

# NATIONAL GUIDELINES FOR COMPREHENSIVE HIV PREVENTION, CARE AND TREATMENT



**Federal Democratic Republic of Ethiopia** | Ministry of Health

**2014**



# NATIONAL GUIDELINES FOR COMPREHENSIVE HIV PREVENTION, CARE AND TREATMENT



**Federal Democratic Republic of Ethiopia** | Ministry of Health

**2014**

# Contents

Foreword	i
Acknowledgement	iii
Acronyms and Abbreviations	iv

---

## Chapter 1

### **INTRODUCTION** **1**

1.1. Background and context	1
1.2. Rationale for the consolidated guideline	1

---

## Chapter 2

### **HIV DIAGNOSIS AND PREVENTION** **4**

2.1. HIV Testing and counseling (HTC) services	5
2.2. HIV testing and counseling in specific populations	11
2.3. Quality Management	14
2.4. Policy, Ethical & Legal considerations for HIV Testing and Counseling	16
2.5. Post Exposure management including Prophylaxis	18
2.6. Combination Prevention	23
2.7. Care of HIV exposed infants	27

---

## Chapter 3

### **CARE AND TREATMENT OF PEOPLE WITH HIV INFECTION** **34**

3.1. General care packages for PLHIV	35
3.2. Pre-ART care package	35
3.3. Preparing people living with HIV for ART	35
3.4. When to Start ART	36
3.5. What ART regimen to start with (first-line ART)	38
3.6. Monitoring response to ART and the diagnosis of treatment failure	42
3.7. Monitoring the response to ART and the diagnosis of treatment failure	53
3.8. What ART regimen to switch to (second-line ART)	56

---

## Chapter 4

### **PREVENTION, SCREENING AND MANAGEMENT OF COMMON CO-INFECTIONS** **60**

4.1. Co-trimoxazole preventive therapy (CPT)	61
4.2. Management of Opportunistic Diseases of the respiratory system	62
4.3. Management of Gastrointestinal Opportunistic Diseases	74
4.4. Management of Opportunistic Diseases of the Nervous System	77
4.5. Cutaneous manifestations	82
4.6. Visceral Leishmaniasis	85
4.7. Screening for co-morbidities	86

---

## Chapter 5

# **GUIDANCE ON OPERATIONS AND SERVICE DELIVERY**

**88**

5.1. Adherence to ART	89
5.2. Disclosure	92
5.3. Retention across the continuum of care	99
5.4. Service delivery	101
5.5. Laboratory and diagnostic services	103
5.6. Pharmaceuticals Supply Management System	105

---

## Chapter 6

# **GUIDANCE FOR PROGRAMME MANAGERS**

**110**

6.1. Guiding principles	111
6.2. National and local HIV epidemiology	113
6.3. Program performance and response analysis	113
6.4. Key parameters for decision-making	114
6.5. Roles and responsibility	115
6.6. Coordination mechanisms	116

---

## Chapter 7

# **MONITORING & EVALUATION**

**118**

Monitoring & Evaluation	119
7.1. Monitoring the implementation of the New recommendation	119
7.2. Key Indicators	120
7.3. Data Reporting, Data Flow and Quality Assurance	120
7.4. Supportive Supervision and Review Meetings	122
7.5. Other monitoring considerations	122

---

## **ANNEXES**

**124**

<b>ANNEX 1:</b> GROWTH CURVES	125
<b>ANNEX 2:</b> DOSAGE OF ANTIRETROVIRAL DRUGS FOR ADULTS AND ADOLESCENTS	130
<b>ANNEX 3:</b> DOSAGE OF ANTIRETROVIRAL DRUGS IN CHILDREN	131
<b>ANNEX 4:</b> PEDIATRIC ARV DRUG FORMULATIONS, SIDE EFFECTS AND SPECIAL CONSIDERATIONS IN CHILDREN	134
<b>ANNEX 5:</b> GRADING OF TOXICITY IN ADULTS AND ADOLESCENTS	137
<b>ANNEX 6:</b> GRADING OF ADVERSE EVENTS IN CHILDREN	138
<b>ANNEX 7:</b> LABORATORY GRADING OF ADVERSE EVENTS IN ADULTS AND ADOLESCENTS (ACTG)	140
<b>ANNEX 8:</b> GRADING TOXICITIES IN CHILDREN BY SELECTED LABORATORY FINDINGS	141
<b>ANNEX 8:</b> PEDIATRIC TB SCREENING TOOL	142
<b>ANNEX 9:</b> ADULT TB SCREENING TOOL	144

---



## Foreword

Antiretroviral Therapy (ART) began in Ethiopia in 2003 and free ART was launched in 2005. An estimated 769,500 Ethiopians are currently living with HIV, of whom 542,600 require ART and 367,000 are currently taking the treatment.

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

Expansion and strengthening HIV care and treatment activities at regional, zonal, woreda and kebele levels through targeted social mobilization and active community participation have been expected to create an enabling environment to prevent and control 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 1045 health facilities providing HIV care and treatment service.

This revised 4<sup>th</sup> edition of guidelines for use of OI and ARV drugs in adult and children is based on recent global evidence and experiences. It is intended to serve as a clear guidance for rational and safe use of OI and antiretroviral drugs. The Federal Ministry of Health believes that this guidelines, along with other national implementation guidelines, will be instrumental in accelerating and scaling up ART uptake.



Kebede Worku, MD, MPH

State Minister of Health,

Federal Democratic Republic of Ethiopia





# Acknowledgement

The Ministry of Health expresses its appreciation for the institutions that participated in the development of this consolidated HIV prevention care and treatment guideline. The printing of the guidelines has been funded by ICAP Ethiopia and WHO country offices.

The ministry also recognizes the following experts for their contribution in the development of the Guideline

Name	Organization
Dr Frehiwot Nigatu	FMOH
Dr Mizan Kiros	FMOH
Mrs Seble Mamo	FMOH
Dr Fethia Keder	FMOH
Mr Tekalign Moges	FMOH
Dr Zelalem Tadesse	FMOH/ICAP-E
Dr Eshetu Gezehagn	ICAP-E
Dr Solomon Amsalu	ICAP-E
Dr Abera Refisa	ICAP-E
Dr Yigeremu Abebe	CHAI
Dr Getchew Feleke	ITECH
Dr Tsegazeab Kahsu	MSH/ENAT-CS
Dr Fahmi Mohammed	WHO
Dr Ghion Tirsite	WHO
Dr Aschalew Endale	WHO
Mr Masresha Assefa	PFSA

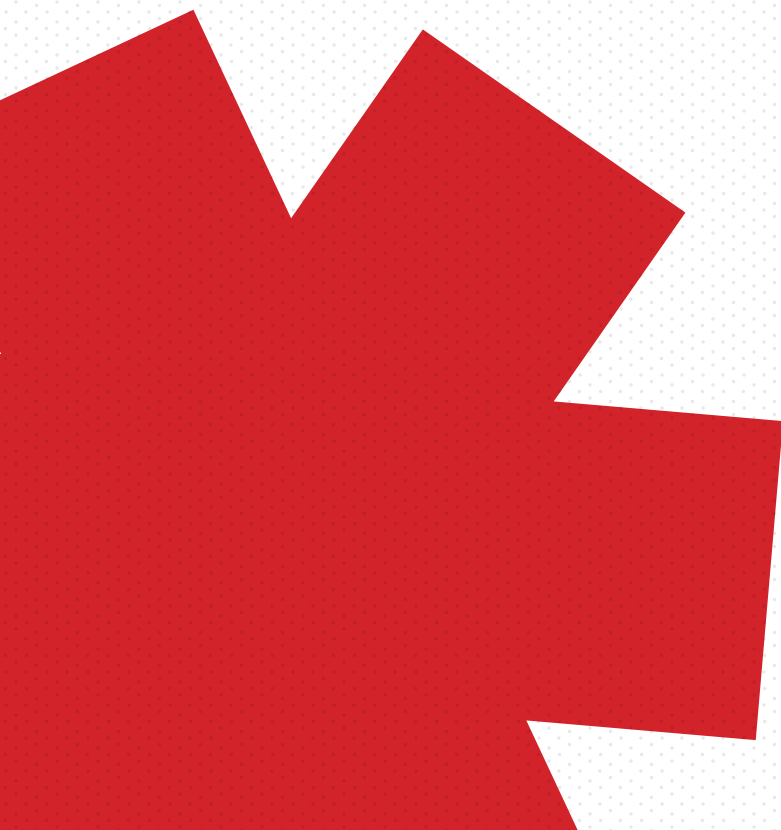
## Acronyms and Abbreviations

<b>3TC</b>	Lamivudine
<b>ABC</b>	Abacavir
<b>AFB</b>	Acid fast bacilli
<b>AIDS</b>	Acquired Immune Deficiency Syndrome
<b>ANC</b>	Antenatal Care
<b>ARV</b>	Antiretroviral
<b>ART</b>	Antiretroviral Therapy
<b>AZT/ZDV</b>	Zidovudine
<b>CBC</b>	Complete Blood Count
<b>CD4 CELLS</b>	Type of T-lymphocyte, white blood cells
<b>CMV</b>	Cytomegalovirus
<b>CPT</b>	Cotrimoxazole Preventive Therapy
<b>DBS</b>	Dried Blood Spot
<b>D4T</b>	Stavudine
<b>DDI</b>	Didanosine
<b>DHS</b>	Demographic and Health Survey
<b>DNA</b>	Deoxyribonucleic acid
<b>DOTS</b>	Directly Observed Therapy Short Course
<b>EFV</b>	Efavirenz, also abbreviated as EFZ
<b>FBOS</b>	Faith-based organizations
<b>FDC</b>	Fixed dose combination
<b>FHAPCO</b>	Federal HIV/AIDS Prevention and Control Office
<b>FMOH</b>	Federal Ministry of Health
<b>HAART</b>	Highly active antiretroviral therapy
<b>HBV</b>	Hepatitis B Virus
<b>HCV</b>	Hepatitis C Virus
<b>HIV</b>	Human Immunodeficiency Virus
<b>IDV</b>	Indinavir
<b>IP</b>	Infection Prevention
<b>IPT</b>	INH Preventive Therapy
<b>IRIS OR IRS</b>	Immune Reconstitution Inflammatory Syndrome also called Immune Reconstitution Syndrome (IRS)
<b>I-TECH</b>	International Training and Education Center on HIV/AIDS

<b>LFT</b>	Liver Function Test
<b>LPV</b>	Lopinavir
<b>MTCT</b>	Mother-To-Child Transmission (of HIV)
<b>MD</b>	Medical Doctor
<b>NFV</b>	Nelfinavir
<b>NGO</b>	Non-governmental Organization
<b>NNRTI</b>	Non-nucleoside reverse transcriptase inhibitor
<b>NRTI</b>	Nucleoside Analogue Reverse Transcriptase Inhibitor
<b>NVP</b>	Nevirapine
<b>OI</b>	Opportunistic Infections
<b>PCR</b>	Polymerase chain reaction
<b>PEP</b>	Post-exposure prophylaxis
<b>PI</b>	Protease Inhibitor
<b>PITC</b>	Provider Initiated Testing and Counselling
<b>PLHIV</b>	People living with HIV
<b>PMTCT</b>	Prevention of mother-to-child transmission (of HIV)
<b>RNA</b>	Ribonucleic acid
<b>RTV, R</b>	Ritonavir
<b>PI/R</b>	Ritonavir boosted Protease Inhibitor
<b>RFT</b>	Renal function test
<b>RT</b>	Reverse transcriptase
<b>STI</b>	Sexually Transmitted Illnesses
<b>TB</b>	Tuberculosis
<b>TLC</b>	Total Lymphocyte Count
<b>U/A</b>	Urine analysis
<b>UNAIDS</b>	The Joint United Nations Program on HIV/AIDS
<b>UP</b>	Universal Precautions
<b>WHO</b>	World Health Organization
<b>ZDV</b>	Zidovudine (also abbreviated as AZT)

CHAPTER 1

# INTRODUCTION



## 1.1. Background and context

The first evidence of HIV epidemic in Ethiopia was detected in 1984. Since then, 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 single point HIV related estimates and projections for Ethiopia 2014, the national HIV prevalence is 1.14%. The recent 2011 EDHS shown that the urban prevalence is 4.2% which is seven times higher than that of the rural (0.6%). The 2011 EDHS also shows that the HIV prevalence varies from region to region ranging from 0.9% in SNNPR to 6.5% in Gambela. Furthermore, the HIV related estimates and projections indicate that the 2013 HIV prevalence in regions ranges from 0.8% to 5.8%.

Currently 367,000 patients, including 23,400 children under the age of 15, are taking ART. Based on the 2014 estimate, the 2014 ART need is 542,121 for adults and 178,500 for children under 15 years of age.

Free ARV service was launched in January 2005 and public hospitals started providing free ARVs in March 2005. Currently, ART service is available in 1045 Health facilities. On the basis of the 2010-2014 strategic plan, ART coverage for adults (age 15+) has reached 76% but the coverage remains low (23.5%) 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 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. Since the National ART treatment guidelines was last published in 2008, new information as well as evidence-based best practices have become available to make HIV treatment more effective and accessible, creating a need to revise the existing guidelines. Hence, this guidelines is developed taking into consideration the current recommendations released by WHO in its 2013 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 National guidelines on using ART among adults and adolescents have been combined with those for children and for 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.

### 1.2.1. 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

### 1.2.2. 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

### 1.2.3. Guiding principles

#### Public health approach

The public health approach seeks to ensure the widest possible access to high-quality services at the population level, based on simplified and standardized approaches, and to strike a balance between implementing the best-proven standard of care and what is feasible on a large scale in resource-limited settings.

#### Strengthening health systems through innovation and learning

HIV services are already being integrated at lower-level health, while services for PMTCT are increasingly becoming core elements of maternal and child health services. As people receiving ART begin to age and HIV infection becomes a chronic, manageable condition, improving the integration of HIV services with care for non-communicable diseases will also become more important.

### Increasing the effectiveness and efficiency of programmes

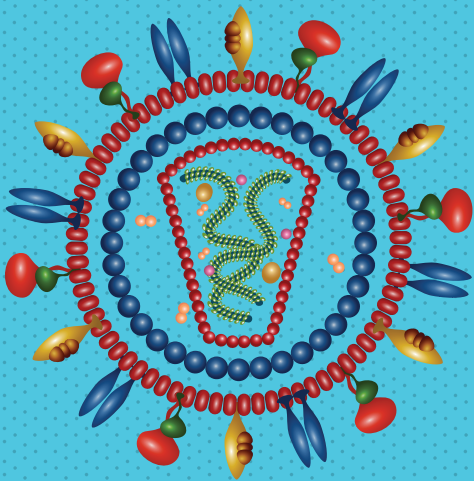
HIV programmes through a strategic approach to using ARV drugs that involves: giving priority to providing ARV drugs to people living with HIV who are eligible for treatment and most in need; exploring opportunities to enhance the impact of ARV drugs on HIV prevention by starting treatment earlier in certain populations; increasing the effectiveness and reach of ARV programmes across the continuum of care through a strategic mix of quality-assured HIV testing approaches, improving adherence and retention, innovative service delivery, integrating ART in a wider range of settings and strengthening links between services; and engaging in both short- and longer-term efforts to optimize and harmonize drug regimens and increase their affordability and to develop and implement simpler and more affordable point-of-care diagnostics and laboratory services.

### Promoting human rights and health equity

Access to HIV prevention, treatment, care and support should be recognized as fundamental to realizing the universal right to health, and these guidelines should be implemented based on core human rights and ethical principles.

## CHAPTER 2

# HIV DIAGNOSIS AND PREVENTION







## 2.1. HIV Testing and counseling (HTC) services

HIV testing is the critical first step in identifying and linking 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 HTC service 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 care, treatment and prevention services.**

- People receiving HIV testing and counseling must be given informed consent (verbal consent is sufficient and written consent is not required) to be tested and counseled. They should be informed of the process for HIV testing and counseling and their right to decline the test.
- 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. Although confidentiality should be respected, it should not be allowed to reinforce secrecy, stigma or shame. Counselors should rise, 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.
- HIV testing and counseling services must be accompanied by appropriate and high-quality pre-test information and post-test counseling.
- HIV testing and counseling providers should strive to provide high-quality testing services.
- 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 and treatment support.

### 2.1.2. Service Delivery Models

There are two major HIV testing and counseling service delivery models and under these models there are different service delivery approaches.

These are **health facility based HIV testing and counseling model and community based HIV testing and counseling model.**



### a. Health Facility Based Model of HIV Testing and Counseling

Currently both VCT and 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 (Voluntary) 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 both public and private, should provide HIV testing and counseling services to their clients by using both VCT and PITC approaches
  - ≡ All health facilities with VCT services must provide couple counseling and testing services
  - ≡ All health facilities should provide PITC for their eligible clients at outpatient, inpatient, labor and delivery , Ante-natal Care, Post natal Care, EPI, Family Planning and TB Clinic departments by using national algorithms.



#### **The eligible clients for routine HIV testing and counseling by using PITC approach are:**

1. All pregnant women with unknown HIV status and their partners
2. All laboring mothers with unknown HIV status and their partners
3. All postpartum mothers with unknown HIV status and their partners
4. All patients at TB clinics with unknown HIV status
5. All STI patients with unknown HIV status and their partners
6. All family members of index cases
7. All under five children visiting health facility
8. Children Orphaned by AIDS and vulnerable children
9. All family planning clients with unknown HIV status and their partners
10. All key populations and adolescent/youth clients (15-24 years),
11. Clients coming with clinical signs and symptoms of HIV/AIDS visiting health facilities at OPD and Wards
12. Discordant couples

1.

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 case.



## b. Community Based Model of HIV Testing and Counseling

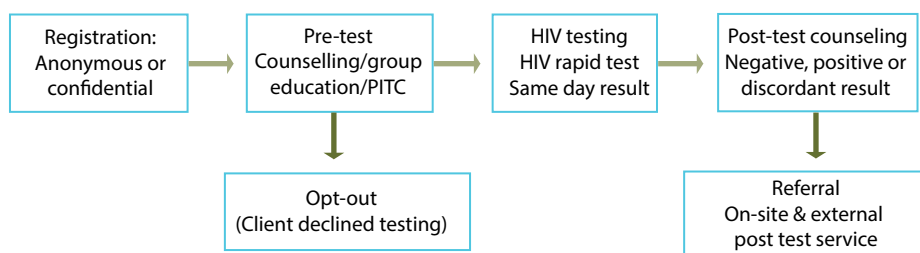
Community based model is one approach of addressing eligible clients who don't appear at health facilities for HIV testing and counseling for different reasons. This model builds public trust and also mitigates issues related to stigma and discrimination. It has also importance to identify HIV positives earlier than facility based approach as well as reaching populations that 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 at the following settings:

- Home-based testing targeting specific sub-population group
- Outreach HIV testing and counseling services. Targeting specific geographic areas with high HIV prevalence (hot-spots). While planning outreach HTC, effective linkage of the identified HIV infected clients is very critical.
- Work place HTC 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 hydro-electric etc.)
  - ≡ Big factories and mining sites

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

### 2.1.3. Procedures of HTC service delivery

Figure-2.1 HIV counseling and testing protocol with workflow.



A user-friendly site guide for VCT, quick reference manual, SOPs for HTC, counseling protocol and HIV testing algorithm should be available at all health facilities providing HTC service. Same day results should be respected at all times irrespective of the type of delivery model. VCT and PITC service providers should follow the national HTC protocol, cue-card and job-aids while providing HTC services.

## a. Client registration

At VCT sites clients will be registered using unique identifiers (code numbers) however at PITC sites 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 year age) can give verbal consent by themselves.

Unconscious or patient who is not in status of 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 patient. 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 quality of service delivery, acceptability and uptake of HTC, for many 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 national, accepted RDTs following national HIV testing algorithm.

### e. Providing HIV test results

Test results should be declared in person (not by telephone, e mail or letter). HCT 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 including 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, importance of medical care and treatment, disclosure and partner testing, prevention messages and positive living referral for care and treatment.

The post-test counseling session for negatives should include meaning of test result, prevention message (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 HCT services -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 (2-3 within two weeks) 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.



#### **Note:**

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.

#### h. Follow-up counseling

After counseling a client on test results, counselors should take opportunity to review or share information that may not have been absorbed. 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.

#### 2.1.4. Retesting

There is a need to reduce unnecessary re-testing among persons who have previously been tested and learnt their results. Most people do not require re-testing to validate an HIV-negative result. However, it is important to accurately identify persons who do require re-testing. 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 discordant test results; the same assays are used and, where possible, the same specimen.

**Re-testing** – 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 sharing injecting equipment. Re-testing 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.

### Recommendations for re-testing

General Recommendation:

Re-testing is warranted in all epidemic types:

1. If an individual has previous or ongoing risk for HIV infection (i.e. sex workers, having a high-risk or known HIV positive partner; having clinical indications for re-testing such as newly acquired sexually transmitted infections [STI]) OR
2. If an individual can identify a specific incident of HIV exposure in the three months prior to HIV testing (i.e. history of occupational exposure, unprotected sex with a known HIV-positive person).



### Re-testing is specifically recommended for:

1. A person who has occupational exposure or sexually assaulted client who started PEP; re-test 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. Person who has an STI: re-test after 3 months
4. Person who has continuing or ongoing risk of acquiring HIV (MARPs); every 12 months but for female sex workers consider retesting every six month
5. Person who has specific incidents of known HIV exposure within the past three months, re-test after 3 months
6. Discordant Couple, retest after 6-12 months

**Referral and linkage:** Clients with HIV positive result should be referred to relevant facility, or community services for prevention or treatment services based or linked with relevant clinic for follow-up and support.



## 2.2. HIV testing and counseling in specific populations

### a. Couples

**Couple:** Two persons in an ongoing sexual relationship; each of these persons is referred to as a “partner” in the relationship.

Studies in several countries have shown that couples HIV testing and counseling is acceptable, feasible and effective. It can identify sero-concordant couples who can be linked to prevention, care and treatment services. Services should be offered to married and cohabiting couples, premarital couples, polygamous unions and any other partnerships. As with all HIV testing and counseling approaches, couples HIV testing and counseling should be voluntary. Health providers must be aware of the potential for intimate partner-based violence and should support individuals when they do not want to test with their partners. Couples HIV testing and counseling can be offered at VCT, PMTCT and ART sites.

Support to encourage the testing of the partners of people living with HIV is also an efficient and effective way of identifying additional people living with HIV, who then can benefit from treatment. Offering family counseling and testing to couples where one or both are living with HIV can identify children, adolescents and other household members who have not previously been diagnosed.



### Recommendations

Couples and partners should be offered HIV testing at all HIV testing points with support for mutual disclosure

### 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 care settings.
- Re-testing 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



are essential. Final diagnosis (or definitive diagnosis) at the end of the risk period for mother to-child transmission (breast feeding period) should be ensured. For children 18 months of age and older (who are not being breast fed or who stopped breast feeding at least six weeks earlier), standard HIV serological tests such as rapid diagnostic tests can be used to reliably determine HIV infection status.



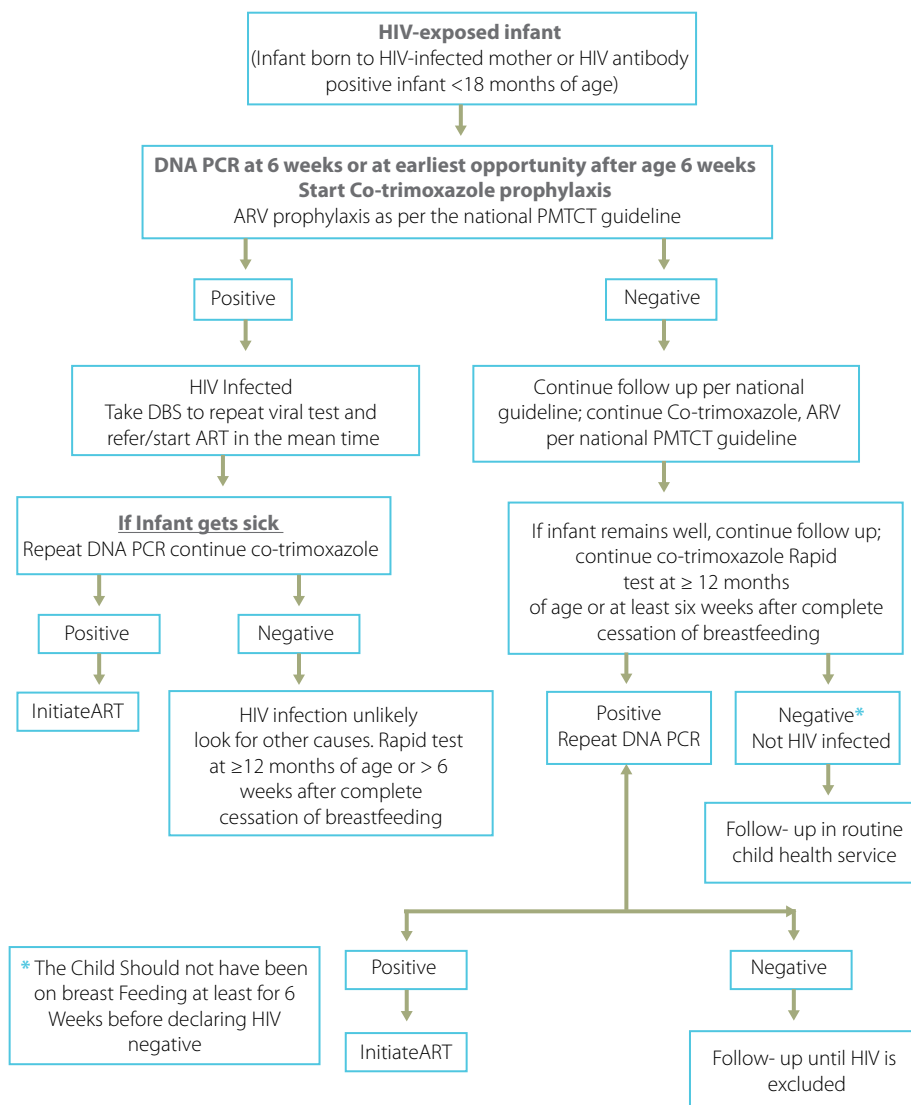
### **Recommendations**

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 2.2 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).

## Adolescents

Adolescents are often underserved and given insufficient priority in many HIV programs, with poor access to 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 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 HTC service by giving self-consent.



### Recommendations

- HIV testing and counseling with other prevention services and linkage to treatment and care is recommended for all adolescents and youth age 15-24 years
- Adolescents should 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

### Most at Risk Populations

HIV testing and counseling has been provided to most at risk 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, mobile workers, in-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 MARPS at health facilities and community service model.

## 2.3. Quality Management

Quality HTC can be defined as accessible HTC services that meet the need of clients and providers, in an equitable and acceptable manner, within the resources available 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 HCT services: issues that need to be addressed while assessing for QA:

- Did the counselors/service provider received basic HTC training packages approved by FMOH?
- Is there enough physical space to provide HCT that ensures privacy of the clients and point of care testing?
- Are basic supplies and provider support tools available to provide HCT services?
- 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?

HTC services should be supervised by well-trained program supervisors on regular basis to ensure HTC 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.

**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.

## 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. Quality can be controlled and ensured by looking at:

- How consistently the national testing protocol is followed
- How valid the testing algorithm is in terms of specificity and sensitivity
- If the laboratory operating procedures are observed
- If infection prevention practice is in place



**Note:** 10% of negative and 30% of positive samples must be sent to the regional laboratory for external quality control at sites which perform more than 500 tests per month. For others, combined on-site evaluations with proficiency testing will be conducted once or twice a year.

In addition, trained laboratory technicians may regularly retest samples tested by counselors and other lab technicians as an internal quality control. Sites failing the proficiency tests need to receive additional technical supervision and support.

Supervision and Quality Assurance: for testing standards and bio- safety;

- proficiency testing
- quality control testing in central laboratory
- Standardized laboratory log book
- Technical support on the quality of HCT service

## 2.4. Policy, Ethical & 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 HCT services to individuals, couples, and community groups of all ages especially to vulnerable and high-risk groups regardless of gender.

##### *Policy Statements*

- HCT services shall be integrated into existing health and social welfare services and promoted in all settings: government, non-governmental, private sector, cooperatives, workplace, faith based organizations etc.
- HCT services shall be strengthened through effective networking, consultation and collaboration among stakeholders.
- HCT services 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, 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.



- No results will be provided in certificate form, however referral will be offered to access post-test services (prevention, care, treatment and support).
- 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.
- Provider-initiated testing and counseling (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 HCT during pregnancy, labour, post natal and at family planning 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 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 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*

- HCT service 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.
- HCT 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. Post Exposure management including Prophylaxis

### **2.5.1. 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 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, janitors 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**

1. Assign one trained physician / HO / 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 coordinated PEP activity 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 tool algorithm for determination of the severity of exposure (Exposure Code) and PEP register should be available in the facility.

### **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 artery or vein
- Visible blood on device
- Deep and extensive injury





Table 2.1 Interpretation of exposure code (Severity of Exposure)

Exposure Code	Type of exposure
<b>1. EC 1</b>	Is a minor mucocutaneous exposure to small volume of blood for short period (few seconds to minutes)
<b>2. EC 2</b>	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)
<b>3. EC 3</b>	Severe Percutaneous exposure (Large bore hollow needle, Deep puncture, Visible blood on device, Needle used in patient artery/vein)

Table 2.2- 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
<b>1. HIV SC 1</b>	The Source patient is HIV Positive but is asymptomatic and has reasonably good immune status
<b>2. HIV SC 2</b>	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 )
<b>3. HIV SC unknown</b>	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)

### Recommendation of PEP based on Risk assessment

Table 2.3. Recommended HIV post exposure prophylaxis for percutaneous injuries and mucous membrane or non-intact skin exposure

Status code	Exposure code		
	EC 1	EC 2	EC 3
<b>SC 1</b>	Basic 2 drug PEP	Basic 2 drug PEP	Expanded 3 drug PEP
<b>SC 2</b>	Basic 2 drug PEP	Expanded 3 drug PEP	Expanded 3 drug PEP
<b>SC unknown</b>	No PEP is warranted	No PEP is warranted	Generally no PEP is warranted
	Consider basic 2 drugs PEP for source with HIV risk factors		
<b>HIV negative</b>	No PEP warranted	No PEP warranted	No PEP warranted





Table 2.4 Recommended drugs and administration guide.

ARV drug regimen	Dose	Frequency	Duration
<b>2-Drug Regimen:</b>			
<b>Tenofovir (TDF) + Lamivudine (3TC)</b>  or <b>Zidovudine (AZT) + Lamivudine (3TC)</b>	TDF 300mg 3TC 300mg  AZT 300mg 3TC 150mg	Once daily  12 hourly	28 days  28 days
<b>3-Drug Regimen:</b>			
<b>Triple FDC</b>  <b>Tenofovir (TDF) / Zidovudine (AZT) + Lamivudine (3TC) + Efavirenz (EFV)</b>  or <b>Lopinavir/ritonavir (LPV/r)</b>  or <b>Atazanavir/ritonavir (ATV/r)</b>	Triple FDC (TDF 300mg, 3TC 300mg, EFV 600mg)  AZT 300mg 3TC 150mg EFV 600mg (daily)  LPV/r400mg/100mg  ATV/r300mg/100mg	Once daily  12 hourly  12 hourly  Once daily	28 days

**Timing of initiation of prophylaxis:**

To be effective, post-exposure prophylaxis 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. Don't consider PEP beyond 72 hours post exposure. Prophylaxis is to be given for 28 days.

**Testing and monitoring after occupational exposure:**

- Testing source: rapid 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.



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.

### 2.5.2. Prevention of the transmission of the Human Immunodeficiency Virus (HIV) after sexual assault:

1. All women 15 years and older 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.
  - e. It is strongly recommended that the implementation of post-rape prophylaxis should be carefully monitored and evaluated for:
    - Psychosocial and legal support
    - Screening for conventional STIs and follow up management
    - Drug side effects
    - Sero-conversion

#### Note

PEP is not recommended

- a. If victim presents more than 72 hours after exposure
- b. Following condom leak or tear

Recommended regimen

AZT Or TDF + 3TC + EFV for 28 days.

Alternatively, Kaletra or boosted Atazanavir can substitute EFV.



## Follow-up of client Exposed to HIV

### Post exposure Testing

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

### Monitoring and Management of PEP Toxicity

- Exposed clients 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.

## 2.6. Combination Prevention

HIV prevention approach based solely on one element does not work and can hinder the AIDS 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 by both HIV-infected and uninfected persons. We need to use a mix of behavioral, biomedical and structural HIV prevention actions and tactics which suit with our country's actual epidemic.

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/AIDS (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 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 through HEP and HDA 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
- Behavioral change communication (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 and 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, and 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 counseling and testing services to eligible patients
- Ensure access and enhance uptake of PMTCT services
  - ≡ Strengthen the integration of PMTCT with MNCH in all health facilities.
  - ≡ Mobilize the community to be actively involved in PMTCT.
  - ≡ Promote PITC for all pregnant women attending ANC and delivery services.
  - ≡ Ensure male involvement in PMTCT service.



- ≡ Promote & educate PMTCT by the health development armies.
    - ≡ Provide education to households on PMTCT by health development armies.
    - ≡ Expand PMTCT services.
    - ≡ Provide PMTCT training for service providers to people with disability.
    - ≡ Involve private health facilities to provide PMTCT services.
  - Increase availability and utilization of STI services
- STI services should be provided through implementation of syndromic case management.
- ≡ Create strong leadership for STI programs in all health facilities.
    - ≡ Expand STI services to all health facilities.
    - ≡ Intensify health education to improve treatment seeking behaviour and utilization of STI services.
    - ≡ Promote partner notification during STI case detection.
    - ≡ 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.
  - Friendly health services
  - Increase supply, distribution and utilization of male and female condoms
    - ≡ Ensure adequate supplies of condoms.
    - ≡ Conduct targeted condom distribution, particularly to MARPs.
  - Ensure infection prevention and safe blood supplies in Health system
  - Avail post exposure prophylaxis (PEP) treatment
  - Accelerate male circumcision in areas needed
  - Intensifying positive prevention

### Structural Interventions

- Community mobilization and awareness through HDA
- Access to health services
- Address socio-cultural factors
  - ≡ Address harmful traditional practices that fuel HIV/AIDS.
- Address stigma and discrimination
- Reduce economic vulnerability
- Legal & Policy Environment (Legal support system and partnership)

- Promote gender equality and prevention of gender-based violence
- Supportive interventions designed to enhance referrals, adherence, retention and community mobilization

## 2.7. Care of HIV exposed infants

### 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 HIV exposed infants (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 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 HIV exposed infant

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 and development
5. Infant feeding: Nutrition and feeding history should be assessed regularly.
6. Immunization: All HIV exposed infants should be immunized according to EPI recommendations





Table 2.3: Immunization schedule for HIV exposed infants.

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

## 7. ARV prophylaxis:

- NVP should be given to all babies born to HIV infected mothers
  - Give NVP syrup to the baby once daily for the first six weeks of life
  - For HIV exposed infants identified after birth (through infant or maternal HIV antibody testing)

### Infant on breastfeeding:

- Initiate ART for the mother
- Provide NVP syrup for the infant for 6 week (consider extending it for 12weeks if mother is diagnosed during labor or immediate postpartum)
- Collect specimen for DNA PCR testing at 6 weeks of age

### Infant not breast feeding

- Initiate ART for the mother based on eligibility criteria
- If the infant is brought within 72 hours of birth provide Nevirapine prophylaxis otherwise there is no need to provide NVP syrup for the infant
- Collect specimen for DNA PCR testing at 6 weeks of age

Table 2.4 – Dosage of NVP syrup for different age groups

Infant age	NVP daily dosing	Dose in ml
<b>Birth to 6 weeks</b>		
<b>Birth weight 2000 - 2499 g</b>	10 mg once daily	1ml
<b>Birth weight &gt; 2500 g</b>	15 mg once daily	1.5ml
<b>Age 6 weeks to 6 months</b>	20 mg once daily	2ml
<b>Age 6 months to 9 months</b>	30 mg once daily	3ml
<b>Age &gt; 9 months</b>	40 mg once daily	4ml





- NVP concentration is 50mg/ml.
- Dose listed in the table is given once daily
- 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.
- Low birth weight infants (<2000mg) should receive mg/kg dosing, suggested dose is 2 mg/kg once daily.
- NVP infant dose: 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.
- Dosing beyond 6 weeks of age in special situations in which prolonged dosing of up to 12 weeks should be considered (such as the mother having had limited ART and not being likely to be virally suppressed; the infant is identified as HIV exposed after birth and is breastfeeding).

#### **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 HIV exposed infants from 6weeks of age. CPT for HIV exposed infants should be continued 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 (CXR) if clinically indicated

#### **10. Determination and evaluation of infection status**

One of the goals of follow up of HIV exposed infants is to identify and treat HIV infected ones early. All HIV exposed infants 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) 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 HIV exposed infant 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 2.5: Follow up visit schedule for HIV exposed infants

Age in weeks / months	At birth	6 wk	10 wk	14 wk	5 mo	6 mo	9 mo	12 mo	15 mo	18 mo
History	•	•	•	•	•	•	•	•	•	•
Physical exam*	•	•	•	•	•	•	•	•	•	•
Growth Assessment	•	•	•	•	•	•	•	•	•	•
Developmental assessment	•	•	•	•	•	•	•	•	•	•
Infant Feeding counseling	•	•	•	•	•	•	•	•	•	•
Determination of HIV status		D N A P C R	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		
Co-trimoxazole Preventive Therapy		•	Continue until HIV is excluded and infant is no longer at risk from breastfeeding							
TB Risk Assessment	At each visit									
Immunizations	•	•	•	•			•			
Adherence counseling	•	•	•	•	•	•	•	•	•	•

\* 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

## 2.8. Linking people diagnosed with HIV infection

It is critical for people living with HIV to enroll in care as early as possible. This enables both early assessment of their eligibility for ART and 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 HTC 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 HTC service sites:

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



- Prepare SOP for inter and intra- facilities service outlets referral linkage system
- Establish site level support groups to improve escorting and feedback practices for intra-facility referral
- Mapping and establishing network between available HCT, chronic care, and other support services in the area

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

- Harmonize site level HCT and chronic care registers, reporting formats, referral and feedback formats (in line with HMIS)
- Ensure the availability and sustainability of recording and reporting formats
- Ensure a referral and linkage feedback mechanism in health facilities

**Ensure standardization of HCT guidelines and training materials on referral and linkage issues, the priority interventions are:**

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

**Improve the involvement of Health Extension Workers (HEW), PLHIVs in awareness creation activities as to improve referral and linkages through the following priorities interventions:**

- Support HEWs in their day to day IEC/BCC activities in relation to HIV
- Establish and strengthen PLHIV associations and support groups to be involved on the facilitation of referral and linkage through escorting and other mechanisms

**Reduce stigma and discrimination through community involvement, the priority interventions:**

- Develop IEC/BCC material focusing on stigma and discrimination
- Avoid 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 HEWs and other sectors such as agricultural extension workers, education workers, youth associations, women's associations, PLHIV and etc. are aware of the problem of referral and linkage and collaborate to resolve it.



## CHAPTER 3

# **CARE AND TREATMENT OF PEOPLE WITH HIV INFECTION**





Early enrollment in care will enable early assessment of eligibility for ART and timely initiation of ART as well as access to interventions to prevent the further transmission of HIV, prevent other infections and co-morbidities.

### 3.1. General care packages for PLHIV

Not all people living with HIV are eligible for ART and, of those eligible, not all will be able to access ART immediately. Enrolment in care provides an opportunity for close clinical and laboratory monitoring and early assessment of eligibility for ART and timely initiation, and aims to minimize lost to follow-up. 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.

#### Key elements at enrolment into chronic HIV care

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

### 3.2. Pre-ART care package

If patient is not eligible for ART he/she should be seen **every three months regularly**. During every visit the patient needs to be evaluated according to the key elements of care mentioned above. Patients in pre-ART care should receive intensive education and linked to social support networks with proactive follow up. Clients failing to show up in the clinic on their schedule should be traced.

### 3.3. Preparing people living with HIV for ART

Before people start ART, it is important to have a detailed discussion with them about their willingness and readiness to initiate ART, the ARV regimen, dosage and scheduling, 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 should consider nutritional status, any co-morbidities and potentially interacting medications for possible contraindications or dose adjustment.



The choice to accept or decline ART ultimately lies with the individual person or his or her caretaker, and if they choose to defer initiation, ART can be offered again at subsequent visits. If there is mental health, substance use or other problems that are major barriers to adherence, appropriate support should be provided, and readiness to initiate ART should be reassessed at regular intervals. A wide range of patient information materials as well as community and peer support can 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.

**Requirements for initiation of ART**

- 1. HIV positive test result with written documentation
- 2. Start only patients with medical eligibility for ART
- 3. Ensure readiness of patient for ARV therapy

3.4. When to Start ART

**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 community level. ART should be provided to all eligible people with a confirmed HIV diagnosis.

Table 3.1 Summary of recommendations on when to start ART in adults, adolescents, pregnant and breastfeeding women.

<b>All Adults and adolescents</b>	HIV infection with CD4 count ≤500 cells/mm3 should be started on HAART irrespective of WHO clinical stage.
	HIV infection and WHO clinical stage 3 and 4 should be started on HAART irrespective of CD4 cell count.
	HIV infection and active TB disease should be started on HAART irrespective of CD4 cell count. All HIV positive pregnant and breast feeding women irrespective of CD4 count.
	Provide ART to all HIV infected partners of sero-discordant couple regardless of CD4 cell count (to reduce the risk of HIV transmission to the negative partner).





## When to start ART in pregnant and breastfeeding women

ARV drugs are used for pregnant and breastfeeding women with HIV primarily for the mother's health and to prevent the exposed child from becoming infected. All pregnant and breastfeeding women with HIV should initiate lifelong triple ARVs (ART), which should be maintained at for the duration of mother-to-child transmission risk as well as then after (Option B+). Infants should be put on NVP prophylaxis for 4-6 weeks and exclusive breast feeding for the first six months

Table 3.2: Summary of recommendations on when to start ART in pregnant and breastfeeding women and prophylaxis for their infants

PMTCT program	Pregnant and breast feeding women with HIV	HIV exposed infant prophylaxis
Use lifelong ART for all pregnant and breastfeeding women ("Option B+")	Initiate lifelong ART Regardless of WHO clinical stage or CD4 cell count	6 weeks of infant prophylaxis with once-daily NVP

## When to start ART in discordant couple

It has been shown that viral load is the greatest risk factor for HIV transmission and lowering the viral load is critical to interrupt transmission and preventing morbidity and mortality. Studies showed that the risk of transmission is near zero when the viral load is very well controlled. Data from observational and ecological studies confirmed that when ART is given to the infected partner at a higher CD4 count the risk of transmission is decreased by 96% when compared with those who started ART at CD4+ counts  $<350\text{cells/mm}^3$ . ART is recommended for all HIV infected partners of Sero-discordant couple regardless of CD4 cell count.

## When to start ART in children

Infants and young children have an exceptionally high risk of poor outcomes from HIV infection. Up to 52% and 75% of children die before the age of two and five years respectively in the absence of any intervention. By five years of age, the risk of mortality and disease progression in the absence of treatment falls to rates similar to those of young adults.

Diagnosing and retaining children exposed to HIV and children infected with HIV in care also presents unique challenges because of their dependence on a caregiver. Loss to follow-up has been particularly high along the continuum of care, with retention especially challenging for children who are in HIV care but not yet eligible for ART. Where access to immunological testing is limited, the burden of pediatric HIV disease is high and pediatric ART coverage is low, simplifying the eligibility criteria for initiating ART may significantly improve the overall health outcomes for children with HIV.

ART is recommended for HIV infected all children less than 15 years regardless of CD4 count and WHO clinical stage. Treating all children younger than fifteen years of age is expected to simplify pediatric treatment and facilitate a significant expansion of



ART coverage for young children. Note that late diagnosis is still occurring, and a large proportion of the children identified as infected with HIV would already be eligible for ART based on previous recommendations.

<b>Children &lt;15 years</b>	All children with HIV infection regardless of CD4 count and WHO clinical stage.
------------------------------	---

3.5. What ART regimen to start with (first-line ART)

Using simplified, less toxic and more convenient regimens as fixed-dose combinations is recommended for first-line ART. Once-daily regimens comprising NRTI backbone (TDF + 3TC) and one NNRTI (EFV) are maintained as the preferred choices in adults, adolescents and children older than ten years. For children younger than three years a PI-based regimen is the preferred approach (Table 3.3).

Table 3.3:- Summary of first-line ART regimens for adults, adolescents, pregnant and breastfeeding women and children

Population	Preferred first Line regimens	Alternative First Line regimens <sup>b</sup>
<b>Adults (including pregnant and breastfeeding women and adults with TB co-infection)</b>		AZT + 3TC + EFV AZT + 3TC + NVP TDF + 3TC + NVP
<b>Adolescents (10 to 19 years) ≥35 kg</b>	TDF + 3TC + EFV(FDC)	AZT + 3TC + EFV AZT + 3TC + NVP TDF + 3TC + NVP ABC + 3TC + EFV
<b>Children 3 years to less than 10 years and adolescents &lt;35 kg</b>	AZT/ABC + 3TC + EFV	ABC + 3TC + NVP AZT + 3TC + NVP TDF + 3TC + EFV TDF + 3TC + NVP
<b>Children &lt;3 years</b>	ABC or AZT + 3TC + LPV/r	ABC + 3TC + NVP AZT + 3TC + NVP

<sup>b</sup>ABC, d4T or boosted PIs (ATV/r, LPV/r) can be used in special circumstances.

ART for TB/HIV co-infected adults

Timing of ART for adults: Antituberculosis treatment and Co-trimoxazole (CPT) 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 immunosuppression such as CD4 counts less than 50 cells/mm3 should receive ART immediately within the first two weeks of initiating TB treatment.

<b>Preferred regimen for TB/HIV co-infected patients TDF +3TC+EFV</b>
---



## ARV for HIV/HBV co-infection

When the co-infected patient is eligible **based on the HIV eligibility criteria** the regimen should contain TDF+3TC+EFV.

## First-line ART for pregnant and breastfeeding women and ARV drugs 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 childbearing age. Infants of mothers who are receiving ART and are breastfeeding should receive six weeks of infant prophylaxis with daily NVP. If infants are receiving replacement feeding, they should be given six weeks of infant prophylaxis with daily NVP. Infant prophylaxis should begin at birth or when HIV exposure is recognized postpartum.

Table 3.4 Summary of maternal and infant ARV prophylaxis for different clinical scenarios.

Scenario	Maternal ARV prophylaxis <sup>a</sup>	Infant ARV prophylaxis <sup>b</sup>	Duration of infant ARV prophylaxis
<b>Mother diagnosed with HIV during pregnancy<sup>c,d</sup></b>	Initiate maternal ART	NVP	6 weeks
<b>Mother diagnosed with HIV during labour or immediately postpartum and plans to breastfeed</b>	Initiate maternal ART	NVP	6 weeks; consider extending this to 12 weeks
<b>Mother diagnosed with HIV during labour or immediately postpartum and plans replacement feeding</b>	Refer mother for HIV care and evaluation for treatment	NVP	6 weeks
<b>Infant identified as HIV exposed after birth (through infant or maternal HIV antibody testing) and is breastfeeding</b>	Initiate maternal ART	NVP	Perform infant PCR early infant diagnosis test and then immediately initiate 6 weeks of NVP – strongly consider extending this to 12 weeks
<b>Infant identified as HIV exposed after birth (through infant or maternal HIV antibody testing) and is not breastfeeding</b>	Refer mother for HIV care and evaluation for treatment	No drug	Do HIV PCR test in accordance with national recommendations on early infant diagnosis; no infant ARV prophylaxis; initiate treatment if the infant is infected



Scenario	Maternal ARV prophylaxis <sup>a</sup>	Infant ARV prophylaxis <sup>b</sup>	Duration of infant ARV prophylaxis
<b>Mother receiving ART but interrupts ART regimen while breastfeeding (such as toxicity, stock-outs or refusal to continue)</b>	Determine an alternative ART regimen or solution; counsel regarding continuing ART without interruption	NVP	Until 6 weeks after maternal ART is restarted or until 1 week after breastfeeding has ended

- Ideally, obtain the mother's CD4 cell count at the time of initiating or soon after initiating ART
- If infant NVP causes toxicity or NVP is not available, 3TC can be substituted.
- If the mother is using replacement feeding, infant AZT can be substituted for infant NVP; 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.
- If it is known that the mother has initiated ART less than 4 weeks before delivery, consider extending infant NVP for infants who are breastfeeding to 12 weeks.

### First-line ART for children

Treatment recommendations for children should be easy to implement at all levels of the health system, including the primary care level, and by all ART service providers, rather than pediatric specialists alone.

### Infants and children younger than 3 years

Optimizing first-line ART in children younger than three years is critical to achieving 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 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 infants and children infected with HIV 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. (See table 3.5).

### Children 3 years and older (including adolescents)

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 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 adult dual and triple fixed-dose combinations and the dose of EFV in adult triple fixed-dose combinations are acceptable for use in adolescents (Table 3.3).

### 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. The recommended regimens for children diagnosed with TB and starting ART are consistent with the previous recommendations (Table 3.5). ART should be started as soon as tolerated within 8 weeks of initiating anti-TB.

Table 3.5 Summary of recommended ART regimens for children who need TB treatment

Recommended regimens for children and adolescents initiating ART while on TB treatment <sup>a,b</sup>		
Younger than 3 years		Two NRTIs + NVP, ensuring that dose is 200 mg/m <sup>2</sup> or Triple NRTI (AZT + 3TC + ABC) <sup>c</sup>
3 years and older		Two NRTIs + EFV or Triple NRTI (AZT + 3TC + ABC) <sup>c</sup>
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, ensuring that dose is 200 mg/m <sup>2</sup> Or Triple NRTI (AZT + 3TC + ABC) <sup>c</sup>
	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) <sup>c</sup>



Recommended regimens for children and adolescents initiating ART while on TB treatment <sup>a,b</sup>		
<b>Child on standard PI based regimen (two NRTIs + LPV/r)</b>	Younger than 3 years	Triple NRTI (AZT + 3TC + ABC) <sup>c</sup> or Substitute NVP for LPV/r, ensuring that dose is 200 mg/m <sup>2</sup>
	3 years and older	If the child has no history of failure of an NNRTI-based regimen: Substitute with EFV <sup>d</sup> or Triple NRTI (AZT + 3TC + ABC) <sup>c</sup> or If the child has a history of failure of an NNRTI-based regimen: Triple NRTI (AZT + 3TC + ABC) <sup>c</sup> Consider consultation with experts for constructing a second line regimen

- Ensure optimal dosing of rifampicin based on new dosing guidelines
- Substitute ARV drugs based on an age-appropriate ART regimen in line with nationally recommended first-line ART.
- 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.
- 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.

## 3.6 Monitoring response to ART and the diagnosis of treatment failure

### 3.6.1. What to expect in the first months of ART

Although taking ART is a lifelong commitment, the first six months of therapy are especially important. Clinical and immunological improvement and virological suppression are expected when individuals adhere to ART, but opportunistic infections and/or immune reconstitution inflammatory syndrome (IRIS) may develop, as well as early adverse drug reactions, such as drug hypersensitivity, especially in the first three months of ART. ART significantly decreases mortality overall, but death rates are also highest in the first three months of ART. These complications are commonest when the people starting ART already have advanced HIV disease with severe immunodeficiency and existing co-infections and/or co-morbidities, severely low hemoglobin, low body mass index and very low CD4 counts or are severely malnourished.



### 3.6.2. CD4 recovery

In most adults and children, CD4 cell counts rise when ART is initiated and immune recovery starts. 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. Failure to achieve some CD4 recovery 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 opportunistic infections such as co-trimoxazole preventive therapy.

### 3.6.3. Immune reconstitution inflammatory syndrome (IRIS)

IRIS is a spectrum of clinical signs and symptoms thought to be associated with immune recovery brought about by a response to ART. It is a widely recognized phenomenon that 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, cryptococcosis, Kaposi's sarcoma and hepatitis. BCG vaccine-associated IRIS (localized and systemic) may occur in infants infected with HIV in settings where BCG immunization is routine. A low CD4+ cell count (<50 cells/mm<sup>3</sup>) at ART initiation, disseminated opportunistic infections or tumors and a shorter duration of therapy for opportunistic infections before ART starts are the main risk factors. 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.

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

- A low pretreatment CD4 count (often less than 100 cells/ $\mu$ L). One important exception to this general rule is tuberculosis( IRIS secondary to preexisting M. tuberculosis infection may occur in individuals with CD4 counts >200)
- A positive virologic and 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 malabsorption after appropriate evaluation for the clinical presentation.



- The presence of clinical manifestations consistent with an inflammatory condition
- A temporal association between HAART initiation and the onset of clinical features of illness- usually within the first 6 months

### Management of 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/mm<sup>3</sup>; 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.

- Patients should generally be treated for the underlying opportunistic infection 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 we choose to treat with corticosteroids, initiate therapy with prednisone at a dose of 1 mg/kg/day (maximal dose 60 to 80 mg). A rapid taper over a 10 to 14 days period. IRIS in closed spaces (e.g. CNS OIs) should be managed promptly or referred to appropriate center to avert significant morbidity and mortality.



#### Note

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 OIs should be treated using standard guidelines and in critically sick patients short course of corticosteroid might be indicated to control severe symptoms.

### 3.6.4. Clinical and Laboratory monitoring before and after initiating ART

Standardized clinical assessment of patients and, when available immunological, are mandatory at baseline to decide on initiation of antiretroviral therapy. Patients who do not qualify for this have a follow up protocol that monitors disease progression and starts antiretroviral therapy before life-threatening immunodeficiency sets in. Patients qualifying for antiretroviral therapy are thoroughly evaluated at baseline and for the rest of their lives to monitor toxicity, intolerance, response or failure to treatment. Before ART initiation and thereafter patient readiness and adherence to therapy are always assessed and necessary support provided. Opportunistic infections including TB, IRIS, and co morbidities are always looked for and managed. Such standardized procedures ensure HIV- infected persons a reasonable quality of care.





Table 3.6: Procedure of Baseline Assessment and Follow up

Objectives	Activities	Decision
<b>Baseline assessment, week 0</b>		
<b>Assess patient eligibility</b>	<ul style="list-style-type: none"><li>• Check HIV test document or request test</li><li>• Adherence counseling and ensure readiness</li><li>• For transfer-ins check referral form</li><li>• Register, fill intake format</li><li>• Clinical assessment: Hx of any HIV related illnesses in the past, OIs, co-morbidities, pregnancy, past and current medication</li><li>• Stage with WHO staging</li><li>• Counselling and education: determine treatment readiness, social background, disclosure,</li><li>• Lab assessment<sup>1</sup>: CD4, (if available CBC, ALT, creatinine). If TB suspect sputum smear. Pregnancy and other tests as necessary.</li></ul>	<ul style="list-style-type: none"><li>• Develop impression on treatment readiness</li><li>• Start CPT if clinically indicated</li><li>• Treat OI</li><li>• Determine eligibility</li><li>• Refer if necessary</li><li>• Continue ART for transfer-ins</li><li>• Give appointment of 1 week</li></ul>
<b>2<sup>nd</sup> Visit, 1 week after baseline visit</b>		
<b>To decide on Initiation</b>	<ul style="list-style-type: none"><li>• Review clinical and lab data</li><li>• Adherence counselling and ensure readiness</li><li>• Drug counseling and education</li><li>• Encourage disclosure and discuss with family for support</li></ul>	<ul style="list-style-type: none"><li>• Decide eligibility</li><li>• Non-eligible patients come every 3/12</li><li>• Start CPT or IPT (as indicated)</li><li>• Treat OI including TB</li><li>• Manage any drug toxicity and intolerance</li><li>• Determine treatment readiness</li><li>• Decide on regimen and initiate ART</li><li>• Provide education on drug adverse reactions</li><li>• Appointment to return after 2 weeks</li></ul>
<b>3<sup>rd</sup> visit, 2 weeks after initiation</b>		
<b>To determine toxicity/intolerance, adherence, and IRIS</b>	<ul style="list-style-type: none"><li>• Clinical assessment</li><li>• Assess and support adherence</li><li>• Provide counseling support</li><li>• Lab tests if necessary</li></ul>	<ul style="list-style-type: none"><li>• Decide escalation of nevirapine</li><li>• Manage toxicity as indicated</li><li>• Treat OI if diagnosed</li><li>• Give appointment to return in 2 weeks</li></ul>



Objectives	Activities	Decision
<b>4<sup>th</sup> visit 4 weeks after initiation</b>		
<b>Same as 3<sup>rd</sup> visit</b>	<ul style="list-style-type: none"> <li>• Same as 3<sup>rd</sup> visit</li> <li>• Hg if patient is on ZDV</li> <li>• Assess and support adherence</li> </ul>	<ul style="list-style-type: none"> <li>• Refill ART and other drugs as necessary for one month</li> <li>• Treatment of OI</li> <li>• Manage toxicity and intolerance</li> <li>• Refer if necessary</li> <li>• Appointment to return after 4 weeks</li> </ul>
<b>5<sup>th</sup> visit 8 weeks after initiation</b>		
<b>Same as 4<sup>th</sup> visit</b>	<ul style="list-style-type: none"> <li>• Same as 4<sup>th</sup> visit</li> </ul>	<ul style="list-style-type: none"> <li>• Refill ART and other drugs as necessary for 1 month</li> <li>• Treatment of OI</li> <li>• Manage toxicity and intolerance</li> <li>• Refer if necessary</li> <li>• Appointment to return after 4 weeks</li> </ul>
<b>6<sup>th</sup> visit 12 weeks after initiation</b>		
<b>Same as 5<sup>th</sup> visit</b>	<ul style="list-style-type: none"> <li>• Same as 5<sup>th</sup> visit</li> </ul>	<ul style="list-style-type: none"> <li>• Refill ART and other drugs as necessary for 1 month</li> <li>• Treatment of OI</li> <li>• Manage toxicity and intolerance</li> <li>• Refer if necessary</li> <li>• Appointment to return after 4 weeks</li> </ul>
<b>7<sup>th</sup> visit 16 weeks after initiation</b>		
<b>Same as 6<sup>th</sup> visit</b>	<ul style="list-style-type: none"> <li>• Same as 6<sup>th</sup> visit</li> </ul>	<ul style="list-style-type: none"> <li>• Refill ART and other drugs as necessary for 2 months</li> <li>• Treatment of OI</li> <li>• Manage toxicity and intolerance</li> <li>• Refer if necessary</li> <li>• Appointment to return after 8 weeks</li> </ul>
<b>8<sup>th</sup> visit 24 weeks after initiation</b>		
<b>Same as 7<sup>th</sup> visit</b>	Same as 7 <sup>th</sup> visit	<ul style="list-style-type: none"> <li>• Determine CD4</li> <li>• Refill ART and other drugs as necessary for 3 months</li> <li>• Treatment of OI</li> <li>• Manage toxicity and intolerance</li> <li>• Refer if necessary</li> <li>• Appointment to return after 12 weeks</li> </ul>

**NB:**

- After the 24th week of initiation of antiretroviral therapy patients are 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 are done. Lab tests including ALT are requested when indicated. CD4 is repeated every 6/12.
- Patients should be encouraged to come any time if they have concerns. Clients may be seen out of the above schedule whenever necessary.
- At every visit conduct screening for TB



Table 3.7 summarizes recommended laboratory tests for HIV screening and monitoring, as well as approaches to screen for co-infections and non-communicable diseases.

Management	Recommended	Desirable (if feasible)
<b>HIV diagnosis</b>	HIV serology	HBV (HBsAg) serology <sup>a</sup> Screening for sexually transmitted infections Assessment for major non-communicable chronic diseases and co-morbidities <sup>b</sup>
<b>Follow-up before ART</b>	CD4 cell count every 6 months	
<b>ART initiation</b>	CD4 cell count Hemoglobin test for AZT <sup>c</sup>	Urine dipsticks for glycosuria and estimated glomerular filtration rate (eGFR) and serum creatinine for TDF <sup>d</sup> Alanine amino-transferase for NVP <sup>e</sup>
<b>Receiving ART</b>	CD4 cell count (every 6 months) HIV viral load based on need	Urine dipstick for glycosuria and serum creatinine for TDF
<b>Treatment failure</b>	CD4 cell count HIV viral load if available	HBV (HBsAg) serology (before switching ART regimen if this testing was not done or if the result was negative at baseline)

- If feasible, HBsAg testing should be performed to identify people with HIV and HBV coinfection and who therefore should initiate TDF-containing ART.*
- Consider assessing the presence of chronic conditions that can influence ART management such as hypertension and other cardiovascular diseases, diabetes and TB.*
- Among children and adults with a high risk of adverse events associated with AZT (low CD4 or low BMI).*
- Among people with a high risk of adverse events associated with TDF: underlying renal disease, older age group, low BMI, diabetes, hypertension and concomitant use of a boosted PI or potential nephrotoxic drugs.*
- 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 cells/mm<sup>3</sup> and HCV co-infection. However, liver enzymes have low predictive value for monitoring NVP toxicity.*

### 3.6.5. Monitoring for drug toxicities and substitutions for ARV

#### Guiding principles

- Establish whether the adverse event is due to ARV drugs, other drugs, or clinical illness.
- Try to identify the responsible ARV drug.
- Assess the severity using ACTG (AIDS Clinical Trial Group) grading system

#### 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; therefore, they must be closely monitored. They occur from few weeks to months. The most frequent drug adverse reactions include:



- Toxicities of NRTIs (NVP and EFV) occur in the first few weeks, and may be life-threatening
- ABC hypersensitivity reaction starting from first week following initiation
- Anaemia and neutropenia due to ZDV 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 ZDV induced gastrointestinal problems, are important barriers to adherence unless appropriate measures are taken.

Table 3.8 Types of toxicities associated with first and second line ARV drugs

ARV Drug	Major types of toxicity	Risk factors	Suggested management
<b>ABC</b>	Hypersensitivity reaction	<ul style="list-style-type: none"> <li>• Presence of HLA-B*5701 Gene</li> </ul>	<ul style="list-style-type: none"> <li>• If ABC is being used in first-line ART, substitute with TDF or AZT</li> <li>• If ABC is being used in second line ART, substitute with TDF</li> </ul>
<b>ATV/r</b>	Electrocardiographic abnormalities (PR interval prolongation)	<ul style="list-style-type: none"> <li>• Pre-existing conduction disease</li> <li>• Concomitant use of other drugs that may prolong the PR interval</li> </ul>	LPV/r.
	Indirect hyperbilirubinaemia (clinical jaundice)	<ul style="list-style-type: none"> <li>• Underlying hepatic disease</li> <li>• HBV and HCV coinfection</li> <li>• Concomitant use of hepatotoxic drugs</li> </ul>	
	Nephrolithiasis and risk of prematurity	<ul style="list-style-type: none"> <li>• Risk factors unknown</li> </ul>	
<b>AZT</b>	Anaemia, neutropaenia, myopathy, lipodystrophy or lipodystrophy	<ul style="list-style-type: none"> <li>• Baseline anaemia or neutropaenia</li> <li>• CD4 count <math>\leq 200</math> cells/mm<sup>3</sup></li> </ul>	<ul style="list-style-type: none"> <li>• If AZT is being used in first-line ART, substitute with TDF or ABC</li> <li>• If AZT is being used in second-line ART consult specialist</li> </ul>
	Lactic acidosis or severe hepatomegaly with steatosis	<ul style="list-style-type: none"> <li>• BMI <math>&gt;25</math> (or body weight <math>&gt;75</math> kg)</li> <li>• Prolonged exposure to nucleoside analogues</li> </ul>	



ARV Drug	Major types of toxicity	Risk factors	Suggested management
<b>LPV/r</b>	Electrocardiographic abnormalities (PR and QT interval prolongation, torsades de pointes)	<ul style="list-style-type: none"> <li>• People with pre-existing conduction system disease</li> <li>• Concomitant use of other drugs that may prolong the PR interval</li> </ul>	<ul style="list-style-type: none"> <li>• If LPV/r is used in first-line ART for children, use an age-appropriate NNRTI (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</li> <li>• 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, consult specialist</li> </ul>
	QT interval prolongation	<ul style="list-style-type: none"> <li>• Congenital long QT syndrome</li> <li>• Hypokalemia</li> <li>• Concomitant use of drugs that may prolong the QT interval</li> </ul>	
	Hepatotoxicity	<ul style="list-style-type: none"> <li>• Underlying hepatic disease</li> <li>• HBV and HCV co-infection</li> <li>• Concomitant use of hepatotoxic drug</li> </ul>	
	Pancreatitis	<ul style="list-style-type: none"> <li>• Advanced HIV disease</li> </ul>	
	Risk of prematurity, lipoatrophy or metabolic syndrome, dyslipidemia or severe diarrhoea	<ul style="list-style-type: none"> <li>• Risk factors unknown</li> </ul>	
<b>NVP</b>	Hepatotoxicity	<ul style="list-style-type: none"> <li>• Underlying hepatic disease</li> <li>• HBV and HCV Co-infection</li> <li>• Concomitant use of hepatotoxic drugs</li> <li>• Baseline CD4 &gt;250 cells/mm<sup>3</sup> in women</li> <li>• Baseline CD4 &gt;400 cells/mm<sup>3</sup> for men</li> <li>• First month of therapy (if lead-in dose is not used)</li> </ul>	<ul style="list-style-type: none"> <li>• EFV. If the person cannot tolerate either NNRTI, use boosted PI</li> </ul>
	Severe skin rash and hypersensitivity reaction (Stevens-Johnson syndrome)	<ul style="list-style-type: none"> <li>• Risk factors unknown</li> </ul>	<ul style="list-style-type: none"> <li>• Use boosted PIs</li> </ul>



ARV Drug	Major types of toxicity	Risk factors	Suggested management
<b>d4T</b>	Peripheral neuropathy, lipoatrophy or lipodystrophy	<ul style="list-style-type: none"> <li>Older age CD4 count <math>\leq 200</math> cells/mm<sup>3</sup></li> <li>Concomitant use of isoniazid or ddl</li> </ul>	<ul style="list-style-type: none"> <li>If d4T is being used in first-line ART, substitute with TDF or AZT or ABC</li> <li>If d4T is being used in second-line ART (after TDF or ABC are used in first-line ART), substitute with AZT</li> </ul>
	Lactic acidosis or severe hepatomegaly with steatosis, acute pancreatitis	<ul style="list-style-type: none"> <li>BMI <math>&gt; 25</math> (or body weight <math>&gt; 75</math> kg)</li> <li>Prolonged exposure to nucleoside analogues</li> </ul>	
<b>EFV</b>	Persistent central nervous system toxicity (such as abnormal dreams, depression or mental confusion) <sup>2</sup>	<ul style="list-style-type: none"> <li>Depression or other mental disorder (previous or at baseline)</li> <li>Daytime dosing</li> </ul>	<ul style="list-style-type: none"> <li>NVP. If the person cannot tolerate</li> <li>either NNRTI, use boosted PIs</li> </ul>
	Hepatotoxicity	<ul style="list-style-type: none"> <li>Underlying hepatic disease – HBV and HCV co-infection</li> <li>Concomitant use of hepatotoxic drug</li> </ul>	
	Convulsions	<ul style="list-style-type: none"> <li>History of seizure</li> </ul>	
	Hypersensitivity reaction, Stevens-Johnson syndrome Potential risk of neural tube birth defects (very low risk in humans) Male gynaecomastia	<ul style="list-style-type: none"> <li>Risk factors unknown</li> </ul>	<ul style="list-style-type: none"> <li>Use boosted PI</li> </ul>



ARV Drug	Major types of toxicity	Risk factors	Suggested management
TDF	TDF Tubular renal dysfunction, Fanconi syndrome	<ul style="list-style-type: none"><li>Underlying renal disease</li><li>Older age BMI &lt;18.5 (or body weight &lt;50 kg)</li><li>Untreated diabetes mellitus</li><li>Untreated hypertension</li><li>Concomitant use of nephrotoxic drugs or a boosted PI</li></ul>	<ul style="list-style-type: none"><li>If TDF is being used in first-line ART, substitute with AZT or ABC</li><li>If TDF is being used in second-line ART (after d4T + AZT use in first-line ART), substitute with ABC</li></ul>
	Decreases in bone mineral density	<ul style="list-style-type: none"><li>History of osteomalacia and pathological fracture</li><li>Risk factors for osteoporosis or bone loss</li></ul>	
	Lactic acidosis or severe hepatomegaly with steatosis	<ul style="list-style-type: none"><li>Prolonged exposure to nucleoside analogues</li><li>Obesity</li></ul>	
	Exacerbation of hepatitis B (hepatic flares)	<ul style="list-style-type: none"><li>Discontinuation of TDF due to toxicity</li></ul>	<ul style="list-style-type: none"><li>Use alternative drug for hepatitis B treatment consult specialist</li></ul>

### 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 with 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. People with HIV with severe anemia at baseline (hemoglobin <7.0 g/dl) should avoid AZT 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/mm<sup>3</sup> and men who have CD4 cell counts >400 cells/mm<sup>3</sup> 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.

### 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 common adverse events clinical grading system in adults and adolescents (ACTG)





## 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 3.10 Key ARV drug interactions and suggested management

ARV drugs	Key interactions	Mechanism	Suggested management
<b>NVP</b>	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)
<b>EFV</b>	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
<b>Boosted PI (ATV/r, LPV/r)</b>	Rifampicin		Substitute rifampicin with rifabutin Adjust the PI dose or substitute with three NRTIs (for children)
	Lovastatin and simvastatin	Increase concentration	Use an alternative dyslipidaemia agent (for example pravastatin)
	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

## 3.7. Monitoring the response to ART and the diagnosis of 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. The value of viral load testing as a



more sensitive and early indicator of treatment failure is increasingly recognized. Viral load testing should be done after 6 months of initiating ART and every 12 months then after in order to detect treatment failure proactively. Viral load testing should be used aside from the routine testing whenever there is clinical or immunologic suspicion of treatment failure.

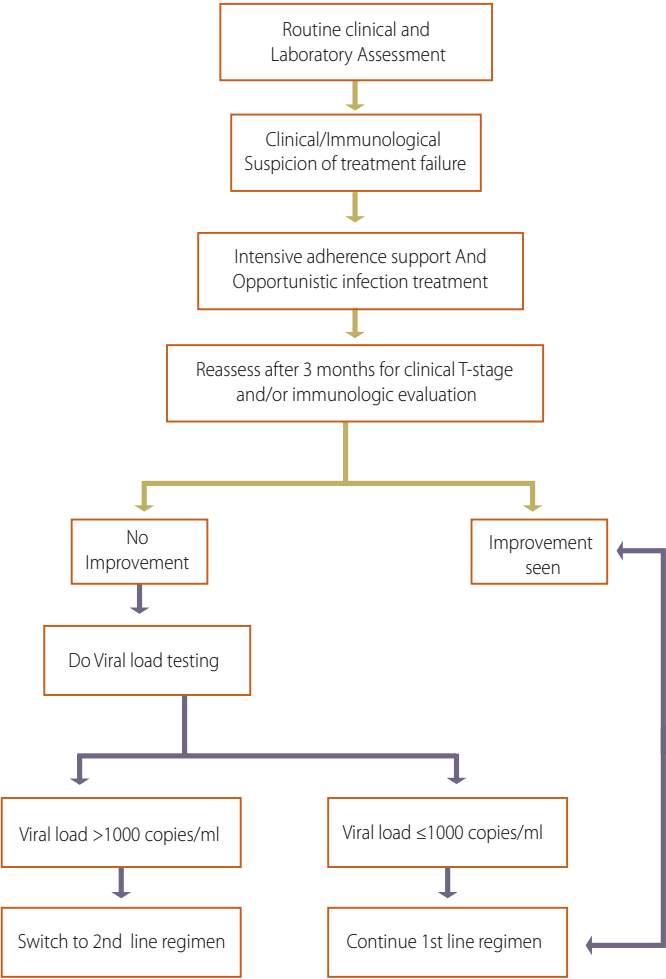
Table 3.11 Definitions of clinical, immunological and virological failure for the decision to switch ART regimens

Failure	Definition	Remark
<b>Clinical failure</b>	<p><b>Adults and adolescents</b></p> <p>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</p> <p><b>Children</b></p> <p>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</p>	The condition must be differentiated from immune reconstitution inflammatory syndrome occurring after initiating ART.
<b>Immunologic failure</b>	<p><b>Adults and adolescents</b></p> <p>CD4 count falls to the baseline (or below) or</p> <p>Persistent CD4 levels below 100 cells/mm<sup>3</sup></p> <p><b>Children</b></p> <p>Younger than 5 years:</p> <p>Persistent CD4 levels below 200 cells/mm<sup>3</sup> or &lt;10%</p> <p>Older than 5 years:</p> <p>Persistent CD4 levels below 100 cells/mm<sup>3</sup></p>	<p>Without concomitant or recent infection to cause a transient decline in the CD4 cell count.</p> <p>Current WHO clinical and immunological criteria have low sensitivity and positive predictive value for identifying individuals with virological failure.</p>
<b>Virologic failure</b>	Plasma viral load above 1000 copies/ ml	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.



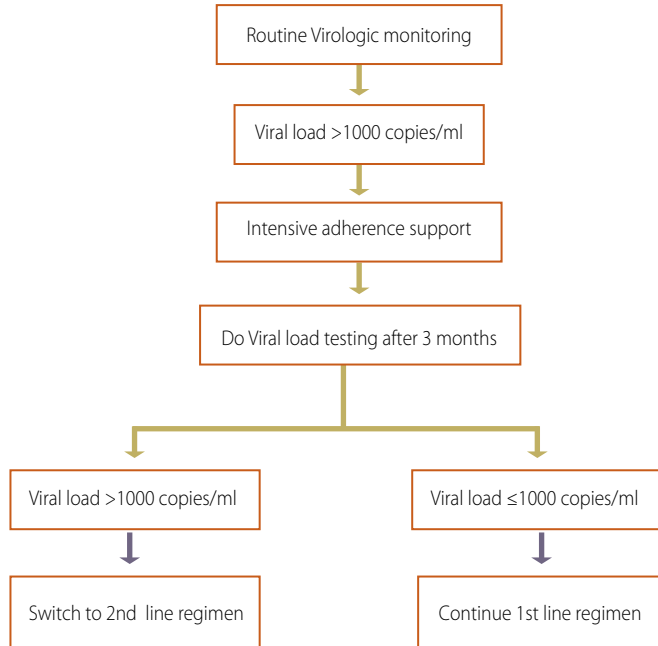
Figure 3.1 Algorithms for diagnosis and management of clinical/immunological and virological treatment failures

**a. Algorithm for diagnosis of clinical/immunological treatment failure**





### b. Algorithm for diagnosis of virological treatment failure



### 3.8. What ART regimen to switch to (second-line ART)

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 with age.

#### Second-line ART for adults and adolescents

It is recommended that second-line adult 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

- Assess adherence and address barriers
- Drug interactions
- Don't add one drug to a failing regimen
- Consider resistance & cross resistance
- Quality of life in end stage disease

- Get advice from experienced clinicians
- At least 2 new drugs
- Preferably 1 new drug class
- Premature changing in ARV can limit future options



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

Target population	Preferred Second line regimen	
<b>Adults and adolescents (≥10 years)<sup>a,b</sup></b>	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
<b>HIV and TB co-infection</b>		Standard PI-containing regimens as recommended for adults and adolescents  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)
<b>HIV and HBV co-infection</b>	AZT + TDF + 3TC + (ATV/r or LPV/r)	

a. Adult clients taking ABC and ddl can be shifted to TDF and 3TC.  
 b. For pregnant women same regimens recommended as for adults and adolescents

### 3.8.1. Second-line ART for children (including adolescents)

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 switch 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 is containing



AZT or d4T + 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 (including adolescents)

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

- 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.
- TDF may only be given to children >2 years.
- ATV/r can be used as an alternative to LPV/r in children older than 6 years.



## CHAPTER 4

# **PREVENTION, SCREENING AND MANAGEMENT OF COMMON CO-INFECTIONS**







Although initiation of ART is at a higher CD4 count of  $<500\text{cells/mm}^3$ , 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. Main areas affected 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 (CPT )**

Co-trimoxazole preventive therapy (CPT) 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 & diarrhoea 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
<b>HIV exposed Infants</b>	In all, starting at 4–6 weeks after birth irrespective of CD4 level	Until the risk of HIV transmission ends or HIV infection is excluded	Clinical at 3-monthly intervals
<b>&lt;1year</b>	In all	Until 5 years of age regardless of CD4% or clinical symptoms or never	
<b>1-5 years</b>	WHO clinical stages 2, 3 and 4 regardless of CD4 % or Any WHO stage and CD4 $<25\%$	Never stop	
<b><math>\geq 5</math> years, including Adults</b>	Any WHO stage and CD4 count $<350\text{ cells/mm}^3$ Or WHO 3 or 4 irrespective of CD4 level	Never or when CD4 $\geq 350\text{ cells/mm}^3$ after 6 months of ART	

*\*Discontinue also if the person has Stevens-Johnson syndrome, severe liver disease, severe anaemia, 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.*



Table 4.2 Dosage of Co-trimoxazole for adults, adolescents, children & infants

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

Table 4.3 Adverse Effects of CPT & management

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

## 4.2. Management of Opportunistic Diseases of the respiratory system

### 4.2.1 Tuberculosis

TB is the most frequent life-threatening opportunistic infection 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 challenge of high impact of TB on HIV and vice versa. Therefore, 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;
  - 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, INH Preventive Therapy and Infection control)
  - Intensify TB case finding and ensure quality TB treatment;
  - Initiate TB prevention with earlier initiation of ART and Isoniazid preventive therapy (IPT);
  - 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;
  - Provide antiretroviral therapy for HIV positive TB patients.

Table 4.4 Timing of ART for adults and children with TB

<b>Patients with Tuberculosis found to be HIV positive</b>	<b>HIV positive patients taking ART diagnosed with TB</b>
<ul style="list-style-type: none"><li>• ART should be started in all TB-HIV co-infected patients, including those with drug-resistant TB, irrespective of the CD4 count.</li><li>• 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 counts less than 50 cells/mm<sup>3</sup>) should receive ART immediately within the first two weeks of initiating TB treatment</li><li>• ART should be started in any child with active TB disease as soon as possible within eight weeks following the initiation of anti-tuberculosis treatment irrespective of the CD4 count and clinical stage.</li><li>• Efavirenz should be used as the preferred drug in patients starting ART while on anti-tuberculosis treatment</li></ul>	<ul style="list-style-type: none"><li>• Start anti-TB</li><li>• Modify ART regimen to avoid drug-drug interaction</li><li>• Evaluate for treatment failure</li></ul>



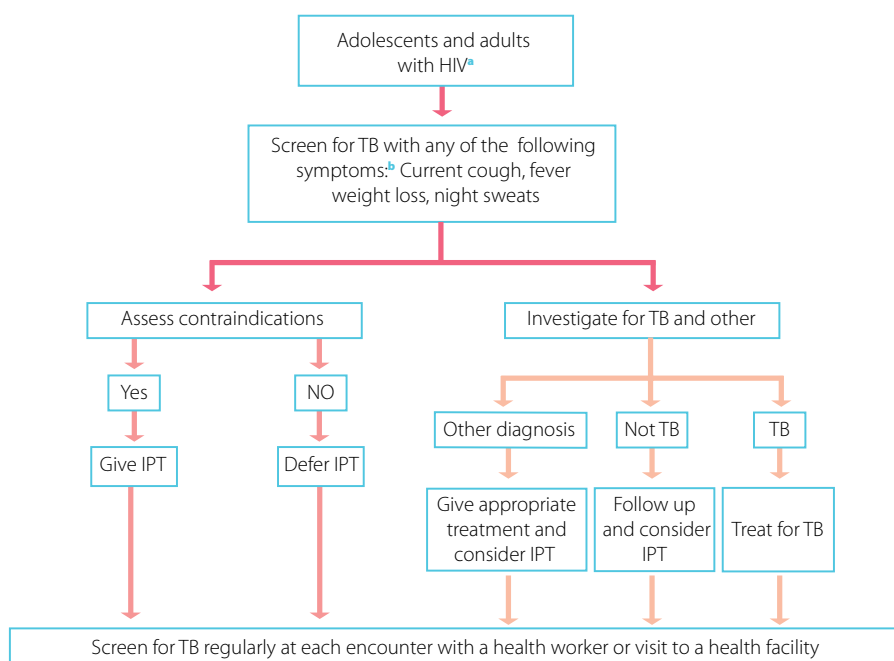
## The 3Is intervention

The 3 Is stand for intensified TB case finding, Isoniazid Preventive Therapy (IPT), and infection control. Each will be discussed below.

### 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 HCT 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.

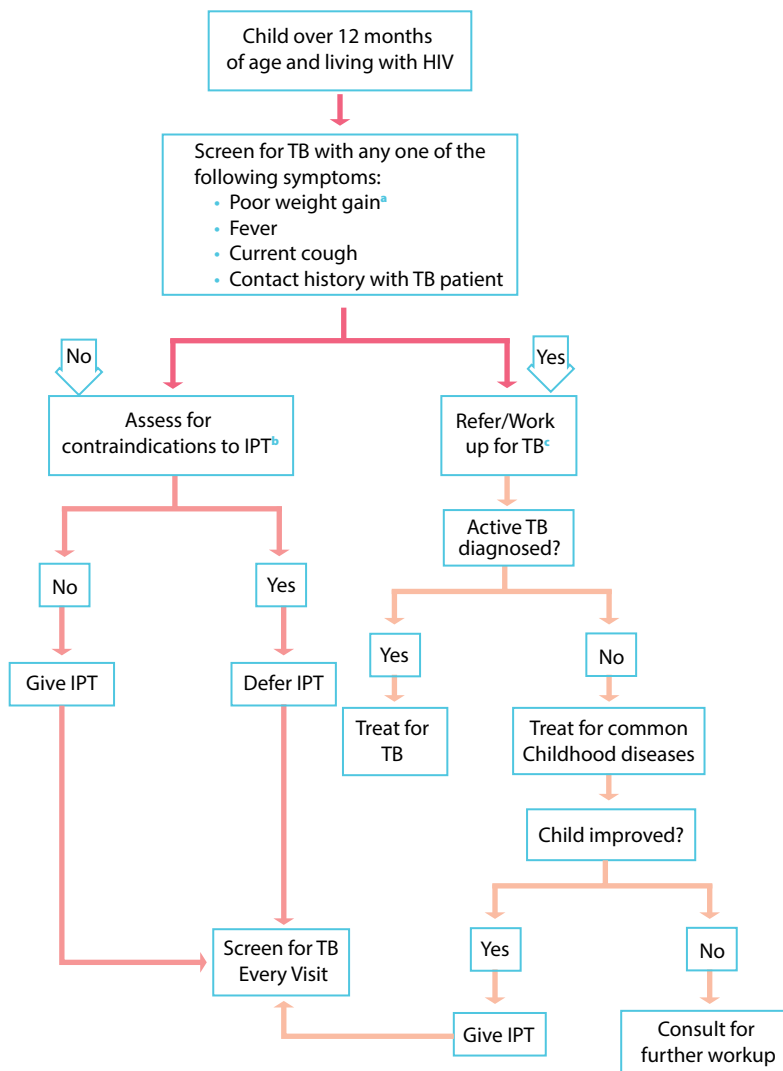
Figure 4.1 Algorithm for TB screening among adults and adolescents living with HIV in HIV-prevalent and resource-constrained settings



- Every adult and adolescent should be evaluated for eligibility to receive ART. Infection control measures should be given priority to reduce M.TB transmission in all settings that provide care
- 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.
- Contraindications include: active hepatitis (acute or chronic), regular and heavy alcohol consumption and symptom of requirement for initiating IPT
- Investigations for TB should be performed in accordance with existing national guideline.

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.

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

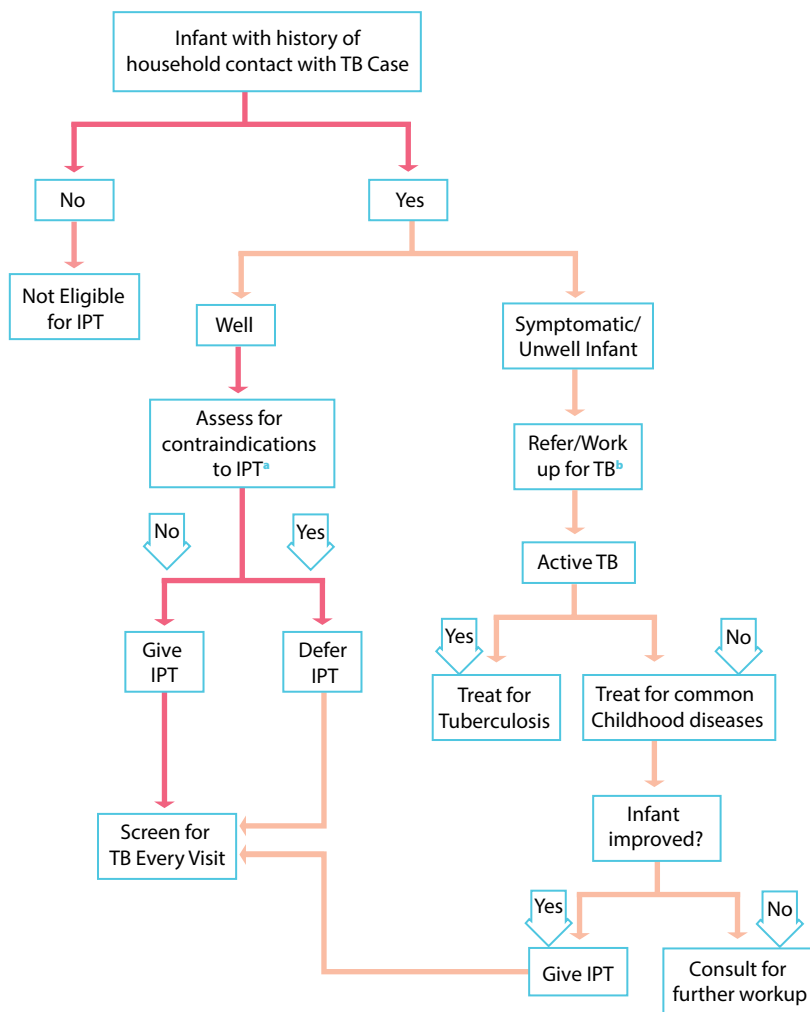


- Poor weight gain is defined as (1) reported weight loss or very low weight (weight for age less than  $-3$  z-score), (2) underweight (weight for age less than  $-2$  z-score), (3) confirmed weight loss ( $>5\%$ ) since the last visit or (4) growth curve flattening.
- Contraindications include: active hepatitis (acute or chronic) and symptoms of peripheral neuropathy
- 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



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

### 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 OIs, 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 (PCP), 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 in 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.

**AFB microscopy:** AFB Microscopy is indicated for HIV infected presumptive TB cases when access to XPERT MTB/RIF test is limited.

**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.

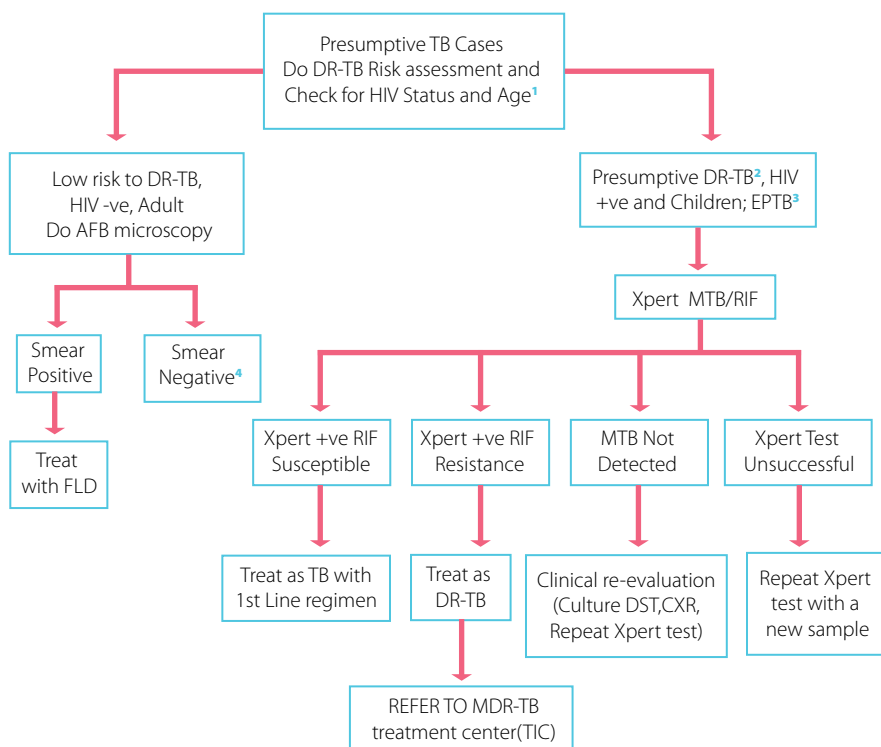
**Sputum culture:** sputum culture is the gold standard for the diagnosis of tuberculosis in general. In patients with XPert negative results, sputum culture may be indicated as part of the diagnostic procedure for people living with HIV if clinical suspicion persists.

### 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.



Fig 4.4 National TB and MDR TB diagnostic algorithm at health facility level



**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 in 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
<b>Lymph Node TB</b>	2 cm 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.
<b>Pleural effusion</b>	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.
<b>Tuberculosis Meningitis</b>	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.
<b>Pericardial Effusion</b>	Heamodynamically significant pericardial effusion, often with pleural effusions, Lung fields clear and intra-thoracic lymphadenopathy. Usually patients with weight loss, night sweats, fever. N.B. 90% of Pericardial Effusions in HIV positive patients in high-TB burden areas is due to TB.	CXR, Echocardiogram or chest ultrasound; pericardiocentesis, and pericardial biopsy; routine TB Workup. Start anti-TB as soon as possible
<b>Disseminated TB</b>	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)
<b>TB of the Spine</b>	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. Initiate TB prevention with Isoniazid Preventive Therapy** 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 4.5 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 of IPT.

## Follow-up of Patients on IPT

Patients should be given one-month supply of Isoniazid and 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 OIs.
- Stop IPT if active TB is diagnosed and to immediately start anti-TB.



### 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

#### 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 that in 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 *Hemophilus 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:

Amoxicillin is the drug of choice for community-acquired bacterial pneumonia. Start with 500mg tid for ten days in adults. In children amoxicillin syrup with a dose of 40mg/kg for seven days is the recommended approach. In patients with penicillin allergy use erythromycin 500mg qid for the same duration. Follow up is necessary to document resolution of initial symptoms or to monitor complications. Moreover, the patient has to be staged to determine eligibility for ART. 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.

#### 4.2.3. Pneumocystis Pneumonia

Pneumocystis pneumonia is caused by *Pneumocystis jiroveci* formerly known as *pneumocystis carini pneumonia* (PCP), 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<200cells/mm<sup>3</sup> or CD4 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 often 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 methylamine 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 started (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 (LIP)

**Epidemiology:** LIP is one of the most common chronic lower respiratory conditions occurring in up to 25% of children with HIV/AIDS.

**Clinical manifestations:** Range 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:** Usually based on clinical exam 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 GI OI diseases commonly manifest with diarrhoea, 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 providing supportive care to monitor situations such as fluid loss. A number of drugs can cause adverse effects that present with clinical manifestations referable to GIS which are similar to OIs 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 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:** 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 are referred or investigated if facilities are available, to rule out other causes.

Drug of choice: Fluconazole 200 mg(3mg/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 eosophagitis use acyclovir 400mg po five times for 14 to 21 days.

4.3.2. Diarrhoea

Diarrhoea is defined as passing more than four loose or watery stools/day. It may be acute or chronic, persistent or intermittent. Diarrhoea is among the most frequent symptoms of HIV disease. Delay in treatment can result in fluid loss and hemodynamic instability. Chronic diarrhoea 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 and stool culture when indicated (optional)

Management:

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

If specific enteric pathogen is identified or strongly suspected on clinical grounds, it should be treated accordingly.

Table 4.6: 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



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 4mg stat then 2mg 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 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 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 (augmentin) 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  $<100$  cell/mm<sup>3</sup>.

The lesions become extensive, persistent, severe and sometimes 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 Acycovir is gratifying if it is done in sufficient dose (400mg 4 to 5 X/d) 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.

Cervical cancer screening is an important test to prevent significant morbidity and mortality associated with HPV in women.

77

#### 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 section 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, d drugs, 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 reflex
- 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, like 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/ $\mu$ L. 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 p.o.q 6h for six weeks or 3 weeks after resolution of lesion  
S/E: crystal urea, rash C/I: severe liver, renal and hematological disorders; known hypersensitivity to Sulfonamides

Dosage/form: 500 mg tablets,

PLUS

Pyrimethamine

Loading dose of 200 mg once, followed by:

Pyrimethamine 50-75 mg/day

S/E: rash, fever and bone marrow depression (neutropenia and thrombocytopenia)

C/I: folate deficiency

Dosage/form: 25 mg tablets

PLUS

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

S/E: allergy

Dosage/form: 5 and 10 mg tablets

OR

ii. Pyrimethamine and Folinic Acid (Leucovorin): (standard dose)

PLUS

Clindamycin: 600 mg q 6 hrs

S/E: 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. 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 cerebrospinal fluid (CSF) absorption, or yeast infection of the brain.





## Diagnosis

LP and CSF analysis:

- The opening pressure may be markedly elevated.
- CSF analysis

Protein = 30–150 mg/dl

WBC = 0–100 /mm<sup>3</sup> (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 in two divided doses):

**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/mm<sup>3</sup> (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 cell count less than 20 cells/ $\mu$ L
- High CSF cryptococcal antigen titer

### 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 (ddI, d4T, 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
- Substitute or switch drugs such as d4T/DDI when the neuropathy is severe
- Remove other drugs associated with peripheral neuropathy
- Supplement vitamin intake for all patients including concomitant administration of pyridoxine with INH.
- Adjuvants for pain management (such as Amitriptylin, carbamazepin) indicated for patients with pain and paresthesias.

### 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 OIs; early manifestations of HIV infections frequently occur in the skin. Different kinds of OIs, 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.

Pruritis 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 not amenable to available therapy. The most common skin conditions associated with pruritis in patients with AIDS include the following:

1. Excessive dryness of the skin ( Xerosis cutis)
2. Eczemas like seborrheic dermatitis or contact dermatitis
3. Folliculitis that may include infections by *Staphylococcus aureas* or hypersensitivity to insects
4. Drug eruptions
5. Scabies
6. 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:

Infections	Disease	Clinical Presentations	Treatment	Remark
Bacterial	Cellulitis	Poorly defined erythema. pus and crust at the site plus signs of inflammation	Amoxicillin 500mg tid for ten days or erythromycin 500mg 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 antibiotic: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 tid for ten days. <i>In children 20 mg/kg/dose 4X daily</i>	If Chronic (> one month) indicates eligibility for ART.
	Herpes Zoster	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.



Infections	Disease	Clinical Presentations	Treatment	Remark
Viral	Warts/veruccar	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 immune deficiency state.	May not require therapy; HAART if eligible	Contagious
Parasitic infestation	Scabies	Pruritic lesions ranging from pinpointed erythematous papules involving interdigital and gluteal places 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.*





### 4.5.3. 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 a 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 they 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. HAART 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 (anaemia, leucopenia and thrombocytopenia). Presentation may not be typical. The bone marrow is packed with parasites but two-thirds of cases have no detectable anti-Leishmanial antibodies. CD4+ cell count in co-infected patients is usually  $<300 \text{ cells/mm}^3$ .

#### Diagnosis:

Parasitological diagnosis: Isolation of the organism from material taken from reticuloendothelial tissue and examined with Giemsa, Wright's or Leishmanial stain.

#### Immunological diagnosis

- Antibody detection
- Leishmanial test is negative

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

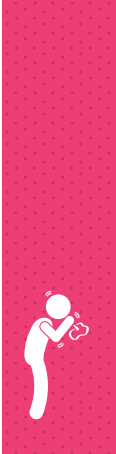
**Treatment of relapsed patients:** These are patients who are slower to respond and have a higher chance of further relapse and of becoming unresponsive to anti-monial drugs.

**Treatment:** same as above.



#### 4.7. Screening for co-morbidities

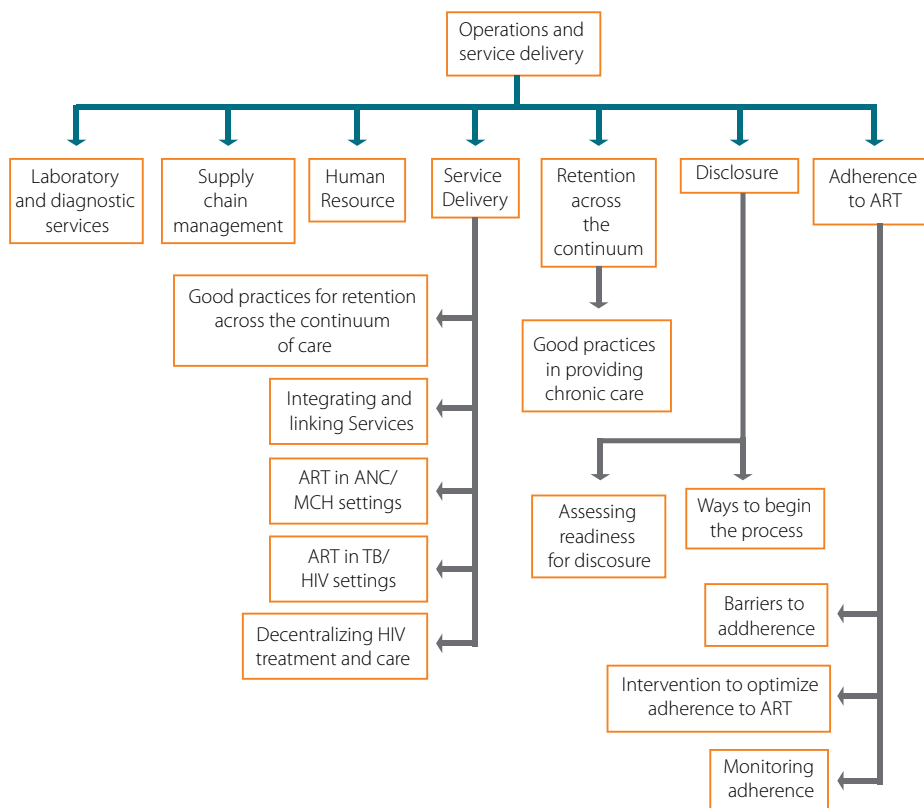
People living with HIV have got increased risk of non AIDs defining chronic diseases such as diabetes mellitus, cardiovascular illnesses, malignancies, chronic liver disease and chronic renal disease. With the advent of ART people are living longer, hence they are at risk for age related diseases. Therefore,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



## CHAPTER 5

# **GUIDANCE ON OPERATIONS AND SERVICE DELIVERY**





## 5.1. Adherence to ART

### Barriers to adherence

WHO defines treatment adherence as “the extent to which a person’s behaviour – 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.

Multiple factors related to 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; traveling 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.

**Programme-level interventions for improving adherence to ART include:**

Avoiding imposing out-of-pocket payments at the point of care, 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 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. Adherence preparation should not delay treatment initiation, when prompt action is necessary.

**Other interventions to optimize adherence to ART**

**Patient education and 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 intervention studies indicate that improving well-being by treating depression and managing substance use disorders improves HIV treatment outcomes.

**Nutritional support**

Nutrition assessment, care and support are essential components of HIV care. HIV programmes 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**

New recommendations like mobile phone text messages could 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 and are used to send brief reminders about the timing of ARV drugs, drug dosage and appointments.

**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. Effectively monitoring 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. Although treatment failure is often caused by lapses in adherence to ART, it may also result from other factors (such as drug stock-outs, drug interactions or malabsorption). **However, viral load monitoring does not provide an opportunity for care providers to monitor non-adherence in real time and prevent progression to treatment failure.** Viral load monitoring must therefore be combined with other approaches to monitoring 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 because they want to be perceived as being adherent and 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.



## 5.2. Disclosure

Pediatric disclosure is an ongoing process and 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.

### Advantages of Disclosure

#### For the child

- ≡ May feel relief at learning the cause of his/her illness
- ≡ May help to stop self-blaming as cause of the sickness.
- ≡ May feel more in control
- ≡ May have greater open involvement in medical care decisions
- ≡ Avoid situation of accidental disclosure (e.g., child overhears caregiver discussing)
- ≡ May decrease disruptive behaviors
- ≡ May improve adherence to medication
- ≡ May improve social functioning and school performance
- ≡ May be more willing to access health education, social support, peer support
- ≡ Communicates respect for the child and builds trust

#### For the care giver

- ≡ Relieves the stress and anxiety that accompanies secrecy and deception
- ≡ Opportunity to develop trusting relationship and more open communication with child
- ≡ Improved cooperation from a child
- ≡ Sharing positive messages with their child will lead to caregiver feeling less helpless and hopeless
- ≡ Allow easier access to other services, care and support

### Disadvantage of non-disclosure

- Child blames him/herself
- Maintains false understanding of illness including the belief that they are being cured
- Parents may use forceful means to ensure child takes medication





- Child's imagination creates unnecessary worry
- Becomes sexually active without knowing status
- No access to support
- Child may find out his /her status inadvertently/traumatic way
- Child may not trust caregiver in future



### **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

93

### **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 5.1). 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



Table 5.1 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?

Source: Columbia Paediatric Clinical Manual 2005

**5.2.1. 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 (Table 5.2). 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. This is addressed in the adult disclosure section.

**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 them 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, reinforce previous messages (while looking into possible causes)
- 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.

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.

### Stage 3

- 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.



### Post –disclosure assessments

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.

#### 5.2.2. Disclosure in adults

Among other priorities, testing and counselling programmes 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 serostatus. 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 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.

### 5.3. Retention across the continuum of care

Retaining people living with HIV across the continuum of care is essential for optimal health outcomes. Among those who do not have immediate indications for ART, care visits provide opportunities for screening, prevention and treatment of other conditions and comorbid illnesses, including providing co-trimoxazole prophylaxis, PMTCT, isoniazid preventive therapy and regular screening for TB and clinical and laboratory monitoring to allow timely initiation of ART once the indications arise.

For people who are eligible for ART at the time they test HIV-positive, rapid linkage to care is critical; delays of days or weeks with people already being ill with TB or other opportunistic infections increases the risk of mortality. For people living with HIV who are receiving treatment, uninterrupted ART and continual monitoring are essential for sustained viral suppression and optimal treatment outcomes.

Retaining people living with HIV in care especially people who are not yet eligible for ART and those who are eligible but have not yet initiated treatment poses a great challenge. People who discontinue care especially those who are not eligible for ART at initial assessment – frequently return to care only after they become ill with advanced HIV disease, when early mortality after initiating ART is significant. Multiple factors relating to the health care delivery systems and patients could facilitate or hinder retention in HIV 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 priorities in implementation research and public health.

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.

Many people living with HIV who are not yet eligible for ART may not attend clinic appointments and may not return to care until they are symptomatic. Regularly following up these individuals is important to ensure continual monitoring and timely initiation of ART. Key populations generally experience more barriers to accessing health services.

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.

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

<b>Factors related to the health system</b>	<b>Possible interventions</b>
<b>High direct and indirect costs of receiving care</b>	<ul style="list-style-type: none"> <li>• ART and related diagnostics and services free of charge at the point of care</li> <li>• Decentralize ART where feasible</li> <li>• Scheduled facility visits</li> <li>• Reduce waiting time at the facility level:</li> <li>• Appointment system</li> <li>• Separate clinical consultation visits from appointments for picking up medicines</li> <li>• Link, integrate and coordinate care</li> </ul>
<b>Stock-outs of ARV drugs</b>	<ul style="list-style-type: none"> <li>• Optimize pharmaceutical supply management systems to forecast, procure and deliver ARV drugs.</li> <li>• Use fixed-dose combinations to simplify forecasting and supply management systems</li> </ul>
<b>Lack of a system for monitoring retention in care</b>	<ul style="list-style-type: none"> <li>• Implement systems for patient monitoring across the continuum of care, including cohort analysis and patient tracking systems</li> </ul>
<b>Lack of a system for transferring people across different points of care</b>	<ul style="list-style-type: none"> <li>• 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</li> </ul>
<b>Pill burden and complex ARV drug regimens</b>	<ul style="list-style-type: none"> <li>• Use fixed-dose combinations to reduce the pill burden and simplify the regimens</li> </ul>
<b>Lack of accurate information for patients and their families and peer support</b>	<ul style="list-style-type: none"> <li>• Engage and integrate community health workers, volunteers and people living with HIV in peer support, patient education and counseling, and community-level support</li> </ul>





<b>Factors related to the health system</b>	<b>Possible interventions</b>
<b>Adherence support</b>	<ul style="list-style-type: none"><li>• Task shifting for involving community health workers</li><li>• Linking with community-level interventions and resources such as peer adherence support</li><li>• Using known effect reminder methods (such as text messaging)</li><li>• Peer support also provides opportunities for in-person reminders</li></ul>
<b>Poor relationship between patient and care provider</b>	<ul style="list-style-type: none"><li>• 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</li></ul>
<b>Lack of time for educating people in HIV care</b>	<ul style="list-style-type: none"><li>• Task shifting and sharing among clinic team members</li><li>• People living with HIV as patient experts and peer supporters</li><li>• A team approach to care</li></ul>
<b>Adverse drug effects</b>	<ul style="list-style-type: none"><li>• Preparedness and knowledge of how and when to self-manage adverse effects and when to return to the clinic</li></ul>
<b>Forgetfulness, life stress, stigma and discrimination</b>	<ul style="list-style-type: none"><li>• Using text messaging to keep patients engaged</li><li>• Peer and family support</li><li>• Link to community support group</li></ul>
<b>Comorbidity, substance and alcohol use disorders and mental health disorders</b>	<ul style="list-style-type: none"><li>• Manage HIV with mental health disorders, alcohol and other substance use disorders and link with community and social support</li></ul>
<b>Patient knowledge and beliefs related to HIV infection, its course and treatment</b>	<ul style="list-style-type: none"><li>• Integrate the education of patients and their families and counseling, broader community literacy and education and community engagement</li></ul>

## 5.4. Service delivery

### Good practices in providing chronic care

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.

### **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 and TB need to collaborate to successfully implement ART and related services at different levels of the health system.

### **Delivering ART in antenatal care and maternal and child health 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 ART in TB treatment settings**

ART should be initiated for an individual living with HIV in TB treatment settings, with linkage to ongoing HIV care and ART.

### **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.



## Human resources

### Building human resource capacity

Within the past decade, in the context of the rapid scaling up of HIV care and treatment, in-service training has assumed a key role in rapidly upgrading the competencies of health workers. All health workers, including community health workers, need to be regularly trained, mentored and supervised to ensure high-quality care and the implementation of updated national recommendations. Given the rapidly evolving knowledge on HIV care and treatment, the country needs to consider a system for supporting health workers' continuing education, including clinical mentoring and regular supportive supervision. The use of new technologies such as computer-based self-learning, distance education, online courses and phone-based consultation may supplement classroom in-service training and support the efficient use of health workers' time and other resources. It is also important to fully embrace and strengthen HIV care and treatment in existing pre-service courses leading to health workers graduating and being certified in various disciplines. Health workers also need to be equipped to manage HIV as a chronic condition, and to work in a team and need to be familiar with the national guidelines and care protocol.

### 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.

## 5.5. Laboratory and diagnostic services

The consolidated national HIV guidelines support an increased access to HIV care and treatment, which will also requires 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. This guidance to strengthen laboratory and diagnostic services emphasizes the importance of leadership and governance, high-quality laboratory services and developing the health workforce:

- to strengthen and expand laboratory and diagnostic services;
- to support a dedicated specimen referral system;



- 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; and
- to ensure high-quality diagnostics and plans for implementation, including quality assurance.

### **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 sample 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). 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 call for routine 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 CD4 and early infant diagnosis networks;
- ensuring that laboratories have adequate infrastructure, technical testing expertise and quality assurance and quality improvement programmes;
- 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. 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.

#### **5. Implementing comprehensive quality management systems**

Developing a comprehensive quality management system including external quality assessment (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.

#### **6. 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.

### **5.6. Pharmaceuticals Supply Management System**

The provision of complete health care necessitates the availability of safe, effective and affordable drugs and related supplies of the required quality, in adequate quantity at all times.



The Integrated Pharmaceutical Logistics System (IPLS) integrates the management of essential pharmaceuticals including the following pharmaceuticals that were used to be managed vertically: HIV/AIDS, Malaria, TB and Leprosy, EPI, MCH and purchased essential drugs. It is the primary mechanism through which health facilities obtain essential and vital pharmaceuticals. Products included on the National Pharmaceuticals Procurement List (NPPL) are supplied and managed through the IPLS.

The Pharmaceutical Fund and Supply Agency (PFSA) is responsible for the selection, quantification, procurement planning, procurement, storage, distribution, inventory management and rational drugs use of the pharmaceuticals and delivery of health products to health facilities.

### **1. Selection of ARV Drugs and Related Supplies:**

The National List of Drugs for Ethiopia describes the antiretroviral drugs and related supplies for use in Ethiopia. This list will be updated as required. Forms containing information about strength and dosage of individual drugs will also be made available.

### **2. Quantification:**

National quantification of pharmaceuticals need for the Ethiopian Antiretroviral Treatment program will be conducted by PFSA in collaboration with stakeholders such as HAPCO, FMOH, RHBs and development partners. Different orders of ARVs and related commodities will be managed according to the quantities estimated in the quantification exercise. However, due to various changes in the program regarding regimen proportions, dynamic ARV preparations, and changes in the guidelines, it is found that it is necessary to review the national level quantification exercise every year to update the previous quantification exercise assumptions and results so that the forecast meets the current demands of the program.

### **3. Procurement:**

All antiretroviral drugs and related products for use in the public or private sector should be procured at affordable prices, with assured quality and adequate shelf life, from a reliable supply. This will enable organizations and institutions supporting ART to determine the minimum safety stock of ARVs they need in order to prevent stock-outs.

ARVs and related commodities are procured and distributed by PFSA. It follows the national and international procurement regulation.

### **4. Storage and Distribution:**

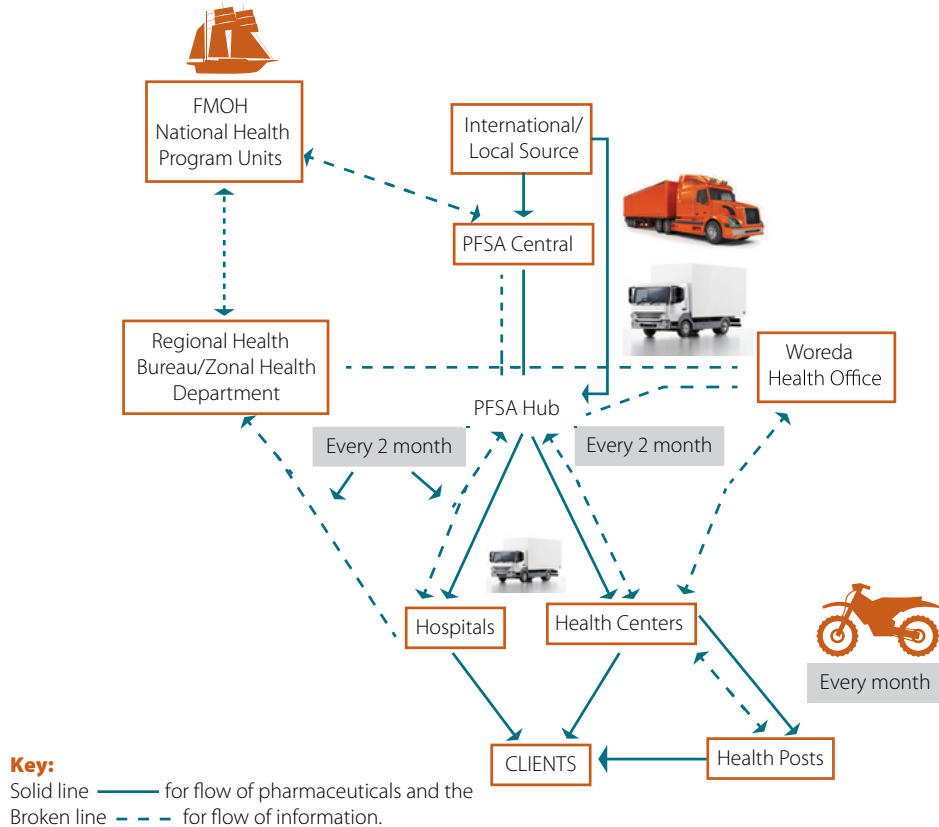
Proper storage of ARVs, including refrigeration, is critical to maintain the quality of the drugs and related supplies. Adequate space and facilities for proper handling must be ensured at various levels.

Pharmaceuticals and health products distribution will follow the existing delivery system and it extends from the central level to the Facility. PFSA will be the main system that will be used to deliver the products to its hubs; subsequently the hubs distribute the commodities to districts and health facilities.



Pharmaceuticals are ordered every two months by hospitals and health centres from the PFSA and delivered by PFSA to these facilities. Health posts report to health centres monthly and collect pharmaceuticals from those health centres.

### 5. Inventory Control:



The Pharmaceutical Logistics Information Tracking System (PLITS) and PFSA MIS system are electronic systems that collect data on the consumption at the facility level and the inventory at the facility and PFSA warehouses. PLITS summarizes the consumption and the inventory data to give regional and national picture about the status of the pharmaceuticals at the different levels. This information along with the assumptions set during the yearly forecasting exercises are used for decision on the quantities to procure and timing of procurement.

**NB.** PFSA is responsible for collecting, validating, analyzing, and utilizing the information to ensure an uninterrupted supply of health products through electronic report that coming every two months.



## **6. Rational use of medicines:**

Patients must receive the prescribed dose of medications appropriate to their clinical needs for an adequate period of time free of charge.

Rational use of drugs implies promotion of rational prescribing, ensuring good dispensing practice and encouraging appropriate drug use by the patient and the community at large. This should be part and parcel of programmatic activities at each and every level and the implementation is the responsibility of all stakeholders, including PFSA, FMOH, HAPCO and other partners.

## **7. Quality Assurance:**

Mechanisms are 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 ARVs is developed and is being implemented by FMHACA. Quality assurance of drugs and supplies will be maintained using simple visual methods: a First-In-First-Out (FIFO) system will be used to avoid expiration and ensure fresh supplies at all levels.





CHAPTER 6

# **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 are discussed in an open manner.

### 6.1. Guiding principles

- 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 (PLHIV), 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/AIDS 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/AIDS and the workplace (employment); blood safety; etc.) and are linked to other pre-existing services.

As the HIV/AIDS policy framework was being developed, the Ministry of Health coordinated a process of strategic planning and program development in Ethiopia's nine regions and two city administrations. This process involved national and regional governmental institutions, the major regional sector NGOs and religious organizations, and other key stakeholders. The framework focuses on reducing the transmission of HIV and associated morbidity and mortality, and its impact on individuals, families, and society at large. The strategy is built on four issues:

- 1.** Multi-sectoralism,
- 2.** Participation,
- 3.** Leadership, and
- 4.** Efficient management (including adequate monitoring and evaluation).

The strategy highlights the following priority areas for action: -

- 1.** Intensifying HIV Prevention.
- 2.** HIV Prevention Programs.
- 3.** Reducing vulnerability of young people, women, orphan and vulnerable children and others to HIV.
- 4.** Increasing the availability and accessibility of basic facility based HIV services, and utilization of preventive services.
- 5.** Increase access and quality of chronic care and treatment.
- 6.** Strengthen care and support to mitigate the impact of HIV/AIDS.
- 7.** Strengthen generation and use of strategic information.

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 mobilized for strengthening HIV strategic information.

National HIV program managers play a unique role in managing the process for adapting and implementing the HIV guideline recommendations. First, convening a broad, inclusive and transparent consultative process can help to define what program changes are relevant and necessary, such as revising national protocols, guidelines and regulations. Second, in parallel, it is necessary to secure the financial resources and political support required to implement the proposed changes. Third, systems 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. Lastly, 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. 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 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.

### **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 several economic evaluation tools used to measure the value of delivering particular services.

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.

### **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

Identifying individuals with CD4 counts between 350 and 500 cells/mm<sup>3</sup> provides an important opportunity to link them into care and initiate ART early. 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.

As coverage of ART increases and programs mature, expanding access to second-line regimens increasingly becomes a programmatic priority. Scaling up viral load monitoring will be important to adequately identify treatment failure and to avoid switching unnecessarily to second-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 programme managers should ensure effective coordination (a) with other health programmes, (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 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 AIDS Programme of the Ministry of Health should provide technical leadership and coordination of the health



sector response to HIV. The AIDS Programme Manager should serve as a leader, manager, facilitator and innovator and should liaise regularly with other health programmes 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. Regional Health Bureaus (RHBs) 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/AIDS programs and service deliveries in the region, zones and woredas. .

### **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**

### **National AIDS Council (NAC)**

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, nongovernmental organizations, and people living with HIV, faith-based organizations, and private sector and development partners.

### **HIV/AIDS Prevention and Control Office (HAPCO)**

HAPCO is responsible for resource mobilization and coordination of the multi-sectoral HIV/AIDS response in Ethiopia.

### **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 their 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 AIDS 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 7

# MONITORING & EVALUATION





## Monitoring & Evaluation

Effective HIV prevention, care and treatment require proper and 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 and analyzed.

The reporting of HIV prevention, care and treatment activities is integrated into the Health Management Information System (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.

The expansion of HIV prevention care and treatment must be accompanied by effective M&E and operational research to guide implementation and to see that efficiency, effectiveness, quality of care and acceptability are established and maintained.

This national consolidated guide on monitoring and evaluation of HIV in the health sector that brings together the various elements of monitoring and evaluation systems for HIV programmes. 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)

### 7.1. Monitoring the implementation of the New recommendation

Summary of the new recommendation area	Implication for monitoring
<b>HIV testing and Counseling</b>	<ul style="list-style-type: none"><li>• Monitor the uptake of community-based HIV testing strategies and testing</li><li>• services for adolescents, including systems for linkages to care</li></ul>
<b>When to start ART</b>	<ul style="list-style-type: none"><li>• Monitor the number and percentage of different populations (such as adults, adolescents, children and pregnant and breastfeeding women) who have initiated ART based on the new eligibility criteria</li><li>• Review the monitoring system to assess what disaggregation is needed for what purpose (such as CD4 counts <math>\leq 200</math> cells/mm<sup>3</sup> to routinely monitor late diagnosis or CD4 counts <math>\leq 350</math> cells/mm<sup>3</sup> and 350–500 cells/mm<sup>3</sup> to periodically assess the distribution of CD4 when ART is initiated) and how to best collect the relevant data, and age disaggregation of children (such as &lt;2 years and &lt;5 years)</li></ul>



Summary of the new recommendation area	Implication for monitoring
<b>Which ART regimen to start</b>	<ul style="list-style-type: none"> <li>• Monitor the first- and second-line ART regimens people are receiving Monitor the phasing out and/or introduction of specific drugs (such as d4T and TDF)</li> <li>• Monitoring tools may need to be adjusted to reflect new regimen options</li> </ul>
<b>Response to ART and diagnosing treatment failure</b>	<ul style="list-style-type: none"> <li>• Monitor the percentage of people receiving ART who had a viral load test and received the results</li> <li>• Monitor the reasons for switching ART regimen</li> </ul>

## 7.2. Key Indicators

List the key indicators based on the revised HMIS

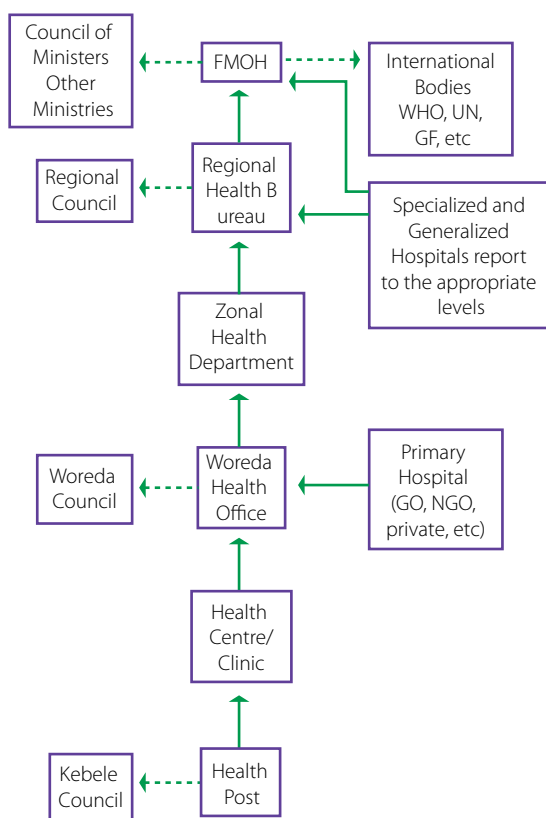
- 1. Number of individuals Tested and counseled for HIV and who received their test results:-** is the Number of individuals who have been tested for HIV and who received their test results
- 2. Number of PLHIV newly enrolled in Pre-ART care:-** is the Number of adults and children with HIV infection newly enrolled and receiving pre-ART care
- 3. HIV positive persons receiving co-trimoxazole prophylaxis:-** is the percentage of adults and children enrolled in HIV care and eligible for co-trimoxazole (CTX) prophylaxis (according to national guidelines) who are currently receiving CTX prophylaxis
- 4. Number of PLHIV ever started on ART:- is the Cumulative number of adults and children with advanced HIV infection started on antiretroviral therapy**
- 5. Number of adults and children receiving antiretroviral therapy (ART) (CURRENT):-** is the Number of adults and children with HIV infection receiving antiretroviral therapy
- 6. Number of adults and children with HIV infection newly started on ART:- is the Number of adults and children with HIV infection newly started on antiretroviral therapy during the reporting period**
- 7. Survival on ART:-** is the Percent of adults and children with HIV known to be alive and on treatment 12 months after initiation of antiretroviral therapy (survival at 12 months)

## 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 office 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 desegregation 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.



### 7.3.1. Data Quality Assurance (DQA)

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 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 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 ISSs, in-depth TB Program-Specific supervisions using standardized TBL 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 TBL and TB/HIV program performance is reviewed as part of the overall review meeting.

## 7.5. Other monitoring considerations

Programmes 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, programmes 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 programmes.

## **HIV drug resistance**

The use of early warning indicators to help 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 programmes, 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.



An abstract graphic design featuring a large, dark blue, angular shape on the left side of the page. This shape has several sharp points and a jagged, mountain-like top edge. Overlapping the right side of this blue shape is a smaller, bright yellow, angular shape. The word "ANNEXES" is printed in a bold, yellow, sans-serif font, centered within the yellow shape. The background of the entire page is a light gray with a fine, repeating dot pattern.

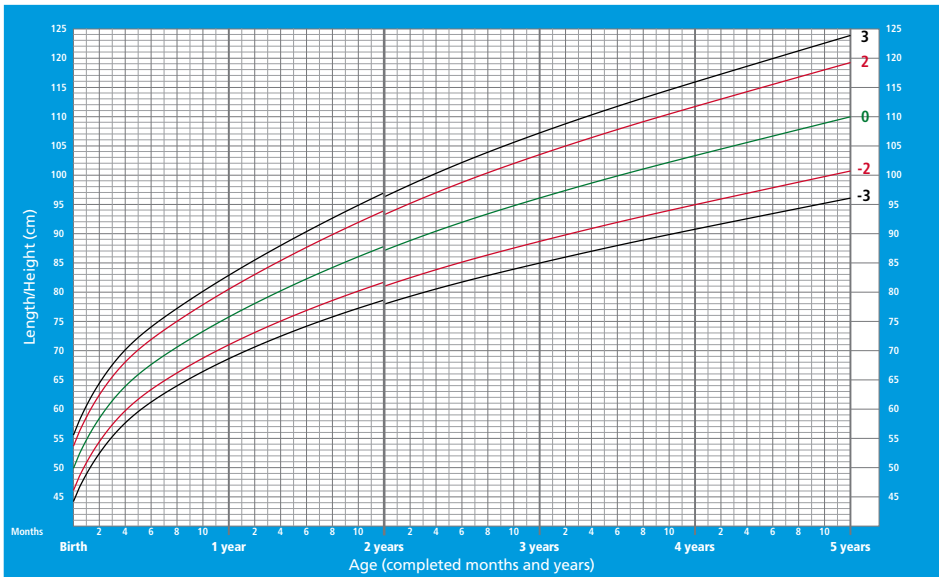
**ANNEXES**



# ANNEX 1: GROWTH CURVES

## Length/height-for-age BOYS

Birth to 5 years (z-scores)

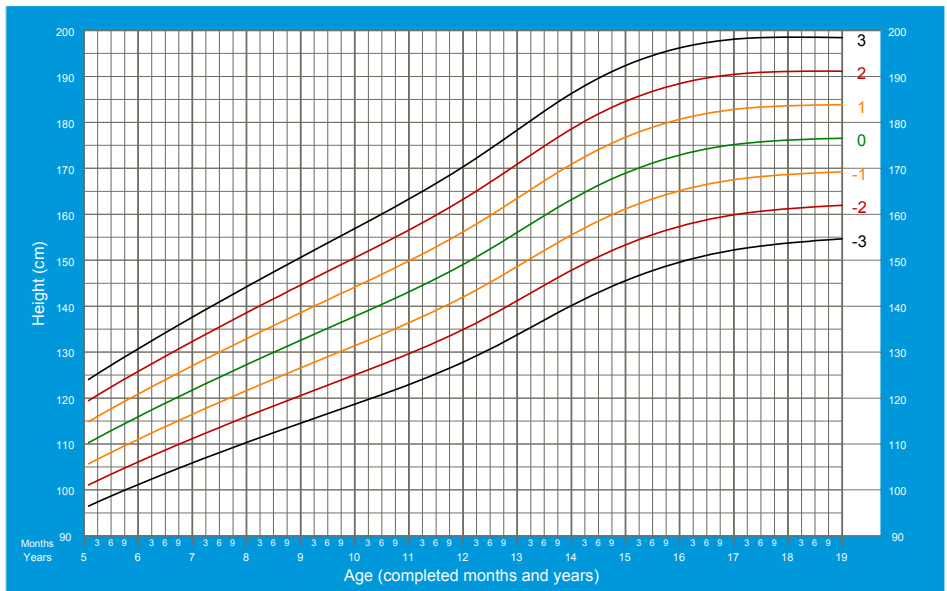


WHO Child Growth Standards

125

## Height-for-age BOYS

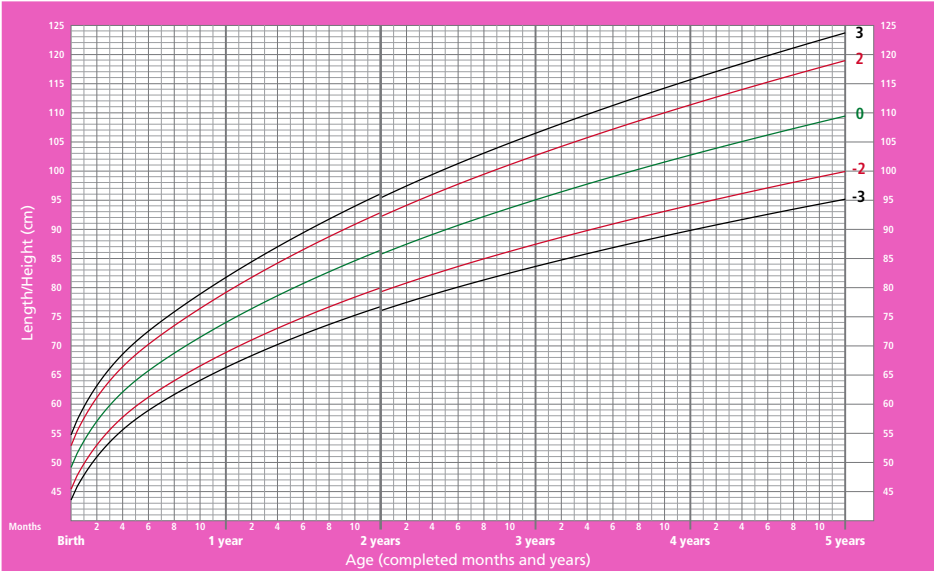
5 to 19 years (z-scores)



2007 WHO Reference

Length/height-for-age GIRLS  $\hat{E}$

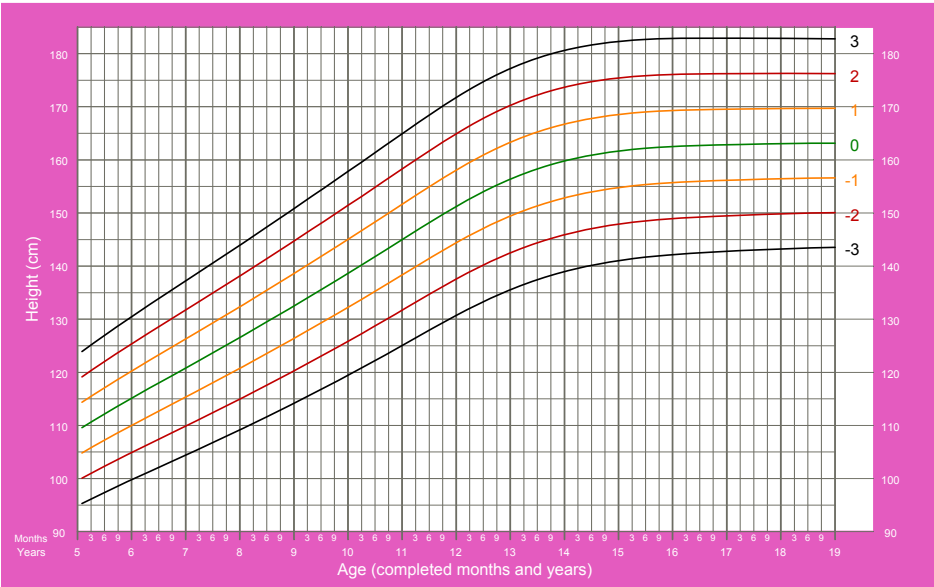
Birth to 5 years (z-scores)



WHO Child Growth Standards

Height-for-age GIRLS

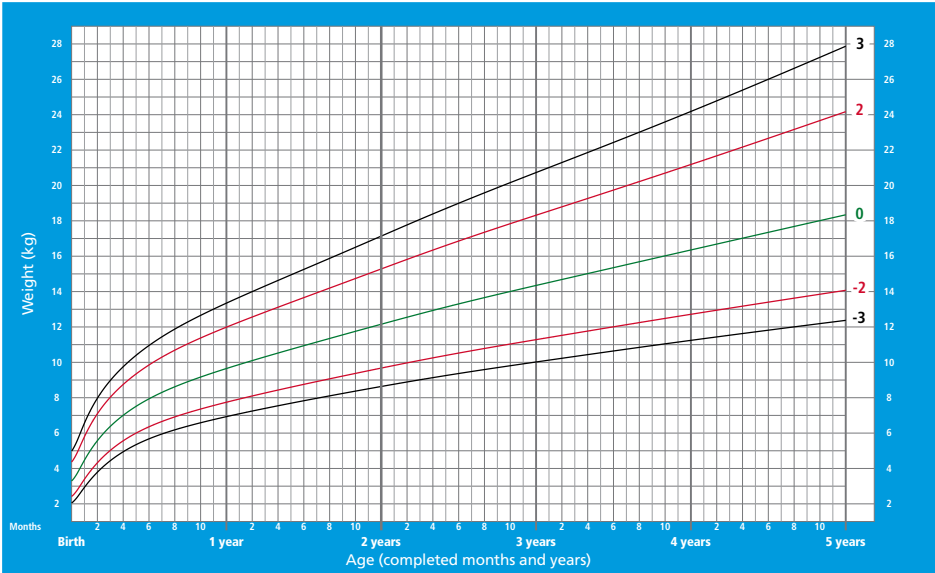
5 to 19 years (z-scores)



2007 WHO Reference

# Weight-for-age BOYS Ê

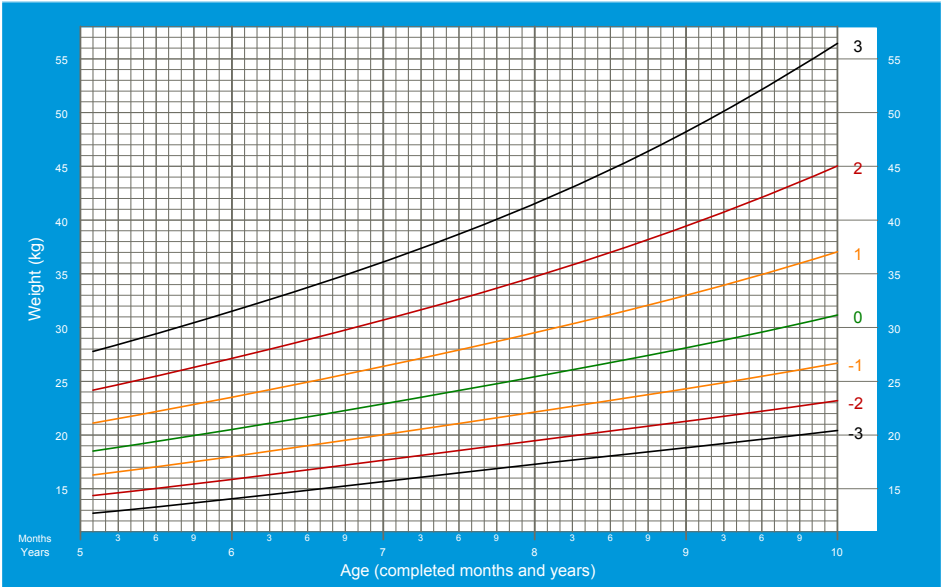
Birth to 5 years (z-scores)



WHO Child Growth Standards

# Weight-for-age BOYS

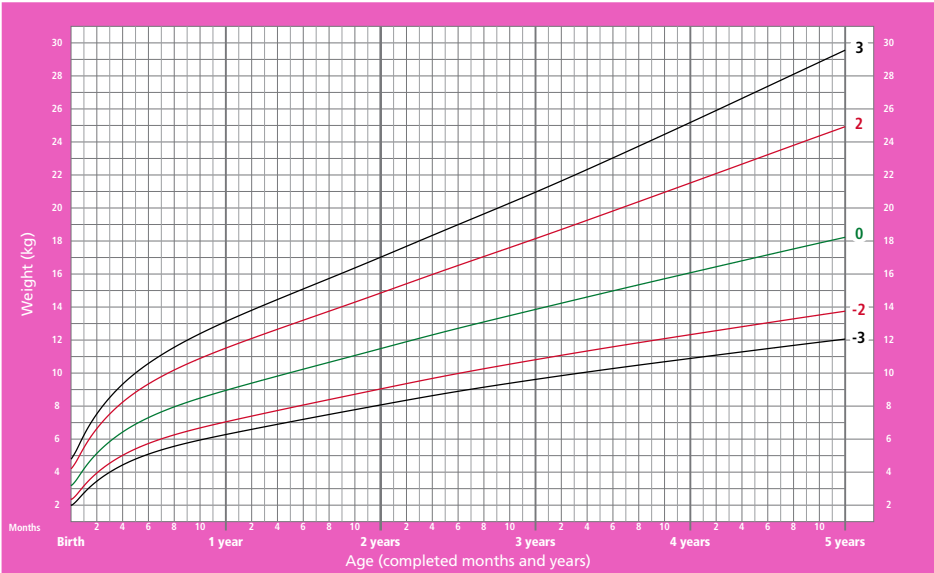
5 to 10 years (z-scores)



2007 WHO Reference

Weight-for-age GIRLS <sup>Ê</sup>

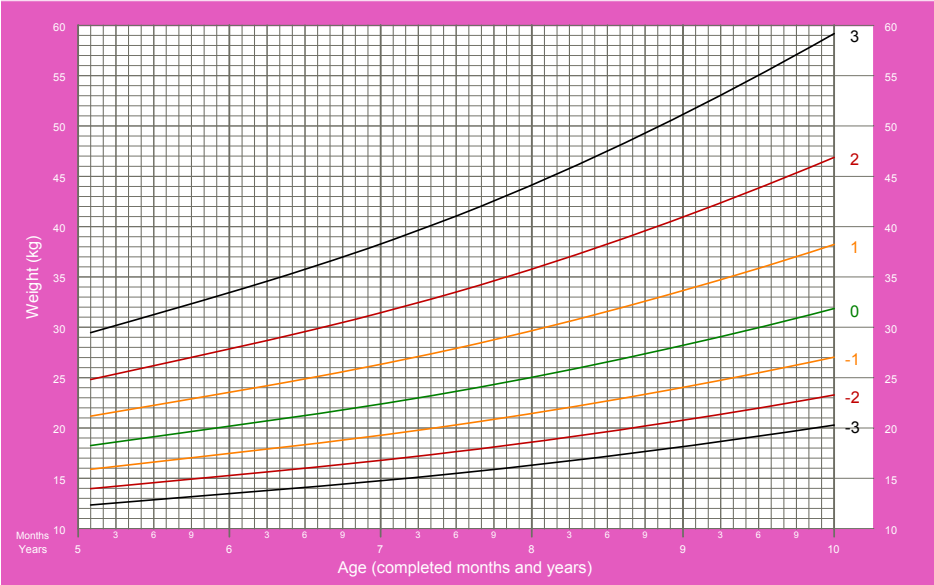
Birth to 5 years (z-scores)



WHO Child Growth Standards

Weight-for-age GIRLS

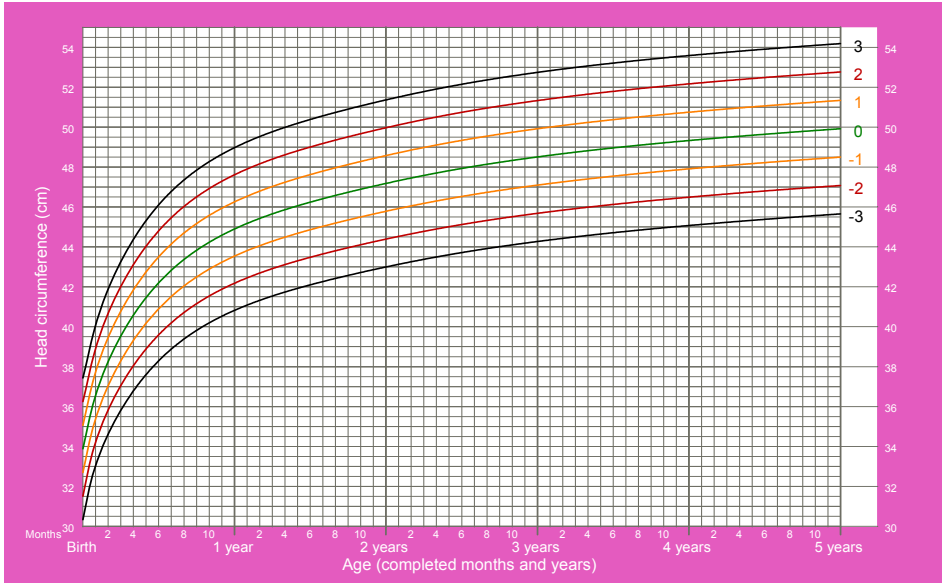
5 to 10 years (z-scores)



2007 WHO Reference

# Head circumference-for-age GIRLS

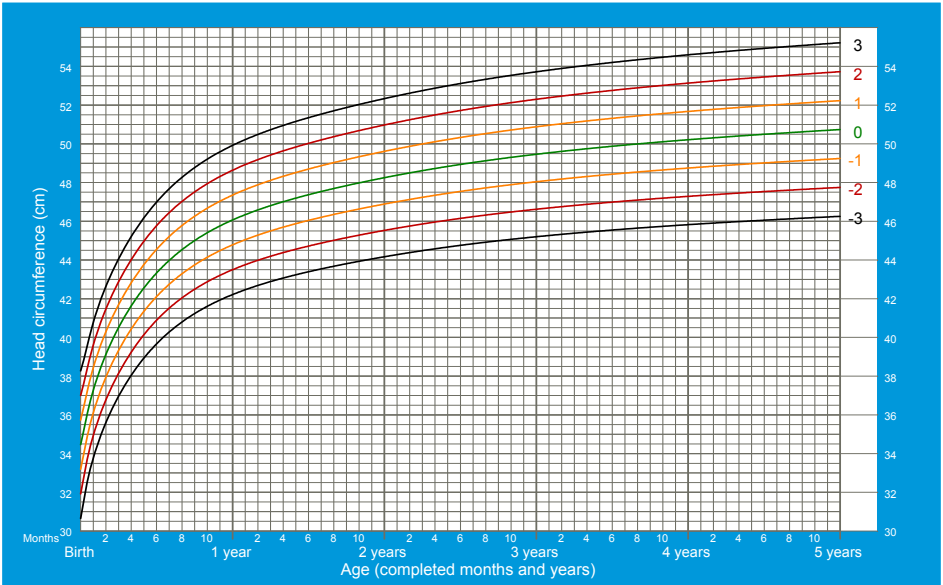
Birth to 5 years (z-scores)



WHO Child Growth Standards

# Head circumference-for-age BOYS

Birth to 5 years (z-scores)



WHO Child Growth Standards

## ANNEX 2: DOSAGE OF ANTIRETROVIRAL DRUGS FOR ADULTS AND ADOLESCENTS

Generic Name	Dose
<b>Nucleoside Reverse-Transcriptase Inhibitors (NRTIs)*</b>	
Abacavir (ABC)	300 mg twice daily or 600 mg once daily
Didanosine (dd)	400 mg once daily (> 60 kg) 250 mg once daily (≤60 kg)
Emtricitabine (FTC)	200 mg once daily
Lamivudine (3TC)	150 mg twice daily or 300 mg once daily
Stavudine (d4T)	30 mg twice daily
Zidovudine (AZT)	250–300 mg twice daily
<b>Nucleoside Reverse-Transcriptase Inhibitors (NRTIs)</b>	
Tenofovir (TDF)	300 mg once daily
<b>Non-Nucleoside Reverse-Transcriptase Inhibitors (NRTIs)</b>	
Efavirenz (EFV)	600 mg once daily
Etravirine (ETV)	200 mg twice daily
Nevirapine (NVP)	200 mg twice daily for 14 days, followed by 200 mg twice daily
<b>Proteases Inhibitors (PIs)</b>	
Atazanavir + ritonavir (ATV/r)	300 mg +100 mg once daily
Darunavir + ritonavir (DRV/r)	800 mg +100 mg once daily or 600mg +100 mg twice daily
Lopinavir/ritonavir (LPV/r)	400 mg/100 mg twice daily
<b>Considerations for individuals receiving TB therapy</b>	
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 twice daily) or (SQV 400 mg + RTV 400 mg twice daily), with close monitoring.	
<b>Integrase Strand Transfer Inhibitors (INSTIs)</b>	
Raltegravir (RAL)	400 mg twice daily

\* for adolescents weighing less than 35 kg, see the next page for weight-based dosing for ARV formulations for Children

## ANNEX 3: DOSAGE OF ANTIRETROVIRAL DRUGS IN CHILDREN

Drug	Strength of Tablet or sprinkle sachet or capsule (mg)	Number of Tablet or sprinkle/capsule sachets by weight band											
		3 – 5.9 Kg		6 – 9.9 kg		10 – 13.9 kg		14 – 19.9 kg		20 – 24.9 kg		25 – 34.9 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
ABC/3TC/NVP LPV/r sprinkles	60mg/30mg/50mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	4	4
	40mg/10mg	2	2	3	3	4	4	5	5	6	6		
ABC/3TC/LPV/r	30 mg/15mg/40mg/10mg	2	2	3	3	4	4	5	5	6	6		
	30 mg/15mg/40mg/10mg	2	2	3	3	4	4	5	5	6	6		
DRV	240mg/40mg					1	1	1	1	2	1		
ATV/r	100mg/33mg					1	1	1	1	2			
ABC/3TC	120mg/60mg	1		1.5		2	2	2.5		3			
	75mg/75mg					1.5	1.5	2		2.5		3 – 3.5 <sup>a</sup>	
TDF/3TC/EFV	75mg/75mg/150mg					1.5	1.5	2	2	2.5	2.5	3 – 3.5 <sup>a</sup>	
	300mg/300mg					one third	one third	one half	one half	two third	two third	1	
TDF/3TC adult double scored <sup>b</sup>						one third	one third	one half	one half	two third	two third	1	
TDF/3TC/EFV adult double scored <sup>b</sup>	300mg/300mg/600mg					one third	one third	one half	one half	two third	two third	1	

<sup>a</sup> 3 tablets for 25 – 29.9 kg and 3.5 tablets for 30 – 34.9kg

<sup>b</sup> A double-scored tablet has two score lines on one side of the tablet and one score line on the other side, enabling it to be divided into thirds or halves as needed

Drug	Strength of Paediatric Tab (mg) or Liquid (mg/ml)	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 AM + PM	30 – 34.9 kg AM + PM
		3 – 5.9 Kg AM + PM	6 – 9.9 kg AM + PM	10 – 13.9 kg AM + PM	14 – 19.9 kg AM + PM	20 – 24.9 kg AM + PM				
d4T/3TC	6/30	1 + 1	2 + 1	2 + 2	3 + 2	3 + 3	30/150	1 + 1	1 + 1	
	12/60	0.5 + 0.5	1 + 0.5	1 + 1	1.5 + 1	2 + 1				
d4T/3TC/ NVP	6/30/50	1 + 1	2 + 1	2 + 2	3 + 2	3 + 3	30/150/200	1 + 1	1 + 1	
	12/60/100	0.5 + 0.5	1 + 0.5	1 + 1	1.5 + 1	2 + 1				
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 /d	200 & 2 x 50 once /d	50, 200, 600	200 & 3 x 50 once /d	2 x 200 once daily	
NVP	10 mg/ml	5ml + 5ml	8ml + 8ml	10ml + 10ml	1 + 0.5	1 + 0.5	200	1 + 1	1 + 1	
AZT	200 (adult)									
	10 mg/ml	6ml + 6ml	9ml + 9ml	12ml + 12ml				1 + 1	1 + 1	
d4T	300 (adult)				0.5 + 0.5	1 + 0.5	300	1 + 1	1 + 1	
	1 mg/ml	6 ml + 6ml	9ml + 9ml	15ml + 15ml						
3TC	10 mg/ml	3ml + 3ml	4ml + 4ml	5 ml + 5ml						
	150 (adult)			0.5 + 0.5	0.5 + 0.5	1 + .5	150	1 + 1	1 + 1	
ABC	20 mg/ml	3ml + 3ml	4ml + 4ml	6ml + 6ml						
	60	1 + 1	2 + 1	2 + 2	3 + 2	3 + 3				
ABC/3TC	300 (adult)				0.5 + 0.5	1 + 0.5	300	1 + 1	1 + 1	
	60/30	1 + 1	2 + 1	2 + 2	3 + 2	3 + 3	600/300	1 once daily	1 once daily	



Drug	Strength of Paediatric Tab (mg) or Liquid (mg/ml)	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 AM + PM	30 – 34.9 kg AM + PM
		3 – 5.9 Kg AM + PM	6 – 9.9 kg AM + PM	10 – 13.9 kg AM + PM	14 – 19.9 kg AM + PM	20 – 24.9 kg AM + PM				
Lop/r	80/20 mg/ml	1ml + 1ml	2ml + 1ml	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			
ddl	25 chewable tablet;	2 x 25 +	2 x 25 +	125 EC once	200 EC once	250 EC once	250 EC	1 once daily	2 + 1	2 + 2
	125, 200, 250 EC	2 x 25	2 x 25	daily	daily					

Note: A 1:1 ratio of Lopinavir and Ritonavir is required when Lop/r is co-administered with enzyme-inducing drugs such as rifampicin; n/r = not recommended

ANNEX 4: PEDIATRIC ARV DRUG FORMULATIONS, SIDE EFFECTS AND SPECIAL CONSIDERATIONS IN CHILDREN

Drug Formulation	Comments	Side Effects
Nucleoside reverse transcriptase		
Lamivudine (3TC) Oral solution 10mg/ml Tablet: 150mg	Can be given with food. Store solution at room temperature (use within one month of opening). Tablet can be mixed with small amount of water and taken immediately. Side effects are rare.	Common: head ache, nausea, abdominal pain. Less common: pancreatitis, neutropenia, increased LFTs.
Stavudine (d4T) Oral solution 1mg/ml Capsules: 15mg 20mg, 30mg, 40mg	Keep liquid refrigerated.Stable for 30 days. Capsules can be opened and mixed with small amount of food or water. DO NOT USE WITH AZT.	Common: head ache, and GI intolerance. Less common: peripheral neuropathy, lipoatrophy. Life threatening: lactic acidosis with severe hepatomegaly and steatosis.
Zidovudine (AZT or ZDV) Oral solution 10mg/ml Tablet: 300mg Capsule:300mg	Can be given with food. Syrup is light sensitive, store in a glass jar.Capsule can be opened and contents dispersed or tablet crushed and combined with food or small amount of water.Large volume of syrup not well tolerated in older children. DO NOT USE WITH d4T.	Common: neutropenia, anemia, granulocytopenia, macrocytosis, and head ache. Less common: myositis, myopathy, mitochondrial disease.
Non-nucleoside reverse transcriptase		
Efavirenz (EFV) Syrup: 30mg/ml Capsule:50mg, 100mg, 200mg	Only for children > 3 yrs.Syrup requires higher dose than capsules.Can be given with food (but avoid high fat foods). Capsule can be opened and added to food: to avoid peppery taste mix with sweet food or jamBest given at night time to avoid CNS effects.	Common: skin rash, somnolence, insomnia, abnormal dreams, confusion, hallucinations. Less common: increased LFTs.
Nevirapine (NVP) Oral solution 10mg/ml Tablet: 200mg	Store at room temperature.Can be given with food.Tablets can be divided and combined with small amount of water or food and immediately administered. Patients should be warned of rash. Do not escalate dose if rash occurs.For SJS and TEN discontinue drug and do not rechallenge. Multiple drug interactions.	Common: skin rash, head ache, nausea, diarrhea. Less common: increased LFTs. Life threatening: Steven Johnsons syndrome, TEN, fatal hepatitis.

Drug Formulation	Comments	Side Effects
Nucleoside reverse transcriptase		
<b>Abacavir (ABC) Oral solution 20mg/ml Tablet: 300mg</b>	Can be given with food. Tablet can be mixed with small amount of water and taken immediately. Instruct patient on how to recognize and respond to potentially fatal hypersensitivity reaction. Patients should not interrupt therapy without consulting their healthcare provider. DO NOT rechallenge after hypersensitivity reaction.	Common: head ache, GI upset and rash. Less common: lactic acidosis, hepatomegaly with steatosis. Life threatening: potentially fatal hypersensitivity reaction (fatigue, rash, N/V, sore throat, joint and muscle pain, cough, and dyspnea).
<b>Didanosine(ddI) Powder for oral solution: reconstituted 10ml/ml Chewable tablets: 25mg, 50mg, 100mg, 150mg Enteric coated capsules: 200mg, 250mg, 400mg</b>	If tablets are dispersed in water, at least 2 tablets of appropriate strength should be dissolved to ensure adequate buffer. Keep suspension refrigerated, shake well, stable for 30 days. Enteric formulation may be better tolerated.	Common: diarrhea, abdominal pain, N/V. Less common: increased LFTs, lactic acidosis with hepatomegaly and steatosis, peripheral neuropathy, hyperuricemia. Life threatening: pancreatitis which is rare in children.
<b>Lamivudine (3TC) Oral solution 10mg/ml Tablet: 150mg</b>	Can be given with food. Store solution at room temperature (use within one month of opening). Tablet can be mixed with small amount of water and taken immediately.Side effects are rare.	Common: head ache, nausea, abdominal pain. Less common: pancreatitis, neutropenia, increased LFTs.
<b>Stavudine (d4T)Oral solution 1mg/mlCapsules: 15mg 20mg, 30mg, 40mg</b>	Keep liquid refrigerated.Stable for 30 days.Capsules can be opened and mixed with small amount of food or water. DO NOT USE WITH AZT.	Common: head ache, and GI intolerance. Less common: peripheral neuropathy, lipoatrophy. Life threatening: lactic acidosis with severe hepatomegaly and steatosis.
<b>Zidovudine (AZT or ZDV)Oral solution 10mg/ml Tablet: 300mgCapsule:300mg</b>	Can be given with food. Syrup is light sensitive, store in a glass jar.Capsule can be opened and contents dispersed or tablet crushed and combined with food or small amount of water.Large volume of syrup not well tolerated in older children. DO NOT USE WITH d4T.	Common: neutropenia, anemia, granulocytopenia, macrocytosis, and head ache.Less common: myositis, myopathy, mitochondrial disease.

Drug Formulation	Comments	Side Effects
<b>Non-nucleoside reverse transcriptase</b>		
<b>Efavirenz (EFV) Syrup:</b> 30mg/ml Capsule: 50mg, 100mg, 200mg	Only for children > 3 yrs. Syrup requires higher dose than capsules. Can be given with food (but avoid high fat foods). Capsule can be opened and added to food: to avoid peppery taste mix with sweet food or jam. Best given at night time to avoid CNS effects.	Common: skin rash, somnolence, insomnia, abnormal dreams, confusion, hallucinations. Less common: increased LFTs.
<b>Nevirapine (NVP) Oral solution 10mg/ml Tablet: 200mg</b>	Store at room temperature. Can be given with food. Tablets can be divided and combined with small amount of water or food and immediately administered. Patients should be warned of rash. Do not escalate dose if rash occurs. For SJS and TEN discontinue drug and do not rechallenge. Multiple drug interactions.	Common: skin rash, head ache, nausea, diarrhea. Less common: increased LFTs. Life threatening: Steven Johnsons syndrome, TEN, fatal hepatitis.
<b>Protease Inhibitors</b>		
<b>Lopinavir /ritonavir (LPV/r)</b> Oral solution 80mg/ml LPV plus 20mg/ml r capsules: 133.3mg LPV plus 33.3mg r	Preferable to store capsules and liquid in a refrigerator. Can be stored at room temp 25°C for 2 months. Should be taken with food. Capsules should not be opened or crushed, swallow whole. Liquid has low volume but bitter taste. Tablets require no cold chain; can be used in children on full adult dose.	Common: diarrhea, head ache, nausea, vomiting, increase in blood lipids. Less common: pancreatitis, diabetes, hyperglycemia, hepatic toxicity, fat redistribution.
<b>Nelfinavir (NFV) Powder for oral suspension (mix with liquid): 200 mg per level teaspoon (50mg per 1.25 ml scoop) Tablet: 250mg</b>	Take with food. Store at room temperature. Crushed tablet preferred even for infants. Drug interactions less than with RTV/PI	Common: diarrhea, nausea, vomiting, head ache. Less common: asthenia, abdominal pain, rash, lipodystrophy.
<b>Ritonavir (RTV) Suspension: 80mg/ml Capsule: 100mg</b>	Take with food to increase absorption and reduce GI side effects. 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. If given with dd there should be 2 hours between taking each drug.	Common: N/V, diarrhea, headache, abdominal pain, anorexia. Less Common: circumoral paraesthesia, increased LFTs, lipodystrophy, elevated cholesterol and triglycerides, hyperglycemia.

## ANNEX 5: 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
<b>Peripheral neuropathy</b>	<b>Grade 1 (mild)</b> Transient or mild discomfort, no limitation of activity no medical intervention/treatment required	<b>Grade 2 (moderate)</b> Moderate limitation of activity, some assistance might be needed Non-narcotic analgesia required	<b>Grade 3 (Severe)</b> Marked limitation in activity, some assistance usually required, medical intervention/therapy required, hospitalization possible severe discomfort and/or severe impairment (decrease or loss of sensation up to knees or wrists) narcotic analgesia required	<b>Grade 4 (Severe Life threatening)</b> 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
<b>Cutaneous/Rash/Dermatitis**</b>	Erythema, pruritus	Diffuse, maculopapular rash or drydesquamation	Vesiculation or moist desquamation or ulceration*	Erythema multiforme or suspected Stevens-Johnson syndrome or Toxic Epidermal Necrolysis (TEN)
<b>Management</b>	Continue ARV Provide careful clinical monitoring Consider change of a single drug if condition worsens		substitute responsible drug	Stop ARV and consult experienced physician

## ANNEX 6: GRADING OF ADVERSE EVENTS IN CHILDREN

Parameter	Grade 1 Mild	Grade 2 Moderate	Grade 3 Severe	Grade 4 Severe Life-threatening
<b>Diarrhoea</b> ≥1 year of age <1 year of age	Transient or intermittent episodes of unformed stools OR increase of ≤3 stools over baseline per day. Liquid stools (more unformed than usual) but usual in number.	Persistent episodes of unformed to watery stools or increase of 4-6 stools over baseline per day. Liquid stools with increased number of stools or mild dehydration.	Grossly bloody diarrhoea or increase of ≥7 stools per day or IV fluid replacement indicated. Liquid stools with moderate dehydration.	Life-threatening consequences (e.g. hypotensive shock). Liquid stools resulting in severe dehydration with aggressive rehydration indicated or hypotensive shock.
<b>Nausea</b>	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.
<b>Vomiting</b>	Transient or intermittent vomiting with no or minimal interference with oral intake.	Frequent episodes of vomiting with no or mild dehydration.	Persistent vomiting resulting in orthostatic hypotension or aggressive rehydration indicated (e.g. IV fluids).	Life threatening consequences (e.g. hypotensive shock).
<b>Acute systemic allergic reaction</b>	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.

Parameter	Grade 1 Mild	Grade 2 Moderate	Grade 3 Severe	Grade 4 Severe Life-threatening
<b>Pancreatitis</b>	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).
<b>Rash</b>	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 ulcerations of mucous membrane limited to one site.	Extensive or generalized bullous lesions or Stevens-Johnson syndrome or ulceration of mucous membrane involving two or more distinct mucosal sites or Toxic Epidermal Necrolysis.
<b>Alteration in personality-behaviour or mood</b>	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.	Behaviour potentially harmful to self or others or with life-threatening consequences.
<b>Altered Mental Status</b>	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 7: 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 <sup>3</sup>	750-990 mm <sup>3</sup>	500-749 mm <sup>3</sup>	<500 mm <sup>3</sup>
Platelets	-75,000- 99,000	50,000-74,999	20,000-49,999 mm <sup>3</sup>	<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
<b>Cholesterol*</b> 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				
<b>MANAGEMENT</b>	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 8: 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 (mm3 )	750 – <1,000	500 – 749	250 – 500	<250
Platelets (mm3 )	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	<sup>3</sup> 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 8: 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: Gastric Aspirate/ Induced sputum/ Sputum for AFB	date ordered					
	date result received					
	result (+, -ve, Not Done)					
Radiology: CxR, etc.	date ordered					
	date received					
	result (Suggestive, inconclusive, other dx, Not Done)					

<b>Other: FNA, etc</b>	date ordered					
	date received					
	result (+, -ve, Not Done)					
<b>TB diagnosis date: / / Circle type of TB: PTB :- smear pos, smear neg, EPTB TB Rx start date / /</b>						
<b>Is the child eligible for IPT? Yes ___ No ___ If no, reason If yes, start IPT and use the chart below</b>						
<b>Contraindications for IPT: Active TB, active hepatitis, allergy to INH, peripheral neuropathy</b>						
<b>Date INH collected</b>	TB Symptoms [cough, fever, failure to gain wt or wt loss] (yes, no)	Hepatitis Sx [abd 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 \_\_\_/\_\_\_/\_\_\_

Key: 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. NB 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 9: ADULT TB SCREENING TOOL

		Follow Up Visit					
Children TB screening questions		Date: _/_/_	Date: _/_/_	Date: _/_/_	Date: _/_/_	Date: _/_/_	Date: _/_/_
Current cough							
Fever							
Weight lose							
Night seats							
Evaluate for TB if “yes” to anyone of the above (positive TB screening)							
Bacteriology: Sputum for AFB (+/- induced)		Done = yes/no					
		result (+, -ve, unknown )					
Radiology: CxR, etc.		Done = yes/no					
		Result (Suggestive, inconclusive, other dx, Not Done)					
FNA, culture, ultrasound etc		Done = yes/no					
		If done result					
TB diagnosed		Yes (write type of TB)/No					
Is patient eligible for IPT		Yes/No					

Children TB screening questions		Follow Up Visit				
Date: ____/____/____		Date: ____/____/____	Date: ____/____/____	Date: ____/____/____	Date: ____/____/____	Date: ____/____/____
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, 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 \_\_\_\_/\_\_\_\_/\_\_\_\_

Patient stopped \_\_\_\_/\_\_\_\_/\_\_\_\_ Stopped \_\_\_\_/\_\_\_\_/\_\_\_\_ Transferred out \_\_\_\_/\_\_\_\_/\_\_\_\_

(Footnotes)

1 For those eligible without CD4 count ART initiation should not be delayed for the CD4 test, however do the test at earliest opportunity for monitoring purpose.

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





