatment. • ART should be started in any child with active TB disease as soon as possible within eight weeks following the initiation of anti-TB treatment irrespective of the CD4 count and clinical stage. • Efavirenz should be used as the preferred drug in patients starting ART while on Anti-tuberculosis treatment. • When second line is initiated LPV/r is preferable.	• Start anti-TB • Modify ART regimen to avoid drug-drug interaction • Evaluate for treatment failure

The 3Is intervention

I. Intensify TB case finding and ensure quality TB treatment

Tuberculosis case finding should be intensified in all HIV testing and counseling services for HIV positive clients by using a set of simple questions for early identification of presumptive TB cases. HIV positive clients coming through HTS services should be informed about the advantages of being screened for TB. Once informed about the risk of developing active TB, they should undergo screening for it. Adults and adolescents living with HIV should be screened for TB with clinical algorithm, those who report any one of the symptoms of current cough, fever, weight loss or night sweats may have active TB and should be evaluated for TB and other diseases.



^a Every adult and adolescent should be evaluated for TB before ART is initiated. Infection control measures should be given priority to reduce TB transmission in all settings that provide care.

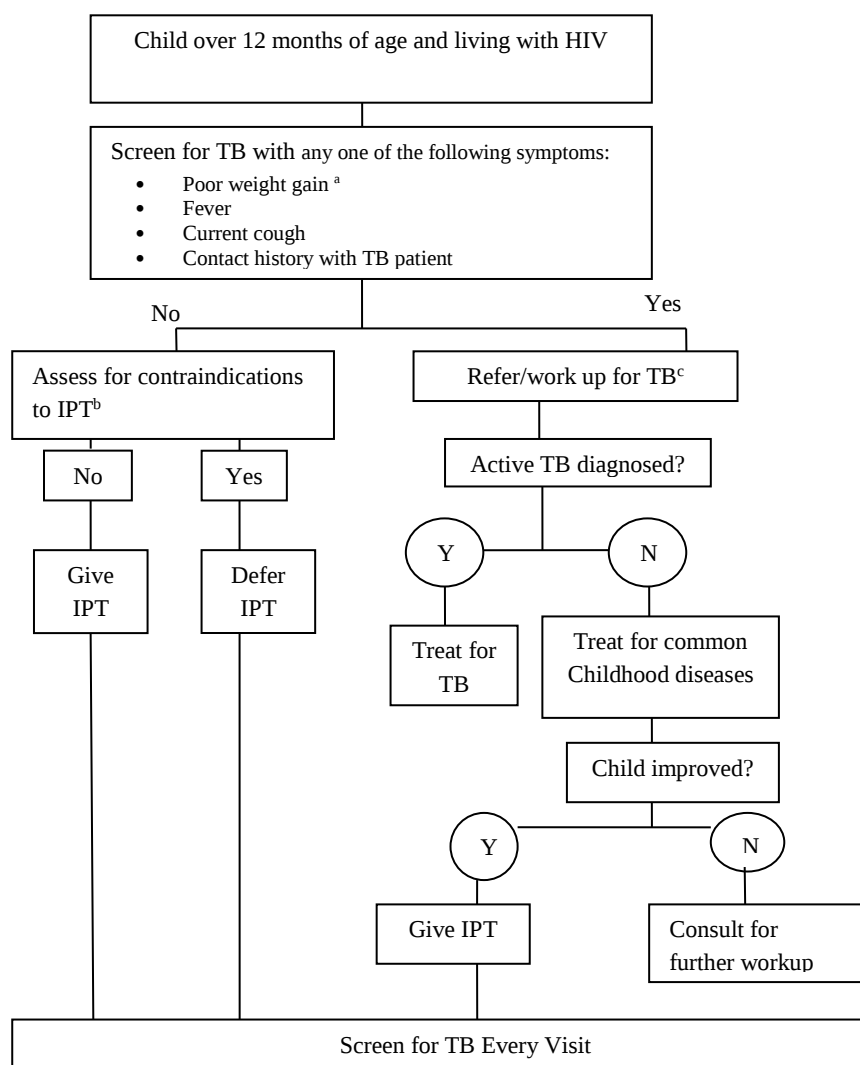
^b Chest radiography can be done if available but is not required to classify people into TB and non-TB groups. In settings with high HIV prevalence and high TB prevalence among PLHIV (such as exceeding 10%), strong consideration must be given to adding other sensitive investigations.

^c Contraindications include: active hepatitis (acute or chronic), regular and heavy alcohol consumption and symptom of requirement for initiating IPT.

^d Investigations for TB should be performed in accordance with existing national guideline.

Figure 4.1 Algorithm for TB screening among adults and adolescents living with HIV in HIV-prevalent and resource-constrained settings.

Children living with HIV who have any of the symptoms of poor weight gain, fever, current cough or contact history with TB case may have active TB and should be evaluated for TB and other conditions. If the evaluation shows no TB, children should be offered IPT regardless of their age.

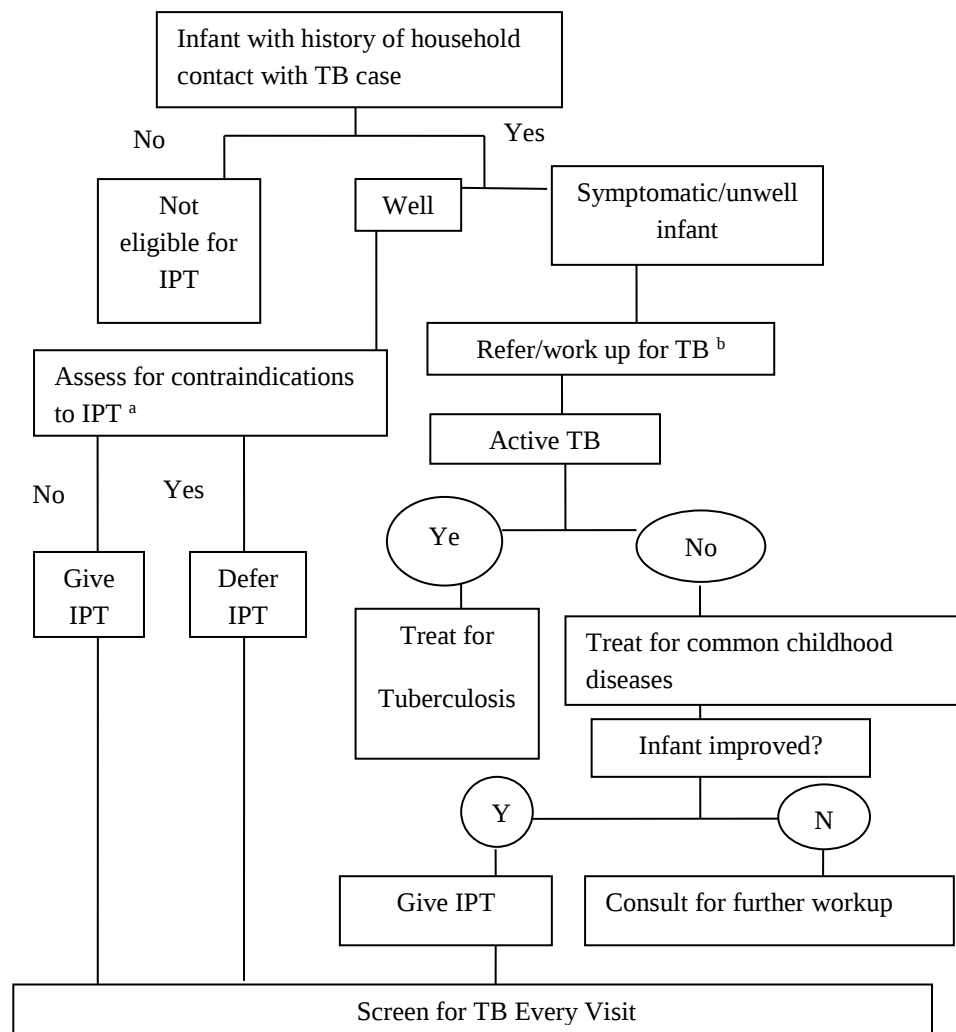


^a Poor weight gain is defined as (1) reported weight loss or very low weight (weight for age less than -3 z-score), (2) underweight (weight for age less than -2 z-score), (3) confirmed weight loss ($>5\%$) since the last visit or (4) growth curve flattening.

^b Contraindications include: active hepatitis (acute or chronic) and symptoms of peripheral neuropathy.

^c Investigations for TB must be performed in accordance with existing national guidelines.

Figure 4.2: Algorithm for TB screening and IPT for children more than one year old and living with HIV.



^a Contraindications include: active hepatitis (acute or chronic) and symptoms of peripheral neuropathy.

^b Investigations for TB must be performed in accordance with existing national guidelines.

Figure 4.3: Algorithm for TB screening and IPT for infants less than one year old and living with HIV.

Diagnosis of TB in HIV infected people

Diagnosis of TB is challenging in HIV positive individuals, especially when the stage of the disease is advanced. Standard TB diagnostic approaches and clinical algorithms should be followed to guide the diagnosis of TB in PLHIV.

Clinical assessment: thorough clinical evaluation of the patient, including exclusion of other OI, should be done. For patients with respiratory symptoms in whom tuberculosis is less likely and who are treated empirically for bacterial pneumonia or pneumocystis pneumonia, clinical response should not automatically exclude the diagnosis of tuberculosis. Acute bacterial pneumonia or PCP may occur in patients with underlying tuberculosis and patients should therefore be reevaluated for tuberculosis, particularly if respiratory symptoms persist after treatment.

Xpert MTB/RIF Test (GeneXpert Test): The GeneXpert MTB/RIF system is a fully automated nested real time PCR system, which detects MTB complex DNA in sputum and other sample types (i.e pleural, lymph node aspirate or tissue, CSF, gastric fluid and tissue other than lymph node). It simultaneously identifies mutations in the *rpoB* gene, which are associated with rifampicin resistance. The assay detects M.TB and rifampicin resistance; conferring mutations using three specific primers and five unique molecular probes. It provides results less than 2 hours and has minimal bio-safety requirements and training.

Xpert MTB/RIF test (GeneXpert Test) is recommended as an initial diagnostic test for all presumptive TB cases (individuals with TB symptoms) among HIV infected people.

- Xpert MTB/RIF should be used rather than conventional microscopy, culture and drug susceptibility testing (DST) as the initial diagnostic test in adults and children suspected of having HIV-associated TB or multidrug resistant TB.
- Xpert MTB/RIF should be used in preference to conventional microscopy and culture as the initial diagnostic test for cerebrospinal fluid (CSF) specimens from patients suspected of having TB meningitis.
- Xpert MTB/RIF may be used as a replacement test for usual practice (including conventional microscopy, culture or histopathology) for testing specific non-respiratory specimens (lymph nodes and other tissues) from patients suspected of having extra pulmonary TB.

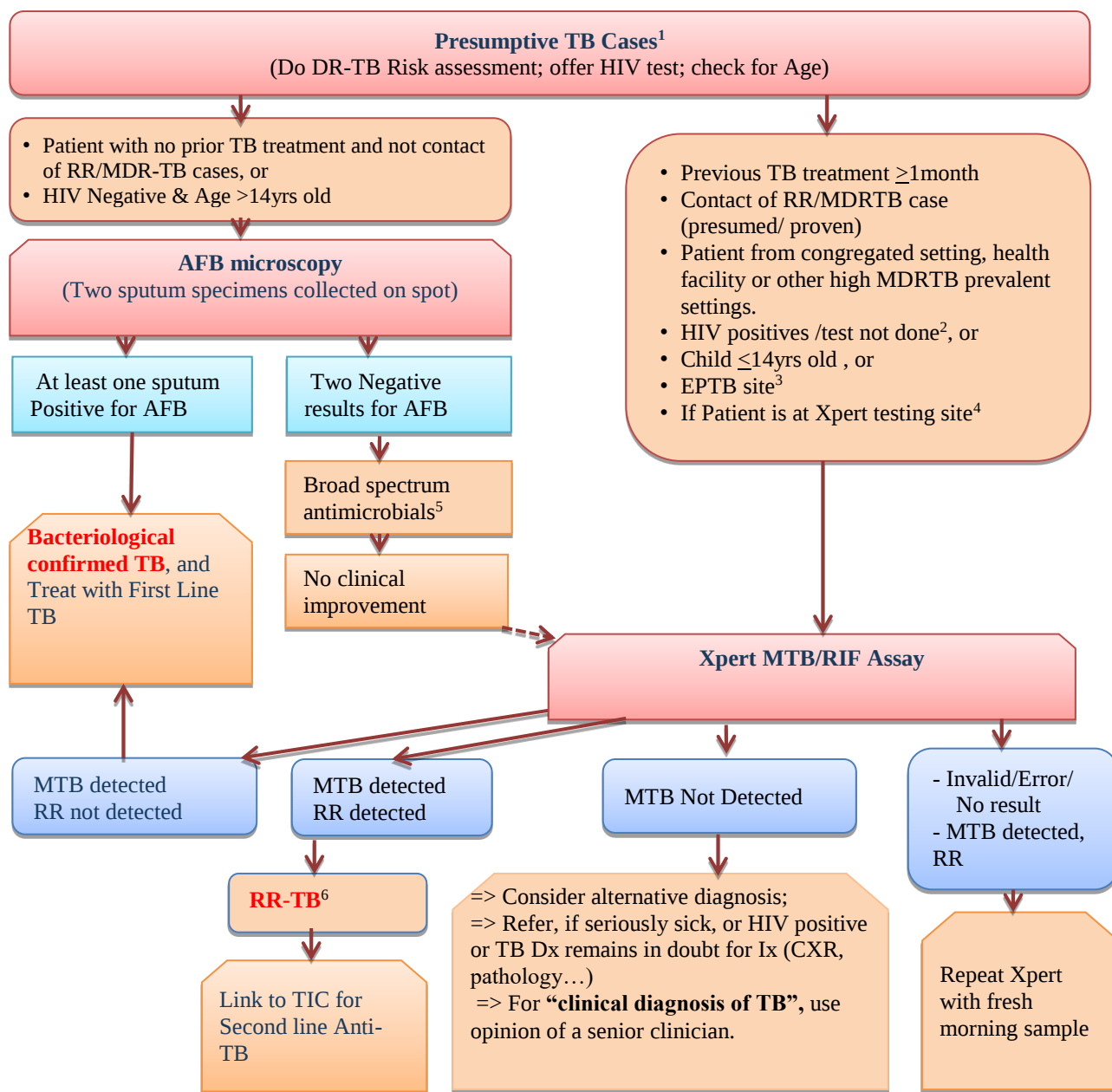
AFB microscopy: AFB microscopy is indicated for HIV infected presumptive TB cases when access to XPert MTB/RIF test is limited. The recommendation for AFB microscopy is 2 spot tests with in 1 hour.

Chest radiography: Chest X-ray plays a significant role in shortening delays in diagnosis of TB in PLHIV. It can also be an important entry point to diagnose non-tubercular chest diseases, which are common among HIV positives.

Sputum culture: sputum culture is the gold standard for the diagnosis of tuberculosis in general. In patients with XPert negative results, sputum culture may be indicated as part of the diagnostic procedure for people living with HIV if clinical suspicion persists.

Diagnosis of extra-pulmonary tuberculosis in HIV positive

Extra-pulmonary tuberculosis is more HIV-related than pulmonary tuberculosis. The accurate diagnosis of extra-pulmonary tuberculosis is complex and difficult, particularly in peripheral health facilities with limited diagnostic capacity. Therefore, it is important for healthcare workers to have high-index of suspicion and critically evaluate through clinical algorithms. For other sites, do organ specific investigations.



¹ Presumptive TB is defined as having symptom and signs consistent with TB; mainly persistent cough of two or more weeks (or cough of any duration if HIV positive).

² For patients in whom "HIV test is not done" at time of TB evaluation, Xpert test may be the initial test if the clinician has strong clinical suspicion of HIV infection or if the patient possesses risk behavior to acquire HIV infection.

³ Liquid specimens from EPTB site (in particular CSF) may be subjected to Xpert test without additional processing.

⁴ Xpert test is preferred test to examine presumptive TB patients identified at facility where the machine is available.

⁵ Broad spectrum antimicrobials, excluding fluoroquinolone or anti-TB drugs is to be given for 10-14days.

⁶ RR-TB result in patients considered to be low risk for MDR-TB warrants DR-TB risk re-assessment and a repeat Xpert test on fresh specimen, and if result shows RR-TB again; link the patient to TIC for Second line TB treatment; but if the repeat test result identifies TB but not RR-TB, initiate first line TB regimen as bacteriologically confirmed susceptible TB at TB clinic.

Note:

- ✓ *Xpert MTB/RIF test is recommended as initial diagnostic test for CSF in patients presumed to have TB meningitis.*
- ✓ *One sputum sample for the facility which have Xpert test and two sample for sample referring facilities.*

Antibiotic trial: Antibiotic trial has a role to treat concomitant bacterial infection for PLHIV with cough or serious illness. However, antibiotic trial is not helpful in the diagnosis of TB in HIV positives.

Table 4.5: Extra pulmonary TB diagnostic approaches in HIV positive patients.

Type of TB	Evidences Strongly Suggestive of EPTB	Investigations and recommendations
Lymph Node TB	2cm or more in size, Asymmetrical/localized; Painless swelling; Firm/fluctuated; Cervical location; patient with weight loss, night sweats, fever	LN Aspirate for AFB has 85% yield, if not possible to do FNAC of LN, start anti-TB.
Pleural effusion	Unilateral effusion; Aspirate of fluid is clear and straw colored and clots on standing in a tube without anti-coagulants or pleural fluid analysis shows protein >30g/L & >50% lymphocytes; Patients with weight loss, night sweats, fever, or evidence of TB elsewhere	Start anti-TB as soon as possible.
Tuberculosis Meningitis	Patients with weight loss, night sweats, fever; Cerebrospinal fluid clear with high protein, low glucose and lymphocytes; Cryptococcal antigen (or Indian Ink and fungal culture) negative in CSF Evidence of TB elsewhere	Admit patient, start anti-TB with steroids as soon as possible. Start treatment for cryptococcal meningitis based on clinical or lab evidences. Note: GeneXpert test has to be conducted on CSF specimen as an initial diagnostic test as much as possible.
Pericardial Effusion	Hemodynamically significant pericardial effusion, often with pleural effusions, Lung	CXR, Echocardiograph or chest ultrasound; pericardiocentesis, and

	fields clear and intra-thoracic lymphadenopathy. Usually patients with weight loss, night sweats, fever. <u>N.B.</u> 90% of Pericardial Effusions in HIV positive patients in high-TB burden areas is due to TB.	pericardial biopsy; routine TB Workup. Start anti-TB as soon as possible
Disseminated TB	Patients with weight loss, night sweats, fever and cough; Abnormal CXR (which can include military pattern); Large spleen/liver, Anemia	Start anti-TB treatment (add antibiotics if critically ill)
TB of the Spine	Pain over localized area, children/adolescents –often thoracic vertebrae. Adults: frequently lumbar vertebrae.	Spinal imaging (e.g. X-Ray, MRI); FNA of vertebral lesions and /or paraspinous abscesses when feasible.

II. TB prevention with isoniazid preventive therapy

IPT is the use of Isoniazid to sterilize latent TB infection. Thus, isoniazid is given to individuals with latent infection with *Mycobacterium tuberculosis* in order to prevent reactivation to active disease. Screening for exclusion of active TB in HIV infected persons is the single most important step that should precede the decision to initiate IPT. So far, evidences strongly favor the benefit of IPT in eligible individuals. Studies have shown that providing IPT to people living with HIV does not increase the risk of developing INH-resistant TB. Therefore, concerns regarding the development of INH resistance should not be a barrier to providing IPT. The dose of INH is 300mg/day for adults and 10mg/kg for children. The duration of IPT is for six months. It is also desirable to provide vitamin B6 (25mg / day) to prevent INH-induced peripheral neuropathy.

Table 4.6: INH dosage for children and adolescents.

Weight ranges for Children (kg)	Number of 100 mg tablets of INH to be administered per dose	Dose given (mg)
< 5	½ tablet	50
5.1-9.9	1 tablet	100
10-13.9	1 ½ tablet or ½ adult tablet	150
14 -19.9	2 tablets	200
20 -24.9	2 ½ tablets	250
>25	3 tablets or one adult tablet	300

Contraindications of IPT

Individuals with any one or more of the following conditions should not receive IPT:

- Symptoms compatible with tuberculosis even if the diagnosis isn't yet confirmed.
- Active hepatitis (chronic or acute)
- Regular and heavy alcohol consumptions
- Prior allergy or intolerance to isoniazid
- Symptoms of peripheral neuropathy

NB: Past history of TB and current pregnancy should not be contraindications for starting IPT.

National policy:

- IPT should be administered at enrolment to HIV care after ruling out active TB.
- IPT is to be administered once and should not be repeated unless there is strong indication on its benefits which is to be decided by senior physician.
- IPT should be administered only for six months.
- IPT should not be administered right after completing full course of TB treatment
- IPT can be administered for patients who had history of TB treatment before three years.

Follow-up of patients on IPT

Patients should be given monthly supply of Isoniazid for the first three months and three months' supply for the remaining months. They will be assessed at each follow-up visit to:

- Evaluate adherence to treatment and to educate client.
- Evaluate for drug toxicity.
- Evaluate for signs and symptoms of active tuberculosis or other OI.
- Stop IPT if active TB is diagnosed and to immediately start anti-TB.

Treatment interruption management

If a patient has interrupted IPT without the medical personnel advice, the client should be traced (by adherence case managers/adherence supporters, HEW or through the index person) and treatment must be resumed after identifying and addressing the adherence barriers.

IPT is said to be completed if a patient completed the full course of therapy within nine months period (i.e. the six months doses should be finished in nine months' time).

If the client discontinues treatment for a period of less than three months:

- Resume the same course by adding for the missed doses at the end.

If the client discontinues treatment for a period of more than three months:

- Re-initiate new course of IPT for six months.

Repetition and prolongation of IPT: there are different experiences in different countries on IPT recommendation considering the local HIV and TB epidemiology. Repeating INH preventive therapy after the first cycle of IPT or the provision of IPT after completion of full course of TB therapy is not recommended.

III. Infection control

People living with HIV are at high risk of acquiring TB in health care facilities and congregate settings. Each health care facility should have a TB infection control plan for the facility that includes administrative, environmental and personal protection measures to reduce the transmission of TB in health care and congregate settings and surveillance of TB disease among workers. Health care workers with HIV should be provided with ART and IPT if they are eligible.

Summary of recommendations for key actions for infection control

Administrative (facility-level infection control committee and protocols):

- A triage system to identify people suspected of having TB.
- Separate people with suspected or confirmed TB.
- Cough etiquette and respiratory hygiene.

Health workers and care providers

- Surveillance and information.
- Package of care for HIV-positive workers (ART and isoniazid preventive therapy).
- Protective equipment (particulate respirator masks that meet or exceed N95 standards).
- Relocation for health care workers living with HIV to a lower-risk area.

Environmental

- Ventilation (mechanical)
- Ventilation (natural)

Personal

- Spend as much time as possible outside.
- Cough etiquette.
- Sleep alone while smear-positive.
- Avoid congregate settings and public transport while smear-positive.

Reduce the burden of HIV in patients with presumptive and confirmed TB

Provide HIV testing and counseling to presumptive and confirmed TB patients

HIV testing is an entry point for HIV care and treatment services including ART. This equally applies to TB patients. Significant proportions of TB patients are co-infected with HIV. Among TB patients who are also HIV-infected, other OIs are significant causes of morbidity and mortality even with a successful treatment of TB. Hence, HIV testing and counseling should be routinely offered to all TB patients.

Presumptive treatment of TB for people living with HIV

The rationale for presumptive TB treatment is to prevent the death of people with HIV in situations where expedited diagnosis of TB is not possible or feasible due to the clinical condition of the patient or limited access to TB diagnostic services. While there is no case definition of presumptive TB, WHO algorithms include initiation of TB treatment for people with HIV in peripheral facilities based exclusively on clinical suspicion (without TB investigations) for seriously sick patients (with respiratory distress) based on the judgement of the clinician. This approach is based on expert opinion and emphasizes that every effort should be made to confirm the diagnosis of TB after initiation of presumptive treatment and that treatment should be stopped only if there is bacteriological, histological or strong clinical evidence of an alternative diagnosis.

Introduce HIV prevention interventions for presumptive and confirmed TB patients

All clients attending TB clinics should be screened for STI using a set of simple questions. Those with symptoms of STI should be treated or referred to the treatment providers. (Refer to the National Guideline for the Treatment of STI using the Syndromic Approach.) Condoms should be made available in TB clinics.

Provide co-trimoxazole preventive therapy for HIV positive TB patients

Co-trimoxazole is a safe and broad-spectrum antibiotic with activity against a broad range of bacterial, fungal and protozoal infections that are common cause for morbidity and mortality in HIV infected populations. Therefore, CPT is recommended to all TB/HIV co-infected patients

regardless of their CD4 Count. All PLHIV with TB and receiving CPT should be registered on the unit TB register, as well as the Pre ART/ART Register. They should also be monitored monthly.

Ensure HIV prevention, treatment and care for HIV positive TB patients

Referral linkages between TB and HIV services must be strengthened to provide comprehensive HIV prevention services for TB patients and their families. Tuberculosis control program should implement procedures for prevention of occupational and nosocomial exposure to HIV infection in their services. Health units should be equipped with protective materials and routinely follow standard precautions to prevent HIV transmission in the healthcare settings. Linkage should be ensured for pregnant and non-pregnant HIV positive clients to access services for prevention of mother to child transmission. TB clinics should establish linkage with HIV services to provide the continuum of care and support for HIV positives during and after completion of anti-TB treatment.

Provide antiretroviral therapy for HIV positive TB patients

ART should be provided to all HIV positive TB patients regardless of CD4 count or WHO stage. Ant-tuberculosis treatment should be provided first, followed by ART as soon as possible within the first 8 weeks of treatment.

Management consideration for TB/HIV Co-infections

In the management of TB/HIV co-infection, treatment of tuberculosis is always given priority over ART. As soon as HIV is identified in a TB patient, the patient should be enrolled to HIV chronic care. Ideally, the HIV care can be delivered at the TB clinic for the duration of TB treatment. In settings where this is not possible, there should be a strong referral system in place to link the TB/HIV co-infected patient to the HIV clinic promptly. Appropriate clinical, psychosocial and laboratory evaluations (including complete blood count, chemistry tests and CD4 count tests) as per the national guidelines for ART should be performed as soon as possible. Patients should be initiated on CPT and ART regardless of CD4 count or WHO clinical stage and ART regardless of CD4 count or WHO clinical stage. ART is recommended for all HIV infected TB patients regardless of CD4 count or WHO clinical stage. CD4 cells count shall preferably be determined for all HIV infected TB patients. The preferred regimen for TB/HIV co-infected adult patients is TDF+3TC+EFV, regardless of pregnancy status.

Multidrug-resistant TB and HIV

Multidrug-resistant TB (MDR-TB) is defined as TB that is resistant to at least isoniazid and rifampicin. Patients with both HIV and MDR-TB face complicated clinical management, fewer treatment options and poor treatment outcomes.

Outbreaks of MDR-TB among people with HIV have been documented in hospital and other settings, especially in Eastern Europe and in Southern African countries with a high HIV prevalence. People with HIV with suspected drug-resistant TB should be tested using Xpert MTB/RIF where possible, since this test is more sensitive for detecting TB among people with HIV and rapidly detects rifampicin resistance, thus greatly shortening the time to diagnose and treat MDR-TB.

The burden of MDR-TB can be reduced by strengthening HIV prevention, improving infection control and improving collaboration between HIV and TB control activities, with special attention to the groups at the highest risk of MDR-TB and HIV infection, such as people who inject drugs and those exposed in congregate settings.

4.2.2. Bacterial pneumonia

This can occur in immune-competent individuals but in HIV-infected patients, particularly those infected with *S. pneumoniae*; incidence of bacteremia accompanying pneumonia is increased compared with individuals who are not HIV infected. Bacterial pneumonia occurs during the whole spectrum of HIV disease, but tends to be more severe and recurrent as the CD4 counts drops significantly. In addition pneumonia can concomitantly present with sinusitis and/or bacteremia. If not treated promptly, extra pulmonary complications like empyema, meningitis, pericarditis, hepatitis and arthritis can follow. *Streptococcus pneumoniae* and *Haemophilus influenzae* are the most common etiologies of community acquired pneumonia.

Clinical manifestation

Typically the patient presents with sudden onset of cough, sputum production, chest pain, fever and/or shortness of breath.

Diagnosis

The clinical suspicion is based on a history of acute symptoms presented over days to a few weeks and/or abnormal physical signs of systemic infection and consolidation in the affected lung/s. Radiologic imaging can assist in confirming the diagnosis of pneumonia.

Treatment

For none sever pneumonia Amoxicillin 1000mg TID or erythromycin 500 mg QID or doxycycline 100 mg BID for seven days. Avoid doxycycline in pregnancy. Alternative, Azithromycin 500 mg PO per day for three days, Clarithromycin 500 mg twice daily for seven days. If not improving after three days and if patient is adherent to the antibiotic, review and consider switching to IV regimen, Ceftriaxone 1-2gm IV once per day plus erythromycin 500 mg oral or IV four time a day.

For pediatric age groups: For none sever pneumonia Amoxicillin 40mg/kg divided in to three doses per day for seven days. In children and infants allergic to penicillin, use Erythromycin; for infants aged one month up to two years, erythromycin 125 mg four times daily for seven days; for age groups 2-8 years, erythromycin 250 mg four time per day for seven days; for age groups above 8 years give erythromycin adult dose. If not improving after three days and if patient is adherent to the antibiotic, review and consider switching to IV ceftriaxone 75-100gm per kg IV/IM once a day or equally divided dosed twice a day for 7 to 10 days. Maximum dose 2-4gm per day for seven days.

When the patient has presented with clinical evidence of severe pneumonia, which includes tachypnea (RR>30/minute), old age (>70 years), cyanosis, hypotension, systolic blood pressure <80mm Hg, multi-lobar involvement and altered mental status in adults, and chest in-drawing, grunting and presence of danger signs in children, admit for parenteral antibiotic treatment and supportive therapy or refer the patient if admission is impossible. Tachypnea for children: Birth to 2 months RR >60/minute, 2 months to 1 year RR> 50/minute, 1 year to 5 years > 40 and 5 years and above RR> 30/minute.

4.2.3. *Pneumocystis pneumonia*

Pneumocystis pneumonia is caused by *Pneumocystis jiroveci*, formerly known as *pneumocystis carinii pneumonia*, a ubiquitous organism that is classified as a fungus but also shares biologic characteristics with protozoa. It commonly occurs when patients have significant immune suppression ($CD4 < 200 \text{ cells/mm}^3$ or $CD4 \text{ percentage} < 14\%$).

Clinical manifestation

Typical clinical presentations are characterized by insidious onset of low grade fever, dry cough, and dyspnea exacerbated by exertion. Physical examination reveals fever, tachypnea, tachycardia and scattered rales in the lungs but examination of the lungs can appear normal in some patients. In children highest incidence is seen between 2-6 months of age and is characterized by abrupt onset of fever, tachypnea, dyspnea and cyanosis.

Diagnosis

Presumptive diagnosis of PCP is based on clinical judgement and typical chest X-ray findings revealing a perihilar interstitial infiltration with tendency to spread outwards. Note that the chest X-ray can be normal in 20% of patients. Definitive diagnosis of PCP is based on demonstration of the organism from an induced sputum sample using special stains like Giemsa or methylene silver stains, but these tests are not routinely done in Ethiopia. .

Treatment

Use Trimethoprim 15-25 mg/Kg, three or four times daily for 21 days. Close monitoring is necessary during the initial five days of treatment and if patient grows sicker, administration of oxygen is useful. In severely ill patients with marked respiratory distress and extensive chest X-ray findings, prednisolone has to be given simultaneously; 80mg for the first five days, 40 mg until 11 days and 20 mg until completion of intensive co-trimoxazole therapy. For severe cases of PCP in children provide prednisolone 2mg/kg per day for the first 7 - 10 days followed by a tapering regimen for the next 10 - 14 days. Toxicity of co-trimoxazole, like skin rash, bone marrow suppression, hepatitis and renal failure can be troublesome in some patients with advanced HIV disease and requires close monitoring.

Secondary prophylaxis after completion of the course of treatment with co-trimoxazole should be continued. (Refer Table 4.2).

Alternative regimens for mild to moderate cases of PCP include:

1. Clindamycin 600 mg qid plus primaquine 15 mg bid; or
2. Clindamycin 600 mg qid plus dapsone 100 mg daily.

Consider spontaneous pneumothorax in patients with sudden deterioration in clinical condition.

4.2.4. *Lymphoid interstitial pneumonitis*

Lymphoid interstitial pneumonitis (LIP) is one of the most common chronic lower respiratory conditions occurring in up to 25% of children with HIV/AIDS.

Clinical manifestations

It ranges from asymptomatic disease with isolated radiographic findings to bullous lung disease with pulmonary insufficiency. Symptomatic children present with insidious onset of tachypnea, cough, and mild to moderate hypoxemia with normal auscultatory findings or minimal rales or wheezing. Progressive disease is accompanied by digital clubbing and symptomatic hypoxemia. Associated physical findings include generalized lymphadenopathy, hepatosplenomegaly and parotid enlargement.

Diagnosis

It is usually based on clinical examination findings. Diffuse bilateral reticulonodular infiltrate on X-ray with mediastinal lymphadenopathy. It is important to exclude tuberculosis and other infectious etiology.

Treatment

Provide symptomatic treatment (hydration, oxygen). Use antibiotics if there is a superimposed bacterial infection. Bronchodilators may be helpful in mild to moderate disease. Corticosteroids

are usually reserved for children with significant hypoxemia and symptoms of pulmonary insufficiency. Give prednisolone 1 – 2 mg/kg/24 hrs for 6 – 8 weeks and then taper as tolerated.

4.3. Management of gastrointestinal opportunistic diseases

The gastrointestinal (GI) OI diseases commonly manifest with diarrhea, nausea and vomiting, dysphagia and odynophagia among others. There are a number of opportunistic and pathogenic organisms causing GI disease in patients infected with HIV most common ones being *Isospora belli*, *cryptosporidium*, *shigella* and *salmonella*, CMV etc. A scenario of multiple concurrent GI infections is fairly common. The general principle of managing GI opportunistic infections is identifying and treating the specific offending agent and providing supportive care to monitor situations such as fluid loss. A number of drugs can cause adverse effects that present with clinical manifestations which are similar to OI of the GI, posing challenges in differential diagnosis.

4.3.1. Dysphagia and odynophagia

Dysphagia (difficulty in swallowing) and odynophagia (painful swallowing) are symptoms of esophagitis occurring at advanced stages of AIDS. They are usually caused by candida, HSV, CMV, and aphthous ulcers. As well as a sign of severe immunodeficiency, esophagitis also seriously impairs the patient's nutritional status. Therefore prompt diagnosis and treatment are mandatory to avert nutritional complications and inability to swallow prescribed medications. Children will present with reluctance to eat, excessive salivation, or crying while feeding. If thrush is associated with dysphagia, odynophagia, and/or retrosternal pain, consider oesophageal candidiasis but this can also occur in the absence of oral thrush. Thrush or oropharyngeal candida is characterized by white, painless, plaque-like lesions on the buccal surface and/or tongue.

Diagnosis

It is frequently made on clinical grounds, but when facilities are available upper GI endoscopy with or without biopsy or contrast imaging may be done.

Treatment

Dysphagia and/or odynophagia are treated as oesophageal candida on clinical grounds, in particular when oropharyngeal candida is present. Patients are empirically treated with Fluconazole in presumptive oesophageal candida. If the response is unsatisfactory they should be referred or investigated if facilities are available, to rule out other causes.

- Drug of choice: Fluconazole 200 mg (3 mg/kg/day in children) PO daily for 14 days.
- Alternatively, ketoconazole 200 mg (3-6mg/kg/day daily in children) twice daily for 4 weeks.

Risk of recurrence after completing treatment may be high. If the patient is on ART, s/he should be investigated for treatment failure. Take necessary precautions regarding drug interactions especially with ketoconazole. Patients may need hospital admission for supportive care till the oesophageal symptoms improve and necessary long term treatments are started. If diagnosis suggests HSV esophagitis use acyclovir 400mg po five times for 14 to 21 days.

4.3.2. Diarrhoea

Diarrhea is defined, as passing more than three loose or watery stools per day. It may be acute or chronic, persistent or intermittent. Diarrhea is among the most frequent symptoms of HIV disease. Delay in treatment can result in fluid loss and hemodynamic instability. Chronic diarrhea may also lead to nutritional deficiencies and wasting. Diarrhoea is caused by opportunistic or pathogenic organisms, such as viruses (including HIV), bacteria, protozoa, fungi, helminthic, non-infectious causes and drugs. (Diarrhoea occurs as an adverse reaction to a number of drugs).

Check the duration, volume, frequency, consistency of stools as well as any history of abdominal pain, tenesmus, nausea, vomiting, and presence of constitutional symptoms such as fever. Thorough physical examination is necessary to find out the state of hydration and the status of HIV disease.

Laboratory evaluation

Stool microscopy including modified acid fast stain. Stool culture when indicated (optional).

Management

The most important first step is correction of fluid loss. Depending on the severity of dehydration, oral rehydration solution (ORS) or IV fluid therapy can be given. Patients with severe dehydration need to be admitted for intravenous fluid administration. In children zinc 20mg per day for 10-14 days (10mg per day for infants < 6 months of age) should be added.

If specific enteric pathogen is identified or strongly suspected on clinical grounds, it should be treated accordingly. (Refer to the IMNCI module to manage dehydration).

Table 4.7: Treatment of specific enteric pathogens.

Agent	CD4	Symptom	Diagnosis	Rx
E. histolytica	any	Bloody stool, colitis	Stool microscopy	Metronidazole
Giardia	any	Watery diarrhoea	Stool microscopy	Metronidazole
Cryptosporidium	<150	Watery diarrhoea	Modified AFB	ART*
Isospora belli	<100	Watery diarrhoea	Modified AFB	TMP-SMX
Microsporidium	< 50	Watery diarrhoea	Giemsa stain	Albendazole
CMV	<50	Watery/bloody diarrhoea, colitis	Tissue biopsy	Ganciclovir

*No specific treatment for Cryptosporidium but it will improve with immune restoration following ART.

Patients with bloody diarrhoea but repeatedly negative stool results: empirical treatment with ciprofloxacin or norfloxacin (co-trimoxazole in children) can be given, especially when patient has constitutional symptoms such as fever.

Symptomatic treatment

In adults use anti-diarrhoeal agents Loperamide 4 mg stat then 2 mg after each bowel motion or Diphenoxylate 5mg QID. Necessary caution should be taken to avoid anti-diarrhoeal agents in bacterial or parasitic infectious colitis or enteritis, since toxic mega colon may occur.

Patients with chronic diarrhoea will develop nutritional deficiencies of variable severity; therefore proper nutritional assessment and support are helpful.

4.3.3. *Peri-anal problems*

A number of chronic or acute peri-anal problems commonly occur in patients with HIV disease, particularly in advanced stages of immunodeficiency. These include recurrent peri-anal abscesses, chronic peri-anal fistula, peri-anal herpes (severe, persistent and extensive), and peri-anal warts (sometimes large with obstructive problems). Patients with peri-anal problems frequently go to local healers and receive different kinds of local therapy that usually complicate the situation.

Treatment of peri-anal abscess in adolescents and adults

It is not difficult to make the clinical diagnosis of peri-anal abscess. All patients with acute or chronic peri-anal condition must be thoroughly evaluated and per rectum examination should be done routinely. Peri-anal abscess may extend depending on the immunological status of the patient; therefore early treatment is mandatory to avoid this and more serious morbidity. If patients require surgical incision, it should be done promptly on first visit, or referral made if the surgery is unavailable. Otherwise, broad spectrum antibiotics such as amoxicillin-clavulanic acid or alternatively amoxicillin or ampicillin must be administered in sufficient dose for at least 10 days. Palliative care including Sitzz baths and analgesics are also important.

Peri-anal and/or genital herpes

Latent or active infection with HSV I and II are common in the general population, and is usually mild in immune-competent persons. Severe cutaneous disease or visceral involvement is usually restricted to patients with advanced immunosuppression with a CD4 count $<100 \text{ cell/mm}^3$.

The lesions become extensive, persistent, severe and sometimes with bleeding. Unless thorough evaluation with regular inspection of genital and peri-anal areas is done, patients very often don't complain about genital lesions. The response to Acyclovir is gratifying if it is done in sufficient dose (400mg 4-5 time/day) and sufficient duration (10 days to 2 weeks in moderately severe or severe cases). There is risk of recurrence with severe immunodeficiency. In such cases repeat

treatment and put patient on chronic HIV care including ART. Herpetic oro-labial infection is treated the same way as ano-genital herpes.

The treatment of anal and genital warts is particularly frustrating when they are large. Unlike other opportunistic infections, the response to ART is not satisfactory. Patients who have very well responded immunologically with ART continue to suffer from the warts. Depending on the size, cauterization, podophyllin treatment and surgical debulking, etc. may be tried. Patients should be referred to where these services are available.

Sexually transmitted infections and cervical cancer

The epidemiological synergy between HIV and sexually transmitted infections is well established, and they frequently coexist. Most of these infections are asymptomatic, especially among women. However, even asymptomatic STIs can cause complications, be transmitted to sexual partners and enhance HIV transmission. STI services should be an important part of comprehensive HIV care among adults and adolescents. Refer the revised STI guideline for syndromic management of STIs

Cervical cancer is a preventable disease and is curable if diagnosed and treated early. Women living with HIV have a higher risk of pre-cancerous lesions and invasive cervical cancer. The risk and persistence of HPV infection increases with low CD4 count and high HIV viral load. Cervical cancer screening leads to early detection of precancerous and cancerous cervical lesions that will prevent serious morbidity and mortality. Cervical cancer screening is an important test to prevent significant morbidity and mortality associated with HPV in women. All women with HIV should therefore be screened for cervical cancer. (Refer to guideline for cervical cancer prevention and control in Ethiopia, 2015).

HCV/HIV and HBV/HIV co-infection management

HCV HIV co-infection management

HIV patients are among high risk groups for HCV and should be given priority for screening. Therefore all HIV patients should be screened and confirmation VL test should be done for HCV screened positives.

Anti-HCV rapid diagnostic test (RDT) or immunoassay (IA) can be used for screening and HCV RNA viral load test using either quantitative or qualitative PCR should be used to confirm chronic HCV infection.

All chronic HCV infected individuals should be treated to eradicate the virus and achieve cure so that complications can be avoided. Follow up quantitative or qualitative HCV RNA viral load is required to confirm if the patient has achieved Sustained Virologic Response (SVR). This should be performed 12 weeks after the completion of therapy.

Treatment of HCV in HIV infected individuals is not different from non-HIV infected or HCV mono-infected. All combination of direct acting antiviral (DAA) including SOF/LDV, SOF/RIB and SOF/DCV can safely be used. However attention should be given to drug-drug interactions and shared side effects like head ache, fatigue and anemia.

According to the viral hepatitis prevention and control guideline, the following are treatment cited options (please consult the national viral hepatitis prevention and control guideline for further reference):

- Sofosbuvir 400 mg oral once daily + Daclatasvir 60mg oral once daily for 12 weeks (dose of DCV be adjusted to 90 mg with Efavirenz and 30 mg with Atazanavir/r)
- Sofosbuvir 400mg oral once daily + Ledipasvir 90mg oral once daily for 12 weeks.
- For cirrhotic patient the treatment duration will be extended to 24 weeks for the above treatment options.
- Sofosbuvir 400mg oral once daily + Ribavirin 1000mg (weight < 75kg), 1200mg (weight ≥ 75Kg) twice on divided doses for 24 weeks.

It is recommended to thoroughly evaluate Chronic HCV infected person with cirrhosis and treatment duration be decided according to the genotype, type of drug selected and addition of ribavirin.

HBV/ HIV co-infection management

HIV co-infection has been shown to have a profound impact on almost every aspect of the natural history of HBV infection and includes more rapid progression to cirrhosis and hepatocellular

carcinoma (HCC), higher liver-related mortality, and decreased treatment response compared with persons without HIV coinfection

HIV/HBV-co-infected persons also demonstrated more rapid HIV disease progression compared to those who were HIV-infected alone, and had an impaired recovery of CD4 cells. HIV patients are among the high risk groups for HBV and should be given priority for screening. i.e all HIV patients should get screened for HBV and evaluated for chronic infection as per the national viral hepatitis prevention and control guideline. After test result, vaccination or treatment and care for reactive patients are recommended when resources permit.

Treatment options for patients with HIV–HBV Co-infection:

- ART should be initiated in all individuals with HIV regardless of WHO clinical stage or CD4 count in the following situations:
 - Individuals co-infected with HIV and HBV with evidence of severe chronic liver disease. During HBV/HIV co-infection if treatment is indicated for HBV, combination antiretroviral therapy should be initiated with drugs containing TDF+3TC (or FTC) + EFV as a preferred regimen
- For HIV positive patients who are co infected with HBV and qualify for treatment of both the diseases i.e. HIV and HBV, oral drug therapy is first line for these patients with at least 2 of the drugs having activity against HBV like combination of Tenofovir, Emtricitabine/ lamuvidine and Efavirenz.
- The use of lamivudine as mono-therapy in any of these diseases is contraindicated due to high YMDD resistance.
- When switching treatment in patients with HIV on ART failure, the regimen that will continue should have two of the drugs having activity against HBV.
- If tenofovir-associated renal toxicity occurs, the dose of tenofovir should be adjusted according to the renal clearance.

NB: For further reference please consult the national Viral Hepatitis prevention and control guidelines

4.4. Management of opportunistic diseases of the nervous system

Neurological manifestations of HIV can occur at any time from viral acquisition to the late stages of AIDS. They are varied and may affect any part of the nervous system including the brain, spinal cord, autonomous nervous system and the peripheral nerves. HIV affects the nervous system in 70-80% of infected patients. The effect may be due to direct effect of the virus, opportunistic infections and/or malignancies. For certain neurological manifestations, a single aetiology is responsible while in others it is due to multiple causes.

Most life-threatening neurological complications of HIV occur during the severe immunodeficiency state and specific aetiological diagnosis in the Ethiopian setting is often a major challenge. Thus, this unit attempts to guide the management of common opportunistic infections and other treatable conditions in the nervous system.

Neurological complications in HIV patients may be due to:

- HIV (HIV encephalopathy)
- OIs (toxoplasmosis, cryptococcal meningitis)
- Neurosyphilis
- Malignancies (primary CNS lymphoma); and
- Drugs (e.g. EFV, etc.)

Diagnosis of neurological disorders in HIV in our setting depends on the history and standard neurological examinations. In view of this, health care providers must be able to perform a physical examination to detect neurological abnormalities. There can be single or multiple abnormal neurological findings in the same patient necessitating holistic neurological evaluation. Thus the examination should include assessment of:

- Mental status comprising cognitive function, orientation and memory.
- Cranial nerves.
- Motor function including deep tendon reflexes (DTR).
- Sensation.

4.4.1. *Toxoplasma gondii* encephalitis

Toxoplasmic encephalitis (TE) is caused by the protozoan *Toxoplasma gondii*. Disease appears to occur almost exclusively because of reactivation of latent tissue cysts. Primary infection occasionally is associated with acute cerebral or disseminated disease. Sero-prevalence varies substantially in different communities; in Ethiopia, general prevalence is about 80%.

Clinical Manifestations

Among patients with AIDS, the most common clinical presentation of *T. gondii* infection is focal encephalitis with headache, confusion, or motor weakness and fever. Patients may also present with non-focal manifestations, including only non-specific headache and psychiatric symptoms. Focal neurological abnormalities may be present on physical examination, and in the absence of treatment, disease progression results in seizures, stupor, and coma.

Diagnosis

HIV-infected patients with TE are almost uniformly seropositive for anti-toxoplasma immunoglobulin G (IgG) antibodies. The absence of IgG antibody makes a diagnosis of toxoplasmosis unlikely but not impossible. Anti-toxoplasma immunoglobulin M (IgM) antibodies usually are absent. Quantitative antibody titres are not useful for diagnosis. Definitive diagnosis of CNS toxoplasmosis requires a compatible clinical syndrome; identification of one or more mass lesions by CT, MRI, or other radiographic testing; and detection of the organism in a clinical sample. In the absence of imaging support, empirical treatment is justified when patients present with focal neurological findings and the CD4 count is < 200 cells μl . Failure to respond to conventional therapy, based on presumptive clinical diagnosis within a week or two of initiation of therapy, suggests the diagnosis to be unlikely. With empirical treatment for toxoplasmosis, nearly 90% of patients will demonstrate clinical improvement within days of starting therapy. Radiological evidence of improvement is usual after 14 days of treatment.

Treatment

1st line regimen in the Ethiopian context is:

Trimethoprim/sulfamethoxazole 80/400, oral, 4 tablets 12 hourly for 28 days, followed by 2 tablets 12 hourly for 3 months in adults.

In children 10mg of trimethoprim + 50mg of sulfamethoxazole/kg per dose every 12 hours for 28 days followed by maintenance therapy at 50% reduced dosage for three months.

Secondary prophylaxis: use co-trimoxazole 960mg daily for adults and in children. Refer to Table 4.2

Alternative regimen

- I.** Sulfadiazine, 1-2 gm PO QID for six weeks or 3 weeks after resolution of lesion

Side effects: crystal urea, rash

Contraindication: severe liver, renal and hematological disorders; known hypersensitivity to Sulphonamides.

Dosage/form: 500 mg tablets,

PLUS

Pyrimethamine: loading dose of 200 mg once, followed by 50-75 mg/day.

Side effects: rash, fever and bone marrow suppression (neutropenia and thrombocytopenia).

Contraindication: folate deficiency

Dosage/form: 25 mg tablets

PLUS

Folinic acid (Leucovorin): 10-20 mg/d

Side effects: allergy

Dosage/form: 5 and 10 mg tablets

OR

- II.** Pyrimethamine and Folinic Acid (Leucovorin): (standard dose)

PLUS

Clindamycin: 600 mg QID

Side effects: toxicities include fever, rash, nausea and diarrhoea (including pseudomembranous colitis or diarrhoea related to Clostridium difficile toxin).

Adjunctive corticosteroids should be used for patients with radiographic evidence of midline shift, signs of critically elevated intracranial pressure or clinical deterioration within the first 48 hours of therapy. Dexamethasone 4 mg every six hours (0.15mg/kg/dose every 6 hours for children) is usually chosen and is generally tapered over several days and discontinued as soon as possible.

Anticonvulsants should be administered to patients with a history of seizures, but should not be given routinely for prophylaxis to all patients with the presumed diagnosis of TE. Careful attention needs to be paid to any potential drug interactions.

4.4.2. Cryptococcal infection

Cryptococcal meningitis is one of the most important opportunistic infections and a major contributor to high mortality before and after ART is initiated. The main reasons for this high death rate include delayed presentation, together with poor availability and high cost of treatment. Furthermore, there are no standardized guidelines applicable to resource-limited settings for the diagnosis and management of cryptococcal disease. Most HIV-associated cryptococcal infections are caused by *Cryptococcus neoformans*. In HIV-infected patients, cryptococcosis commonly presents as a subacute meningitis or meningoencephalitis with fever, malaise, and headache. Classic meningeal symptoms and signs, such as neck stiffness and photophobia, occur in only one-quarter to one-third of patients. Some patients experience encephalopathic symptoms, such as lethargy, altered mentation, personality changes, and memory loss that are usually a result of increased intracranial pressure, thought to result from impaired CSF absorption, or yeast infection of the brain.

Diagnosis

1. Lumbar puncture (LP) and CSF analysis:
 - The opening pressure may be markedly elevated.
 - CSF analysis
 - Protein: 30-150 mg/dl
 - WBC: 0-100 /mm³ (monocyte)
 - Culture: positive 95-100%
 - Indian ink: positive 60-80%

- Cryptococcal: Ag > 95 % sensitive and specific

If it is not possible or contraindicated to do LP, serum cryptococcal antigen can be used for diagnosis.

Management

Requires hospitalization and evaluation by physician

Phases of management:

1. Induction phase (2 weeks)

Option A. High dose fluconazole- Fluconazole 600 mg twice daily alone (In children 12mg/kg twice daily):

Option B. Amphotericin B + fluconazole:

Amphotericin 0.7-1 mg/kg/day + fluconazole 800 mg/day

2. Consolidation phase (8 weeks)

Option A: Fluconazole 800 mg/day (In children 12mg/kg/day)

Option B: Fluconazole 400-800 mg/day

Maintenance treatment (or secondary prophylaxis) - Fluconazole 200 mg daily (in children 6mg/kg/day).

Additional points about cryptococcal meningitis

1) Management of elevated intracranial pressure (ICP):

Management of increased ICP is critical as >90% of deaths in the first two weeks and 40% of deaths in weeks 3-10 are due to increased ICP. Failure to manage elevated ICP is the most common and most dangerous mistake in management (since the ICP is non-communicating hydrocephalus there is no risk of CSF tapping within the recommended volume).

- Daily serial LP should be done to control increased ICP by drawing 20-30 ml of CSF based on patient's clinical response. Signs of ICP include headache, altered mental status, meningismus and changing in hearing or vision should be closely monitored, if possible opening pressure should be measured.
- There is no role for acetazolamide, mannitol, or corticosteroids to reduce intracranial pressure.

2) Discontinuation of maintenance treatment (secondary prophylaxis)

When patients are stable and adherent to ART and anti-fungal maintenance treatment for at least one year and have a CD4 cell count of greater than or equal to 200 cells/mm³ (two measurements six months apart).

3) Timing of ART initiation

- Immediate ART initiation is not recommended in HIV-infected patients with cryptococcal meningitis due to the high risk of IRIS, which may be life-threatening.
- ART initiation should be deferred until there is evidence of a sustained clinical response to anti-fungal therapy, and
- After 2-4 weeks of induction and consolidation treatment with amphotericin B-containing regimens combined with fluconazole, or
- After 4-6 weeks of induction and consolidation treatment with high-dose oral fluconazole regimen.

Poor prognostic signs

- Extra CNS manifestation (especially pulmonary)
- Altered mental status
- Low CSF WBC count less than 20 cells/ μ L
- High CSF cryptococcal antigen titer

Prevention of cryptococcal disease

According to a pilot study conducted in Ethiopia from June 2015 to July 2016, in 22 high case load facilities in all regions, the proportion of newly enrolled clients with CD4 count less than 100 cells/mm³ was 25.88%. In the same study the prevalence of clients screened positive for cryptococcal antigenemia was high (9.9%).

The use of routine serum or plasma CrAg screening in ART-naïve adults followed by pre-emptive antifungal therapy if CrAg screening is positive to reduce the development of cryptococcal disease, should be considered prior to ART initiation:

- ✓ Where patients with a CD4 count less than 100 cells/mm³; and
- ✓ Where this population also has a high prevalence (>3%) of cryptococcal antigenemia.

The following algorithm or decision making guide shows how to decide whether a patient needs prophylactic fluconazole treatment to CrAg screening positive and asymptomatic patients with CD4 count less than 100cells/ μ l.

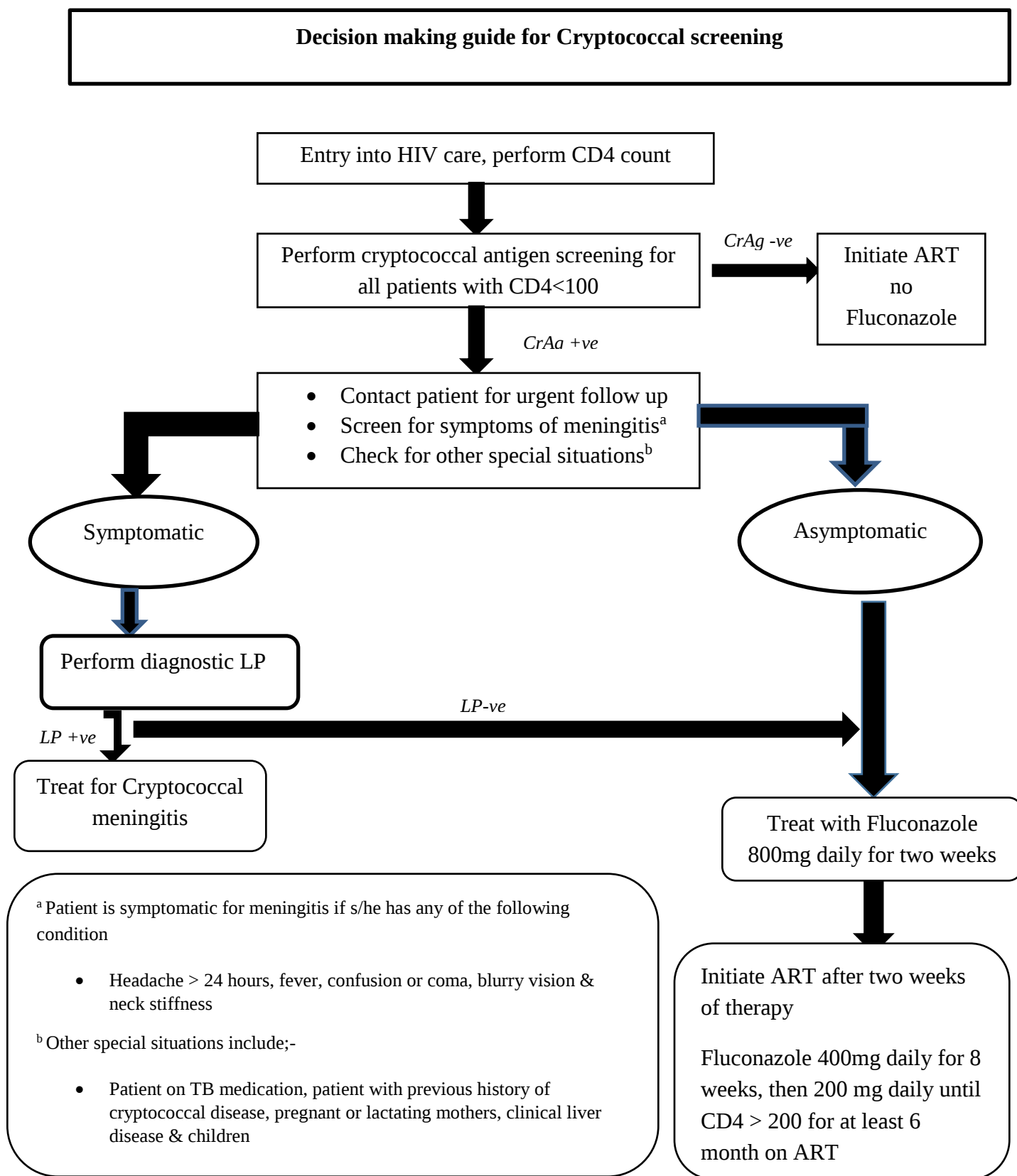


Figure 4.5: Decision making guide for cryptococcal screening

4.4.3. *Peripheral neuropathies*

Peripheral neuropathies are among the most common causes of painful legs in HIV infection; they arise as a complication of HIV infection itself, of drug therapy, or of other metabolic or organ dysfunction or nutritional deficiencies.

Distal symmetrical sensory polyneuropathy is the most common presentation but mono-neuropathies can also occur. The neuropathies associated with HIV can be classified as:

- Primary, HIV-associated.
- Secondary causes related to medications (INH), OIs or organ dysfunctions.

Diagnosis

Peripheral neuropathy diagnosis in HIV-infected patients is based on the clinical picture presenting with pain, tingling sensations, paresthesia or numbness. Physical examination can reveal depressed or absent ankle reflex, decreased sensitivity to different modalities of sensation and in severe cases, difficulty in walking. The feet and sometimes the hands are involved in symmetrical distribution. The diagnosis can be supported by electro diagnostic studies including electromyography (EMG) and nerve conduction studies (NCS) when available. Blood tests are frequently obtained to exclude other causes of neuropathy. In most instances, however, diagnosis is almost always clinical.

Treatment

- Avoid the offending agent if identified.
- Remove other drugs associated with peripheral neuropathy.
- Supplemental vitamin intake for all patients including concomitant administration of pyridoxine with INH.
- Adjuvants for pain management (such as Amitriptlin, carbamazepin) indicated for patients with pain and paraesthesia.

Monitoring of events

- Recognize presence of peripheral neuropathy.
- Assess severity at each clinical visit.
- Avoid drugs causing neuropathy.

4.5. Cutaneous manifestations

The skin is an organ frequently affected by OI; early manifestations of HIV infection frequently occur in the skin. Different kinds of OI, such as herpes zoster, and other viral, fungal and bacterial infections occur in the skin. Manifestations of adverse drug reactions and non-infectious conditions also occur in the skin. Some skin reactions to drugs such as Nevirapine may be life-threatening. In most instances diagnoses of skin disorders with HIV disease are made on clinical grounds. Most skin disorders in HIV disease can be cured or ameliorated, but a few fail to improve even with good general clinical and immunological responses to ART.

Pruritus is the most common dermatologic symptom in HIV infected patients. It can be localized indicating primary skin lesion, or generalized that may or may not indicate primary skin lesions. In many patients pruritus may be severe and may not be amenable to available therapy. The most common skin conditions associated with pruritus in patients with HIV include the following:

2. Excessive dryness of the skin (Xerosis cutis)
3. Eczemas like seborrheic dermatitis or contact dermatitis
4. Folliculitis that may include infections by *Staphylococcus aureus* or hypersensitivity to insects
5. Drug eruptions
6. Scabies
7. Intertrigo (*Candida*, tinea, herpes simplex)

In most patients, diagnosis can be established by examining the lesions. However, as immune deficiency advances it may be useful to use investigations such as biopsy to diagnose specific dermatosis or use staining and culture to diagnose specific infections.

4.5.1. Etiological classification of skin disorders in HIV disease

Skin disorders in HIV infected patients can occur due to infections, neoplasm, and hypersensitivity to foreign agents including drugs, or to unknown causes. Nevertheless, infections are commonly seen in clinical practice; refer to the following table:

Table 4.8: Common skin infections in HIV disease.

Infections	Disease	Clinical Presentations	Treatment	Remark
Bacterial	Cellulitis	Poorly defined Erythema. Pus and crust at the site plus signs of inflammation.	Amoxicillin 500 mg TID for 14 days or erythromycin 500 mg QID if allergic to penicillin.	Mostly encountered lower extremities and often unilateral.
	Impetigo	Erythematous small papules usually limited to few lesions coalescing in to crusted plaques.	Use topical antibiotics: use Amoxicillin for extensive disease.	Usually a superficial lesion.
	Carbuncle	Nodular Lesion with extensions to the deeper Structure. Signs of Inflammation present.	Use Cloxacillin 500mg qid for ten days.	Involves the trunk as well as extremities.
Viral	Herpes simplex	Painful vesicular lesion around mouth or genitalia. Recurrent and extensive, difficult to eradicate during advanced immune deficiency.	Acyclovir 400mg t.i.d for ten days. In children 20 mg/kg/dose 4X/d	If Chronic (> one month) patient will benefit from immediate ART initiation if not on ART
		Painful and vesicular eruptions with dermatomal distribution. When healed, scar will remain.	Acyclovir 800mg 5X per day for seven days. Monitor renal function.	When it involves the eyes, it is a medical emergency. Do not give Acyclovir* if duration is >72 hours.
	Warts / verrucae	Painless flat to raised warts over fingers or genitalia in advanced immune deficiency, they tend to be multiple and exophytic.	Podophyllin, Imiquimod, Cryotherapy Consult experts	Premalignant and risk for cervical cancer.
	Molluscum Contagiosum	Umbilicated and raised facial lesions that tend to be very big during immunodeficiency state.	May not require therapy;	Contagious

Parasitic infestation	Scabies	Pruritic lesions ranging from pinpointed erythematous papules involving interdigital, axillae and groin areas to varying degrees of hyperkeratotic plaques associated with significant skin thickening and crusting.	BBL, lindane or permethrin to be applied to whole body. Ivermectin 200 microgram/kg stat orally.	Burrows are visible in mild infestations but in crust scabies may not be evident leading to misdiagnosis.
Fungus	Dermatophytosis	Superficial causing ringworm or athlete's foot	Topical antifungal for limited skin affected. Fluconazole for extensive lesion 100mg daily for ten days.	
	Thrush	White plaques on the buccal mucosa including the tongue that can be scraped off leaving red base. Can be associated with candida paronychia or intertrigo.	Miconazole gel 2% apply bid Fluconazole 100 mg daily for ten days for recurrent or oropharyngeal thrush.	
	Deep Fungal infection	Presentation varies from fungating nodules and tumors to ulcers and diffuse papulonodular disease	Disseminated Cryptococcus can be confused for Molluscum contagiosum. Treat with amphotericin induction and/or fluconazole maintenance.	

*If patient has ophthalmic involvement refer to ophthalmic specialist.

4.5.2. Pruritic papular eruption

Pruritic papular eruption is common among HIV infected patients causing substantial morbidity in sub-Saharan Africa. Its prevalence ranges from 12-46% and it is uncommon in HIV negative patients (PPV of 82-87%, and may play role in diagnosing HIV). The pathogenesis is unknown but it may be related to hypersensitivity to arthropod bites. In extreme form, eosinophilia and eosinophilic infiltrates of the skin are present. Severity of rash often correlates with CD4 count. The clinical manifestation is intensely pruritic, discrete, firm papules with variable stages of

development and predilection for extremities, though it can involve trunk and face. Excoriation results in pigmentation, scarring and nodules. Treat with topical steroid and oral antihistamines. However it is often refractory to treatment and hence short course prednisolone may be used. ART is often effective.

4.6. Visceral leishmaniasis

Visceral Leishmaniasis (VL) is a systemic parasitic illness, transmitted primarily by the phlebotomine sand fly from animal or human reservoirs. Visceral Leishmaniasis is endemic in Ethiopia, with patchy distribution in the southern and north-western lowlands. The causative parasite is *L. Donovanii*. VL has emerged as a major OI associated with HIV. In HIV patients, VL represents reactivation of latent infection with *Leishmania* parasite.

Clinical features

The cardinal signs of VL in patients with HIV infection are unexplained fever, splenomegaly and pancytopenia (anemia, leucopenia and thrombocytopenia). Presentation may not be typical. The bone marrow is packed with parasites but two-thirds of cases have no detectable anti *Leishmania* antibodies. CD4+ cell count in co-infected patients is usually <300cells/ml.

Diagnosis

Parasite Detection- Visualization of the amastigote form of the parasite by microscopic examination of aspirates from lymph nodes, bone marrow or spleen aspiration. *Culture improves the detection of the parasites. However, this technique remains restricted to referral hospitals or research centers.

Antibody Detection- DAT and rK39 have been extensively evaluated and used for the diagnosis of VL in the field and in laboratory settings.

Antigen Detection Test- It is more specific than the antibody-based immunodiagnostic test. Evaluation of the performance of A urine latex agglutination (KATEX) at the Indian subcontinent and East Africa has shown that this test has a good specificity but only a low to moderate sensitivity.

Molecular Techniques- Compared to the other diagnostic techniques available, the molecular approaches remain expensive and technically highly demanding. Their applicability in the endemic areas is highly questionable.

Treatment:

Ambisome 40mg/kg, require longer treatment and more liable to relapse.

Treatment of relapsed patients: These are patients who are slower to respond and have a higher chance of further relapse and of becoming unresponsive to anti-monal drugs. Treatment is the same as above.

4.7. Screening for co-morbidities

People living with HIV have got increased risk of non-AIDs defining chronic diseases such as diabetes mellitus, cardiovascular illnesses, malignancies, chronic liver disease and chronic renal disease. With the advent of ART, people are living longer; hence they are at risk for age related diseases. **Therefore, screening of PLHIV for these co-morbidities during every visit is a critical component of the care and treatment package.**

Chronic HIV care provides the opportunity for screening, monitoring and managing NCDs, especially through primary care. Integrating interventions such as nutrition assessment, dietary counselling and support, smoking cessation, promoting exercise, monitoring blood pressure and where available cholesterol as part of HIV care are opportunities for reducing the risks of NCDs among people living with HIV. WHO has defined a package of essential NCDs (WHO PEN) interventions along with recommendations on screening for and treating NCD.

HIV and Mental Health Illnesses

The co-occurrence of mental illness for individuals living with HIV significantly magnifies the burden of their disease. Mental illness has been associated with increased risk for HIV infection, and has been noted to occur at higher rates for HIV-infected individuals around the time of diagnosis or during the course of their illness. Further complicating the course of illness are the strong associations between the occurrence of psychiatric symptoms and poor adherence to antiretroviral treatments. Evidence suggests that treatment of co-morbid psychiatric conditions

may improve adherence to ART, underlining the importance of recognition and treatment of psychiatric conditions.

Evidence further points to continued under-recognition and under treatment of these conditions among HIV-infected individuals. Factors contributing to under-recognition of psychiatric symptoms relate to:

- The overlap between the symptoms of depression and symptoms of HIV disease.
- The recognition of certain psychiatric disorders, specifically depression and anxiety, is the mistaken belief that these symptoms are expected in those diagnosed with HIV disease. Depressive or anxiety symptoms that are more severe or that persist beyond the period of initial discovery of HIV infection should prompt evaluation and treatment.
- The neuropsychiatric side effects associated with some ARVs. Zidovudine, nevirapine, abacavir, and efavirenz have been associated with neuropsychiatric symptoms.

Another reason why mental health problems are more common among people with HIV/AIDS is that having a mental health problem is one of the risk factors for becoming infected with HIV. People with mental health problems are more likely to be exploited by others and less able to negotiate safe sexual relationships with partners. They may be less likely to stay in the kind of steady, long-term relationships in which partners can protect each other from getting HIV. Some kinds of mental health problems (in particular substance abuse) make it less likely that people will take precautions (using condoms, avoiding impulsive sexual activity) to avoid getting infected.

FMOH has developed a National Mental Health Strategy to guide the development and implementation of mental health services, training, and research. The strategy guides the integration of mental health services into the existing health system. As the issue of mental illness and substance abuse were identified as key contributors to non-adherence or lost to follow-up of HIV patients in chronic care, the integration of mental health services into HIV services was envisioned to enhance adherence and retention. Accordingly, the ministry has initiated integration of mental health into HIV services particularly using trained case managers and ART clinicians. To this end, screening tool, SOP and training curriculums for case managers and clinicians were developed and being implemented. The model used case managers for screening of common mental health disorders by using a brief screening tool to screen, identify and link clients to ART

clinicians who are trained to manage common mental health disorders. ART clinicians can refer difficult cases to psychiatry units within or outside the health facility.

Priority mental health disorders (WHO)

1. **Psychosis:** this is the collective name for a group of serious disorders characterized by changes in behavior (for example poor self-care, restlessness), strange thoughts or beliefs (for example believing that others wish to do the individual harm) and related dispositions.
2. **Mania:** a form of severe mental illness in which a person is excessively happy or irritable (experiences extreme mood swings), appears over-active and sleeps poorly. People with mania have poor reasoning skills (they have difficulty understanding what is good and what is bad), and display excessive self-confidence.
3. **Depression:** this is the most common priority disorder and is characterized by excessive sadness, loss of interest, lack of energy and related symptoms.
4. **Suicide:** refers to the intentional ending of one's own life.
5. **Abuse of alcohol and other substances:** this is the excessive use of these substances to the detriment of one's health.
6. **Childhood mental disorders:** these are different types of mental disorders related to childhood developments.
7. **Dementia:** is characterized by memory problems and broader problems with thinking and understanding.
8. **Epilepsy:** this is a chronic or longstanding condition caused by abnormal electrical conduction in the brain. In its most obvious form, it is characterized by episodic loss of consciousness and repetitive jerky movements of the body.

Introduction

Most of the time health services are organized primarily to provide episodic acute care. As HIV begins to become a manageable chronic condition, program managers and care providers need to consider how current health delivery systems can be reorganized to provide chronic care.

Once people are diagnosed and enrolled in chronic care, follow-up visits should be scheduled and planned. Waiting until people present with symptoms or preventable complications is costly and inefficient. People living with HIV require care that anticipates their needs at different stages of the care continuum. Compared with the acute care model, planned chronic care models provide opportunities for prevention, early identification of issues and timely intervention.

Chronic care requires broad support for people living with HIV from their communities and health care teams to stay in care, adhere to treatment and cope with stigma. People living with HIV and their families need to be informed about HIV infection and the anticipated side effects of medicines and supported to adhere to treatment. Health care teams play an important role in linking people living with HIV with community-level interventions, resources and support.

This chapter provides broad guidance on three operational and service delivery areas:

1. Differentiated care: addressing the diversity of needs of people in care such as appointment spacing.
2. Recommendations to strengthen the continuum of treatment and care:
 - Linkage from HIV testing to enrollment in care;
 - Retention;
 - Adherence;
 - Frequency of clinic visits;
 - Task shifting;
 - Decentralization;
 - Integration; and
 - Adolescent-friendly health services.

3. Special considerations for continuity and high quality of service delivery:

- Quality service delivery;
- Ensuring a stable supply chain of ARVs, and
- Laboratory and diagnostic services.

5.1. Differentiated HIV service delivery

Continuing to provide ART to a large and growing number of individuals poses a significant challenge to health systems in resource limited setups where there is a shortage of clinical staff. The challenge is highlighted by substantial rates of attrition reported across ART programs. The pace of ART enrolment will likely further increase in the coming years with recommendations issued by WHO in 2016 to change the eligibility criteria for ART initiation as Ethiopia has also endorsed the recommendations.

The challenges of further scaling up ART to those in need and improving retention in care for those on ART require continued adaptations in the models of healthcare delivery to the reality of people's lives. As national, regional and district teams address the various challenges, lessons from innovative models of ART delivery can help shape the next stages of HIV care and treatment scale-up.

To accommodate the growing number of stable individuals on ART and improve retention in care and health outcomes, innovative service delivery models have been developed and WHO reported on their emerging importance in 2014. Of these models, Ethiopia adopted appointment spacing model of HIV care.

The appointment spacing model (ASM) of care will be implemented as per the outline presented in the framework below (see table 5.1). Clients classified as “stable” will be included in this care model. For the time being, the country endorsed ASM for HIV differentiated care, but for the future, the country will consider other models depending on the results through piloting different models.

In the appointment spacing care model, stable clients will be appointed every six months for clinical visit and medication refill. Clients in the new care model should also get additional supports like arrangement of treatment supporter at home level among their family members and arrangement of adherence reminders like alarm and education on how to maintain the drug quality

at home level. Clients should be counselled and encouraged to disclose their status and to participate in peer support groups or to be a member of PLHIV associations. Those clients who disclosed their status will get adherence support from PLHIV associations via home visits or telephone follow up.

After appropriate classification based on the criteria below, clients should be informed and give verbal consent on the frequency of the service delivery. Eligibility for each category and adherence should be monitored continuously according to the appointment spacing model of HV care client classification tool. Through continuous assessment and based on their current needs, patients may move between the categories or groups over the course of their lifetime in care.

The implementation of appointment spacing

- The MDT will be responsible to monitor and support the implementation at facility level.
- Clients will be classified into each category based on their care need and using a standardized tool.
- In addition to the appointment spacing, high load facilities are expected and encouraged to do consent based transfer out or offloading of clients to the nearby low load facilities.
- The recommended care and follow up will be implemented as suggested for their category.
- Those stable clients (category 4) will be given appointment every six months for clinical follow up and medication refill with the health care providers (Nurse/HO/Physician). In addition, these clients need additional supports like:
 - Enhanced counseling to disclose to their family members and at least one treatment supporter will be arranged for each client (among their own family members).
- Ensure clients are supported on innovative and simple ways regarding Medication safety techniques to maintain the quality of the drugs over the six months' period.
- Clients included in the appointment spacing need to be linked to adherence case managers and adherence supporters to get additional counseling and support.
- Adherence case managers and adherence supporters will link the clients included in the appointment spacing to community based adherence support based on consent.
- Community based or peer adherence support will be arranged and coordinated through PLHIV associations and their networks.

- Couple clients will be counseled to have the follow up visits alternatively and each of them will pick the medication of the other partner during their visit.
- All clients will be assessed for possible reclassification as their care need will be changed over time.

Patient classification based on their care needs in the Ethiopian context:

Category 1a: People, who present when well, potentially with higher CD4 cell counts.

Category 1b: Pregnant/breast feeding women with no other complications, **rapidly growing children** (0–5 years old) and **adolescents** with no advanced disease or other complications.

Category 2: People with advanced disease are defined as those presenting to care with a CD4 count below 200 cells/mm³ or WHO clinical stages 3 and 4.

Category 3: Those who are already on ART but need careful monitoring to ensure timely action as required (treatment failure suspects, patients with other chronic comorbidities, patients with identified adherence barriers, etc.).

Category 4: Stable individuals are defined as those who have received ART for at least one year and have no adverse drug reactions that require regular monitoring and have good understanding of lifelong adherence and evidence of treatment success. Evidence of treatment success can be seen using:

- Two consecutive viral load measurements below 1000 copies/mL) with no current illnesses, excluding children, adolescents, pregnant and lactating women. **OR**
- In the absence of viral load monitoring, rising CD4 cell counts or CD4 counts above 200cells/mm³, an objective adherence measure either from the clients self-report or by doing pill count, can be used to indicate treatment success.

Table 5.1 Frame work for appointment spacing model of HIV service delivery in Ethiopia

Patient group/category	Minimum care package/services	Location of Service delivery	Provider of service	Frequency of service delivery	Additional support required	Remark
Category 1a: People, who present when well, potentially with higher CD4 cell counts.	- Clinical and lab evaluation. - OI screening and prophylaxis if needed. - ART initiation. - Additional and targeted adherence and retention support in order to commit to lifelong ART.	HC or Hospital based on consensus between the provider and the client.	Prescriber nurse/HO/ Physician	Biweekly during the 1 st month, monthly during month 2 to 6, every three months then after, Assess for possible change of category after 12 months.	Intensive adherence support during the first six months as they feel well and may be reluctant.	
Category 1b: Pregnant/Breast feeding women with no other complications, rapidly growing children (0–5 years old) and adolescents	- Clinical and lab evaluation. - OI screening and prophylaxis if needed. - ART initiation if not already started. - Additional and targeted adherence and retention support in order to commit to lifelong ART.	HC or Hospital based on consensus between the provider and the client.	Prescriber nurse/HO/ Physician	If the client is newly initiated, Biweekly during the 1 st month, monthly during month 2 to 6, Every three months then after.	Intensive adherence support.	Rapidly growing children and adolescents may need dose adjustment based on their weight.
category 2: People presenting to care with advanced disease	- Systematic screening for OI. - Provision of IPT and CPT;	Hospital or HC with experienced clinicians	Prescriber nurse/HO/ Physician	As per the national treatment guideline and may be assessed	Additional adherence counseling and	

	• Rapid initiation of ART (after appropriate base line evaluation). • Intensive follow-up and monitoring • Lab monitoring as per the guideline			for reclassification after stabilization.	support by case managers.	
Category 3: Those who are already on ART but need careful monitoring to ensure timely action as required.	• Clinical care and lab monitoring. • Additional adherence support. • Timely switch to second-line or third line ART regimen in case of treatment failure.	Hospital or HC with experienced clinicians	Prescriber Nurse/HO /Physician	Monthly and change of category if stabilized or issue settled.	Provide enhanced adherence counseling and support if there is high viral load.	
Category 4: Stable individuals who are already on ART for $\geq$ 1year excluding children, adolescents, pregnant and lactating women.	• Clinical review and medication refill. • Adherence assessment and support. • Adherence counseling to Re-enforce the adherence practice. • Lab monitoring as per the guideline.	HC or Hospital	Nurses/HO	Every 6 months for clinical follow up and drug refill. If the client is not willing to be included in the six monthly follow up, will continue every three months follow up.	Additional adherence counseling and support by case managers (at the facility) and community adherence groups, encourage disclosure, involve treatment/adherence supporters at home.	Treatment supporter at home level, safety box.

The role of PLHIV and PLHIV associations

Networks of PLHIV offer a key mechanism for enhancing support to those who are affected, and ameliorating negative experiences of living with HIV. As programs encourage greater involvement of PLHIV, there is increasing engagement of affected communities in national responses to HIV, and PLHIV networks have the potential to maximize stakeholder contributions. In addition, approaches that increase engagement and empowerment can potentially shift the focus of PLHIV's roles from representation to the building of individual and community capacity to promote health.

Expected outcomes

Assessments of the implementation of the appointment spacing service delivery model showed significant positive outcomes in other setups. From the patients' perspective, the main benefit of the appointment spacing to ART delivery is to reduce the financial and time costs associated with frequent clinic visits and longer patient waiting time at the health facilities. The relationship between social support and improved adherence to treatment is also well established and the engagement of people living with HIV in service delivery can provide an additional accountability mechanism to ensure continuity and quality of care.

From the health system perspective, reducing clinic contact required for clinically stable ART populations and refocusing resources towards managing sick patients with complex clinical problems is a key objective, with anticipated reduction of staff workload and improvements in quality of care and program outcomes. At a wider perspective implementation of the appointment spacing model of care will have important contributions for meeting the targets of the three 90's through improved adherence and retention in care.

5.2. Linkage from HIV testing to enrollment into care

Patient attrition following an HIV diagnosis is a huge global challenge, contributing to delayed ART initiation resulting in avoidable morbidity and mortality, suboptimal treatment outcomes, increased cost of care, and preventable HIV transmission. Multiple factors may hinder successful linkage to care, including distance from HIV care sites, transport costs, disclosure-related concerns, stigma and long waiting times at the facility.

Following an HIV diagnosis, a package of care and support interventions should be offered to ensure timely linkage to care for all people living with HIV. The following interventions have demonstrated benefit in improving linkage to care following an HIV diagnosis:

- **Streamlined interventions** to reduce time between diagnoses and engagement in care including:
 - Enhanced linkage with case-management;
 - Support for HIV disclosure;
 - Patient tracing for those who failed to engage in care;
 - Training of staff to provide multiple services, and
 - Streamlined services to accelerate time to initiation;
- **Peer support** & navigation approaches for linkage, and
- **Quality improvement approaches using data to improve linkage**

Good practices for linkage from HIV testing services include:

- Integrated services, where HIV testing, HIV prevention, treatment and care, TB and STI screening and other relevant services are provided together at a single facility or site;
- Providing on-site or immediate CD4 testing with same-day results;
- Decentralized ART provision;
- Support and involvement of trained lay providers who are peers and act as peer navigators, expert patients/clients and community outreach workers to provide support and to identify and reach people lost to follow-up;
- Intensified post-test counselling by community health workers;
- Promoting partner testing may increase rates of HIV testing and linkage to care, as may approaches in PMTCT settings that encourage male involvement.
- Intimate partner notification by the provider, with permission, is feasible in some settings; it identifies more HIV-positive people and promotes their early referral to care.

5.3 Disclosure

5.3.1. Disclosure in Children

Pediatric disclosure is an ongoing process and even in the best of circumstances may be difficult. Adults struggle with the question of whether, when or how to tell children that they have HIV, often agonizing over how to find the right words. All families are unique and there are no set rules regarding when and how to disclose to children.

Children react to HIV disclosure in different ways and it is not uncommon for relatives to disagree about disclosing HIV-related information to children. Even amongst the HIV/care team there may be disagreement on the best approach. Disclosure has to be individualized taking into consideration the particular child, parent/s, family, household and community.

Barriers to Disclosure

- Fear that the infected child will inappropriately disclose his/her HIV status, especially in families in which the diagnosis remains closely guarded.
- Fear of stigma, rejection, and loss of support by the family/community.
- Desire to protect the child from worrying about his/her future.
- The possibility that the burden of learning of his/her HIV status will lead to depression or other mental health issues.
- Feelings of guilt and shame may prevent HIV-infected caregivers from disclosing their own infection to their child.

Ways to begin the process

HIV disclosure is not a topic that comes naturally for family discussion, especially when children are involved. The best way for child to learn about his/her HIV status is through age-appropriate information shared by a loving and trusted caretaker. Disclosure to children should never happen casually, inadvertently or in the heat of anger or conflict. A child's maturity and cognitive capacity varies and is not only dependent on age. It is important to tailor the discussion to the child's cognitive level and to the child's personal and individual situation. It is important to assess

readiness of the entire family for disclosure and address potential barriers to disclosure (Table 12-1). It is also important to discuss benefits of disclosure which have both short and long term impact on the family.

Disclosure can:

- Help create a sense of closeness in the family.
- Help reduce feelings of anxiety and isolation on the part of the parents/ caregiver.
- Relieve the burden of living with the secret of being HIV-positive.
- Help build social support networks.
- Reduce the anxiety children experience when they suspect something is wrong; they will now have information to make better sense of the situation.
- May improve adherence in a non-adherent child.

Assessing readiness for disclosure
The child • Is the child symptomatic? Taking medications? • How old is the child? • Is the child living with a sick parent or family member? • Is the child asking questions about HIV? • Does the child appear distressed, anxious or worried? • Is the child sexually active and at risk of contracting or spreading HIV? The parent or caregiver • Has the parent or caregiver been tested for HIV? • Is the parent or caregiver infected? Symptomatic? Taking medication? • Is the adult ill? Is s/he in need of help from children in the household? • Is the infected adult an important attachment figure for the child?

The family or household

- Are there any adults in the household with HIV infection? Who is aware?
- Are other children in the household HIV-infected? Who is aware?
- How many family members are taking HIV-related medications?
- Is the family unit cohesive, or characterized by separations and/or conflict?

The community

- Are testing and treatment generally available in the community?
- Are there people in the community who are open about their own HIV status? Does the child know anyone in the community who is open about his/her HIV status?
- How strong is the stigma surrounding HIV in the community?
- Are there risks to the family (isolation, discrimination) if inadvertent disclosure occurs?
- Are there resources within the community for children – a youth group and/or trusted adults they can talk to?

5.3.2. Planning for disclosure

Disclosure is not an event or a one-off conversation. It is a **PROCESS** that takes time and constant communication in an age-appropriate manner. It is important to prepare adequately for disclosure. This involves preparation, education, planning and follow-up. Once the decision has been made to disclose to the child, it is important to understand that the topic will have to be visited over and over again. It is important to give a clear message and listen actively; take cues from the child and avoid lecturing; the emphasis should be on asking directly and indirectly and listening. The following examples can serve as a guide:

- **Pre-schooler (4-6 years old):** Younger children if symptomatic generally want to know what will happen to them. They do not need to know their diagnosis but the illness must be discussed with them. Young children may feel responsible for the parent's illness or just pretend nothing is happening. It is important to give reassurance and take cues from younger children.
- **School aged children (7-13 years):** Some may have difficulty coping with disclosure information leading to changes in behavior (acting out in school, i.e. fights, low grades,

absenteeism, anger, crying fits, or no expression of emotion). Others may have concerns that other children in the school or community will make fun of them. Encourage them to ask questions; do not be disappointed if they do not react in the manner you expected.

- **Adolescents (14 years and older):** Adolescents should know of their HIV status. They must be fully informed in order to appreciate consequences for many aspects of their health, including sexual behavior and treatment decisions. Be supportive and non-judgmental.

Stages of disclosure:

Stage 1 This is for children around the age of six. If they are symptomatic they want to know what will happen to them. They do not need to be informed of their diagnosis but the illness must be discussed with them.

Start providing partial disclosure; communicate with the child as follows:

- You are taking medicines to keep you healthy.
- You have body soldiers that keep you healthy.
- Your medicines increase the number of body soldiers and keep them strong so you can stay healthy.
- As long as your body soldiers are strong and you have many, you can do what you want to do in life.
- You need to take your medicines in the morning and evening, when your (mother . . .) gives it to you.

Stage 2 Once stage 1 understood, or if the child is school age (7-13years) move on to Stage two and then to Stage three.

- Your body soldiers became weak because something was attacking them (“a germ”).
- If you take your medicines every day you keep the “germ” asleep so it can’t attack your body soldiers.
- Body soldiers can then increase in number and stay strong to keep you healthy.
- If you don’t take your medicines the, “germ” could wake up and start attacking your soldiers.
- May consider asking the child if he/she would like to know how many body soldiers they have.
 - Check the file carefully first

- If CD4 trend is up, show child that their own “body soldier” numbers are going up because they have taken their medicines
- If CD4 trend not up, re-enforce previous messages (while looking into possible causes).
- If viral load is suppressed, show child that the “germ” inside their body is under control because they are taking their medication properly.
- Build on the story, introducing the concept of resistance
 - If you forget your medicine and the “germ” wakes up too often, he can become “tricky”; then your medicines may not work to keep him asleep

Stage 3

Make sure the child and caregiver are ready for disclosure. Some may have difficulty coping with disclosure information leading to changes in behavior (acting out in school, i.e. fights, low grades, truancy, anger, crying fits, and no expression of emotion). Others may have concerns that other children in the school or community will make fun of them. Encourage them to ask questions; do not be disappointed if they do not react in the manner you expected.

- Introducing the words HIV and CD4.
 - Only proceed if child and caregiver are ready.
 - Anticipate how the child might react.
- In presence of caregiver.
 - As usual, ask child why taking medicines; congratulate for what he/she has learned.
 - Ask child if he/she wants to know the other names for the soldiers and the bad guy.
 - “Germ” is a virus called HIV.
 - “Body soldiers” are called CD4 cells.
- Ask child what he/she has heard about HIV and correct any misconceptions.
- Choose words that avoid assigning blame, e.g. if child asks where he/she got HIV.
 - “Some children are born with the virus / HIV, and we think that is what happened to you”.
 - **NOT** “your mother gave it to you”.
- Put new information back in the context of what the child has already learned.
 - “as long as you keep taking your medicines well, keep the germ asleep and the soldiers strong, you can do everything you want to do in life”
- Continue to check understanding at each visit.

N.B: Full disclosure can be provided to most children over 10 years. Each steps of disclosure should be documented on the patient's chart.

Adolescents 14 years and older

Adolescents should know of their HIV status. They should be fully informed in order for them to appreciate consequences for many aspects of their health, including sexual behavior and treatment decisions. Be supportive and non-judgmental.

Post –disclosure assessments and follow-up

Disclosure is a process that does not end with telling an HIV-infected child the name of their illness or diagnosis. After the HIV diagnosis has been disclosed to the infected child, follow-up visits are needed to monitor the child and family's understanding of the illness and their emotional and psychological adjustment.

Once the diagnosis has been explained to a child, it needs to be reinforced or regularly discussed as the child develops because many children will not have understood the full implications of the disease or diagnosis at the time of disclosure. For example, preadolescent children can cognitively understand the concepts about the virus but may be less likely to think of the future implications, such as transmission risks and safe sexual practices. As the child ages and matures, he/she will slowly understand and integrate the implications of the diagnosis into his/her life. Children's perception of self, health, illness, and death evolve as they mature through different developmental stages.

Some children who learn of their HIV status may experience guilt and shame and may isolate themselves as a result of the stigma and secrecy surrounding the disease. Changes in behavior and school functioning may occur in these children and may be symptoms of depression. Patients and families who have a difficult adjustment to HIV disclosure without progress over time should be referred for mental health services and additional support. In young adolescents it will be important to discuss about modes of HIV transmission, sexuality and reproductive health.

For details of psychosocial support in children, refer the pediatric psychosocial support manual.

5.3.3. Disclosure in adults

Among other priorities, testing and counselling programs emphasize the importance of people with HIV disclosing their HIV status, particularly to sexual partners. Informing the sexual partners of an individual's HIV infection is not only an effective means of halting the transmission of HIV, but informing partners allows access to care and support as well as further prevention efforts among the client's partners and family.

Two main processes for informing partners of an individual's HIV infection are disclosure and partner notification. Disclosure, or beneficial disclosure as it is often known, refers to actions by individuals themselves to notify their partners of their HIV sero status. UNAIDS and WHO strongly recommend beneficial disclosure, when appropriate, as this process is voluntary, respectful of the autonomy and dignity of the affected individuals and mindful of maintaining confidentiality. Providers of testing and counseling prefer that individuals use beneficial disclosure to inform those who need to know that they are infected. For the individual, his or her sexual partners, and family, beneficial disclosure allows for greater openness about HIV in communities and meets ethical imperatives. To encourage beneficial disclosure, it is needed to establish safe social and legal environments in which more people are willing and able to get tested for HIV and are empowered and encouraged to change their behavior according to the results. This can be done by expanding access to counseling and testing services; providing incentives to get tested in the form of greater access to community care, treatment and support; and removing disincentives to testing and disclosure by protecting people from stigma and discrimination and removing legal barriers.

Disclosure can be difficult as people may be afraid of the consequences: for example, the threat of rejection and violence by partners and family or discrimination in the community and workplace. In some cases, people may have limited knowledge of their partners and how to locate them, or may not know the identity of their partners or where they can be located. Although evidence of effectiveness of partner notification is limited in resource-limited settings, UNAIDS advises that partner notification—or ethical partner counseling—be based on the informed consent of the source client, and maintain the confidentiality of the source client, and where possible, protect individuals from physical abuse, discrimination and stigma that may result from partner notification. Ideally, partners of infected individuals should be encouraged to seek HIV testing and counseling, as this is a critical prevention and treatment tool in the control of HIV.

How to discuss disclosure in adults

- Ask the patient if he/she has disclosed his/her HIV test result or is willing to disclose the result to anyone.
- Discuss concerns about disclosure to partner, children, other family and friends.
- Assess readiness to disclose HIV status and to whom.
- Assess social support and needs (refer to support groups).
- Provide skills for disclosure (rehearsal can help).
- Help the patient make a plan for disclosure if now is not the time.
- Encourage attendance of the partner to consider testing and explore barriers. As couples may have different HIV status, partner testing is important.
- Reassure the patient that you will keep the result confidential and that disclosure is voluntary.

If the patient does not want to disclose the result:

- Reassure that the results will remain confidential.
- Explore the difficulties and barriers to disclosure. Address fears and lack of skills (help provide skills).
- Continue to motivate the client.
- Advise the client not to harm others.
- Offer to assist in disclosure (for example, talk with spouse).
- Offer another appointment and more help as needed (such as peer counselors or trained counselors).

For women, discuss benefits and possible disadvantages of disclosure of a positive result and involving and testing male partners. Men are generally the decision makers in most families and communities. Involving them will have greater impact on:

- Increasing acceptance of condom use, practicing safer sex and making appropriate reproductive choices.
- Helping to decrease the risk of suspicion and violence.
- Helping to increase support to their partners.
- Motivating to get tested.

Disadvantages of involving and testing the partner: danger of blame, possible violence, abandonment. Health worker should assess the risk of violence or suicide and discuss possible steps to ensure the physical safety of patients. Health worker should try to counsel the couple together, when possible.

5.4. Retention in care

Retaining people living with HIV across the continuum of care is essential for optimal health outcomes. For people living with HIV who are receiving treatment, uninterrupted ART and continual monitoring are essential for sustained viral suppression and optimal treatment outcomes. Retention in ART program is more challenging in pediatric populations, postpartum women and men in general. Multiple factors may play a role in loss to follow-up, including distance to health facilities, lack of transport or inability to cover travel expenses, stigma and disclosure-related issues, being too sick and lack of understanding of the need for lifelong care.

Good practices for retention across the continuum of care

Optimizing retention in HIV care requires interventions at multiple levels of the health care system. Given the broad array of challenges and heterogeneity of barriers across settings, no single approach is likely to work for everyone in all settings. Improving the understanding of barriers and innovative strategies to address them are important.

Related transport costs and loss of income while seeking care serve as disincentives when health facilities are located far from the person's home. Bringing services closer to communities, where feasible, reduces the indirect costs of care for the people living with HIV and their families and improves retention.

Waiting times at the facility during consultation are frequently high, especially in settings with a high burden of HIV infection. Reorganizing services, such as systems for appointment, triage, separating clinical consultation visits from visits to pick up medicine, integrating and linking services and family-focused care may reduce waiting times at the health facility.

Interventions harnessing social support have emerged as a promising approach to counteract the structural, economic, service delivery and psychosocial constraints that affect retention in care.

Specific population considerations

1) *Pregnant and breastfeeding women*

For pregnant women living with HIV, the transition between ART care and antenatal care/MNCH services is a potential point for loss to follow-up.

Interventions include:

- Monitoring approaches to ensure that registers are aligned and that women are tracked and followed across different ART service delivery points;
- Peer support, such as mothers-to-mothers program, may improve transition across service delivery settings, and
- Peer adolescent support groups for adolescent pregnant women living with HIV.

2) *Children*

Caregivers are responsible for understanding the importance of retaining children in care, especially younger children. Disclosure to children typically occurs late, making it challenging to discuss the importance of follow-up. WHO recommends age appropriate disclosure to children.

Interventions include:

- Supporting caregivers to attend for regular follow-up.
 - Reinforcing to the caregivers the importance of the process of disclosing to the child.
- This can begin early with age-appropriate messaging and tools.

3) *Adolescents*

Frequent clinic visits, time spent waiting for services and having to miss school discourages adolescents' engagement in care. Negative health care provider attitudes, concerns regarding privacy and confidentiality and limited opportunity to discuss their concerns also act as barriers to retention for adolescents. Distance to facilities and out of pocket expenses may restrict their engagement.

Interventions include:

- Service delivery models beyond the facility that support adolescents to engage in care, such as peer-based interventions and community-based services;
- Implementing adolescent friendly health service approaches to improve quality;
- Providing adolescent services at specific times or in separate areas with flexible appointment systems that accommodate school hours;
- Comprehensive services that address multiple needs, including psychosocial support and sexual and reproductive health, and

- Close monitoring of adolescents' engagement in care, rapid proactive follow-up and implementation of strategies for re-engagement.

Table 5.2 Summarizes the factors related to the health system and people receiving ART influencing retention and adherence with respective potential interventions.

Factors related to the health system	Possible interventions
High direct and indirect costs of receiving care.	• ART and related diagnostics and services free of charge at the point of care. • Decentralize ART where feasible. • Scheduled facility visits • Reduce waiting time at the facility level. • Client centered appointment system. • Separate clinical consultation visits from appointments for picking up medicines. • Link, integrate and coordinate care.
Stock-outs of ARV drugs.	• Optimize pharmaceutical supply management systems to forecast, procure and deliver ARV drugs. • Use fixed-dose combinations to simplify forecasting and supply management systems.
Lack of a system for monitoring retention in care.	• Implement systems for patient monitoring across the continuum of care, including cohort analysis and patient tracking systems.
Lack of a system for transferring people across different points of care.	• Interlinked patient monitoring system across services for HIV, TB, maternal and child health and PMTCT; system for transitioning from pediatric to adolescent and adult services and from maternal and child health and TB services to chronic HIV care.
Pill burden and complex ARV drug regimens.	• Use fixed-dose combinations to reduce the pill burden and simplify the regimens.
Lack of accurate information for patients and their families and peer support.	• Engage and integrate community health workers, case managers, adherence supporters, volunteers, people living with HIV in peer support, patient education and counseling, and community-level support.
Adherence support	• Task shifting for involving case managers, adherence supporters and community health workers.

	• Linking with community-level interventions and resources such as peer adherence support (community adherence support groups). • Using known effect reminder methods (such as text messaging). • Peer support also provides opportunities for in-person reminders.
Poor relationship between patient and care provider.	• Train health workers on how to: reduce stigma; improve treatment preparedness, adherence and retention; provide adherence support and care for key populations; and provide simplified approaches for educating patients and their families.
Lack of time for educating people in HIV care.	• Task shifting and sharing among clinic team members. • People living with HIV as expert patients and peer supporters. • A team approach to care.
Adverse drug effects.	• Preparedness and knowledge of how and when to self-manage adverse effects and when to return to the clinic.
Forgetfulness, life stress, stigma and discrimination.	• Using text messaging to keep patients engaged. • Peer and family support. • Link to community support group.
Comorbidity, substance and alcohol use disorders and mental health disorders.	• Manage HIV with mental health disorders, alcohol and other substance use disorders and link with community and social support.
Patient knowledge and beliefs related to HIV infection, its course and treatment.	• Integrate the education of patients and their families and counseling, broader community literacy and education and community engagement.

5.5. Adherence to ART

WHO defines treatment adherence as “the extent to which a person’s behavior – taking medications, following a diet and/or executing lifestyle changes – corresponds with agreed recommendations from a health care provider”. For ART, a high level of sustained adherence is necessary to suppress viral replication and improve immunological and clinical outcomes; decrease the risk of developing ARV drug resistance; and reduce the risk of transmitting HIV.

5.5.1. Barriers to adherence

Multiple factors related to the health care delivery systems, the medication and the person taking ARV drugs may affect adherence to ART.

Individual factors: may include forgetting doses; being away from home; changes in daily routines; depression or other illness; a lack of interest or desire to take the medicines; and substance or alcohol use.

Medication-related factors: may include adverse events; the complexity of dosing regimens; the pill burden; and dietary restrictions.

Health system factors: may include requiring people with HIV to visit health services frequently to receive care and obtain refills; travelling long distances to reach health services; and bearing the direct and indirect costs of care. Lack of clear information or instruction on medication, limited knowledge on the course of HIV infection and treatment and adverse effects can all be barriers to adherence to ART. Specific population groups face additional challenges to adherence, and these should be considered when implementing the recommended interventions.

Pregnant and postpartum women

The pregnancy and postpartum period presents significant biological, social and economic challenges that may affect treatment adherence. Pregnancy-related conditions such as nausea and vomiting may negatively affect treatment adherence. Other individual factors include suboptimal understanding of HIV, ART and PMTCT, lack of partner disclosure and support, and fear of stigma and discrimination. Service delivery barriers include poor-quality clinical practices, gaps in provider knowledge and training, poor access to services and health worker attitudes

Adolescents

Adolescents face specific challenges, including psychosocial issues such as peer pressure, the perceived need to conform and inconsistent daily routine. Adolescents are often left out of decisions and have limited opportunities to discuss their concerns, and there is limited availability of adolescent-specific treatment literacy and adherence counselling tools. For adolescents who are transitioning from pediatric to adolescent care, additional challenges may include assuming increased responsibility for their own care, issues relating to disclosure to peers or partners,

difficulties in navigating the health-care system, lack of links between adult and pediatric services and inadequately skilled health workers.

Infants and young children

Successfully treating a child requires the commitment and involvement of a responsible caregiver. Parents and other family members of children living with HIV may themselves be living with HIV, and suboptimal HIV care and treatment for family members could result in suboptimal care for the child. Other challenges include lack of nutrition support, limited choice of pediatric formulations, poor palatability of liquid formulations, high pill or liquid volume burden, large pill size, frequent dosing requirements and difficulties in swallowing tablets.

People with mental health conditions and substance use

People with HIV with uncontrolled depressive symptoms are more likely to have poor adherence to ART. Adherence is complicated by mental health comorbidity that results in forgetfulness, poor organization and poor comprehension of treatment plans. Similarly, use of alcohol and other substances may also contribute to poor adherence to ART. Alcohol and substance use can lead to forgetfulness, poor organization and diversion of monetary resources.

5.5.2. Supportive interventions

Several interventions may also be of value in addressing specific challenges that impact on adherence and/or viral suppression. Interventions to optimize adherence to ART includes using fixed-dose combination regimens for ART and strengthening drug supply management systems to reliably forecast, procure, and deliver ARV drugs and prevent stock-outs. Efforts to support program-level interventions for improving adherence to ART include: avoiding imposing and maximize adherence should begin before ART is initiated. Developing an adherence plan and education are important first steps. Initial patient education should cover basic information about HIV, the ARV drugs themselves, expected adverse effects, preparing for treatment, and adherence to ART.

Patient education, counseling and peer support

Patient education and counseling are essential both when ART is initiated and throughout the course of treatment. Informing and encouraging people receiving ART and their families and peers are essential components of chronic HIV care.

Substance use and mental health interventions

Studies indicate that improving well-being by treating depression and managing substance use disorders improves HIV treatment outcomes.

Nutritional support

Nutrition assessment, counseling and support are essential components of HIV care. HIV programs should ensure that existing national policies on nutritional support are observed when it is necessary and feasible to maximize adherence to ART and achieve optimal health outcomes in food-insecure settings.

Reminder and engagement tools

Mobile phone text messages can be considered as a reminder tool for promoting adherence to ART as part of a package of adherence interventions. Other patient reminder tools include alarms, phone calls, diaries and calendars can be used to send brief reminders about the timing of ARV drugs, drug dosage and appointments.

5.5.3. Monitoring adherence to ART in routine program and care settings

Objective monitoring of adherence to ARV drugs is necessary for effective and efficient treatment planning and ongoing support. Each facility visit brings opportunity for assessing and supporting treatment adherence. Effective monitoring of adherence requires a combination of approaches based on human and financial resource capacity, acceptability to people living with HIV and to health workers and the local context.

Viral load monitoring

These guidelines recommend viral load monitoring to diagnose and confirm treatment response and failure. Viral load monitoring is considered as the gold standard for monitoring adherence and confirming treatment response. Although treatment failure is often caused by lapses in adherence to ART, it may also result from other factors such as drug resistance, drug stock-outs, drug interactions or malabsorption. Viral load monitoring must therefore be combined with other approaches to monitoring adherence. These approaches should also be considered as a way to provide additional information about possible causes of virological failure or to support adherence monitoring in settings where viral load testing is not available.

Following an initial high viral load (>1000 copies/ml), an adherence intervention should be carried out prior to conducting a second viral load test. Viral load monitoring also has a high potential to motivate adherence.

Pharmacy refill records

Pharmacy refill records provide information on when people living with HIV pick up their ARV drugs. When people obtain pharmacy refills at irregular intervals, this may indicate non-adherence to ART; however, in many routine care settings, people may pick up their medications when receiving care irrespective of their adherence level. This behavior could lead health care providers to overestimate adherence by solely using pharmacy refill records. In many settings, pharmacy refill records are already a part of national monitoring and evaluation frameworks and can also provide additional information on adherence to ART when used in combination with other tools.

Self-report

Asking people living with HIV or their caregivers how many doses of medication they have missed since the last visit (or within a specified number of days in the past) can help to estimate non-adherence. However, although this method is commonly used, people may not remember missed doses accurately or may not report missed doses as they may want to be perceived as being adherent and to avoid criticism. Counselling on the importance of remembering and/or documenting ARV drug doses and an environment that promotes and enables honest reporting of non-adherence are critical components of monitoring adherence to ART in routine care settings.

Pill counts

Counting the remaining pills in bottles may help to assess adherence. Pill counts usually take place at routine health care visits. However, some people may throw away tablets prior to health care visits, leading to overestimated adherence. Although unannounced visits at people's homes could lead to more accurate estimates, this approach poses financial, logistical and ethical challenges. Counting pills also requires health care personnel to invest significant time and may not be feasible in routine care settings. Pill count can perform better when combined with self-reported adherence.

5.6. Task shifting for HIV treatment and care

Reorganizing, integrating and decentralizing HIV treatment and care will require re-examining the roles and tasks of teams of health care providers involved in delivering chronic HIV care. Task

shifting involves the rational redistribution of tasks among health workforce teams. With this approach, specific tasks are reassigned, where appropriate, from highly qualified health workers to health workers with shorter training and fewer complementary qualifications to more efficiently and effectively use the available human resources. Task shifting should be implemented alongside other strategies designed to increase the total numbers and capacity of all types of health workers.

The quality of care in task shifting should be ensured by (a) providing training, mentoring, supervision and support for nurses, non-physician clinicians and community health workers; (b) stating clear indications for patient referral; (c) implementing referral systems and (d) implementing monitoring and evaluation systems.

Both initial and ongoing training and mentoring, supportive supervision and administrative planning have been critical to the success of program that have implemented task shifting. Program need to train and establish a system for routine supportive supervision of health workers, including lay providers.

5.7. Decentralizing HIV treatment and care

Although rapidly scaling up HIV programs has significantly improved access to ART and increased the health and survival of people living with HIV, it also poses significant challenges to health systems. Decentralizing ART to primary care settings will ease the burden of routine management on other parts of the health system and will improve equity by promoting access to ART in rural areas. Decentralizing HIV care and treatment could reduce the workload for health care personnel, thereby reducing waiting times for people with HIV and people receiving care at hospitals for other conditions and bring HIV services closer to people's homes. Decentralization and scale-up of HIV care and treatment services will continue based on need assessments to address community groups with high HIV prevalence.

5.8. Integrating and linking services

Chronic care requires integrating and linking related services to ensure comprehensive and consistent patient management over time, including providing related services in single settings, systems to share information and effective referrals across settings and providers.

Integrating and linking services are likely to reduce missed opportunities for initiating ART, enhance long-term adherence support and optimize patient retention in care. Programs for HIV,

sexual and reproductive health, maternal and child health, mental health, non-communicable diseases, viral hepatitis and TB need to collaborate to successfully implement ART and related services at different levels of the health system.

Delivering HIV services in antenatal care, maternal and child health settings

HIV testing should be offered to all pregnant women through provider-initiated approaches as an essential component of MNCH services. It is also recommended to provide couple and risk screening based partner HIV testing for all pregnant women and their partners in maternal and child health care settings.

ART should be initiated and maintained in all pregnant and postpartum women and in infants at maternal and child health care settings, with linkage and referral to ongoing HIV care and ART, where appropriate.

Delivering HIV services in TB treatment settings

All confirmed and presumptive tuberculosis patients should be offered HIV testing services in TB clinics. TB patients co-infected with HIV should be initiated with ART through linkage to HIV care and ART services. All PLHIV enrolled to HIV care need to be screened for TB and those with no sign and symptoms of active TB should be provided with INH prophylaxis. PLHIV who develop TB after the initiation of ART, should be linked to TB clinics for TB treatment.

STI and family planning services in HIV care settings

Sexually transmitted infections and family planning services can be integrated within HIV care settings. WHO recommends routine offer of HIV testing services for persons with an STI in all epidemic settings and for family planning clients in generalized epidemic settings. Likewise, all PLHIV should be screened for STIs and treated as per the National Guidelines for Syndromic Management of STI. Family planning services should be provided in HIV care/ART clinics to avoid unintended pregnancy among women living with HIV.

5.9. Delivering HIV services to adolescents

There is a growing cohort of adolescents living with HIV, which includes those infected from birth and those who have acquired HIV later in childhood and adolescence. While there is still a lack of health outcome data for this age group, emerging evidence indicates that adolescents living with

HIV are underserved by current HIV services and have significantly worse access to and coverage of ART. Adolescents are at high risk of loss to follow-up both before and after ART initiation. People aged 15–24 years and those attending services for the PMTCT of HIV are particularly at risk.

All adolescents, including those living with HIV, face significant barriers to accessing health services, due to inadequate health literacy, limited ability to navigate health services, legal requirements for parental or caregiver consent, and insufficient resources to pay direct and associated service costs. Adolescents face significant levels of stigma and discrimination.

Poor quality of services also limits adolescent engagement in health care. Adolescents often perceive health services as unacceptable due to concerns about confidentiality and negative health provider attitudes. Services are often not organized to accommodate adolescent needs and routines and have inconvenient service schedules, inflexible appointments and unwelcoming environments. Without sufficient consideration and support, adolescents can be lost between paediatric and adult services. The rapid developmental and social changes that occur during adolescence exacerbate the impact of such barriers and can have a profound impact on the way adolescents engage with health services.

Due to their unique needs, adolescents living with HIV require quality comprehensive services and care to support access, retention and adherence. This includes psychosocial support, sexual and reproductive health and mental health care. According to the WHO quality of care framework, adolescent friendly health service is defined as follows:

- **Equitable:** all adolescents, not just certain groups, are able to obtain the health services they need.
- **Accessible:** Adolescents are able to obtain the services that are provided.
- **Acceptable:** Health services are provided in ways that meet the expectations of adolescent clients.
- **Appropriate:** The right health services that adolescents need are provided.
- **Effective:** The right health services are provided in the right way and make a positive contribution to the health of adolescents.

Adolescent-friendly HIV prevention, care and treatment service implementation considerations include:

- Aligning approaches for HIV service delivery with national adolescent-friendly health service standards, protocols and activities;
- Including implementation of adolescent-friendly approaches in HIV health service supervisory and monitoring systems;
- Ensuring training, research and personal development opportunities for health service providers on adolescent HIV treatment and care;
- Engaging service providers, adolescents and other key stakeholders to identify acceptable and feasible activities;
- Implementing adolescent-friendly health service approaches in all HIV services used by adolescents, including antenatal care for pregnant adolescents living with HIV; and
- Establishing linkages and referral pathways to ensure a comprehensive continuum of care, especially for the transition from paediatric to adult HIV services.

5.10. Improving the quality of HIV care services

HIV program should be innovative in addressing local challenges and aim to strengthen programme monitoring and the routine use of programme data to improve the quality of services. Quality of care emphasizes that services should be effective in achieving desired health outcomes and that health-care practices should be people-centred and safe. Strategies to improve the quality of HIV care services are needed both at the programme management level and at health facility and community levels where HIV care services are provided. If an intervention is to achieve the desired health outcomes, it needs to be evidence based, of high quality and achieve a level of coverage that brings desired outcomes at the population level.

Quality care means that people living with HIV receive the care they require to maintain their health and quality of life. For HIV program and health-care providers, quality HIV care optimizes programme effectiveness and efficiency. For policy-makers and funding agencies, quality care is an important requirement for maintaining health at the population level and ensuring the optimal use of available resources.

Quality of care should not be seen as an additional activity to routine HIV services or a short-term project to address implementation issues and gaps; it should be incorporated into daily activities at all levels, from service delivery to national programme management.

5.11. Pharmaceuticals supply management system

The overarching objective of pharmaceuticals supply management system is to support national policy with the adequate and continuous availability of the most safe, effective, quality-assured ARV pharmaceuticals at service delivery sites, in the right quantity, at the lowest possible cost and in a timely manner.

Pharmaceutical Fund and Supply Agency (PFSA) is responsible for quantification, procurement, storage and distribution of pharmaceuticals to health facilities. Health facilities obtain essential and vital pharmaceuticals primarily through the Integrated Pharmaceutical Logistics System (IPLS), a single reporting and distribution system managed by PFSA. Pharmaceuticals used for HIV programs are also managed through IPLS.

The new recommendation that ART should be initiated in all people living with HIV regardless of CD4 cell count will require an integrated national strategic response that considers the resources available and enables strong PSM systems at all levels of the health system. FMOH, PFSA and other stakeholders need to work together to ensure that the national supply system is functioning well in accordance with the increasing national demand and the 90-90-90 target.

1. Selection of ARV drugs and related supplies

Product selection is informed by national policies and ART guidelines. Products are selected from or become part of a National Essential Medicines List (EML) and are based on standard treatment guidelines. If a selected ARV drug is not on EML and/or registered in the country, HIV program managers should coordinate with Food, Medicine and Health Care Administration and Control Authority of Ethiopia (FMHACA) and request that these drugs be put on the list and registered.

2. Quantification

National quantification of ARV pharmaceuticals need is conducted by PFSA in collaboration with FMOH, FHAPCO, other stakeholders and development partners. Normally, the national quantification is done every two years. However, due to various changes in the program regarding regimen proportions, dynamic ARV preparations, and changes in guidelines, it is found necessary

to conduct the national level quantification review exercise every year to update the previous quantification exercise assumptions and results so that the forecast meets the current demands of the program. Based on the forecast produced, supply plan will be prepared allowing sufficient flexibility to adjust for potential changes in the pace of scale-up, regimen switching and/or other unforeseen events affecting consumption

3. Procurement

All ARV pharmaceuticals for use in the public and private sector should be procured at affordable prices, with assured quality and adequate shelf life, from a reliable supplier. ARVs and related commodities are procured and distributed by PFSA. The procurement process follows the national and international procurement regulation, which is a competitive approach through international bidding. Technical evaluation of bidders takes place to select the suppliers and awards the contracts. Purchase orders are given to awarded bidders to deliver the products in a staggered approach so as to avoid expiry and reduce expenses of storage.

4. Storage and distribution

Proper storage of ARVs, including refrigeration, is critical to maintain the quality of the drugs and related supplies. Since the recommendation to offer ART to people with HIV regardless of CD4 cell count will significantly increase commodity volumes and the demands on storage and distribution, adequate space and equipment for proper handling must be ensured at various levels.

Pharmaceuticals and health products distribution will follow the existing delivery system and it extends from the central level to health facilities. Central PFSA will have a major role of delivering the products to its Hubs; subsequently the hubs distribute the commodities to health facilities based on orders placed by health facilities to PFSA hubs every two months.

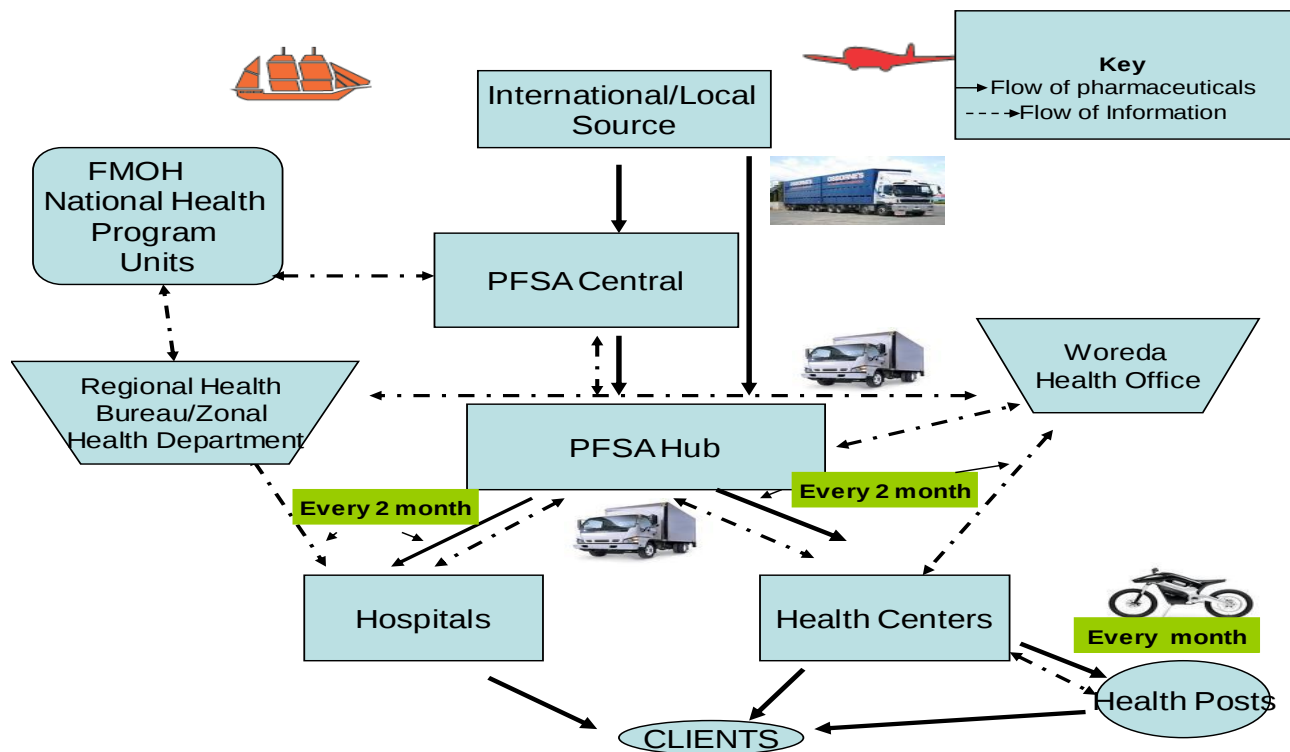


Figure 5.1 Flow of pharmaceuticals and information in the integrated pharmaceutical logistics system.

5. Inventory Control

Inventory control system is mandatory to maintain an appropriate stock level of products at all level of the supply chain to avoid shortage and overstock. IPLS dictates the implementation of max-min inventory control system where there is a set of maximum and minimum months of stock to be kept at each level starting from PFSA central up to health facilities. Health Commodity Management Information System (HCMIS) is an electronic inventory control system which is currently utilized at PFSA central, hubs and some health facilities whereas the remaining health facilities are utilizing a paper based system.

NB: PFSA is responsible for collecting, validating, analyzing, and utilizing product information to ensure an uninterrupted supply of health products.

6. Rational medicine use

Rational medicine use (RMU) dictates that patients must receive medicines appropriate for their clinical needs, in doses that meet their individual requirements, for an adequate period of time and

at the lowest cost to them. RMU implies promotion of rational prescribing, ensuring good dispensing practice and encouraging appropriate medicine use by the patient and the community at large. FMOH in collaboration with FMHACA, PFSA and other stakeholders should implement a strategy to ensure RMU as it is a part and parcel of programmatic activities at each and every level.

7. Quality Assurance

Mechanisms must be put in place to assure the quality of drugs entering the country through pre-procurement certification and post-marketing surveillance. Appropriate quality assurance mechanisms for pharmaceuticals is developed and implemented by FMHACA. Quality standards should also define storage conditions at PFSA warehouses and health facility stores. The national laboratory must have the capacity to assure the quality of ARV pharmaceuticals. Quality assurance of drugs and supplies will be maintained using simple visual inspection methods and a First-Expiry-First-Out (FEFO) system to avoid expiration and ensure fresh supplies are available at all levels.

5.12. *Laboratory and diagnostic services*

The consolidated national HIV guidelines support an increased access to HIV care and treatment, which will also require increased access to laboratory and diagnostic services. To ensure that laboratory services are accurate and reliable, relevant quality assurance systems need to be developed and strengthened. There are multiplicity of diagnostic settings, such as laboratories, maternal and child health clinics, HIV testing and counselling sites and community-based testing. Strategic planning for proper placement and harmonization of testing platforms should be carried out to ensure appropriate use and cost-effectiveness.

This guidance to strengthen laboratory and diagnostic services emphasizes the importance of leadership and governance, high-quality laboratory services, expanding testing services and developing the health workforce:

- To strengthen and expand laboratory and diagnostic services;
- To support a dedicated specimen referral system;
- To increase access to HIV viral load testing;
- To support the expansion of diagnostic services to include testing at the point of care;
- To train and certify health workers who perform the testing;
- To ensure high-quality diagnostics and plans for implementation, including quality assurance; and

- To ensure appropriate deployment of diagnostic technologies to increase their efficient and optimal use.

1) Strengthening and expanding laboratory and diagnostic services

The following areas are important to strengthen the network of laboratory and diagnostic services for implementing the national guidelines:

- Expanding and strengthening current laboratory networks with efficient specimen referral mechanisms to support and monitor the decentralization and integration of laboratory services or to provide access to laboratory tests which are available at limited number of sites (e.g. HIV viral load testing, DNA PCR, CD4 count etc.).
- Standardizing testing methods to streamline procurement, quality assurance and training.
- Incorporating new testing approaches and systems into national laboratory strategic plans and policies.
- Evaluating diagnostics for their performance and operational characteristics to validate testing algorithms (with back-up options) before introduction.
- Carrying out strategic planning for properly placing and harmonizing testing platforms to ensure appropriate use and cost-effectiveness.
- Allocating appropriate resources to ensure the availability of testing services, including human and financial resources.

2) Supporting a dedicated specimen referral system

Laboratory referral systems and procedures for collecting and processing specimens need to be strengthened to increase access to viral load testing and other testing (for example, CD4 and early infant diagnosis). Providing for and strengthening a dedicated, efficient, safe and cost-effective specimen referral system requires reliable specimen transport with adequate conditions for whole blood, plasma and dried blood spot specimens and rapidly and dependably reporting test results back to the referring site with linkage to care. Rapidly reporting results is essential for timely care.

3) Increasing access to HIV viral load testing

The guidelines recommend the use of viral load testing to monitor treatment response and diagnose treatment failure and the use of dried blood spot samples for viral load testing. This will require strengthening the existing laboratory services and phased expansion of monitoring services into peripheral facilities and can include:

- Strengthening and leveraging existing specimen transport and result receiving networks;
- Ensuring that laboratories have adequate infrastructure, technical testing expertise and quality assurance and quality improvement programs;

- Ensuring an appropriate mix of high-volume centralized laboratory testing and testing at the point of care for facilities in remote locations; and
- The use of dried blood spots as a tool to increase access to viral load testing.

4) Planning for appropriate use of CD4 count testing as access to viral load testing increases

As the country eliminated CD4 count-dependent treatment initiation thresholds and viral load monitoring replaces monitoring with CD4 cell count, it is anticipated that the demand for CD4 count testing will decrease. As this transition takes place, program, laboratory, procurement and supply management staff should take into account the following programmatic considerations.

- As demand decreases, reductions in CD4 count testing capacity can be staged through several strategies based on site-level demand.
- Although specimen referral networks for CD4 cell count and viral load testing may overlap, the specimen types require different transport capabilities. The program needs to ensure adequate network capability for specimen referral for viral load testing prior to scaling down CD4 count testing.
- Program planning should include a realistic transition of financial support from CD4 count testing to viral load monitoring. Quantification and forecasting (active supply planning) will be essential to account for commodity shifts. This is particularly important in the early phases of the transition when historical data will not reflect current commodity needs. Supply chain needs, including cold-chain transport and storage, must also be considered during the transition.

Even in settings with full access to viral load testing, CD4 cell count testing capability will continue to be needed as part of HIV programs for baseline assessment, monitoring OI prophylaxis and other clinical assessments.

5) Expanding diagnostic services to point-of-care settings

Decentralizing laboratory and diagnostic services requires that all aspects of testing be in place before implementing services, including:

- Using only high-quality, evaluated and reliable diagnostic tests;
- Supervising and monitoring point-of-care testing for quality and reliability;

- Implementing a strategy for managing supply chain and equipment service; and
- Establishing data management systems for timely identification of quality issues and regional and national data reporting.

6) Implementing comprehensive quality management systems

Developing a comprehensive quality management system including EQA and quality control is essential. The quality management system should:

- Be implemented within the laboratory network and all remote testing sites;
- Be incorporated into the routine testing procedures and monitored;
- Ensure that testing sites undertake quality control, as appropriate;
- Ensure that testing sites are enrolled in an external quality assessment scheme (proficiency testing program);
- Ensure the use of standard operating procedures for all processes, including specimen collection and processing, test methods, interpreting results and reporting;
- Ensure the use of standardized logbooks or electronic data management and reporting, including identifying errors and potential misclassification; and
- Ensure that equipment and facilities are maintained, both preventive and corrective.

7) Providing guidance for developing health workers' capacity, including staff training and certification

There should be guidelines for the qualification of personnel who will perform the laboratory tests. The guidelines should include training requirements for specific tests and the process for certification and re-certification. All health workers assigned to perform point-of-care testing must be trained and proficient on the testing procedure, specimen collection and quality assurance before implementing these services.

CHAPTER SIX: GUIDANCE FOR PROGRAMME MANAGERS

Policy development and review is a dynamic process. Policies change according to the lessons learnt during the implementation of the program as well as evidence and knowledge change over time at national, regional and global level. Policies set early in the development of a program may negatively affect implementation and need to be revised. Policies, therefore, need to be able to respond to these changes. Program managers should be cognizant of changes and challenges affecting the development and implementation of HIV/AIDS policies. These include political commitment, financial implications, administrative reforms, community participation (PLHIV input) and basic legislation.

The key benefits to the global and country HIV response have been that policies have enabled governments, communities, organizations and individuals to break the silence on issues previously deemed taboo. These include matters related to sexual behavior, injecting drug use, socio-cultural attitudes towards diseases, stigma associated with gender, poverty, ethnicity and religious beliefs, entitlement to services and human rights that need to be discussed in an open manner.

6.1 Guiding principles

The following guiding principles are expected to lead the implementation of the national HIV program and services provision:

- I. An effective response to HIV/AIDS requires ownership and active involvement of the community and all other sectors.
- II. Strong leadership commitment at all levels is essential for sustainable and effective response to the HIV/AIDS epidemic.
- III. Establishment of partnership by the government to enhance enabling environment (for the strengthening of the partnership through nurturing local and international initiatives and relationships).
- IV. A multi-sectoral approach that includes partnership, consultations and coordination with all stakeholders in the design, implementation, review, monitoring and evaluation of the national response to HIV/AIDS.
- V. Gender sensitivity must be considered as a corner stone to guarantee the success of HIV/AIDS response with greater and sustained positive impact.

- VI. Public health approaches in HIV prevention, treatment, care and support services through innovative, evidence based, cost effective and high impact interventions.
- VII. Promotion and protection of human rights shall be based on the principles of fundamental human rights, social justice and equity guaranteed by the constitution of the country, including avoidance of stigma and discrimination and addressing criminalization of HIV-related behaviors.
- VIII. As key stakeholders in the fight against HIV/AIDS, greater involvement of people living with HIV, at all levels and areas of the intervention is crucial for an effective response.
- IX. Best use of resources: efficiency, transparency and accountability in and for proper allocation and effective utilization of resources are essential in the national response to HIV/AIDS epidemic at all levels.
- X. The HIV/AIDS programs are designed and implemented in order to ensure equitable and universal access.
- XI. Ensuring sustainability is a cross-cutting and impassable agenda to be put on the forefront of the HIV prevention, treatment, care and support programs design and their implementation.
- XII. Ensuring that HIV program activities are integrated (testing and counseling; access to ART; access to PMTCT services; access to condoms; availability of STI services for youth and most at risk populations; HIV and the workplace (employment); blood safety; etc.) and are linked to other pre-existing services.

The 2015-2020 National HIV /AIDS prevention care and treatment strategic plan was developed in an investment case approach. This investment cases aims to pave the path for ending HIV/AIDS by 2030 through averting 70,000 – 80,000 new HIV infections and saving about half a million lives till 2020. The targets set in this investment case are in line with the three 90's (90-90-90) treatment targets set by UNAIDS to help end the HIV/AIDS epidemic. The three 90's include:

- By 2020, 90% of all people living with HIV will have been diagnosed.
- By 2020, 90% of all people with diagnosed HIV infection will receive antiretroviral therapy.
- By 2020, 90% of all people on antiretroviral therapy will have suppressed viral load.

The HIV Investment Case includes four strategic objectives to achieve the goals and targets. These are:

1. Implement high impact and targeted prevention program.

2. Intensify Targeted HIV testing and counselling services.
3. Attain virtual elimination of MTCT.
4. Optimize and sustain quality care and treatment

In addition, four critical enablers are identified as necessary for the HIV Investment Case to deliver the results.

These include:

- A. Critical enabler 1: Health system strengthening: HMIS/M&E, PHPM & Laboratory services
- B. Critical enabler 2: Enhance Partnership, Coordination and Leadership
- C. Critical enabler 3: Increase Domestic resources for HIV response
- D. Critical enabler 4: Gender equality and equity: Address gender related barriers to HIV and SRH needs of girls and boys, and women and men.

Most HIV/AIDS programs will have HIV strategic Information officers who will be responsible for the technical aspects. For a manager, it is important to note that the key end-product of a functional HIV strategic information system is the availability of adequate and quality data which can be used for policy, program management and clinical care. To achieve this, a manager should ensure that:

- i.** The key components of HIV strategic information systems including its coordination structures and resources are in place.
- ii.** HIV data and information are adequately used at all levels to guide decision making processes, priority setting, choice of interventions and future directions as well as understanding the status of the HIV epidemic and response in the context of ‘Know Your Epidemic’ and ‘Know Your Response’.
- iii.** Clear policies for data collection, storage, retrieval, sharing and confidentiality are articulated and are in line with national health information policies and acts.
- iv.** Resources are available for strengthening HIV strategic information.

In addition, national HIV program managers play a unique role in establishing systems that are required to ensure broad accountability for implementation from all partners at all levels and adequately document performance to inform programming decisions and maintain political support. Implementation and operations research should be supported so that innovative approaches can be assessed and taken to scale. Human rights and ethical principles should guide

the revision of national treatment policies to ensure that they are equitable and meet the specific needs of all beneficiaries.

As HIV programs mature and increasingly focus on the challenges of long-term prevention, treatment, care and support, national responses need to be considered within the broader health and development contexts. The sustainability and effectiveness of HIV programs can be greatly enhanced by creating and strengthening linkages with other health and non-health programs.

6.2. National and local HIV epidemiology

An epidemiological analysis should describe the prevalence levels among the general population and in specific key populations, the rate at which HIV infection is acquired and among whom, including infants, young children, pregnant women and sero discordant couples. Both prevalence and incidence measurements should aim to identify populations at higher risk for HIV infection, including in generalized epidemic settings, and adequate population size estimates for these populations should be available so that results can be interpreted appropriately. Data on the prevalence and incidence of key co-infections (such as TB and hepatitis B and C) and other co-morbidities should also be gathered to inform decision-making.

6.3. Program performance and response analysis

Determining whether current ARV programs are adequate to address the needs that have been identified requires understanding of, who is currently accessing these services. Programs should assess present ARV coverage levels among the general population as well as key populations, the disease stage at which they access care, how well these groups are retained in care and treatment, the ARV regimens used and the impact of ART on viral load suppression, morbidity and mortality. Disaggregated data for various groups enable assessment of ARV needs and establishment of priorities for delivering services.

Data on adherence, retention and viral load suppression are key to assess the quality of the services provided. Surveillance of transmitted and acquired HIV drug resistance can also be instrumental in informing decisions on optimal regimen choices.

Whenever possible, indicators of impact, such as changes in HIV-related incidence, prevalence, morbidity and mortality, should also be reviewed.

Socioeconomic, policy and legal context

A review of epidemiological and programmatic data is incomplete without a deeper understanding of what drives HIV vulnerability and how various political, social, economic and legal factors affect the ability and willingness of various groups – such as men, women, adolescents, sex workers, and people who inject drugs – to seek and access health services. Stigma, discrimination, poverty, gender inequality, education and migration status are key elements that should be taken into account to inform effective HIV programming.

6.4. Key parameters for decision-making

Ethics, equity and human rights

Multiple legal, social and normative obstacles have resulted in inequitable access to HIV treatment and care. Global and national commitments require providing HIV treatment and prevention to everyone in need, following the human rights principles of non-discrimination, accountability and participation. National HIV strategies should be planned and implemented from the outset with the ultimate goal of delivering the full package of services and interventions recommended in these guidelines as soon as possible.

Key ethical principles of fairness, equity and urgency should also be observed in the process of reviewing and adapting guidelines. The design of effective and equitable policies implies that strategies should focus comprehensively on addressing barriers to access testing, prevention and treatment services, particularly those faced by key populations.

Impact and cost–effectiveness

Realizing positive impact for a population is an important goal of public health programs and policies. Examples of the impact of HIV programs include reduced HIV incidence, prevalence, morbidity and mortality and improved quality of life. Impact is often a result of a complex set of factors and a combination of diverse inputs and activities or processes, and it is often not attributable to a single intervention or program.

Cost–effectiveness analysis is one of the several economic evaluation tools used to measure the value of delivering particular services. Economic evaluation measures the costs and consequences of alternative programs, which are then compared to assess how the greatest health benefits can be generated. In cost–effectiveness analysis, impact is often measured using indicators related to a

change in health status, such as disability-adjusted life-years gained, which includes the estimated number of deaths and infections averted. As the experience of scaling up ART in low- and middle-income countries demonstrates, the cost-effectiveness of health interventions also changes over time, as costs fall because of gains in scale, improvements in technology or the design of more efficient delivery systems.

Although evaluating cost-effectiveness and health impact may be useful in systematically comparing various program interventions, they should be considered in the light of the ethical, equity and human rights implications associated with different courses of action, especially in settings in which not all eligible individuals currently have access to ART.

Investments in critical enabler programs (such as integrated treatment and rights literacy programs, legal services, stigma and discrimination reduction programs, training for health care workers and law enforcement) can play a role in overcoming barriers to accessing treatment and other HIV-related services and keeping people connected to care. As such, these programs can contribute to overall cost-effectiveness, in addition to achieving other important objectives, such as reducing discrimination.

Opportunities and risks

The recommendations in these guidelines have the potential to further reduce HIV-related mortality, improve the quality of life, reduce the number of people acquiring HIV infection and enhance treatment effectiveness. The benefits accrued from implementing them are likely to considerably outweigh the upfront investment needed and have the potential to fundamentally change the course of the epidemic. Nevertheless, domestic factors (such as budget cuts, theft of ARV drugs, and attrition of trained health workers and emergence of drug resistance) and external contingencies (such as withdrawal of external financial support, political instability and natural disasters) could negatively affect their implementation. It is essential to design strategies to mitigate such events so that continued service delivery can be assured, especially for those most in need.

Implementations

In concentrated epidemic settings with low ART coverage, it is critical to identify opportunities to expand access to HIV treatment and care, including testing and counseling, to most-at-risk populations, such as sex workers, people who inject drugs and prisoners. This requires addressing

any structural barriers that may prevent these populations from seeking and accessing care. Integrating HIV services into drug dependence treatment and harm reduction services and TB clinics can be a highly effective approach to reaching these populations. In these settings, providing ART during pregnancy and breastfeeding to reduce the risk of mother-to-child transmission of HIV (option B+) are highly effective and relatively low-cost strategies.

Other strategies to improve the overall levels of access to and uptake of ART include decentralizing HIV services to the primary health care level and integrating HIV services with TB and antenatal care and maternal and child health services, and offering pregnant and breastfeeding women living with HIV the option of receiving lifelong ART, based on national program decisions. In addition, as in concentrated epidemics, it is important to identify and reach key and priority population and those with poor access to clinical and community-based services. These may include sex workers, truck drivers, adolescent boys and girls, migrants and other mobile populations, older women and certain high-risk occupational groups.

As coverage of ART increases and programs mature, expanding access to second-line regimens increasingly becomes a programmatic priority. Access to third-line regimens for PLHIV who fail on second-line regimens should be sought. Scaling-up viral load monitoring will be important to adequately identify treatment failure and to avoid switching unnecessarily to second-line or third line regimens. Viral load monitoring is also likely to play a central monitoring role in places in which ART is being broadly expanded to reduce HIV incidence.

As people initiate treatment earlier and stay on it for longer, monitoring the quality of service delivery and strengthening service linkages to improve retention throughout the cascade of care are essential to optimize treatment outcomes and long-term program performance.

6.5. Roles and responsibility

As the response to HIV involves a wide diversity of actors, coordination at various levels of the system becomes important to ensure coherence and cohesion of efforts. HIV program managers should ensure effective coordination (a) with other health programs, (b) between the HIV activities in the health sector and those in other sectors, and (c) for the implementation of the HIV activities in the health sector, between the different levels of the health system (National, regional and district).

Ministry of Health

Some of the functions of the Federal Ministry of Health are to provide policy guidance, regulation, ensuring accountability for health, health intelligence and building partnership across all health actors. The Ministry of Health should also ensure that public health services are of quality and are equitable. The HIV program of the Ministry of Health should provide technical leadership and coordination of the health sector response to HIV. The HIV Program Managers should serve as a leader, manager, coordinator, facilitator and innovator and should liaise regularly with other health program and other health and HIV actors.

Decentralization levels

For effective implementation and follow-up, national strategic plans must be linked and cascaded to the regional, zonal and woreda level. RHB and Zonal / Woreda Health Offices are mandated to manage and coordinate the operation of primary health care services at the respective levels. They are responsible for planning, financing, monitoring and evaluating of all HIV programs and service deliveries in the region and zonal/Woreda.

Partners

The roles and responsibilities of local and international partners include:

- Technical and financial support for implementation of the newly adopted interventions.
- Participate in the national and regional HIV program coordination mechanisms.
- Support the joint planning, monitoring and evaluation of the different program areas.

6.6. Coordination mechanisms

HIV/AIDS control and prevention office (HAPCO)

This is the primary mechanism for multi-sectoral coordination. It ideally includes representation from key actors in the national response to HIV including various government ministries, regional president's non-governmental organizations, and people living with HIV, faith-based organizations, and private sector and development partners.

Coordination in the health sector

High level coordination mechanisms such as the Health Sector Joint Steering Committee, which involves the heads of the Regional Health Bureaus, oversee the different programs in the health sector. The committee is chaired by senior officials in the Ministry of Health and provides general

guidance to the health sector. Technical level coordination between health programs might occur through technical advisory/working groups.

Donor coordination mechanisms

Some funding agencies, such as the Global Fund to fight AIDS, TB and Malaria, the President's Emergency Plan for AIDS Relief (PEPFAR) and other donors might have own types of mechanisms for coordinating their in-country efforts. However, the health sector is involved and often a key member of these coordinating mechanisms and should always work to ensure consistency and harmonization.

Stewardship and advocacy for the HIV response in other sectors

The health sector is often in a position to provide the evidence necessary to leverage action for HIV in other sectors. The Ministry of Health has a crucial role in using its stewardship and advocacy power to ensure that HIV issues are addressed in all policies. This includes engaging ministries of education, social development, gender, transport etc.

CHAPTER SEVEN: MONITORING AND EVALUATION

Effective HIV prevention, care and treatment requires standardized recording and reporting system. Recording and reporting is used to systematically monitor and evaluate progress of patient/s and treatment outcome as well as the overall program performance. Monitoring and evaluation is done at different levels of the health system where epidemiological and operational indicators for monitoring of the HIV prevention, care and treatment are compiled, calculated, analyzed, and used.

The reporting of HIV prevention, care and treatment activities is integrated into the HMIS and all forms and registers are standardized in line with HMIS throughout the country. Health facilities are the primary sources of data. Any information concerning PLHIV should completely and correctly be recorded. Registers and reporting forms should be kept neatly and maintained properly.

M & E will help program and health facility managers assess the effectiveness of interventions and linkages between services along the cascade of testing, treatment and care for HIV and associated conditions. Such information is essential to detect and respond to bottlenecks or gaps in programme performance and to adequately characterize and respond to patient attrition. Patient monitoring systems are also important to support people receiving treatment over time and as they move between clinics and districts, to ensure retention in care. As programs mature, monitoring is also essential of individual- and population-level outcomes, such as toxicity and adverse events, drug resistance, viral suppression, mortality, survival and incidence, to assess and optimize the impact of country program.

This national consolidated guide on monitoring and evaluation of HIV in the health sector brings together the various elements of monitoring and evaluation systems for HIV program. The guide will consolidate and align existing monitoring and evaluation approaches in relevant programmatic areas (such as HIV testing and counselling, ART, PMTCT and HIV drug resistance).

In order to establish a functional national monitoring and evaluation (M & E) system, the following five key elements are important.

1. **Presence of an M & E unit:** Established M & E unit with qualified staff and enough budget. The unit also needs to build links with regions, sector ministries, research institutions, NGO, FBO, civil associations and donors.

2. **Clear goals and objectives of the program:** It needs well-defined national program goals, objectives and targets where regular reviews/evaluations of the progress of the implementation of the National/Regional program is undertaken. Guidelines and guidance need to be put in place on the M & E to regions and sectors.
3. **A core set of indicators and targets:** It is important to identify priority/core indicators and additional indicators that cover program inputs, activities/processes, outputs, outcomes and impact. Also, selection of indicators needs to be through full participation of stakeholders and maintaining relevance and comparability. The process needs also to utilize past and existing data collection efforts (e.g. DHS, BSS and Sentinel Surveillance) to assess national trends.
4. **A plan for data collection and analysis:** An overall national level data collection and analysis plan is important. The plan also has to address data collection and analysis systems at lower levels.
5. **A clear plan for data dissemination and use:** Establishment of an overall national level data dissemination plan is important.

7.1. *Monitoring the implementation of the new recommendation*

Summary of the new recommendation area	Implication for monitoring
• HIV testing and counseling • Re-testing	The monitoring tools should be reviewed to address the following new recommendations: • Services for adolescents, including systems for linkages to care and treatment; • Re-test for individuals with ongoing risk; and • Re-test for verification before ART initiation.
When to start ART	Monitor the number and percentage of different populations (such as adults, adolescents, children and pregnant and breastfeeding women) who have been initiated on ART based on the new eligibility criteria: Test-and- treat – ART should be initiated in all people living with HIV, regardless of WHO clinical stage or CD4 cell count.
Which ART regimen to start	Monitor the first-line, second-line and third-line ART regimens people are receiving. Monitoring tools may need to be adjusted to reflect new regimen options.
Response to ART and diagnosing treatment failure.	Monitor the percentage of people receiving ART who had a viral load test and received the results Monitor the reasons for switching ART regimen

7.2. Key Indicators

1. Percentage of people living with HIV who know their status

Definition	Percentage of people living with HIV who know their status					
Formula	Number of people living with HIV who know their status					
	Estimated Number of people living with HIV X 100					
Interpretation	This indicator can be used as a proxy for the first 90 target of the 90-90-90 HIV targets. It is Critical to determine the proportion of people living with HIV who know their HIV status, as this knowledge is the entry point to the continuum of care for PLHIV. The numerator should be the sum of: 1) PLHIV who were reported as currently on ART in the previous reporting month 2) Total new HIV positives identified through HCT program in the reporting period 3) Total number of lost in the reporting period. Limitation of this indicator: This indicator may miss those previously identified positives and who are alive and not started on ART.					
Disaggregation	Age group: <1, 1-4, 5-9, 10-14, 15-19, 20-24, 25-49, 50+ Sex: Male, Female HIV test result: Positive, Negative Population groups: FCSW, Long distance drivers, Mobile/Daily Laborers, Prisoners, OVC/Children of PLHIV, General population, Other KEY POPULATIONS,					
Sources	PITC tally and VCT register, PMTCT Register, ART register					
Frequency of Reporting	HP	HC	Hospital	WorHO	RHB	FMOH
		Monthly	Monthly	Monthly	Monthly	Monthly

2. Proportion of STI cases tested for HIV

Definition	Proportion of STI cases tested for HIV in the reporting period.					
Formula	$\frac{\text{Number of STI cases tested for HIV in the reporting period}}{\text{Total number of STI cases in the reporting period}} \times 100$					
Interpretation	This indicator is intended to provide information on the proportion of STI cases that are tested for HIV. It is helpful to measure the magnitude of the HIV and STI co-infection and to intensify the HIV prevention interventions. It also helps to track the number of STI cases. Additionally, the proportion of STI cases detected can be tracked by dividing the number of detected STI cases by the estimated number of STI cases in the catchment area.					
Disaggregation	HIV test result: Positive, Negative Sex: Male, Female					
Sources	PICT Tally, OPD and IPD registers					
Frequency of Reporting	HP	HC	Hospital	WoHO	RHB	FMOH
		Monthly	Monthly	Monthly	Monthly	Monthly

3. Percentage of people living with HIV receiving ART

Formula	Number of adults & children receiving ART at the end of the reporting period					X 100
	Estimated number of people living with HIV					
Interpretation	This indicator measures the ongoing scale-up and uptake of ART and retention in ART programs as a critical step in HIV service provision and assesses progress towards coverage of ART. It also measures the progress towards providing antiretroviral therapy to all people living with HIV and the extent to which ART needs are met. Provision of Antiretroviral therapy has been shown to reduce HIV-related morbidity and mortality among those living with HIV, and onward HIV transmission. This indicator measures the second 90 target.					
	Data for this indicator is generated by counting the number of adults and children who are currently receiving ART in accordance with the nationally approved treatment protocol at the end of the reporting period. Patients who have died, stopped treatment, transferred out, lost (patient not seen for 1 to 3 months from last visit) and dropped out (patient not seen for > 3 months from last visit) are NOT counted. Patients on ART who initiated or transferred in during the reporting period should be counted. Some people pick up several months of antiretroviral medicines (ARVs) at one visit, and efforts should be made to include these people in the numerator as receiving antiretroviral even if they do not attend the clinic in the last month of the reporting period.					
	As it will be difficult to get the PLHIV estimate or the expected number of individuals who know their status at the Zone/woreda and lower levels, this indicator will be calculated at these levels based on the target allocation during the planning phase. This indicator includes currently receiving ART clients at ART clinic and those currently receiving ART at PMTCT clinic based on option B+. All option B+ implementing PMTCT only sites are expected to report ART currently receiving clients on monthly basis.					
Disaggregation	Age: <1, 1-4, 5-9, 10-14, 15-19, 20-24, 25-49, 50+; Sex: Male, Female; By Pregnancy Status: pregnant, non-pregnant ; By regimen: ,					
Sources	ART Register, PMTCT register, ARV regimen tally, Electronic ART Database					
Frequency of Reporting	HP	HC	Hospital	WorHO	RHB	FMOH
		Monthly	Monthly	Monthly	Monthly	Monthly

4. Number of adults and children with HIV infection newly started on ART

Definition	Number of adults and children newly enrolled on antiretroviral therapy (ART)					
Formula	Number of adults and children newly enrolled on antiretroviral therapy (ART)					
Interpretation	The indicator measures the ongoing scale-up and up-take of ART programs. This measure is critical to monitor along with number of patients currently on ART in relation to the number of PLHA that are estimated to be eligible for treatment to assess progress in the programs response to the epidemic in specific geographic areas and population as well as at the national level. Reporting the number of new patients enrolled on ART is critical to monitoring the HIV services cascade, specifically the successful linkage between HIV diagnosis and initiating ART. This indicator includes newly initiated clients at ART clinic and those newly started ART at PMTCT clinic based on option B+. All option B+ implementing PMTCT only sites are expected to report ART new initiation on monthly basis. This indicator permits monitoring trends in initiation but does not attempt to distinguish between different lines or regimens of ART or to measure the cost, quality or effectiveness of treatment provided. These will each vary within and between countries and are liable to change over time.					
Disaggregation	Age: - <1, 1-4, 5-9, 10-14, 15-19, 20-24, 25-49, 50+; Sex: - Male, Female , pregnant, non-pregnant					
Sources	ART Register, PMTCT register, ART enrollment tally, e-database					
Frequency of Reporting	HP	HC	Hospital	WorHO	RHB	FMOH
		Monthly	Monthly	Monthly	Monthly	Monthly

5. ART retention rate

Definition	Percentage of adults and children known to be on treatment 12 months after initiation of antiretroviral therapy					
Formula	Number of adults and children who are still on treatment at 12 months after initiating ART					
	$\frac{\text{Total number of adults and children who initiated ART in the 12 months prior to the beginning of the reporting period (net current cohort)}}{\text{Total number of adults and children who initiated ART in the 12 months prior to the beginning of the reporting period (net current cohort)}} \times 100$					
Interpretation	This indicator measures the proportion of adults and children with HIV known to be on treatment 12 months after initiation of antiretroviral therapy and it is one important measure of program success and is a proxy for overall quality of program. The Numerator: Number of adults and children still alive and on ART at 12 months after initiating treatment. A 12-month outcome is defined as the outcome (i.e. whether the patient is still alive and on ART, dead or lost to follow-up) 12 months after starting. The numerator does not require patients to have been on ART continuously for the 12-month period. Patients may be included in the numerator (and denominator) if they have missed an appointment or drug pick-up or temporarily stopped treatment during the 12 months since initiating treatment, as long as they are recorded as still being on treatment at month 12. On the contrary, those patients who have died, stopped treatment, or been lost to follow-up as of 12 months since starting treatment are not included in the numerator. The number of adults and children on ART at 12 months includes patients who have transferred in (and their initiation date is known) at any point from initiation of treatment to the end of the 12-month period and excludes patients who have transferred out during this same period to reflect the net current cohort at each facility. The denominator: Number of adults and children in the ART start-up groups initiating ART at 12 months prior to the end of the reporting period (The denominator is the total number of adults and children in the (monthly) ART start-up groups who initiated ART at a point 12 months prior to the beginning of the reporting period, regardless of their 12-month outcome. This includes all patients, both those on ART as well as those who are dead, have stopped treatment or are lost to follow-up at month 12. Again, the denominator includes patients that have transferred in (and their initiation date is known) and excludes patients that transferred out during the time period. The net current cohort is the number of patients in the start-up group plus any transfers in, minus any transfers out.					
Disaggregation	Disaggregation Age: <1, 1-4, 5-9, 10-14, 15-19, 20-24, 25-49, 50+ Sex: Male, Female, pregnant, non-pregnant					
Sources	ART Register, PMTCT register					
Frequency of Reporting	HP	HC	Hospital	WorHO	RHB	FMOH
		Monthly	Monthly	Monthly	Monthly	Monthly

6. Early viral load suppression rate

Definition	Percentage of ART patients with an undetectable viral load at 6 month after initiation of ART					
Formula	Number of adult and pediatric patients with an undetectable viral load <1,000 copies/ml at 6 months on ART					
	$\frac{\text{Number of adults and children who initiated ART in the 6 months prior to the beginning of the reporting period with a viral load test at 6-month}}{\text{Number of adults and children who initiated ART in the 6 months prior to the beginning of the reporting period}} \times 100$					
Interpretation	This indicator is about those who initiated ART prior to six month of the current reporting period. And is helps to provide information that can contribute to quality improvement activities designed to maximize rates of viral suppression in patients on ART and therefore prevent the acquisition of HIV drug resistance. The increasing ART coverage in resource-limited settings in the absence of routine viral load monitoring is raising concerns about the development of resistance to first-line ART regimens, long-term individual patient outcomes, and increased risk of transmission of HIV, including drug-resistant HIV. To sustain the progress made in reducing morbidity and mortality from HIV through ART, it is important that HIV-infected patients continue to have access to safe, tolerable, and potent ARVs. To accomplish this, the use of viral load testing to monitor HIV treatment will need to be expanded.					
Disaggregation	By Age: <1, 1-4, 5-9, 10-14, 15-19, 20-24, 25-49, 50+; By Sex: Male, Female; Pregnancy status: Non-pregnant and pregnant					
Sources	ART and PMTCT registers					
Frequency of Reporting	HP	HC	Hospital	WorHO	RHB	FMOH
		Monthly	Monthly	Monthly	Monthly	Monthly

7. Viral load suppression

Definition	Percentage of patients on ART with a suppressed viral load (≤ 1000 copies/ml) in the past 12 months					
Formula	$\frac{\text{Number of adult and pediatric patients on ART tested with an undetectable viral load (<1000 copies/ml) in the past 12 months}}{\text{Estimated number of PLWHIV}} \times 100$					
Interpretation	This indicator could provide information that can contribute to quality improvement activities designed to maximize rates of viral suppression in patients on ART and therefore prevent the acquisition of HIV drug resistance. The viral load of patients receiving antiretroviral therapy provides an indication of adherence to treatment, patient compliance with disease monitoring and the quality of care delivered. The increasing ART coverage in resource-limited settings in the absence of routine viral load monitoring is raising concerns about the development of resistance to first-line ART regimens, long-term individual patient outcomes, and increased risk of transmission of HIV, including drug-resistant HIV. To sustain the progress made in reducing morbidity and mortality from HIV through ART, it is important that HIV-infected patients continue to have access to safe, tolerable, and potent ARVs. To accomplish this, the use of viral load test to monitor HIV treatment will need to be expanded. Measuring viral suppression is a key programmatic indicator related to effective treatment. It helps as a proxy indicator to monitor the third 90 of UNAIDS' 90-90-90 treatment target, that 90% of people receiving antiretroviral therapy will have viral suppression by 2020. For the numerator: It can be the actual report or estimated number of people that have suppressed viral loads at the end of the reporting period depending on the viral load testing coverage. In either case, viral load testing should be routine rather than episodic: for example, when treatment failure is suspected. If viral load test is done repeatedly, only the last routine test result should be used. An indication of whether the indicator is direct or adjusted should be included. For the denominator: Estimation models such as Spectrum are the preferred source for the number of people living with HIV. If models other than Spectrum are used, documentation of the estimation method and uncertainty bounds should be provided. Please refer UNAIDS Global AIDS Monitoring 2017 document for further explanation. As it will be difficult to get the PLHIV estimate or the expected number of individuals who know their status at the Zone/woreda and lower levels level, this indicator can be monitored by calculating from the total viral load tested.					
Disaggregation	By Age: <1, 1-4, 5-9, 10-14, 15-19, 20-24, 25-49, 50+; By Sex: Male, Female; By Pregnancy status: Non-pregnant and pregnant					
Sources	ART and PMTCT registers					
Frequency of Reporting	HP	HC	Hospital	WorHO	RHB	FMOH
		Monthly	Monthly	Monthly	Monthly	Monthly

8. Proportion of clinically undernourished People Living with HIV (PLHIV) who received therapeutic or supplementary food

Definition	The proportion of individuals receiving therapeutic or supplementary food among those whose nutritional status was assessed and found to be undernourished						
Formula	No. of clinically undernourished PLHIV on ART who received therapeutic or supplementary food						X 100
	No. of PLHIV on ART who were nutritionally assessed & found to be clinically undernourished.						
Interpretation	Provision of nutritional treatment, care and support for those undernourished PLHIVs is important to prevent morbidity and mortality. Under nutrition significantly increases mortality risk for HIV-infected individuals regardless of treatment status. Among the clinically undernourished PLHIVs, those with severely undernourished (SAM) cases will receive the Ready -To-Use Therapeutic food (RUTF) and those with moderately undernourished (MAM) cases receive Supplementary food (RUSF) based on availability of supplies. Severe acute malnutrition(SAM): Adult: -BMI less than 16 kg/m2. Pregnant and lactating: -MUAC less than 23cm Children: -under 5: MUAC <11cm or WFH (weight for height) <70% or median <-3 Z score, -5-18 years of age: BMI -for-Age <-3 z-score Moderate acute malnutrition(MAM): Adult: BMI 16-18.49 kg/m2 Pregnant and lactating: MUAC 19-23 cm Children: -under 5: MUAC 11cm to <12cm or WFH (weight for height/length) <-3 Z or ≥ 70% to < 80% median or ≥ -3Z to < -2Z score -5-18 years of age: BMI-for-Age between -2 and -3 z-score Normal/No Undernutrition: -Adult: BMI ≥18.5, or MUAC ≥23cm, -Children: WHZ ≥-2 or WHM ≥80%, MUAC ≥ 12 cm, -BMI-for-Age: 5-18 years ≥-2 Z- score. This indicator is the key to measure and work to improve the nutritional intervention service coverage, enabling and supporting adherence and retention to HIV care/ART for improved quality of life. The indicator enables the scale and coverage of these services to be tracked and monitors the extent to which these services are reaching those that need nutrition service.						
Disaggregation	Age: <1, 1-4, 5-14, 15-19, 20+ , Sex: Male/Female Pregnancy status: Non-pregnant and Pregnant, Nutritional status :MAM, and SAM						
Sources	Pre-ART register, ART register and PMTCT registers, ART related tallies, e-databases						
Frequency of Reporting	HP	HC/Clinic	Hospital	WorHO	ZHD	RHB	FMOH
		Monthly	Monthly	Monthly	Monthly	Monthly	Monthly

9. Number of persons provided with Post-Exposure prophylaxis

Definition	Number of persons provided with post-exposure prophylaxis (PEP) for risk of HIV infection through occupational and/or non-occupational exposure to HIV.					
Formula	Number of persons provided with post-exposure prophylaxis (PEP) for risk of HIV infection as per the national guideline.					
Interpretation	Individuals should be counted only if they have received PEP drugs (in accordance with national protocols). This indicator does not intend to capture the type and quality of PEP services provided. PEP services include first aid, counseling, testing, provision of ARVs, medical care, trauma counseling, linkages with police, and other follow-up and support. Simple monitoring of PEP availability through program records does not ensure that all PEP-related services are adequately provided to those who need them. PEP services for occupational exposure include a comprehensive package of services for occupationally exposed health care workers and patients. PEP services for non-occupational exposure include sexual violence. The indicator can be generated by counting the number of individuals receiving PEP for occupational and non-occupational purposes. Individuals should be counted only one (1) time, not incidence. And individuals should only be counted if they have received PEP drugs.					
Disaggregation	Exposure type: Occupational, Non-occupational					
Sources	PEP Register					
Frequency of Reporting	HP	HC	Hospital	WorHO	RHB	FMOH
		Monthly	Monthly	Monthly	Monthly	Monthly

10. Percentage of non-pregnant women living with HIV on ART using a modern family planning method

Definition	Percentage of non-pregnant women living with HIV on ART using a modern family planning method							
Formula	Number of non-pregnant women living with HIV on ART aged 15-49 reporting the use of any method of modern family planning							X 100
	Total number of non-pregnant women living with HIV on ART on ART aged 15-49							
Interpretation	This indicator will be used to monitor HIV/FP integration at ART sites. This indicator is a subset of contraceptive prevalence rate, but focuses specifically on HIV-infected women to measure progress in prong 2 (“prevent unwanted pregnancies among women living with HIV”) of the four prongs of PMTCT. Preventing unintended pregnancies in women living with HIV is a critical step towards reducing mother-to-child transmission and is a core component of the international standards for a comprehensive approach to PMTCT. Inherent within this indicator is the principle that integrated HIV/FP program activities must respect a client’s right to make informed decisions about his or her reproductive life. This means that clients should have access to an appropriate and comprehensive range of contraceptive options; and/or to safer conception/pregnancy counseling depending upon their fertility desire and intentions. All non-pregnant PLHIV women on ART reporting the use of modern contraceptive irrespective of where the service provided will be reported as using modern family planning method.							
Disaggregation	Age:15 - 19, 20–24, 25–49 years Method: - long acting / short acting							
Sources	ART register, PMTCT register, Pre ART Clinical care tally sheet							
Frequency of Reporting	HP	HC/Clinic	Hospital	WorHO	ZHD/ ScHO	RHB	FMOH	
		Monthly	Monthly	Monthly	Monthly	Monthly	Monthly	

7.3. Data reporting, data flow and quality assurance

Routine HIV HMIS data are assembled and reported on a quarterly and annual basis. Facilities aggregate and review their data monthly and report to their respective facility and administrative offices quarterly. The administrative office aggregates the data it receives, adds its own administrative figures, and monitors its own performance based on these reports and self-generated data. It then forwards the HMIS report to the next level. Annual reports include additional data that are not collected quarterly. These reports follow the same line and principles of disaggregation as the quarterly reports. Data aggregation methodology is maintained throughout the reporting chain so that it is possible to disaggregate data by facility type and ownership even at the federal level. HMIS Data flow from the facilities to the federal level is depicted below.

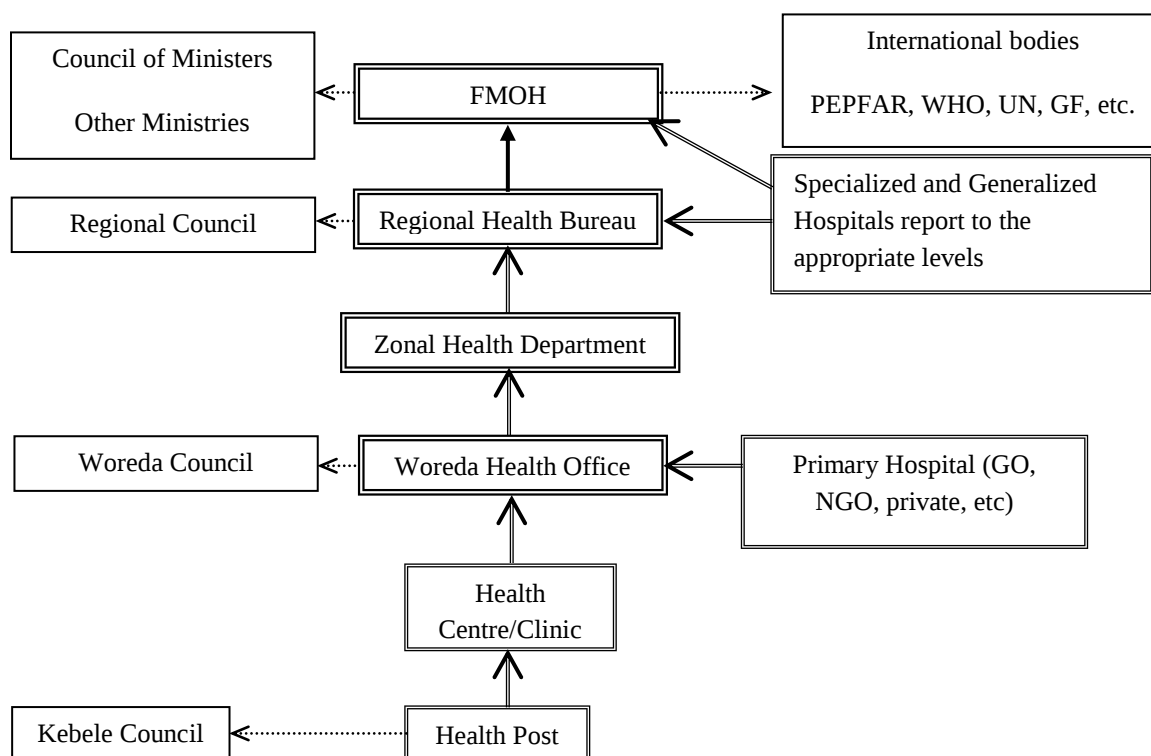


Figure 7.1 HMIS data flow and feedback loop

7.3.1. Data quality assurance

Data quality check is one of the components of the M & E system. Once data are collected, the data are checked for any inaccuracies and obvious errors at every level. The data quality assurance (DQA) is done at two levels: facility level and administrative level (district health offices). At facility level, such a mechanism is the Lot Quality Assurance Sampling (LQAS) methodology which is done on monthly basis. In this procedure randomly selected data elements from the monthly reports are checked against the register or source of the report. The findings are then compared to a standard Data Accuracy Table. The same procedure is done at district health offices on quarterly basis before the data are sent to the next higher reporting unit. Hence, in HMIS all reports are quality checked at every level, from the healthcare institution to the federal level.

7.4. Supportive supervision and review meetings

7.4.1. Supportive supervision

Supervision aims at ensuring and improving quality, effectiveness and efficiency of services provided; it should also enhance competence and satisfaction of the staff at all levels. Supervision consists of observation, discussion, support and guidance. Since it is an essential tool in the management of staff and facilities, it should be done on a regular basis. The overall aim of supervision is the promotion of continuous improvement in the performance of the staff.

Supervisions at all levels are conducted in an integrated manner using standardized checklist clearly identified in the Integrated Supportive Supervision (ISS) guideline. It is done from every administrative level to the respective office and health facility. The ISS guideline shows the actual process of implementation, team composition and checklist.

Besides ISS, in-depth HIV program-specific supervisions using standardized HIV and TB/HIV supportive supervision tool can also be conducted whenever critical gaps that require intensive technical approach are identified during the ISS.

7.4.2. Review meetings

Review meetings organized at various levels create a very good opportunity to review the status of program implementation, achievements and challenges and come up with workable solutions for

the problems and challenges encountered. They are key elements for program management. Furthermore, review meetings are forums for exchange of ideas and experiences among the health professionals and program coordinators. In these meetings, program coordinators from the next lower levels will present activity reports of their respective area, including major achievements and challenges or constraints encountered during the period under review. Integrated review meeting is conducted on regular bases at every level. In this manner, activities taking place at all levels will then be brought forward to the respective review meeting sessions where HIV and TB/HIV program performance is reviewed as part of the overall review meeting.

7.5. Other monitoring considerations

Programs are increasingly moving beyond coverage indicators to focus on critical outcomes, such as viral load suppression and immune reconstitution, and on the broader impact of HIV treatment, including HIV-related mortality and HIV incidence. However, programs also need to measure potential unintended outcomes, such as HIV drug resistance and ARV-related toxicities. Periodic evaluations and implementation research are also central to reviewing programs.

HIV drug resistance

The use of early warning indicators helps to identify deficits in program performance that favor the emergence of HIV drug resistance.

Evaluation, including impact and program performance, and implementation research

Routine monitoring should be complemented by systematic evaluations and program reviews to assess the performance and effects of HIV programs, either comprehensively or with respect to specific priority areas. Social science and implementation research are important to assess perceptions and values of service recipients and communities along with barriers, facilitators and experiences in delivering and receiving services. Impact indicators, such as incidence, morbidity and mortality, are often difficult to measure.

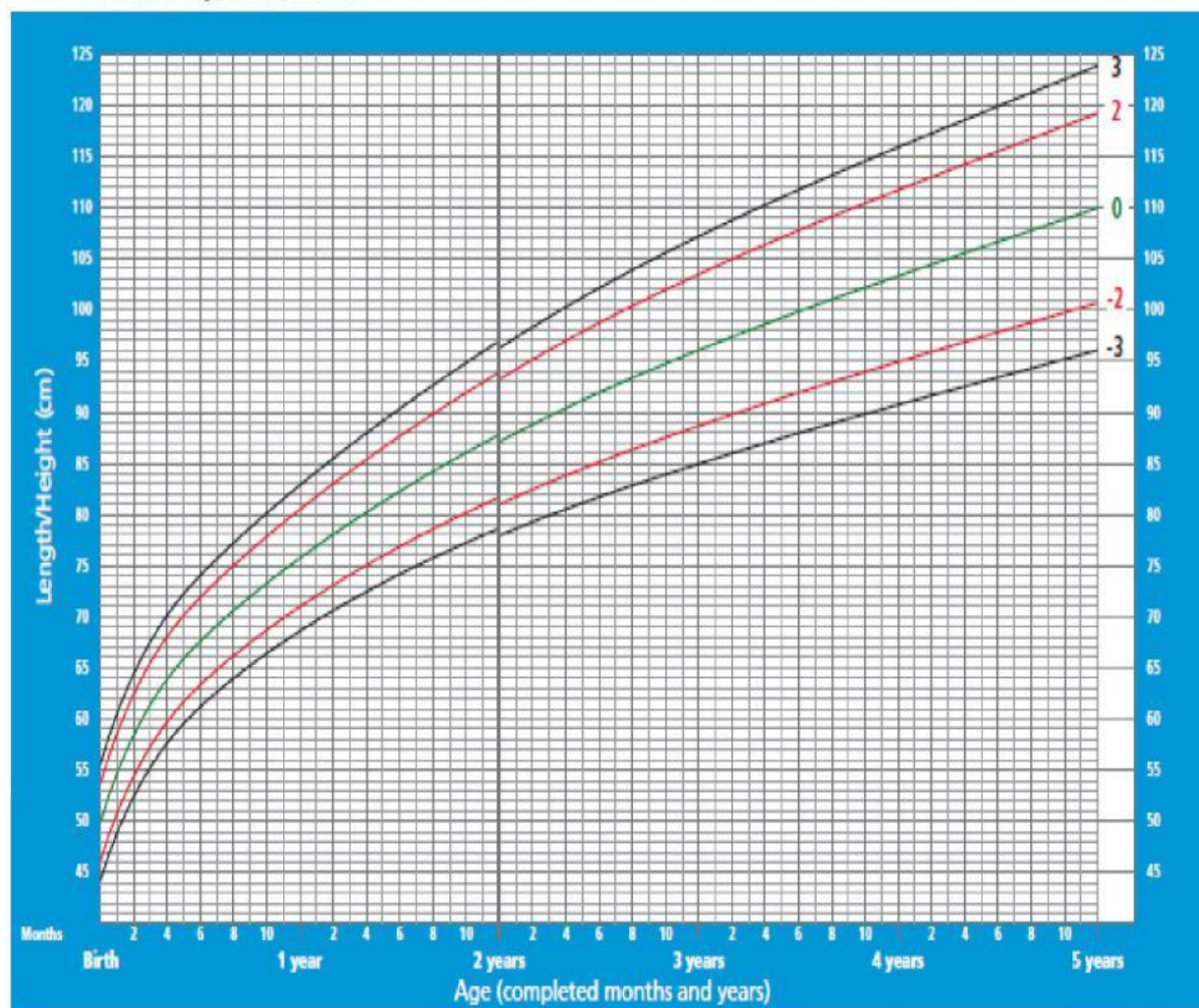
Mathematical modeling is often undertaken to project various scenarios for program planning and evaluating impact. Ensuring the availability of robust data is especially important when estimating the prevention impact of ARV drugs at the population level, as multiple sources of information and uncertainty come into play. Specific data collection efforts and models for particular contexts may provide more accurate estimates.

Annexes

Annex 1: Growth curves

Length/height-for-age BOYS

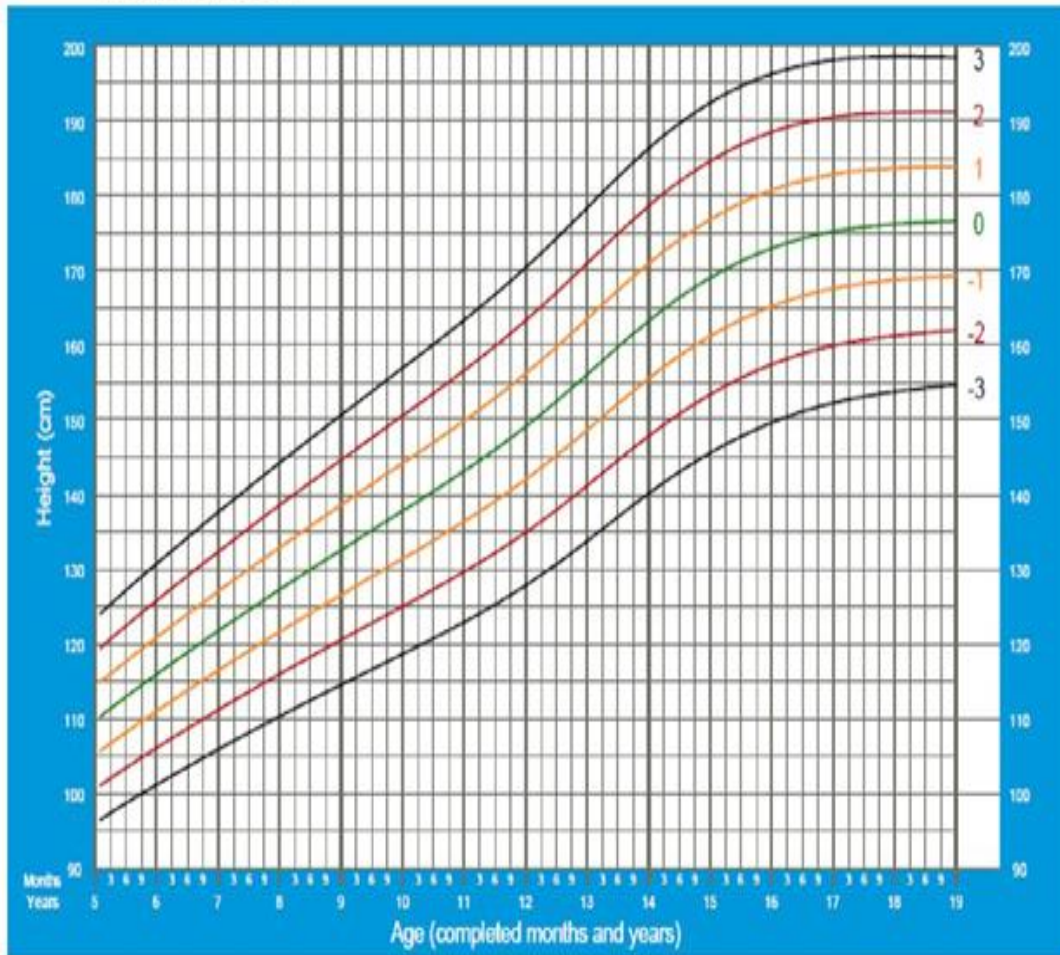
Birth to 5 years (z-scores)



WHO Child Growth Standards

Height-for-age BOYS

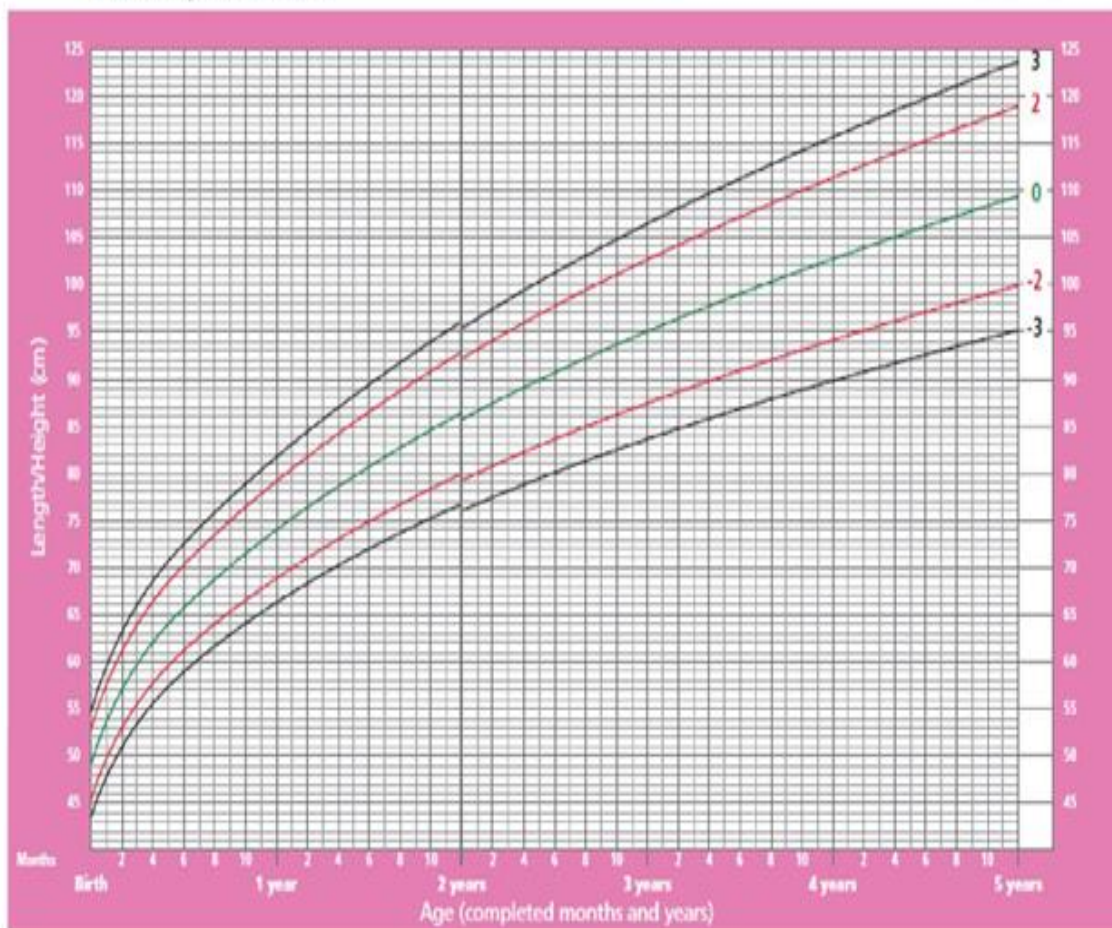
5 to 19 years (z-scores)



2007 WHO Reference

Length/height-for-age GIRLS

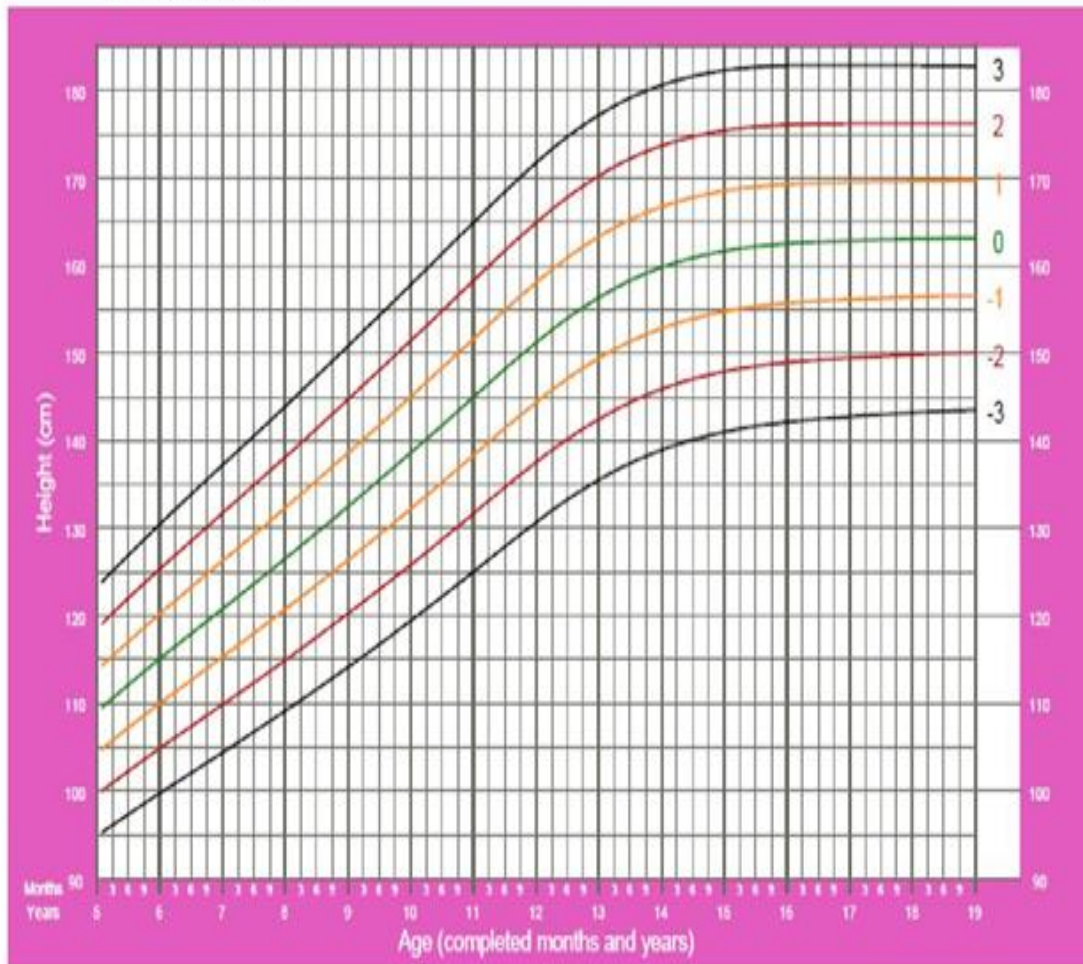
Birth to 5 years (z-scores)



WHO Child Growth Standards

Height-for-age GIRLS

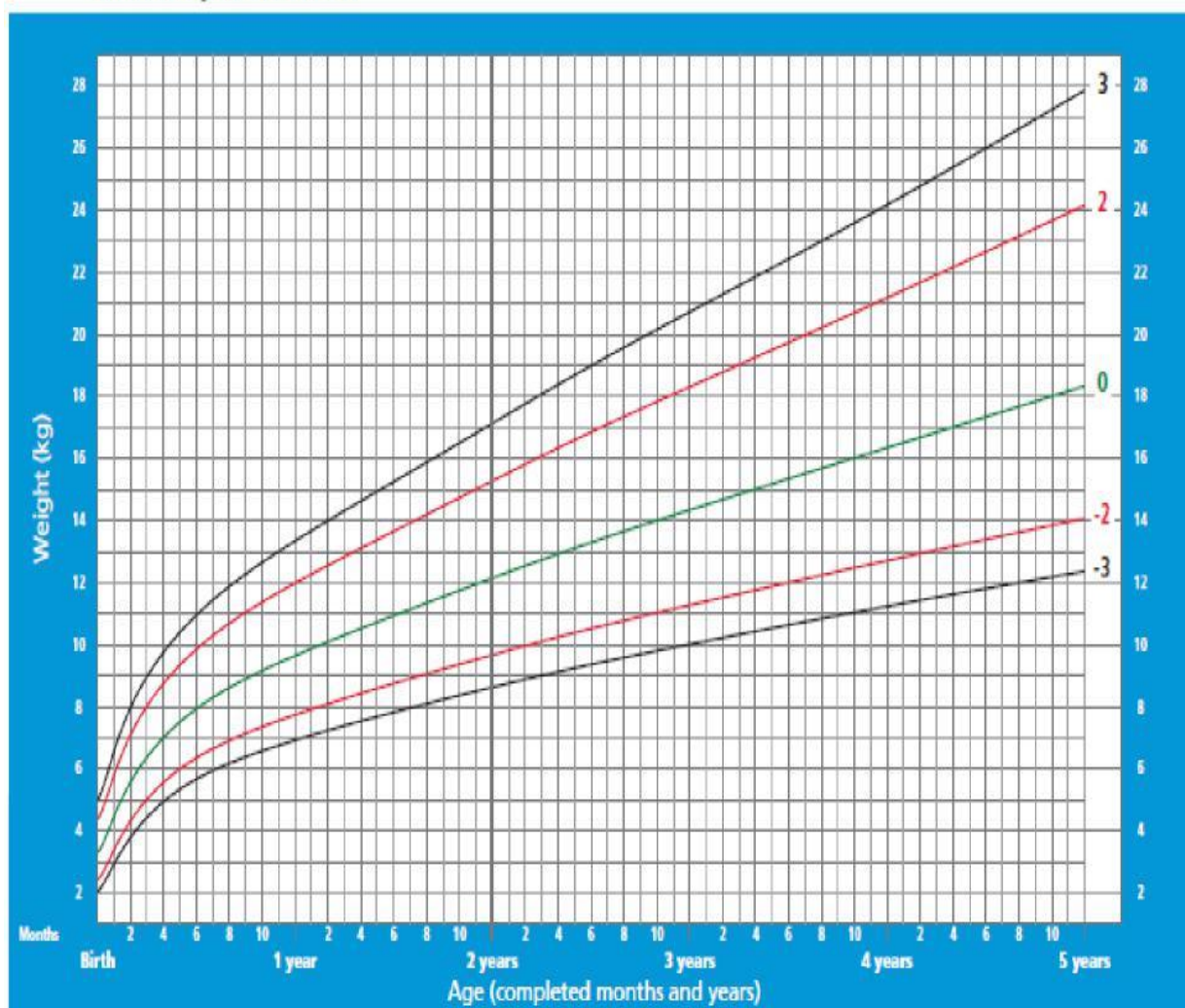
5 to 19 years (z-scores)



2007 WHO Reference

Weight-for-age BOYS

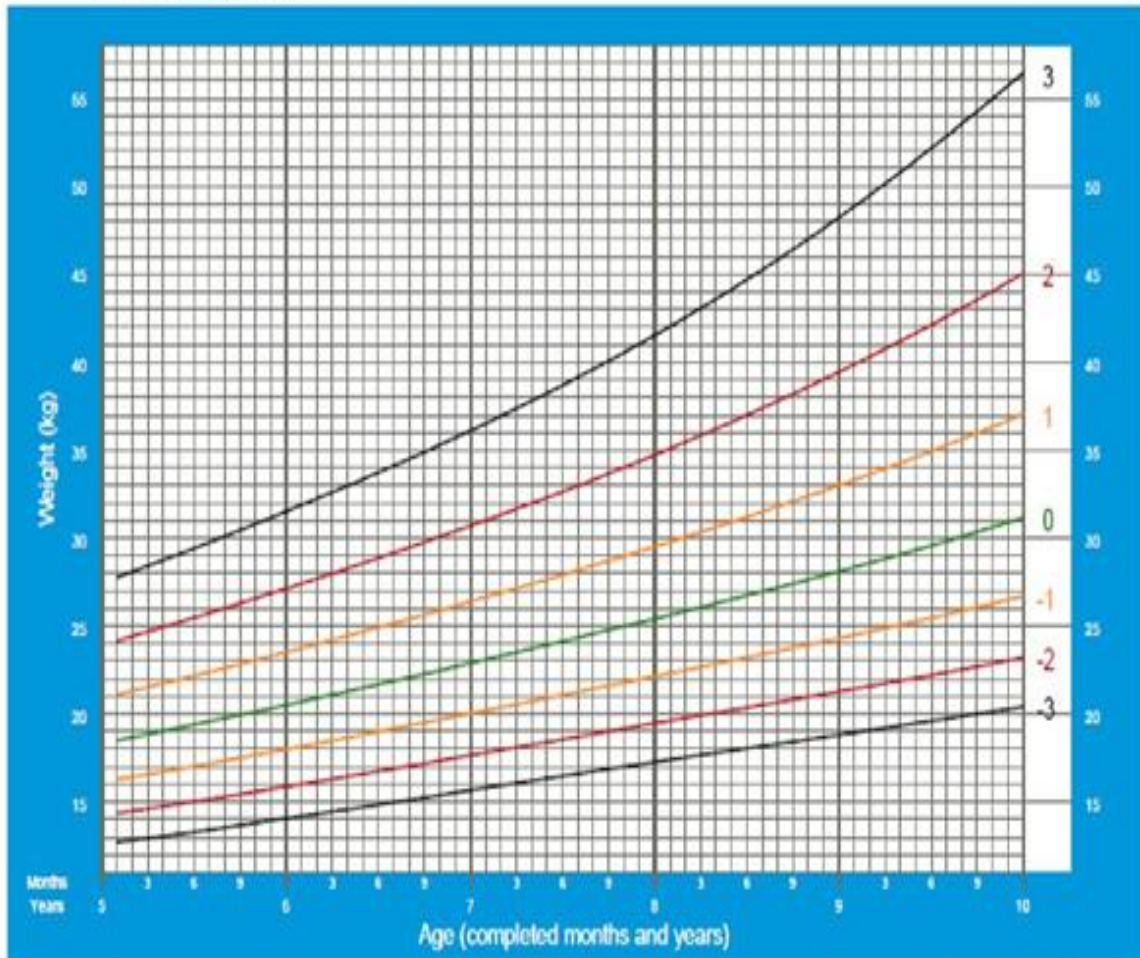
Birth to 5 years (z-scores)



WHO Child Growth Standards

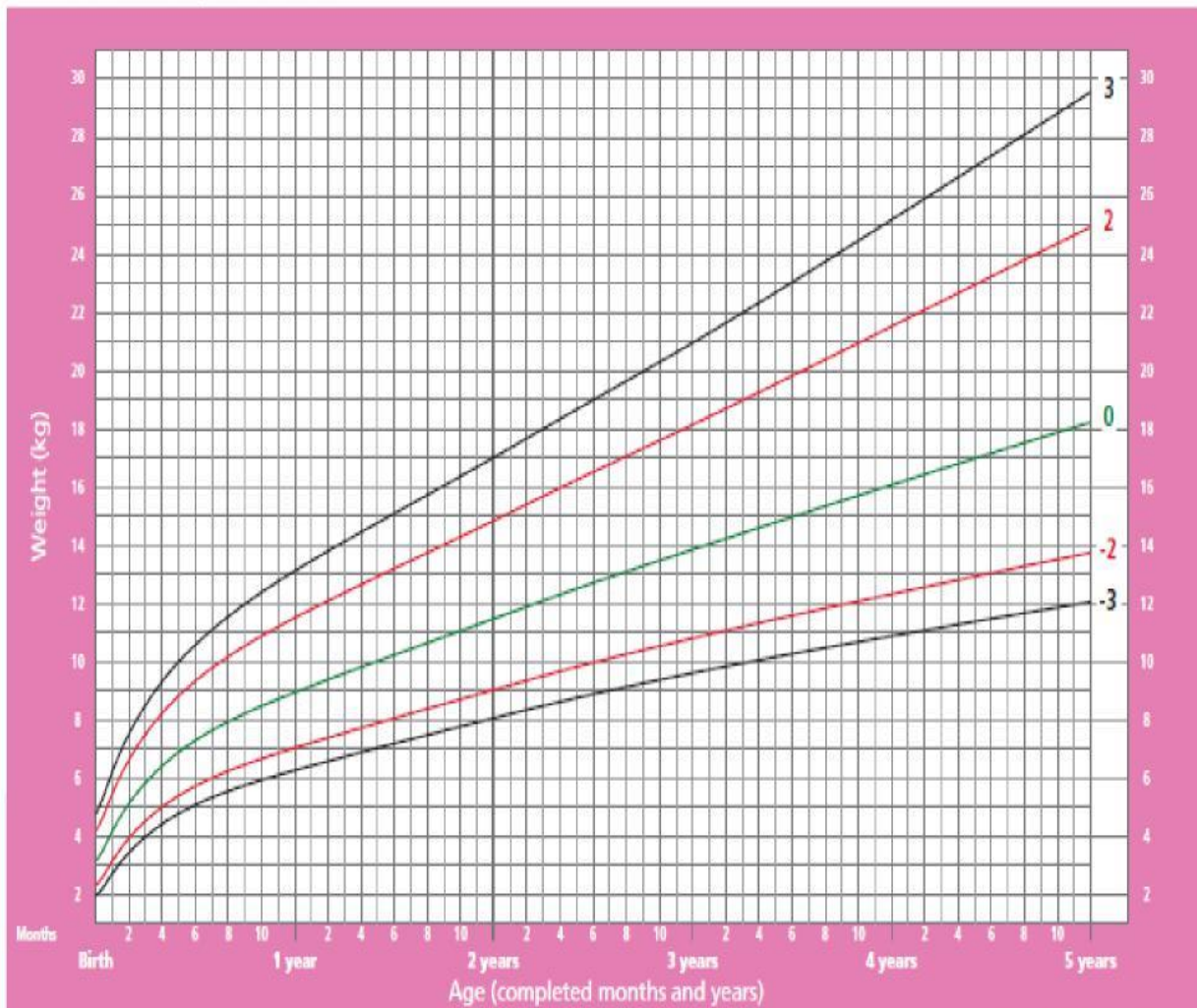
Weight-for-age BOYS

5 to 10 years (z-scores)



Weight-for-age GIRLS

Birth to 5 years (z-scores)



WHO Child Growth Standards

Weight-for-age GIRLS

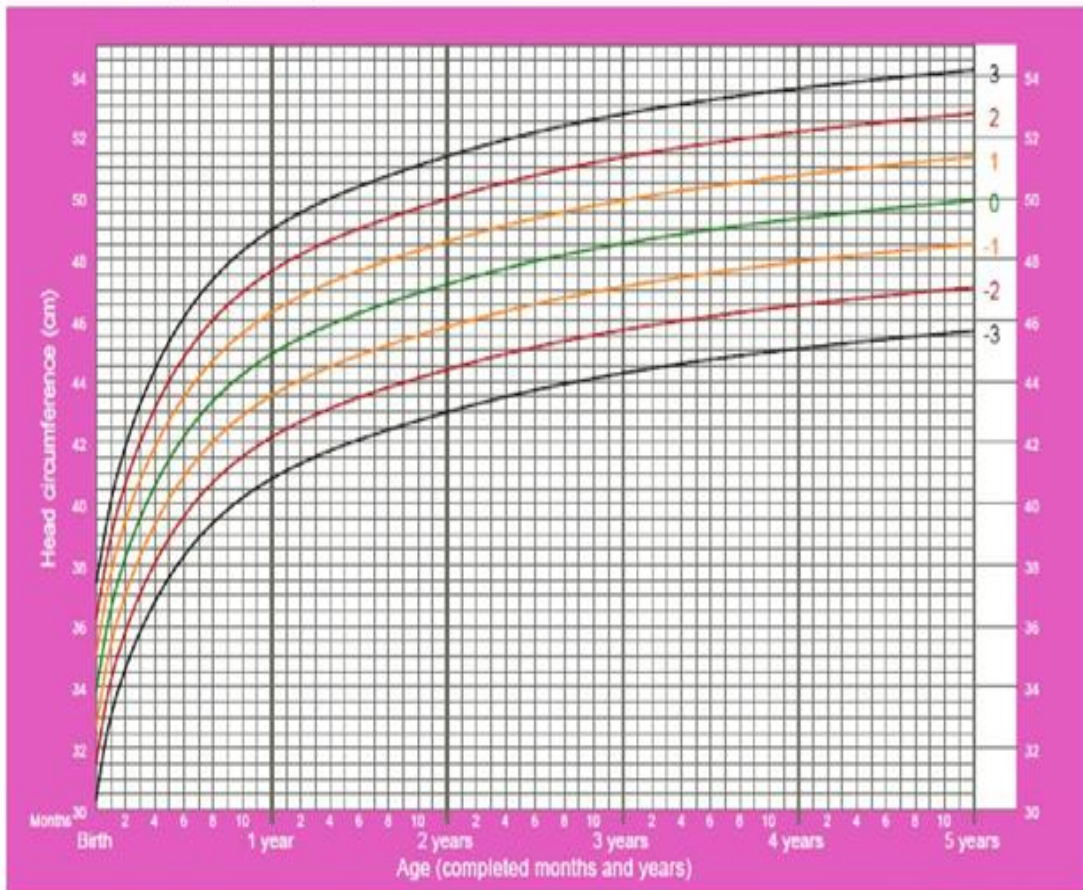
5 to 10 years (z-scores)



2007 WHO Reference

Head circumference-for-age GIRLS

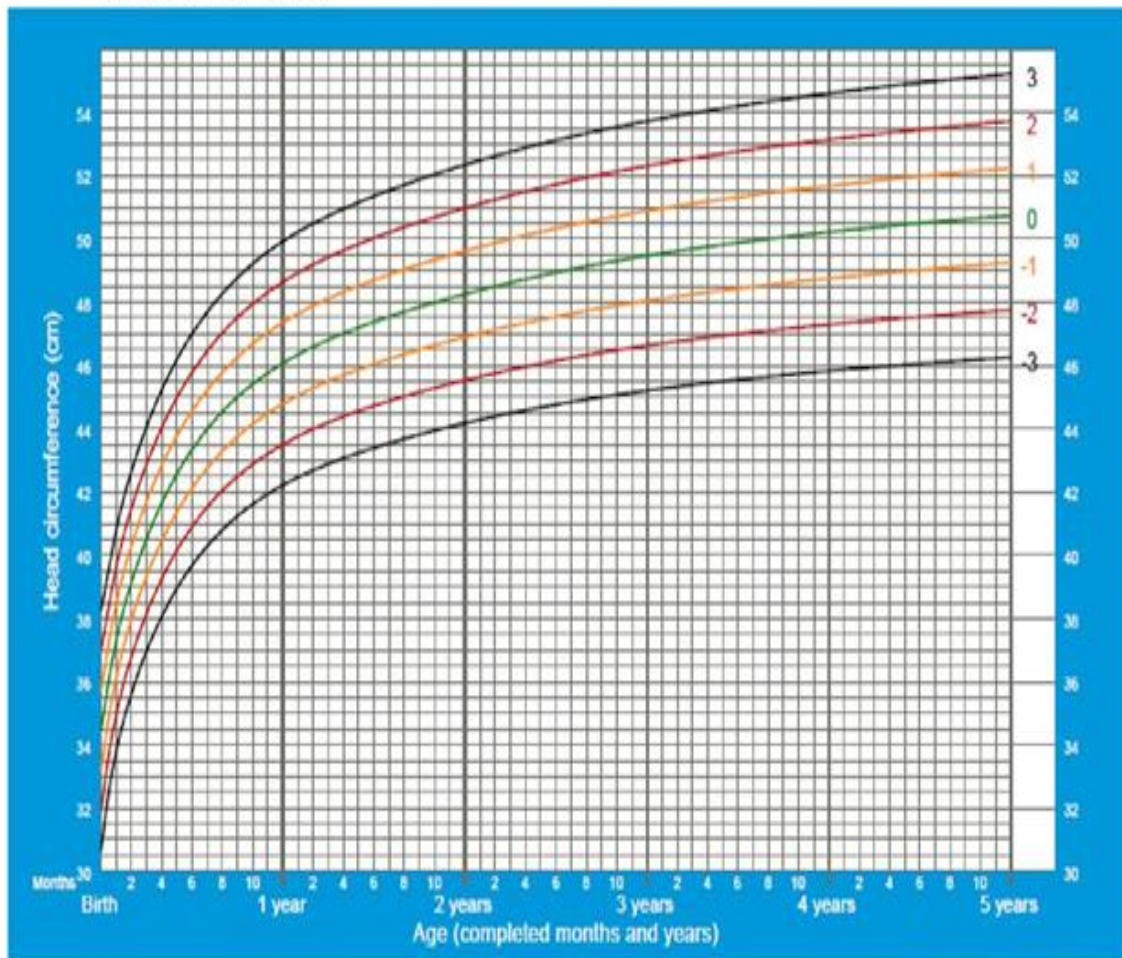
Birth to 5 years (z-scores)



WHO Child Growth Standards

Head circumference-for-age BOYS

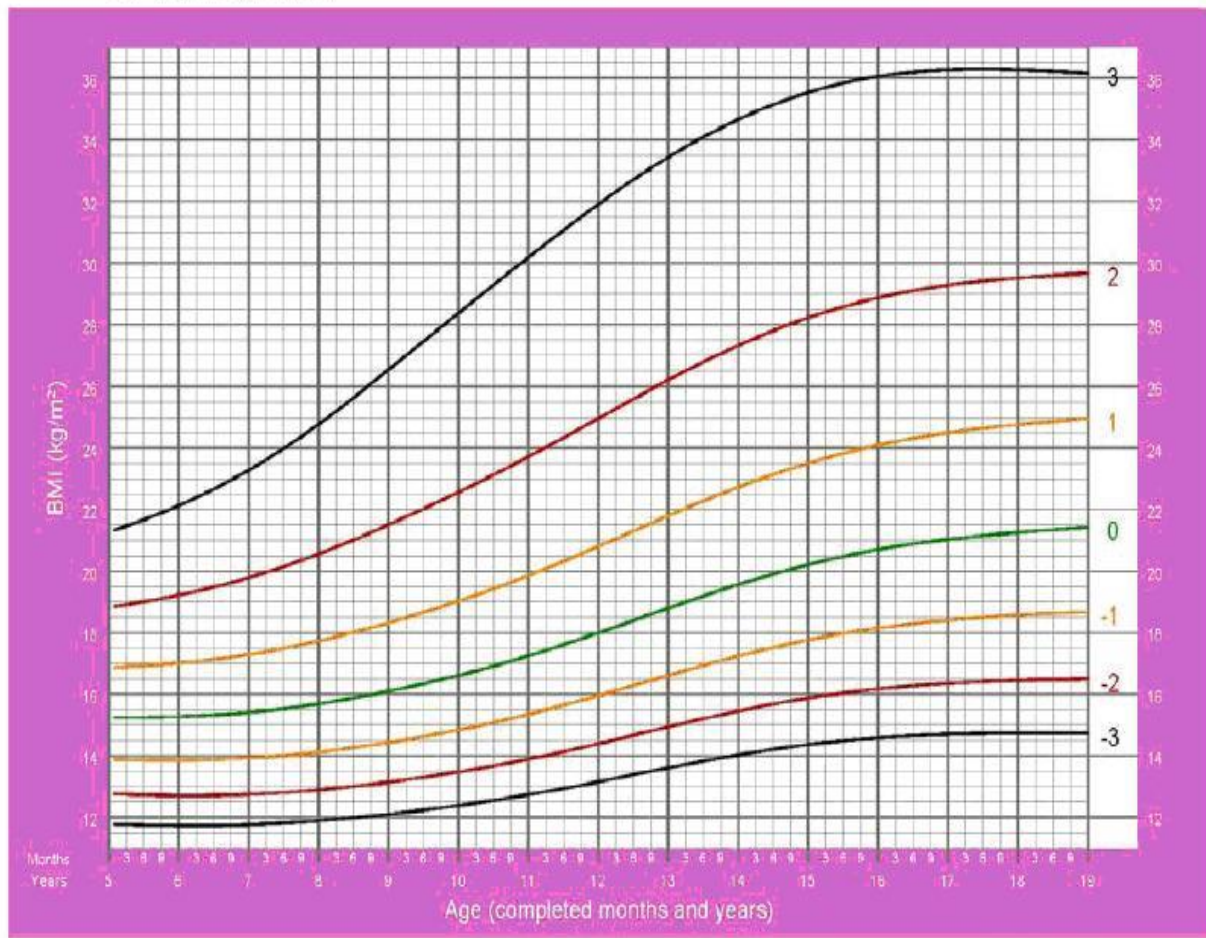
Birth to 5 years (z-scores)



WHO Child Growth Standards

BMI-for-age GIRLS

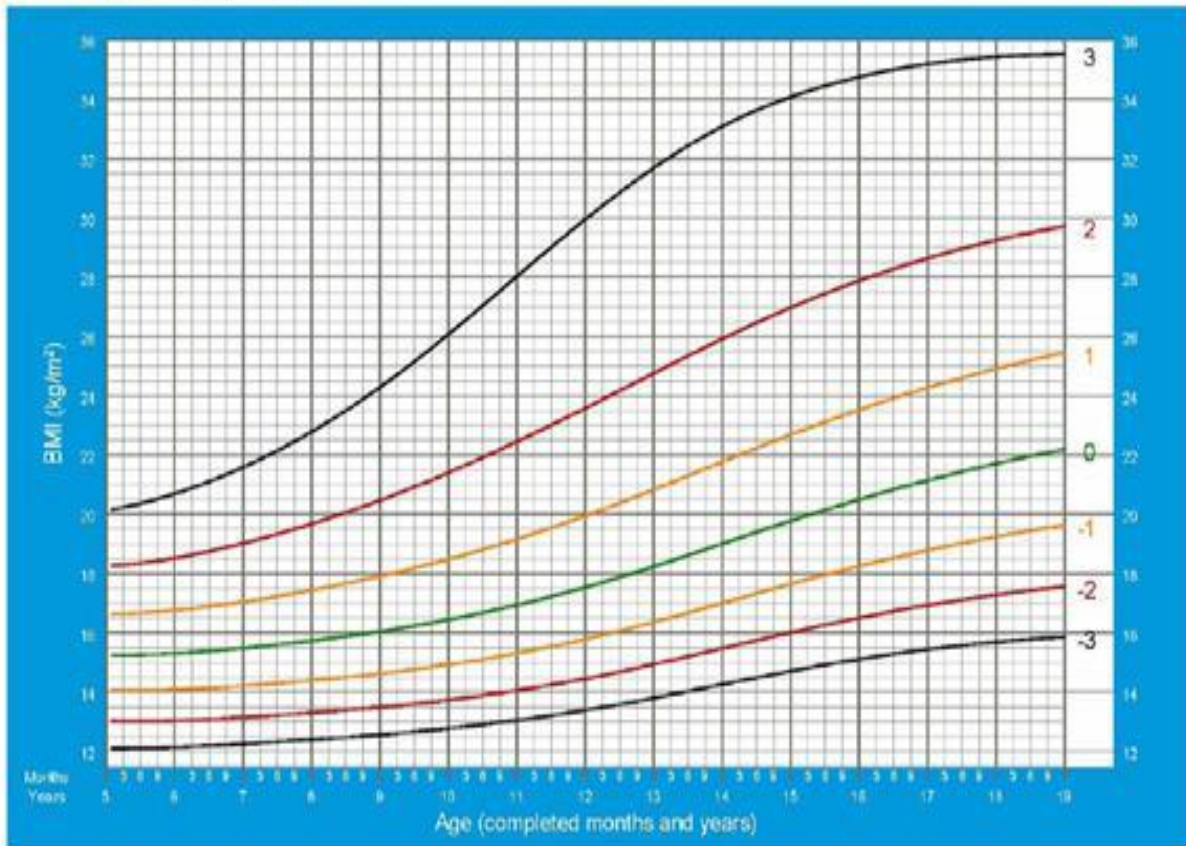
5 to 19 years (z-scores)



2007 WHO Reference

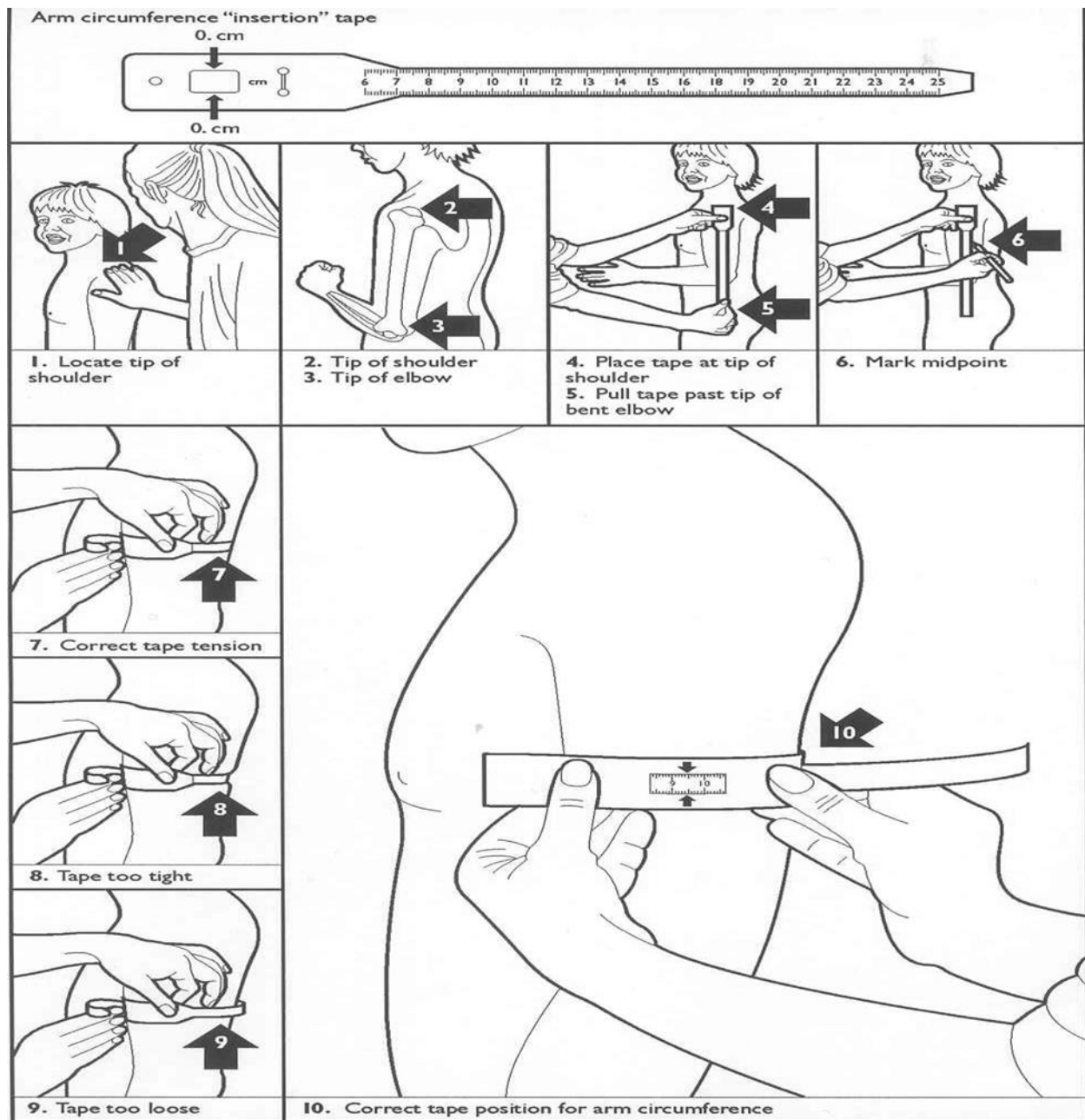
BMI-for-age BOYS

5 to 19 years (z-scores)



2007 WHO Reference

Annex 2. Instruction for MUAC measurement



Source: How to Weigh and Measure Children: Assessing the Nutritional Status of Young Children, United Nations, 1986.

Annex 3: Dosage of antiretroviral drugs for adults and adolescents

Nucleoside reverse-transcriptase inhibitors (NRTIs)	
Abacavir (ABC)	300 mg twice daily or 600 mg once daily
Emtricitabine (FTC)	200 mg once daily
Lamivudine (3TC)	150 mg twice daily or 300 mg once daily
Zidovudine (AZT)	250–300 mg twice daily
Nucleotide reverse-transcriptase inhibitors (NtRTIs)	
Tenofovir (TDF)	300 mg once daily
Non-nucleoside reverse-transcriptase inhibitors (NNRTIs)	
Efavirenz (EFV)	400–600 mg once daily
Etravirine (ETV)	200 mg twice daily
Nevirapine (NVP)	200 mg once daily for 14 days, followed by 200 mg twice daily
Proteases inhibitors (PIs)	
Atazanavir + ritonavir (ATV/r)	300 mg + 100 mg once daily
Darunavir + ritonavir (DRV/r)	800 mg + 100 mg once daily ^a or 600 mg + 100 mg twice daily ^b
Lopinavir/ritonavir (LPV/r)	400 mg/100 mg twice daily
	Considerations for individuals receiving TB therapy
	In the presence of rifabutin, no dose adjustment required. In the presence of rifampicin, adjusted dose of LPV/r: LPV 800 mg + RTV 200 mg twice daily or LPV 400 mg + RTV 400 mg twice daily).or, SQV/r (SQV 400 mg + RTV 400 mg twice daily), with close monitoring.
Integrase strand transfer inhibitors (INSTIs)	
Dolutegravir (DTG)	50 mg once daily
Raltegravir (RAL)	400 mg twice daily

^a For individuals with no previous use of protease inhibitors.

^b For individuals with previous use of protease inhibitors.

Annex 4: Dosage of antiretroviral drugs in children

Drug	Strength of Pediatrics Tab (mg) or Liquid	Number of tablets or ml by weight band (AM + PM)					Strength of Adult Tab (mg)	Number of tablets by Weight band (AM + PM)	
		Children 6 weeks of age and above						25 - 29.9 kg	30 - 34.9 kg
		3 – 5.9 Kg	6 - 9.9 kg	10 - 13.9 kg	14 - 19.9 kg	20 - 24.9 kg			
AZT/3TC	60/30	1 + 1	2 + 1	2 + 2	3 + 2	3 + 3	300/150	1 + 1	1 + 1
AZT/3TC/NVP	60/30/50	1 + 1	2 + 1	2 + 2	3 + 2	3 + 3	300/150/200	1 + 1	1 + 1
EFZ	50, 200	n/r	n/r	200 once daily	200 & 50 once	200 & 2 x 50 once	50, 200, 600	200 & 3 x 50	2 x 200 once
NVP	10 mg/ml	5ml + 5ml	8ml +	10ml + 10ml					
	200 (adult)				1 + 0.5	1 + 0.5	200	1 + 1	1 + 1
AZT	10 mg/ml	6ml + 6ml	9ml +	12ml + 12ml					
	300 (adult)				0.5 + 0.5	1 + 0.5	300	1 + 1	1 + 1
3TC	10 mg/ml	3ml + 3ml	4ml +	5 ml + 5ml					
	150 (adult)			.5 + .5	.5 + .5	1 + .5	150	1 + 1	1 + 1
ABC	20 mg/ml	3ml +3ml	4ml +	6ml + 6ml					
	60	1 + 1	2 + 1	2 + 2	3 + 2	3 + 3			
	300 (adult)				0.5 + 0.5	1 + 0.5	300	1 + 1	1 + 1
ABC/3TC	60/30	1 + 1	2 + 1	2 + 2	3 + 2	3 + 3	600/300	1 once daily	1 once daily
Lop/r ^a	80/20 mg/ml	1ml + 1ml	2ml +	2ml + 2ml	3ml + 2ml	3ml + 3ml			
	100/25	n/r	n/r	2 + 1	2 + 2	3 + 2			
	200/50 (adult)	n/r	n/r	n/r	1 + 1	1 + 1	200/50	2 + 1	2 + 2
TDF / 3TC	75/75	•	-	1.5	2	2.5		3-3.5	3-3.5
TDF/3TC/EFV	75/75/150	-	-	1.5	2	2.5		3-3.5	3-3.5
TDF/3TC adult double scored	300/300	-	--	One third	One half	Two third		1	1

TDF/3TC/EFV	300/300/600	-	-	One third	One half	Two third		1	1
DRV ^b	75 mg	-	-	3 + 3	5 + 5	5 + 5			
	Chewable tablets 25 mg	-	-	3 + 3	4 + 4	6 + 6	400 mg	1 + 1	1 + 1
	100 mg/ml	-	-	2.5 ml + 2.5 ml	3.5 ml + 3.5 ml	-			
RAL ^c	Chewable tablets 100 mg	-	-	-	1 + 1	1.5 + 1.5	400 mg	1 + 1	1 + 1
	Granules (100 mg/sachet)	0.25 + 0.25	0.5 + 0.5	-	-	-		-	-

^a LPV/r liquid requires a cold chain during transport and storage. The LPV/r heat-stable tablet formulation must be swallowed whole and should not be split, chewed, dissolved or crushed.

^b DRV must be administered with 0.5 ml of RTV 80 mg/mL oral suspension if the child weighs less than 15 kg and with RTV 50 mg solid formulation for children weighing 15–30 kg

^c RAL granules are approved for use for children as young as 4 weeks, but the feasibility and acceptability of such formulations has not been widely investigated, and concerns have been raised regarding administration in resource-limited settings.

Annex 5: Pediatric ARV drug formulations, side effects and special considerations in children

Drug / Formulation	Dosing recommendation and instructions	Side Effects
Nucleoside reverse transcriptase		
Lamivudine (3TC) : Formulations: Fixed-Dose Combination Tablets With Abacavir : • 3TC60mg+120mgABC, scored and dispersible tablet With Zidovudine : • 3TC30mg+AZT60mg, dispersible tablet With Zidovudine and Nevirapine: • 3TC30mg+AZT60mg+NVP50mg, dispersible tablet	Instruction for dosing/administration: • Can be given with food. • <u>For those who can't swallow whole tablet, dispersible tablets</u> can be <u>dissolved</u> with 2 teaspoons (10ml) water in a small and clean container and taken immediately. • <u>Scored tablets</u> can be broken to administer lower doses for younger children as recommended in the national ART guidelines. Note: • Adult formulations are to be used for children older than 10 years with body weight > 35kg. • Please see dosing Chart for dose recommendation. Storage: • Can be stored at room temperature	Side effects of 3TC: Common: head ache, nausea, abdominal pain. Less common: pancreatitis, neutropenia, increased LFTs. Hepatitis may exacerbate after discontinuation of lamivudine in the setting of chronic Hepatitis B virus infection. For those patients with HBV and HIV co-infection please consult “the national guideline on management of HBV infection-2016.”
Abacavir (ABC) : Formulations: Fixed-Dose Combination Tablets With Lamivudine :	Instruction for dosing/administration: • Can be given with food. • <u>For those who can't swallow whole tablet, dispersible tablets</u> can be <u>dissolved</u> with 2 teaspoons (10ml) water in a small and clean container and taken immediately.	Side effects of ABC: Common: head ache, GI upset and rash.

• ABC120mg+3TC60mg, scored and dispersible tablet	• <u>Scored tablets</u> can be broken to administer lower doses for younger children as recommended in the national ART guidelines. Note: • Adult formulations are to be used for children older than 10 years with body weight > 35kg. • Please see dosing Chart for dose recommendation. Storage: • Can be stored at room temperature	Less common: lactic acidosis, hepatomegaly with steatosis. Life threatening: potentially fatal hypersensitivity reaction (fatigue, rash, nausea and vomiting, sore throat, joint and muscle pain, cough, and dyspnea). Occurrence of hypersensitivity reactions requires immediate and permanent discontinuation of ABC. Advise patients/care givers what to do if hypersensitivity reactions occur at home. DO NOT re-challenge after hypersensitivity reaction.
Zidovudine (AZT or ZDV) Formulations: Oral solution, 50mg/5ml, 100 ml Fixed-Dose Combination Tablets: With Lamivudine : • AZT60mg + 3TC30mg, dispersible tablet With Lamivudine and Nevirapine: AZT60mg+3TC30mg+NVP50mg, dispersible tablet	Instruction for dosing/administration: • Can be given with food. • The syrup is for infant prophylaxis. • <u>For those who can't swallow whole tablet, dispersible tablets</u> can be <u>dissolved</u> with 2 teaspoons (10ml) water in a small and clean container and taken immediately. • <u>Scored tablets</u> can be broken to administer lower doses for younger children as recommended in the national ART guidelines. Note: • Adult formulations are to be used for children older than 10 years with body weight > 35kg. • Please see dosing Chart for dose recommendation. Storage:	Side effects of AZT: Common: neutropenia, anemia, granulocytopenia, macrocytosis, and head ache. Less common: myositis, myopathy, mitochondrial disease.

	• Can be stored at room temperature • Syrup is light sensitive, store in a brown glass jar and protect from sun light.	
Nucleotide reverse transcriptase inhibitor		
Tenofovir (TDF)	TDF is only approved for use for children 2 years and older. Target dose: 8 mg/kg or 200 mg/m² (maximum 300 mg). In case of TDF toxicity, substitute with AZT or ABC. Do not initiate TDF at eGFR <50 mL/min.	Chronic kidney disease Acute kidney injury and Fanconi syndrome Decreases in bone mineral density Lactic acidosis or severe hepatomegaly with steatosis
Non-nucleoside reverse transcriptase:		
Efavirenz (EFV) Formulations: Efavirenz 200 mg, scored tablet. Efavirenz 50 mg, tablet or capsule	Instructions for dosing/administration: • Used only for children $\geq$ 3 yrs. • Can be given with food but avoid administration with a high-fat meal because of potential for increased absorption that leads to CNS toxicity. • Bedtime dosing is recommended, particularly during the first 2 to 4 weeks of therapy, to improve tolerability of central nervous system side effects. • <u>Scored tablets</u> can be broken to administer lower doses for younger children as recommended in the national ART guidelines. • Efavirenz can be swallowed as a whole capsule or tablet. For children who can't swallow the whole capsule/tablet, the capsule content can be administered by sprinkling on food to avoid/mask peppery taste of EFV.	Side effects of EFV: Common: skin rash, dizziness, somnolence, insomnia, abnormal dreams, confusion, hallucinations, impaired concentration, psychosis, seizures, suicidality. Less common: increased LFTs.

	For sprinkling: • Hold capsule horizontally over a small container and carefully twist to open to avoid spillage. • Gently mix capsule contents with 1–2 teaspoons of an age-appropriate soft food (e.g. yogurt or banana or infant formula milk) at room temperature. • Administer the mixture that contains the sprinkle using a 10-mL syringe. • After administration, an additional 2 teaspoons of food or infant formula must be added to the container, stirred, and dispensed to the patient. Note: • Adult formulations are to be used for children older than 10 years with body weight > 35kg. • Please see dosing Chart for dose recommendation. Storage: • Can be stored at room temperature.	
Nevirapine (NVP) Formulations: Nevirapine oral syrup, 50mg/5ml (10mg/ml) Fixed-Dose Combination Tablets: With Lamivudine and zidovudine : AZT60mg+3TC30mg+NVP50mg, dispersible tablet	Instructions for administration: • Can be given with food. • The syrup is for infant prophylaxis • <u>Scored tablets</u> can be broken to administer lower doses for younger children as recommended in the national ART guidelines. • <u>For those who can't swallow whole tablet, dispersible tablets can be dissolved</u> with 2 teaspoons (10ml) water in a small and clean container and taken immediately. Caution: Multiple drug interactions. Note:	Side effects of NVP: Common: skin rash, head ache, nausea, diarrhea. Patients should be warned of rash. Do not escalate dose if rash occurs. Less common: increased LFTs. Life threatening: Steven Johnsons syndrome, TEN, fatal hepatitis. • For SJS and TEN discontinue drug and do not re-challenge.

	• Adult formulations are to be used for children older than 10 years with body weight > 35kg. • Please see dosing Chart for dose recommendation. Storage: Store at room temperature.	
Protease Inhibitors		
Lopinavir (LPV) Formulations: Combined with Ritonavir: Oral syrup, (LPV 80mg+RTVLPV20mg)/ml Oral pellets, (LPV40mg+Ritonavir10mg)/capsule Tablet, (LPV100mg+Ritonavir25mg)	Instructions for administration: • Do not administer to neonates before a post-menstrual age of 42 weeks and a postnatal age of at least 14 days. • Should be taken with food. • For the capsules: open the capsules, add the pellets from the capsule content onto small soft or milk (not more than 2ml) and administer immediately. • Tablets should not be opened or crushed, swallow whole. Tablets are for older children. • Liquid has low volume but bitter taste. Caution: Multiple drug interactions. Note: • Adult formulations are to be used for children older than 10 years with body weight > 35kg. • Please see dosing Chart for dose recommendation. Storage: • For the syrup, store it in a refrigerator at least until dispensed. Can be stored at room temperature (25°C) for 60 days. • For tablets and oral pellets, store at room temperature.	Side effects of LPV Common: diarrhea, head ache, nausea, vomiting,, increase in blood lipids Less common: pancreatitis, diabetes, hyperglycemia, hepatic toxicity, fat redistribution.
Ritonavir (RTV)	Take with food to increase absorption and reduce GI side effects.	Side effects of RTV:

Formulations: Combined with Lopinavir or Atazanavir:	Oral solution must be refrigerated. Can be kept at room temperature (25°C) if used within 30 days. Bitter taste, coat mouth with peanut butter or chocolate milk.	Common: N/V, diarrhea, headache, abdominal pain, anorexia Less Common: circumoral paraesthesia, increased LFTs, lipodystrophy, elevated cholesterol and triglycerides, hyperglycemia.
Danuravir (DRV) 75 mg tab; chewable tablets 25 mg; 100 mg/ml liquid	Substitute with LPV/r. When it is used in third-line ART, limited options are available. For hypersensitivity reactions, substitute with another therapeutic class.	Hepatotoxicity; severe skin and hypersensitivity reactions
Integrase strand transfer inhibitor		
Raltegravir (RAL) Chewable tablet 100 mg; granules (100 mg/sachet)	RAL granules are approved for use for children as young as 4 weeks, but the feasibility and acceptability of such formulations has not been widely investigated, and concerns have been raised regarding administration in resource-limited settings. In case of toxicity, substitute with another therapeutic class (boosted PIs).	Rhabdomyolysis, myopathy, myalgia; hepatitis and hepatic failure; severe skin rash and hypersensitivity reaction.

Annex 6: Grading of toxicity in adults and adolescents

Item	Grade 1 (Mild toxicity)	Grade 2 (Moderate toxicity)	Grade 3 (Severe toxicity*)	Grade 4 (Severe life-threatening toxicity)
Peripheral neuropathy	• Transient or mild discomfort, no limitation of activity. • No medical intervention/treatment required.	• Moderate limitation of activity, some assistance might be needed. • Non-narcotic analgesia required.	• Marked limitation in activity, some assistance usually required, medical intervention/therapy required, and hospitalization possible. • Severe discomfort and/or severe impairment (decrease or loss of sensation up to knees or wrists) narcotic analgesia required.	• Life-threatening, extreme limitation in of activity, significant assistance required, significant medical intervention/ therapy required, hospitalization/ hospice care. • Incapacitating or not responsive to narcotic analgesia. • Sensory loss involves limbs and trunk.
Cutaneous/Rash/Dermatitis**	Erythema, pruritus	Diffuse, maculopapular rash or dry desquamation	Vesiculation or moist desquamation or ulceration*	Erythema multiforme or suspected Stevens-Johnson syndrome or Toxic Epidermal Necrolysis (TEN).
Management	Continue ARV; provide careful clinical monitoring; and consider change of a single drug if condition worsens.		Substitute responsible drug	Stop ARV and consult experienced physician.

Annex 7- Grading of adverse events in children

Parameter	Grade 1 Mild	Grade 2 Moderate	Grade 3 Severe	Grade 4 Severe Life-threatening
Diarrhoea ≥1 year of age	Transient or intermittent episodes of unformed stools OR increase of ≤3 stools over baseline per day.	Persistent episodes of unformed to watery stools or increase of 4-6 stools over baseline per day.	Grossly bloody diarrhea or increase of ≥7 stools per day or IV fluid replacement indicated.	Life-threatening consequences (e.g. hypotensive shock).
<1 year of age	Liquid stools (more unformed than usual) but usual in number.	Liquid stools with increased number of stools or mild dehydration.	Liquid stools with moderate dehydration.	Liquid stools resulting in severe dehydration with aggressive rehydration indicated or hypotensive shock.
Nausea	Transient (<24 hours) or intermittent nausea with no or minimal interference with oral intake.	Persistent nausea resulting in decreased oral intake for 24-48 hours.	Persistent nausea resulting in minimal oral intake for >48 hours or aggressive rehydration indicated (e.g. IV fluids).	Persistent nausea with no or minimal oral intake resulting in dehydration with aggressive rehydration indicated.
Vomiting	Transient or intermittent vomiting with no or	Frequent episodes of vomiting with no or mild dehydration.	Persistent vomiting resulting in orthostatic hypotension or	Life threatening consequences (e.g. hypotensive shock).

Parameter	Grade 1 Mild	Grade 2 Moderate	Grade 3 Severe	Grade 4 Severe Life-threatening
	minimal interference with oral intake.		aggressive rehydration indicated (e.g. IV fluids).	
Acute systemic allergic reaction	Localized urticaria (wheals) lasting a few hours.	Localized urticaria with medical intervention indicated or mild angio oedema.	Generalized urticaria or angio oedema with medical intervention indicated or symptomatic mild bronchospasm.	Acute anaphylaxis or life-threatening bronchospasm or laryngeal oedema.
Pancreatitis	NA	Symptomatic and hospitalization not indicated (other than emergency treatment).	Symptomatic and hospitalization not indicated (other than emergency treatment).	Life-threatening consequences (e.g. Circulatory failure, haemorrhage, sepsis).
Rash	Localized macular rash	Diffuse macular, maculopapular, or morbilliform rash or target lesions.	Diffuse macular, maculopapular, or morbilliform rash with vesicles or limited number of bullae or superficial	Extensive or generalized bullous lesions or Stevens-Johnson syndrome or ulceration of mucous membrane involving two or more distinct mucosal

Parameter	Grade 1 Mild	Grade 2 Moderate	Grade 3 Severe	Grade 4 Severe Life-threatening
			ulcerations of mucous membrane limited to one site.	sites or Toxic Epidermal Necrolysis.
Alteration in personality-behavior or mood	Alteration causing no or minimal interference with usual social and functional activities	Alteration causing greater than minimal interference with usual social and functional activities.	Alteration causing inability to perform usual social and functional activities and intervention indicated.	Behavior potentially harmful to self or others or with life-threatening consequences.
Altered Mental Status	Changes causing no or minimal interference with usual social and functional activities	Mild lethargy or somnolence causing greater than minimal interference with usual social and functional activities.	Onset of confusion, memory impairment, lethargy, or somnolence causing inability to perform usual social and functional activities.	Onset of delirium, obtundation, or coma.
Source: Antiretroviral therapy of HIV infection in infants and children in resource-limited settings. WHO 2006				

Annex 8. Laboratory grading of adverse events in adults and adolescents (ACTG)

Laboratory Test Abnormalities				
Item	Grade 1 toxicity	Grade 2 toxicity	Grade 3 toxicity	Grade 4 toxicity
Haemoglobin	8.0-9.4 g/dL	7.0-7.9 g/dL	6.5-6.9 g/dL	<6.5 g/dL
Absolute Neutrophil Count	1,000-1,500 mm ³	750-990 mm ³	500-749 mm ³	<500 mm ³
Platelets	-75,000- 99,000	50,000-74,999	20,000-49,999 mm ³	<20,000
ALT	1.25-2.5 X upper normal limit	2.5-5 X upper normal limit	5.0-10 X upper normal limit	10 X upper normal limit
Bilirubin	1-1.5XULN	1.5-2.5 X ULN	2.5-5 x upper limits of normal	>5 x upper limits of normal
Amylase/lipase	1-1.5XULN	1.5-2 X ULN	2-5 x upper limits of normal	>5x upper limits of normal
Triglycerides *	200-399mg/dL	400-750 mg/dL	751-1200mg/dL	>1200mg/dL
Cholesterol *	1.0 –1.3 X Upper normal limit	1.3-1.6 X Upper normal limit	1.6-2.0 X Upper normal limit	2.0 X Upper normal limit
MANAGEMENT	Continue ARV Repeat test 2 weeks after initial test and reassess		substitute responsible drug	Stop ARV and consult experience physician
	Lipid imbalances could be managed with diet, exercise and pharmacologically with the use of fibrates. ALWAYS SEEK EXPERT ADVICE IN CASE OF DOUBT			

Grade 1 (Mild reaction): are bothersome but do not require changes in therapy

Grade 2 (Moderate reaction): consider continuation of ART as long as feasible. If the patient does not improve in symptomatic therapy, consider single-drug substitution.

Grade 3 (Severe reaction): Substitute offending drug without stopping ART. Closely monitor using laboratory and clinical parameters.

Grade 4 (Severe life-threatening reaction): Immediately discontinue all ARV drugs, manage the medical event with symptomatic and supportive therapy, and reintroduce ARV drugs using a modified regimen (i.e. with an ARV substitution for the offending drug) when the patient is stabilised. Life-threatening toxicity includes severe hepatitis, pancreatitis, lactic acidosis or Steven-Johnson syndrome.

Annex 9 - Grading toxicities in children by selected laboratory findings

Parameter	Grade 1 Mild	Grade 2 Moderate	Grade 3 Severe	Grade 4 Severe Life threatening
Haemoglobin (g/dL)	8.5 – 10.0	7.5 – <8.5	6.5 – <7.5	<6.5
ANC (mm ³)	750 – <1,000	500 – 749	250 – 500	<250
Platelets (mm ³)	100,000 – <125,000	50,000 – <100,000	25,000 – <50,000	<25,000 or bleeding
ALT (SGPT)	1.25 – 2.5 x ULN	2.6 – 5.0 x ULN	5.1 – 10.0 x ULN	>10.0 x ULN
AST (SGOT)	1.25 – 2.5 x ULN	2.6 – 5.0 x ULN	5.1 – 10.0 x ULN	>10.0 x ULN
Bilirubin (>2 weeks of age)	1.1 – 1.5 x ULN	1.6 – 2.5 x ULN	2.6 – 5.0 x ULN	>5.0 x ULN
Lipase	1.1 – 1.5 x ULN	1.6 – 3.0 x ULN	3.1 – 5.0 x ULN	>5.0 x ULN
Pancreatic amylase	1.1 – 1.5 x ULN	1.6 – 2.0 x ULN	2.1 – 5.0 x ULN	>5.0 x ULN
Cholesterol (fasting, <18 years old) mg/dL	170 – <200	200 – 300	>300	NA
Glucose, serum, Nonfasting (mg/dL)	116 – <161	161 – <251	251 – 500	>500

Glucose, serum, high: Fasting (mg/dL)	110 – <126	126 – <251	251 – 500	>500
Lactate	<2.0 x ULN without acidosis	≥2.0 x ULN without acidosis	Increased lactate with pH <7.3 without life threatening consequences or related condition present	Increased lactate with pH <7.3 with life threatening consequences (e.g. neurological findings, coma) or related condition present
Triglycerides: Fasting (mg/dL)	NA	500 – <751	751 – 1,200	>1,200
Source: Antiretroviral therapy of HIV infection in infants and children in resource-limited settings. WHO 2006				

Annex 10: Pediatric TB screening tool

		Follow Up Visit					
Children TB screening questions		Date:	Date	Date:	Date:	Date:	Date:
Current cough							
Fever							
Poor weight gain*							
Close Contact history with TB pt.							
*poor wt gain = reported wt loss, very low wt (<-3 Z-score), or underwt (< -2 Z-score), or confirmed wt loss (> 5%) since the last visit or growth curve flattening							
Evaluation for positive TB screening							
Bacteriology:	date ordered						
Gastric	date result received						
Aspirate/Induc	result (+, -ve, Not Done)						
Radiology:	date ordered						
CxR, etc.	date received						
	result (Suggestive, inconclusive, other dx, Not)						
Other: FNA, etc	date ordered						
	date received						
	result (+, -ve, Not Done)						
TB diagnosis date: / / Circle type of TB: PTB :- smear pos, smear neg, EPTB TB Rx start date							
Is the child eligible for IPT? Yes___ No___ If no, reason If yes, start IPT and use the chart below							
Contraindications for IPT: Active TB, active hepatitis, allergy to INH, peripheral neuropathy							
Date INH collected	TB Symptoms [cough, fever, failure to gain wt or wt loss] (yes, no)	Hepatitis Sx [abdominal pain, nausea, vomiting, abnormal LFT] (yes, no)	Neurologic Sx [numbness, tingling, paresthesia] (yes, no)	Rash (yes, no)	Adherence (≥95% =good; 85-94%= Fair <85%=Poor)	Remark	
___/___/___							
___/___/___							
___/___/___							
___/___/___							
___/___/___							
___/___/___							

Outcome of IPT (Write Date): Completed ___/___/___ Defaulted ___/___/___ Died ___/___/___

Interrupted for any reason ___/___/___

Note:

- If there are symptoms suggesting TB during follow up, stop INH and work up for TB.
- If there are symptoms suggesting hepatitis, hold INH. Can resume when liver function normalizes.
- If there are neurologic symptoms, continue INH and give pyridoxine 50mg daily. This side effect is rare if the child is already on pyridoxine skin rash is very rare, if occurs and is extensive, discontinue INH, and give anti histamine.

Annex 11: Adult TB screening tool

		Follow Up Visit					
Children TB screening questions		Date:	Date:	Date:	Date:	Date:	Date:
1.	Current cough						
2.	Fever						
3.	Weight lose						
4.	Night seats						
Evaluate for TB if "yes" to anyone of the above (positive TB screening)							
Bacteriology:	Done = yes/no						
Sputum for AFB (+/- induced)	result (+, -ve, unknown)						
Radiology: CxR,	Done = yes/no						
etc.	Result (Suggestive, inconclusive, other dx, Not Done)						
FNA, culture,	Done = yes/no						
ultrasound etc	If done result						
TB diagnosed	Yes (write type of TB)/No						
Is patient eligible for IPT	Yes/No						
Contraindications for IPT: Active TB, active hepatitis, allergy to INH, peripheral neuropathy							
IPT start date _____							
Date INH collected	TB Symptoms [cough, fever, wt loss] (yes, no)	Hepatotoxicity [abd pain, nausea, vomiting,	Neurologic Sx [numbness, tingling, paresthesia](yes,		Adherence (≥95% =good; 85-94%= Fair <85%=Poor)		Remark
___/___/___							
___/___/___							
___/___/___							
___/___/___							
___/___/___							
___/___/___							

Outcome of IPT (Write Date): Completed ___/___/___ Defaulted ___/___/___ Died
 ___/___/___ Patient stopped ___/___/___ Stopped ___/___/___
 Transferred out ___/___/___

Annex 12: Client with high viral load follow-up form

Name of Health Facility: _____			
1. Patient Information: Name: _____ Age: ____ Sex: ☐ M ☐ F UAN: _____			
2. ARV Information		Viral Load Results	
ARV Regimen	Date of initiation:	1 st VL result: _____ c/ml Date: ____/____/____	
_____	____/____/____	Previous VL (If any): _____ c/ml Date: ____/____/____	
_____	____/____/____		
_____	____/____/____	Date of 1 st VL result & 1 st EAC Session given: ____/____/____	

3. Communicate the viral load **test** result and explain the following to the client

- Viral Load is the number of HIV copies in the blood
- High VL result can be due to poor adherence to medication or can be due to primary resistance.
- When VL result is high in the blood, the CD4 count decreases, OIs are flare up and disease progresses.
- High VL can be reduced as a result of good adherence to medication within three months.

4. Assess current adherence to treatment and document →		Adherence Rate at EAC Session 1		
		>95%	85-94%	<85%
		Good	Fair	Poor
4.1	How many ARV dose/s do you take/day? ☐ Once ☐ Twice	≤2 dose	3-4 doses	≥5 doses
		≤3 doses	4-9 doses	>9 doses
4.2	Did you miss ARV doses in the past one month? Yes/No			
4.3	If Yes, how many dose/s did you miss? ☐ ≤2 ☐ 3-4 ☐ ≥5 ☐ <3 ☐ 4-9 ☐ >9			

5. Explore Medical and Psychosocial Reasons for High VL

EAC

5.1 Identify Medical Reasons for High Viral Load

Session 1

- | |
|---|
| <ul style="list-style-type: none"> • Did you take other drugs than ARVs without consulting your physician? (Yes, No), • If Yes, identify the drug/s, review interaction with ARVs, counsel the client & take measure |
| <ul style="list-style-type: none"> • Have you ever developed recurrent OIs including cough, fever, weight loss, night sweat, diarrhoea, and vomiting in the past? (Yes, No). If yes, investigate for TB and chronic diarrhea and manage |
| <ul style="list-style-type: none"> • Have you ever developed severe ARV drugs side effects in the past? (Yes, No), If Yes, investigate and manage for ARVs side effects. |
| <ul style="list-style-type: none"> • Have you ever taken ART/PMTCT prophylaxis in the past prior to ART initiation? • (Yes, No), If Yes, suspect primary resistance and consult ART physician |
| <ul style="list-style-type: none"> • Did you discontinue your ARV in the past? (Yes, No), If Yes, identify reasons and develop treatment plan with the client. |

If the client is a child, check proper dosing for weight by reviewing chart and readjust ARV dosing for weight.	
5.2 Identify Psychosocial Reasons for High Viral Load	
5.2.1 Cognitive barriers: understanding and expectation - counsel & explain expected outcomes What were the reason/s for missing your ARV dose/s in the past? Identify the reason/s, counsel and motivate the client to develop medication taking plan.	
5.2.2. Socio-economic barriers: lack of social support, disclosure, stigma, & poor living condition - Have you disclosed your HIV status to anyone? If No, provide disclosure counseling and encourage - Do you have treatment supporter?(Yes, No) If No, counsel to designate treatment supporter	
5.2.3 Behavioural barriers: attitude, motivation, confidence & skills – educate, motivate, and empower client to manage medication taking and develop reminder - What do you do to remind yourself to take drugs on time? - Are you confident to take your ARV openly at home?	
5.2.4 Psychological/Emotional barriers: common mental illness: depression, PTSD, substance abuse, and psychosis – link to psychiatric clinic for psychotherapy & treatment Have you ever felt sad for more than 2 weeks? Have you ever lost interest in activities that usually give you pleasure for more than 2 weeks? Have you regularly taken alcohol or chew Khat?	

4. Assess current adherence to treatment and document		Rate at Session 2			Rate at Session 3		
		>95%	85-94%	<85%	>95%	85-94%	<85%
		Good	Fair	Poor	Good	Fair	Poor
4.1	How many ARV dose/s do you take/day? ☐ Once	≤2	3-4	≤5	≤2	3-4	≥5
	☐ Twice	≤3	4-9	>9	≤3	4-9	>9
4.2	Did you miss ARV doses in the past one month? Yes No						
4.3	If Yes, how many dose/s did you miss? ☐ ≤2 ☐ 3-4 ☐ ≥5 ☐ ≤3 ☐ 4-9 ☐ >9						

5. Explore Medical and Psychosocial Reasons for High VL	Date: __/__/__	Date: __/__/__
5.1 Follow-up status of identified medical reason/s for High Viral Load	EAC Session 2	EAC Session 3
5.2 Follow-up status of identified psychosocial reasons for High Viral Load		
5.2.1 Cognitive barriers:		
5.2.2 Socio-economic barriers:		
5.2.3 Behavioural barriers:		
5.2.4 Psychological/Emotional barriers:		

•		
•		



Outcome of EAC Sessions: • Did the patient attend all the appointments? (Yes No) If no, any reason? _____ • Major remaining barriers identified after EAC sessions: ☐ Behavioral ☐ Cognitive ☐ Socio-economic ☐ Emotional. _____ • If patient is defaulted EAC session/s or adherence barriers were not resolved, second Viral Load should be deferred and EAC extended. • Share decision with the team. • Date of collection of 2nd Viral Load: __/__/__, 2nd Viral Load result: ____c/ml Date: ____/____/____ • Your next plan? ☐ continue current regimen ☐ referring to ART Physician ART Nurse: _____ Date of final assessment: ____/____/____
Decision by ART physician What is the plan for this patient? ☐ Shifted to Second-line Regimen. ☐ continue current regimen Comment: _____ ART Physician: _____ Date: ____/____/____

Annex 13: Brief mental health disorders symptom screening tool and referral tool for PLHIV

Patient's Name: _____ MRN: _____ Unique ART No: _____ Date: _____

This checklist is to assist you in assessing and making a timely referral of the client to the treatment team. All behaviors listed below are important and should be taken seriously; they are also designed to help you decide if you should refer the client to the treatment team for further assistance. An answer of "yes" to any one of the following questions should prompt further referral and evaluation by the treatment team or mental health professional. Please put a (✓) to indicate a yes answer.

Questions to Identify Depression: In the past 3 months;

() Was there ever a time when you felt sad, or depressed for more than 2 weeks in a row?

() Was there ever a time lasting more than 2 weeks when you lost interest in most things like hobbies, work, or activities that usually give you pleasure?

Questions to Identify Anxiety: In the past 3 months;

() Did you ever have a period lasting more than 1 month when most of the time you felt worried and anxious?

() Did you have a spell or an attack when all of a sudden you felt frightened, anxious, or very uneasy when most people would not be afraid or anxious?

() Did you ever have a spell or an attack when for no reason your heart suddenly started to race, you felt faint, or you couldn't catch your breath?

Questions to Identify Mania: In the past 3 months;

() *when not high or intoxicated, did you ever feel extremely energetic, elated or irritable and more talkative than usual that stayed for at least a week?*

Questions to Identify Substance Abuse

() Have you ever felt the need to cut down on your use of alcohol or drugs?

() Has anyone annoyed you by criticizing your use of alcohol or drugs?

() Have you ever felt guilty because of something you've done while drinking or using drugs?

() Have you ever taken a drink or used drugs to steady your nerves or get over a hangover (eye-opener)? *A total of ≥2 may be suggestive of a problem.*

Questions to identify suicidal ideation: Since your last visit [or in the last 2 months];

() Have you wished you were dead, or wished you could go to sleep and not wake up?

() Have you had actual thoughts of killing yourself?

() Have you ever attempted to harm/kill yourself?

Questions to Identify Psychosis: Observe or ask families whether the patient (in the last 3 months);

() Talking & acting strangely or becoming very quiet and avoid talking.

() Claiming to hear voices or see things that other people don't.

() Being very suspicious, perhaps claiming that other people are trying to harm him/her.

Questions to Identify Dementia: Interview the patient or families whether the patient (in the last 3 months);

() Has trouble with memory.

() Has diminished orientation to time, place and person

() Has diminished executive function .

Questions to Identify Epilepsy:

() Did you ever have partial or generalized fits [sharp, shaky movements], frothing accompanied by loss of control of bowel or bladder function, sudden loss of consciousness, and stiff limbs?

Referred by: _____

Date: _____

Feedback (confirm the assessment)

The patient has:

() Mental Health Disorder (specify) _____

() Non Mental Health Disorder

Name of clinician: _____

Date: _____

