NATIONAL GUIDELINES ON THE USE OF ANTIRETROVIRAL THERAPY FOR HIV PREVENTION AND TREATMENT

Fifth Edition

Ministry of Health

Government of Lesotho

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ABBREVIATIONS AND ACRONYMS

ABC	Abacavir
AFASS	Affordable, Feasible, Acceptable, Sustainable and Safe
AFB	Acid-fast bacilli
AIDS	Acquired Immune Deficiency Syndrome
ALT	Alanine aminotransferase
ANC	Antenatal care
ART	Antiretroviral therapy
ARV	Antiretroviral
ATT	Anti tuberculosis treatment
ATV	Atazanavir
AZT	Azidothymidine, also known as Zidovudine
CDC	Centres for Disease Control and Prevention
CSF	Cerebro-Spinal Fluid
CTC	Care and Treatment Clinics
CTX	Co-trimoxazole
CRAG	Cryptococcal antigen
CXR	Chest X-ray
d4T	Stavudine
DBS	Dried Blood Spot
DNA	Deoxyribonucleic Acid
DRV	Darunavir
DST	Drug Susceptibility Testing
DTG	Dolutegravir
EC	Emergency Contraceptive
EFV	Efavirenz
ELISA	Enzyme-linked immunosorbent assay
EPTB	Extra-pulmonary tuberculosis
ETV	Etravirine
FBC	Full Blood Count
FP	Family Planning
FTC	Emtricitabine
HCW	Healthcare worker
Hb	Haemoglobin
HBsAg	Hepatitis B surface antigen
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
HRZE	Isoniazid, Rifampicin, Pyrazinamide, Ethambutol
HTS	HIV Testing Services
INH	Isoniazid
IPT	Isoniazid Prophylaxis Therapy
IUD	Intra-Uterine Device
LFTs	Liver Function Tests
LPV/r	Lopinavir/Ritonavir boosted
MCH	Maternal and Child Health
MDR-TB	Multi-Drug Resistant TB
MOH	Ministry of Health
MTCT	Mother-to-Child Transmission of HIV

MUAC	Mid-Upper-Arm Circumference
NGO	Non-Governmental Organisation
NVP	Nevirapine
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NtRTI	Nucleotide Reverse Transcriptase Inhibitor
NNRTI	Non-nucleoside Reverse Transcriptase Inhibitor
NSAIDs	Non-steroidal Anti-Inflammatory Drugs
OI	Opportunistic Infection
PCP	*Pneumocystis jirovecci* Pneumonia
PCR	Polymerase Chain Reaction
PEP	Post-Exposure Prophylaxis
PITC	Provider Initiated Testing and Counselling
PLHIV	People Living With HIV
PMTCT	Prevention of Mother-to-child Transmission of HIV
PrEP	Pre-exposure prophylaxis
RAL	Raltegravir
RH	Rifampicin, Isoniazid
RPR	Rapid plasma regain (syphilis test)
RTV	Ritonavir
RUTF	Ready-to-use Therapeutic Food
SJS	Stevens-Johnson Syndrome
STI	Sexually Transmitted Infection
TB	Tuberculosis
3TC	Lamivudine
TDF	Tenofovir Disoproxil Fumatrate
TLC	Total Lymphocyte Count
TNA	Trained Nurse Assistant
VDRL	Venereal Disease Research Laboratory (syphilis test)
VHW	Village Health Worker
WBC	White Blood Count
WFP	World Food Programme
WHO	World Health Organization
XDR-TB	Extensively Drug Resistant TB
ZDV	Zidovudine; also known as Azidothymidine (AZT)

FOREWORD

With the revision, publication and implementation of the Fifth Edition of the National ART Guidelines, the Government of Lesotho is embracing the most up to date global evidence to redouble its commitment and efforts to halt and reverse the HIV epidemic plaguing Lesotho. In order to do this, Lesotho has adopted the 'Test and Treat' strategy, which means antiretroviral treatment is offered to every person living with HIV in Lesotho as soon as they know their HIV status. In 2004, the Government through the Ministry of Health made a momentous decision to provide comprehensive HIV care and treatment in the public sector utilizing a nurse-driven service delivery model to scale up ART for the Basotho people. Since then Lesotho has continued in the forefront in the adoption and scaling up of the most cost effective interventions to improve the quality of life of people living with and affected by HIV. By November 2007, the CD4 criteria for initiating patients on ART was increased from 200 to 350 cells per mm^3. Since 2010, a tenofovir-based regimen has been used as the preferred first-line ART regimen, including the scaled up use of a single fixed-dose combination pill taken once per day while third-line ARV options with raltegravir, darunavir, and etravirine were introduced. Furthermore, since 2012, ART has been offered to every HIV-positive pregnant woman to prevent mother-to-child HIV transmission and improve their health outcomes. Most recently, treatment was being offered to every HIV-positive adult and child aged 5 years or more with a CD4 <500, those diagnosed with TB or active hepatitis B, those in a discordant relationship with a HIV-negative partner, and all children less than 5 years of age regardless of their CD4 count.

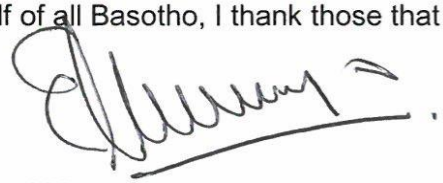
The fifth edition of these guidelines represents a determined commitment of the government to achieve and contribute to the ambitious global target of reaching 90-90-90 by 2020, which aims to diagnose 90% of people living with HIV, place 90% of those diagnosed on ART, and suppress HIV viral replication in 90% of those on ART by 2020. Reaching these goals will help reverse and end the AIDS epidemic by 2030. Lesotho has one of the highest HIV prevalences in the world at 23% and an estimated 319,000 people living with HIV. At the end of 2014, 41% of Basotho infected with HIV were receiving ART: 41% of adults and 40% of children. The Government of Lesotho through the Ministry of Health has made the commitment to scale up the number of people on ART dramatically to reach the 90-90-90 goals by 2020. Embracing the 'Test and Treat' strategy is a key recommendation in these guidelines that will enable the country to reach these bold targets.

Twelve years of establishing and expanding HIV care and treatment services to nearly every health facility in Lesotho, both public and private, and scaling up ART to reach 41% of people with HIV has built a strong foundation for HIV service provision, even in the poorest and most remote areas of the country. The Ministry of Health is committed to decentralizing care even closer to communities, which is essential as the number of people on ART continues to increase.

Studies done across the world have now clearly demonstrated that antiretroviral treatment is the best treatment for HIV. ART reduces HIV-related opportunistic infections and cancers, deaths, as well as diseases not traditionally considered to be associated with HIV, such as non-HIV related cancers, cardiovascular disease, kidney failure, and liver failure. Suppression of HIV replication with ART reduces the risk of HIV transmission by over 90%. 'Test and Treat' is also known to be the most cost effective approach to controlling the HIV epidemic. These guidelines adopt the 'Test and Treat' approach to HIV treatment in order to provide the best care to people living with HIV in Lesotho and help stop the further spread of HIV. These guidelines emphasize the importance of the HIV 'care cascade' – identifying people with HIV as early as possible after infection, promptly linking them to HIV care and beginning preparations for starting ART, and retaining them on treatment through robust adherence support and monitoring systems.

Lesotho is a resource challenged country with high burdens of HIV and TB. These guidelines require everyone to do business differently extending from the Ministry, districts, and health facilities to the communities and people living with and affected by HIV. We must make conscious and innovative changes and invest wisely along the way. And we must build upon the strong foundation established over the first 12 years of the Lesotho ART program and learn from our past experiences as we adopt 'Test and Treat' in Lesotho along with the other recommendations in these guidelines. I am confident that we will reach our goals and end the HIV and TB epidemics if we do so.

On behalf of all Basotho, I thank those that contributed to the development of these guidelines.



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HONOURABLE MINISTER OF HEALTH

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EXECUTIVE SUMMARY

- While the global response to HIV and AIDS has resulted in a more than 15 million people being on ART by the end of 2015 and new HIV infections and AIDS deaths have decreased, the epidemic continues to have devastating effects on communities. According to the most recent UNAIDS report, there were an estimated 36.9 million people living with HIV, 3.3 million of whom were children; 2 million people were newly infected with HIV and 1.2 million people died from AIDS in 2014.

- At 23%, Lesotho has one of the highest adult HIV prevalence rates in the world. There are an estimated 52 new HIV infections and 26 deaths due to AIDS each day. An estimated 319,000 people are living with HIV in Lesotho. Of these, 19,000 are children and 300,000 are adults. Although the HIV epidemic has been stable, there has been no significant change in the national adult HIV prevalence since 2005. The sentinel surveillance conducted in 2013 showed that there is no major difference in HIV prevalence among women attending ANC clinics, which stands at 25.9%. Five districts, Mafeteng, Mohale's Hoek, Maseru, Leribe, and Berea account for 75% of all of the people living with HIV in Lesotho.

- Lesotho continues to focus on scaling up its ART program to reach more people with life-saving ART after reaching universal provision of HIV care and treatment services in public facilities. Currently, 41% of people living with HIV in Lesotho are on ART. The goal is to expand that figure to attain the 90-90-90 targets by 2020: diagnosing 90% of people with HIV, putting 90% of those on ART, and suppressing the viral load of 90% of those on ART. To achieve these targets, the Ministry of Health has put in place programs and developed policies to provide guidance in the areas of HIV Prevention, Care, Support and Treatment.

- These guidelines are focused on HIV prevention, diagnosis, treatment, care and support. Specific issues regarding adults, adolescents, pregnant women and children have been addressed. The guidelines are linked to other HIV-related documents including: HIV testing services; prevention of mother-to-child transmission of HIV; home-based care; nutrition and HIV; male medical circumcision; TB; behavior-change communication strategy; Infection Prevention and Control; HIV post-exposure prophylaxis; programme monitoring and evaluation; and sexually transmitted infections guidelines.

- The decision to revise the National ART Guidelines was based on the need to update Lesotho's HIV treatment guidelines to provide people living with HIV in Lesotho with the best care possible in order to reduce the morbidity and mortality burden caused by HIV and halt further HIV transmission. In particular, the guidelines provide a comprehensive approach to ART and include several important updates such as:
    - Recommend initiation of ART for everyone living with HIV regardless of CD4 or clinical stage ('Test and Treat')
    - Introduction of confirmatory HIV testing before ART initiation to ensure correct diagnosis based on new National HIV Testing Services Guidelines
    - Provision of ARVs to HIV-negative individuals at high risk of being infected by HIV (pre-exposure prophylaxis – PrEP)
    - Increased emphasis on use of viral load to monitor success of ART and identify treatment failure
    - Guidance on evaluation of treatment failure and conducting enhanced adherence counselling sessions
    - Recommended management of patients presenting with advanced HIV
    - Addition of new ARV options for 1st, 2nd and 3rd line ART regimens

- Prompt identification of HIV-infected infants through DNA PCR tests and presumptive HIV diagnosis
- Revision and development of tools and reports to support programme monitoring and evaluation of key indicators

CHAPTER 1: INTRODUCTION

The fifth edition of the National ART Guidelines comes following a review of the fourth edition of the guidelines from 2014 and an adaptation process of the *Early Release Guideline on When to Start Antiretroviral Therapy and on Pre-exposure Prophylaxis for HIV* and *Policy Brief: Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: What's New* released by the World Health Organization in September and November 2015 respectively. The process of developing these guidelines was led by the Ministry of Health and involved multiple stakeholders who reviewed the scientific evidence, rationale, and feasibility of translating the global recommendations into country-specific national ART guidelines.

Recent evidence has clearly demonstrated that starting ART as soon as possible after HIV diagnosis improves the health outcomes of people living with HIV and prevents HIV transmission regardless of the HIV clinical stage or CD4 count. This has led to the World Health Organization, UNAIDS, and the other leading international HIV organizations to support this approach, which is often referred to as 'Test and Treat' or 'Test and Start'.

Highlights of the 2016 National ART Guidelines

Prevention

Pre-exposure prophylaxis with oral TDF/3TC should be offered to HIV-negative individuals at significant risk of HIV infection

HIV diagnosis

Individuals who test positive for HIV should be retested to confirm the diagnosis of HIV prior to starting ART

Antiretroviral treatment

<u>ART Initiation</u>

- Every person living with HIV should be started on ART regardless of their CD4 count or HIV clinical stage

<u>First-line ART</u>

- Fixed-dose combination TDF/3TC/EFV remains the preferred first-line ART regimen for adults and adolescents
- ABC/3TC/EFV remains the preferred first-line ART regimen for children 3-9 years and ABC/3TC/LPV/r remains the preferred first-line regimen for children <3 years

<u>Second-line ART</u>

- Patients failing a NNRTI-based first-line regimen should be switched to a PI-based second-line regimen
- All patients failing a PI-based first-line regimen should receive a genotypic resistance test to determine the best second-line regimen
- When a genotypic resistance result is not available for patients failing a PI-based first-line regimen, the integrase inhibitors dolutegravir and raltegravir are the preferred second-line ARVs in combination with a NRTI backbone

<u>Third-line ART</u>

- All patients failing second-line ART should receive a genotypic resistance test to determine the best third-line regimen

ART monitoring

- Viral load monitoring remains the preferred method for assessing the success of antiretroviral therapy and diagnosing treatment failure
- Viral load should be checked 6 and 12 months after starting ART and annually thereafter if suppressed. Pregnant and breastfeeding women and children under 5 should have viral load checked every 6 months.
- Adherence monitoring should be continuous for all ART patients.
- Patients with treatment failure should receive enhanced adherence counselling and close follow-up
- CD4 still has an important role for assessing degree of immune suppression from HIV, risk of developing opportunistic infections, and need for co-trimoxazole prophylaxis
- The frequency of CD4 monitoring can be reduced to annually if the viral load is <1000 copies/ml and CD4 count is >350 cell/mm^3
- The absence of laboratory monitoring tests should not delay ART initiation

Service delivery

- Stable patients should be given ARV refills lasting 3-6 months
- Community adherence groups should be established for stable patients to decongest health facilities
- Appropriately trained lower-level cadres of health workers can initiate and re-prescribe ART
- ART initiation and refills should be decentralized as close to the community as possible, including health outreaches and health posts

The guidelines present opportunities to reach out to all people living with HIV earlier, in line with the Government of Lesotho's commitment to reach the 90-90-90 treatment targets by 2020. The 90-90-90 treatment targets state that by the year 2020, 90% of all people living with HIV should be diagnosed with HIV, 90% of those people diagnosed with HIV should be receiving antiretroviral treatment, and 90% of those on ART should have their viral load suppressed. The overall goal of the 90-90-90 targets is to end the HIV epidemic in Lesotho by 2030.

The structure of these guidelines is consistent with the HIV treatment cascade from prevention of HIV to HIV diagnosis to enrolment in HIV care and initiation on ART to retention in chronic care and treatment and, ultimately, HIV viral suppression (see Figure 1.1). Specific chapters are dedicated to patient monitoring, ART adherence counseling support, disclosure, management of comorbidities and co-infections, nutrition, infection control, operational and service delivery guidance, and programme monitoring and evaluation.

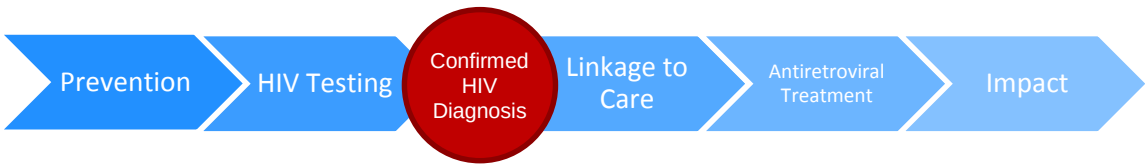


Figure 1.1: The HIV Care Cascade

CHAPTER 2: PREVENTION

Preventing new HIV infections is critical to controlling the HIV epidemic in Lesotho. Providing HIV testing services in health facilities and communities is essential for identifying people who are HIV-negative and providing them with appropriate education, counselling, and prevention strategies to help them stay negative (see Chapter 3). Treating people living with HIV with life-long ART to prevent new HIV infections has emerged as a powerful additional prevention tool benefiting people of all ages. This chapter reviews the major recommended HIV prevention approaches in Lesotho inclusive of those using antiretrovirals and non-medical strategies.

SECTION 2.1 TREATMENT AS PREVENTION

Treating people living with HIV with ART has been shown to be the most effective strategy for preventing new HIV infections – 'Treatment as Prevention'. Studies have demonstrated a 93% reduction in HIV transmission in HIV within serodiscordant couples when the HIV-positive partner was on ART. When the viral load of the HIV-positive partner is fully suppressed by ART, the protective effect of ART on preventing new infections approaches 100%. 'Treatment as Prevention' is an effective strategy regardless of the route of HIV exposure (vaginal, rectal, or percutaneous) and patient group (heterosexual men and women, homosexual men and women, transgender persons, commercial sex workers, and people who inject drugs).

Significantly increasing the number of HIV-positive people on ART with suppressed viral replication is a key strategy for halting the spread of HIV and eliminating the HIV epidemic.

SECTION 2.2 PREVENTION OF MOTHER-TO-CHILD TRANSMISSION OF HIV

Prevention of mother-to-child transmission (PMTCT) of HIV is composed of four prongs:

1. Preventing HIV infection in women
2. Preventing unintended pregnancies among women with HIV
3. Preventing vertical transmission of HIV from mothers to their infants during pregnancy, delivery, and breastfeeding
4. Providing care, treatment, and support for mothers with HIV and their children

Women in Lesotho have higher rates of HIV than men starting from late adolescents until mid-adulthood where the prevalence rates are similar. This discrepancy is due to biological and social factors. Risk of HIV transmission from men to women during vaginal intercourse is greater the risk of transmission from women to men. Societal and gender norms often make it difficult for women and adolescent girls to negotiate safer sexual practices with their partners. It is important to ensure that women and adolescent girls are regularly tested for HIV (see Chapter 3) and provided with comprehensive prevention services if found to be HIV-negative.

Clinicians should discuss pregnancy desires and plans regularly with women and adolescent girls with HIV and family planning services should be provided to those who do not wish to become pregnant.

PMTCT services have evolved over the past 12 years from limited maternal ARV prophylaxis for HIV-positive women with advanced stages of HIV to the provision of life-long ART to all pregnant woman as soon as HIV is diagnosed. HIV care and treatment services for pregnant and postpartum women are well integrated into routine antenatal and postpartum services in Lesotho. Despite this, PMTCT coverage in Lesotho was estimated at 72% and early infant diagnosis (EID) coverage with DNA PCR testing was only 55% at the end of 2014. Additonal efforts are needed to ensure that all pregnant women and adolescent girls are tested for HIV and enrolled into PMTCT services and their infants are

enrolled and retained in exposed infant care. Infant ARV prophylaxis is recommended for all HIV-exposed infants from birth until 6 weeks or 14 weeks of life depending on the mother's ART status and viral load (see Chapter 3.10).

SECTION 2.3 GENERAL HIV PREVENTION METHODS

General HIV prevention methods include condom and lubricant education and provision, risk reduction counselling, and STI diagnosis and management. Risk reduction messages focus on encouraging abstinence, avoiding having multiple concurrent sexual partners if an individual is sexually active, and using condoms consistently and correctly during sexual intercourse (vaginal, anal, and oral).

SECTION 2.4 VOLUNTARY MALE MEDICAL CIRCUMCISION

Voluntary male medical circumcision (VMMC) has been shown to reduce a HIV-negative man's risk of HIV infection by up to 60% in combination with general HIV prevention strategies, such as condom provision. Males of all ages are recommended to be evaluated for VMMC services, which includes provision of HIV testing services to all clients with linkage to HIV care and treatment services for individuals identified as HIV positive. VMMC services for infant boys (early infant male circumcision – EIMC), adolescent boys, and adult men are available in Lesotho. See the National VMMC Guidelines for further recommendations.

SECTION 2.5 PRE-EXPOSURE PROPHYLAXIS

Pre-exposure prophylaxis (PrEP) is the use of antiretroviral drugs in HIV-negative people to reduce their risk of acquiring HIV infection. Studies have demonstrated that oral PrEP containing TDF reduces the risk of HIV infection by 51% in the setting of other HIV prevention services, including condom provision and education, STI treatment, VMMC referral and risk reduction counselling. PrEP has been shown to be effective in many different groups of people, including men and women in serodiscordant couples, men who have sex with men, transgender people, commercial sex workers, people who inject drugs, and incarcerated persons. Adherence to PrEP is crucial in order to realize the protective benefits: the risk of HIV was reduced by up to 90% or more among patients with the highest adherence rates to PrEP.

Oral PrEP is recommended for HIV-negative individuals at 'significant risk' of becoming infected with HIV. 'Significant risk' is defined as a ≥3% risk of being infected with HIV in 1 year. An individualized risk assessment should be performed for HIV-negative individuals in order to determine if PrEP is an appropriate HIV prevention strategy. The risk assessment should inquire about known high risk behaviors for acquiring HIV. Although it is important to conduct a risk assessment for each HIV-negative person before offering PrEP, the following groups of people are suggested for targeting of PrEP services based on high risk behaviors:

- Exchanged sex for money
- Paid for sex
- Men who have sex with men and transgender people
- People who inject drugs
- In serodiscordant relationship and HIV-positive partner is not on ART
- In serodiscordant relationship and HIV-positive partner has been on ART for <12 months
- In serodiscordant relationship and HIV-positive partner's viral load is ≥1000 copies/ml or recent viral load is not known but partner's ART adherence is documented to be poor
- Multiple concurrent sexual partners
- Incarcerated individuals

Table 2.1 Summary of PrEP recommendations	
PrEP regimen	TDF/3TC 300/300mg once daily
Duration	• Until individual is determined to no longer be at significant risk of HIV infection • Stop immediately if patient seroconverts to HIV-positive and start full ART regimen • Patient opts to stop PrEP
Frequency of HIV testing	Every 3 months while on PrEP

Clinic visits	• Initial visits 2 and 4 weeks after PrEP initiation for adherence assessment and monitoring for side effects
	• Routine visits every 3 months thereafter for:
	  • Adherence assessment and monitoring for side effects
	  • HIV testing
	  • Repeat risk assessment
	  • Provision of ongoing HIV prevention counselling and services, such as condom provision and education, STI screening and treatment, and VMMC referral
	  • PrEP refill if repeat HIV testing remains negative

Lab monitoring	• Baseline serum creatinine and urine dipstick for glucose and protein (TDF is contraindicated if creatinine clearance is <50 ml/min) • 6 monthly urine dipstick for glucose and protein. Send serum creatinine if glucose or protein detected in urine

Patients should be counselled when starting PrEP that full protection is not obtained until 4 weeks after initiating PrEP. Patients with known HIV exposure within the past 72 hours should be offered post-exposure prophylaxis (PEP) for 28 days based on PEP guidelines (see Section 2.5). PrEP can then be started after completing PEP if the patient remains HIV-negative. Continuous adherence to PrEP should be reinforced: PrEP ARVs should be taken once daily every day. There are currently no studies demonstrating the effectiveness of intermittent dosing of TDF/3TC for PrEP. Patients discontinuing PrEP should not stop taking the ARVs until 28 days after their last potential HIV exposure.

Providing PrEP should not displace or threaten the implementation of other effective and well-established HIV prevention interventions, such as condom distribution and education and risk reduction counselling.

SECTION 2.6: POST-EXPOSURE PROPHYLAXIS

The term *post-exposure prophylaxis* (PEP) is generally understood to mean the medical response given to prevent the transmission of blood-borne pathogens following a potential exposure. In the context of HIV, post-exposure prophylaxis refers to the set of services that are provided to manage the specific aspects of exposure to HIV and to help prevent HIV infection. The services include first aid; counselling, including the assessment of risk of infection from the exposure; HIV testing; and depending on the outcome of the exposure assessment, a prescription for a 28-day course of ARVs with appropriate support and follow-up.

People exposed to HIV and other pathogens through sexual assault or occupational exposure merit close monitoring. In addition to the risk of infection, these experiences cause significant psychological damage that can be long-lasting. For these reasons, avoidance of occupational exposure and proper management of sexual assault victims should be given top priority.

It is imperative that HIV post-exposure prophylaxis policies reinforce the importance of primary risk prevention in all settings where HIV could be transmitted. PEP should never be provided in isolation but should form part of a wider strategy for preventing exposure to HIV. It should also be associated with measures to prevent other bloodborne diseases, such as Hepatitis B and C.

Non-Discriminative Provision of PEP

The policy for PEP eligibility should be founded on the principles of equity and non-discrimination. Decisions about whether or not to offer post-exposure prophylaxis should be based purely on clinical considerations of risk and should not be tied in any way to a person's decision to file a police report or to pursue legal action.

Individuals should be assessed for PEP regardless of their involvement in any activities considered to be illegal by national legislation such as injection drug use, sex work, or men having sex with men. There should also not be any unnecessary financial or administrative barriers preventing an individual from accessing PEP.

Indications for PEP

PEP is aimed at preventing HIV from invading sites such as the lymph nodes and testis. Within the first 72 hours of HIV exposure, these sites are thought to be invaded by the virus, which remains there permanently. Therefore, administering PEP within 72 hours of exposure to HIV is the most effective way of preventing HIV infection; PEP should NOT be initiated more than 72 hours after the event as it has not been shown to be effective after this time.

Occupational Exposure Incidents

Management of Occupational Exposure

- Cleanse the wound thoroughly with soap and water. Do not use antiseptics or squeeze the injured site
- Report the incident to the supervisor
- Document the incident
- Evaluate the exposure incident
- Evaluate the exposure source

When available, obtain the HIV status and Hepatitis B status of the source patient**.** If the source is HIV-infected and information is available, determine:

- Stage of disease
- Current and previous antiretroviral therapy
- Viral load
- Antiretroviral resistance information

It is also important to know the HIV status and Hepatitis B status of the exposed person. A complete history should be taken to identify other medical conditions (renal disease, liver disease, diabetes, or mental health diagnosis), drug allergies, and pregnancy or breastfeeding status.

Non-healthcare Related Exposures

- Sexual Assault
- Police service men
- Crime scene attendants
- Accident attendants
- Unprotected consensual sexual intercourse
- Condom breakage

Providing PEP

Table 2.2: RECOMMENDATIONS FOR PEP			
Exposure	**HIV status of source patient**		
	Unknown	**Positive**	**High Risk**
Intact Skin	No PEP	No PEP	No PEP
Mucosal splash/non intact skin	Consider 2-drug regimen	Recommend 2-drug regimen	Recommend 2-drug regimen
Percutaneous (sharps)	Recommend 2-drug regimen	Recommend 2-drug regimen	Recommend 3-drug regimen
Percutaneous (needle in vessel or deep injury)	Recommend 2-drug regimen	Recommend 3-drug regimen	Recommend 3-drug regimen

TABLE 2.3: RECOMMENDED PEP DRUG REGIMEN				
Population	**Drug**	**Dose**	**Frequency**	**Duration**
Adults	TDF/3TC	300/300mg	Once daily	28 days
Children	ABC/3TC	Weight-based (Annex 4)	Once daily	28 days
Adults and children	Lopinavir/ritonavir (3rd drug in cases of high risk exposure)	400mg/100mg	12 hourly	28 days

STEP 1: REPORT AND DOCUMENT

Document all HIV exposures in the PEP register, incident report book and exposed person's bukana.

Confidentiality - PEP evaluations for both the exposed and source individual (if known) should be treated with confidentiality.

Circumstances of the exposure and PEP management should be recorded in the exposed person's incident report. Details should include:

- Date and time of exposure
- Details of the incident: where and how the exposure occurred, exposure site(s) on body
- Details of the exposure: type and amount of fluid or material, severity of exposure

STEP 2: EVALUATE THE EXPOSURE

The exposure should be evaluated for potential to transmit HIV based on the type of body substance involved, the route, and HIV status of the source patient.

TABLE 2.4: RELEVANT HISTORY TO OBTAIN REGARDING THE EXPOSURE SOURCE PATIENT	
Known HIV infection	▪ Obtain history of antiretroviral medications, recent viral load, CD4 cell count and date of results ▪ Consider drawing HIV viral load, CD4 cell count and resistance testing ▪ Consider evaluation and testing for other sexually transmitted infections, including Hepatitis B and Hepatitis C
Unknown HIV infection	▪ Obtain risk history and rapid HIV test ▪ Consider evaluation and testing for other sexually transmitted infections, including Hepatitis B

STEP 3: EVALUATE THE EXPOSURE SOURCE

Regardless of HIV status, assess and assist with access to medical care, social support services, and risk reduction counseling.

STEP 4: MANAGEMENT OF POTENTIAL EXPOSURES

1. Baseline Evaluation

For all exposed people, the following baseline tests are recommended:

- HIV testing
- Serologic testing for Hepatitis B
- Pregnancy testing, as appropriate

Exposures from sexual assault, consensual sex, condom breakage also need:

- Screening and prophylaxis for other sexually transmitted infections
- Assess need for emergency hormonal contraception

Note: If consultation is not immediately available, PEP should not be delayed; changes can be made as needed after PEP has been started. If the source patient is found to be HIV uninfected, PEP should be discontinued. If the exposed person found to be HIV infected, eligibility to initiate ART should be assessed.

- Exposed persons are frequently unable to complete PEP regimens due to side effects. Providing prophylactic symptom management can improve adherence.
- A starter pack of 3 days may be prescribed initially with a scheduled follow-up appointment for HIV test, evaluation for potential medication side effects, and continue counseling on risk reduction, support and adherence.

2. Counseling after HIV exposure:

- Advise an exposed person to refrain from donating blood and utilize risk reduction methods including use of condoms during sex, not sharing injection equipment, and/or abstaining from high risk behaviors.
- Offer mental health counseling as needed.
- Counsel the exposed individual about the signs and symptoms of acute retroviral syndrome (flu-like syndrome), and the need to come in for additional testing should these symptoms develop.

SPECIAL CONSIDERATIONS

1. Pregnancy risk
   - Provide emergency contraception
   - Bear in mind drug interactions
2. Known or suspected pregnancy
   - Does not preclude the use of optimal PEP regimens
   - Do not deny PEP on the basis of pregnancy.
3. Children
   - PEP should be offered, using paediatric dosing of ARVs.
   - Offer psychosocial support and counselling for assault victims.
   - Provide prophylaxis or treatment for STIs as needed
   - Offer emergency contraception for all pubertal girls – Tanner Stage 3 and above
4. Sexual assault survivors
   - Provide prophylaxis or treatment for STIs.
   - Offer emergency contraception for any woman who may become pregnant
   - Offer psychosocial support and counselling
   - Do not deny or delay PEP if a patient does not have a Sexual Assault Form (police form) or intention to pursue legal action.
5. Injection-drug users and sex workers
   - PEP should not be refused for high risk incidents and risk reduction strategies should be discussed.

STEP 5: FOLLOW-UP

TABLE 2.5: HIV FOLLOW UP TESTING

Test	Baseline	6 Weeks	3 Months	6 Months
HIV Testing	X	X	X	X
Pregnancy	X	X		
Hepatitis B	X			X

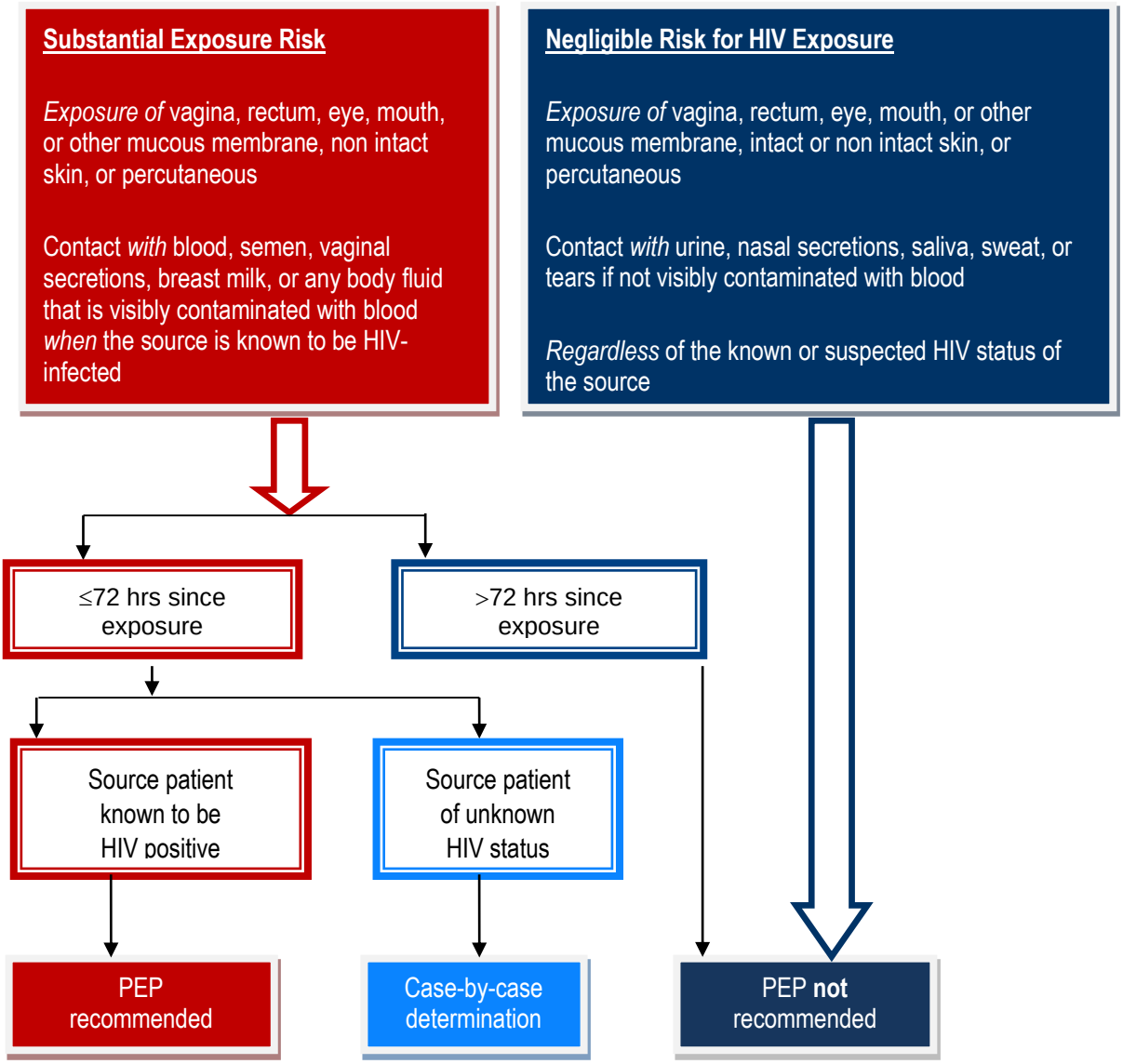
Resistance of the source virus to antiretroviral agents

- If the source person's virus is known or suspected to be resistant to one or more of the drugs considered for the standard PEP regimen, alternate drugs are to be selected in consultation with an HIV expert.

Toxicity of the initial PEP regimen

- Adverse symptoms such as nausea, diarrhea, and headaches are common with PEP.
- Symptoms can often be managed without changing the PEP regimen by prescribing analgesic, antidiarrhoea and/or antiemetic agents.

FIGURE 2.1: ALGORITHM FOR EVALUATION AND TREATMENT OF POSSIBLE NON OCCUPATIONAL HIV EXPOSURES



CHAPTER 3: HIV DIAGNOSIS

SECTION 3.1: HIV TESTING

People access HIV treatment, care, and prevention through the gateway of HIV testing services (HTS). The overall goals of HTS are to properly identify as many people living with HIV as early as possible after acquiring HIV infection, link them appropriately in a timely manner to prevention, care, and treatment services, and link HIV-negative people to appropriate prevention services. Diverse models of HTS are available to increase access to HIV diagnosis, including testing services in health care facilities, free standing sites and a wide range of community based approaches. Priority attention should be given to adolescents, pregnant women, and infants due to the high rates of new infections among adolescents and pregnant women and the rapid progression of HIV disease in infants. However, it is crucial that all Basotho know their HIV status if the HIV epidemic is to be reversed and stopped.

The recommendations in this chapter reflect those in the 2016 National HIV Testing Services Guidelines. Please refer to those guidelines for complete guidance on HTS in Lesotho.

The process of HIV testing services should follow the minimum standards of **C**onsent, **C**onfidentiality, **C**ounselling, **C**orrect results, and **C**onnection (linkage to care and treatment), the so-called 5 C's.

Consent for HIV Testing

Adults and children 12 years and above have the right to give their own informed consent for HIV testing in Lesotho. For children under 12 years, a parent or caregiver who brings the child for care can give written or verbal consent for testing. Pre and post-test counselling must be offered to the patient and/or caregiver.

If the health care provider determines that an adult or child is at risk of HIV exposure or infection, consent is not required, and the provider may initiate testing with the understanding that the individual maintains the right to 'opt out'.

Who Can Conduct Rapid Tests and Perform DBS for DNA PCR?

All those trained and accredited in HTS including:

- Counsellors, including lay counsellors who are adequately supervised
- Midwives
- Nurses
- Trained Nursing Assistants
- Physicians
- Laboratory Technicians and Technologists
- Pharmacists and Pharmacy Technicians
- Social Workers
- Ward Attendants
- Village/Community Health Workers who are adequately supervised
- Expert Patients (PLHIV) who are adequately supervised

Provider-Initiated Testing and Counselling

The need for HIV testing should be assessed for all people at every health care service delivery point during each clinical interaction and those found to be in need of testing should be offered HTS on-site.

The importance of knowing one's HIV status so appropriate care can be received should be emphasised. All individuals should be tested unless they opt out. Those who test should receive post-test counselling whether the result is positive or negative. Individuals who opt out should be further counselled on prevention, the benefits of knowing one's status, and different ways of getting tested if desired in the future.

HIV testing should be offered to all people with unknown status during all clinical interactions with a health facility. The need for HIV testing should be assessed for all people at every health care service delivery point during each clinical interaction and those found to be in need of testing should be offered HTS on-site.

Clients may seek HTS to guide personal life decision making; plan for their future or the future of their families; understand symptoms they might be experiencing; or to support personal HIV prevention efforts.

Frequency of HIV Testing

Most individuals who test negative for HIV in routine clinical and community settings will not be at risk for recent HIV exposure. Retesting to rule out acute infection is needed only for HIV-negative individuals who report recent or ongoing risk of exposure. For most people who test HIV-negative, additional retesting to rule out being in the window period is not necessary and may waste resources. **People who are diagnosed HIV-negative but remain at high risk, such as some people from key populations, may benefit from regular retesting at more frequent intervals (3 monthly)** (see Table 3.1 below)**.** Retesting gives these people both the opportunity to ensure early HIV diagnosis and to receive ongoing health education on HIV prevention. **All sexually active adolescents and adults in Lesotho should be tested *at least* annually. It is important that all individuals are routinely assessed for their need for HIV testing and their risk for recent HIV exposure at every health service delivery point.**

Examples of groups and behaviors with ongoing high risk for HIV exposure and infection include:

- Unprotected intercourse with an HIV-positive partner or partner with unknown HIV status (risk of HIV infection is significantly reduced if HIV-positive partner's viral load is <1000 copies/ml)
- Men who have sex with men and transgender persons
- Commercial sex workers and their clients
- Exchange sex for money or having paid for sex
- Incarcerated individuals
- Injection drug use
- Multiple sexual partners

All HIV-negative individuals receiving antiretrovirals for pre-exposure prophylaxis (PrEP) must be tested every 3 months as a condition for ongoing receipt of PrEP (see Chapter 2.5 on PrEP).

Self Testing

HIV self testing refers to situations where individuals collect their own specimen (usually a oral swab), performs a HIV test, and interprets the test result themselves. Self testing reduces barriers to HIV testing, particularly among certain populations that have low HTS utilization rates, such as, adolescents, key populations, and individuals fearful of testing in health facilities due to stigma or poor treatment by health care providers. Support systems are critical to ensure appropriate linkage to confirmatory HIV testing services as well as HIV care and treatment if HIV infection is confirmed. **HIV self testing does not provide a definitive diagnosis**. *A reactive self test always requires additional testing according to the national HIV testing algorithm*.

Refer to the National HIV Testing Services Guidelines for complete guidance on HIV self testing. HIV-positive clients already on ART should be discouraged from performing HIV self testing as a false negative result can be obtained due to viral suppression from ART leading to low levels of HIV antibodies that are not detected by some rapid tests.

HIV Testing and Counselling for Specific Populations

Index Patient/Family Tree Testing

Ensuring that all partners, children, and other household members of HIV-positive individuals have been tested for HIV is a key strategy for identifying HIV-positive people in the community. Persons living with HIV should be routinely asked about the HIV status of their sexual partners and children and the statuses of these family members should be clearly documented in the index patient's medical record to allow for further follow-up (see Annex 18 for an example index patient / family tree testing form).

Couples

Couples counseling is a key strategy to identify people living with HIV. HTS should be offered to married and cohabiting couples, premarital couples, polygamous unions and any other partnerships. 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 HTS can be offered in all settings where HTS are provided.

Offer couples and partners HIV testing services with support for mutual disclosure

Pregnant and breastfeeding women

PITC for pregnant and breastfeeding women with appropriate linkage and retention to prevention, care and treatment services are needed to promote the mother's health and to prevent new paediatric infections.

- Provide HTS for women as a routine component of antenatal, childbirth, postpartum and paediatric care settings.
- Test pregnant women upon enrolment into ANC services and retest at 36 weeks and every 3 months thereafter during the breastfeeding period for women who test negative at enrollment
- Test all women who present in labour with unknown HIV status immediately.

Adolescents

Adolescents are often underserved and given insufficient priority, with poor access to and uptake of HTS and linkage and retention to prevention, care, and treatment services. Adolescent girls and adolescents from key populations are particularly vulnerable to HIV infection and benefit from access to acceptable and effective HIV testing services.

- Counsel adolescents about the potential benefits and risks of disclosure of their HIV status and empower and support them to determine if, when, how and to whom to disclose.

TABLE 3.1: SUMMARY OF HTS RECOMMENDATIONS

Who to Test	When to Test
Everyone attending health facilities	• At all health care encounters • Retest at least annually for all sexually active adolescents and adults • Retest every 3 months for individuals with high risk for recent HIV exposure§
Partners and couples	• Premarital, pregnancy, after separations, new partnerships, at the start of care and ART • For the HIV-negative person in sero-discordant couples, offer re-testing at least every 6–12 months and more often if the HIV-positive partner is not on ART or viral load is not suppressed
Partners and family members of index HIV patients	• As soon as possible after the index patient is diagnosed
Key populations: MSM, transgender people, sex workers and their clients, prisoners, factory workers, and injection drug users	• At least annually for all adolescents and adults • Every 3 months for individuals with high risk for recent HIV exposure§
Pregnant women and male partners	• At first antenatal care visit • Re-test in third trimester at 36 weeks and every 3 months thereafter during breastfeeding period • Test immediately for women presenting in labor with unknown HIV status or were not retested at 36 weeks • Offer partner testing throughout ANC and PNC
Infants and children <18 months old of HIV-positive mothers or women with unknown HIV status (see Figure 3.1 and 3.2)	• Early infant diagnosis at 6 and 14 weeks for all HIV-exposed infants • Retest based on EID testing algorithm • Determine the final infant HIV infection status after 18 months and/or when breastfeeding ends
Children (>18 months to 9 years)	• Establish HIV status for every child and retest based on risk of HIV exposure (NB: children in this age group who test HIV negative do not need repeat HIV testing unless there has been a possible exposure to HIV)
Adolescents (10 to 19 years)	• Establish HIV status for every adolescent and retest based on risk of HIV exposure • Retest at least annually for all sexually active adolescents and adults • Retest every 3 months for individuals with high risk for recent HIV exposure§
People with disabilities (mental and physical)	• Establish HIV status for every person with a disability and retest based on risk of HIV exposure • Retest at least annually for all sexually active adolescents and adults • Retest every 3 months for individuals with high risk for recent HIV exposure§
Individuals receiving pre-exposure prophylaxis (PrEP)	• Retest every 3 months to ensure they remain HIV negative. If seroconversion to HIV positive occurs, stop PrEP immediately and being full ART

§ Examples of groups and behaviors with ongoing high risk for HIV exposure and infection include:

- Unprotected intercourse with an HIV-positive partner or partner with unknown HIV status (risk of infection is significantly reduced when HIV-positive partner's viral load is <1000 copies/ml
- Men who have sex with men and transgender persons
- Commercial sex workers and their clients
- Exchange sex for money or having paid for sex
- Incarcerated individuals
- Injection drug use
- Multiple sexual partners

COMMUNITY-BASED HIV TESTING AND COUNSELLING

Although facility-based testing is a key HTS approach, HIV-positive people who are diagnosed with HIV at health facilities are often identified late in the course of HIV disease because they have developed clinical signs and symptoms of HIV. In addition, some populations, including men, adolescents, and especially key populations, have low utilization of health care services where they can be reached by facility-based testing aproaches. Community-based testing approaches provide opportunities to reach people living with HIV earlier in the course of their HIV diseaseand engage with populations that may not normally attend health facilities.

The use of HIV rapid tests performed by trained lay and professional counselors and community health workers has facilitated the expansion of HIV testing services in community settings, which include homes, transport stations, religious facilities, schools, universities, workplaces and venues frequented by key populations. Continued expansion of community-based testing is an important strategy in achieving universal knowledge of HIV status and earlier diagnosis with linkage to care and treatment. Community-based HTS include mobile, door-to-door, index, campaign, events, workplace and school-based approaches.

Community health workers who are certified to provide HTS and appropriately supervised should provide HTS to all community members when able and link them to facility-based or other community-based HTS providers if they are not able to provide HTS themselves.

Community-based HIV testing services with linkage to prevention, care and treatment services are recommended as a key strategy for ensuring that all people know their HIV status

SECTION 3.2: HIV DIAGNOSIS IN CHILDREN

More than 90% of HIV infections among children are acquired from the mother during pregnancy, labour and delivery, or through breastfeeding. Because infants and children have an immature immune system, HIV disease progresses much faster in infants and children than it does in adults. If untreated, approximately 40% of HIV-infected children die before their first birthday, 50% by age 2, and 80% by age 5. Please refer to the National PMTCT Guidelines for additional information on HIV diagnosis in HIV-exposed infants and children.

It is of paramount importance to diagnose HIV-exposed and HIV-infected children *early;* with rapid testing or DNA PCR testing before they get sick.

HIV Testing Services for Infants and Young Children

The diagnosis of HIV in infants is challenging because they may carry maternal HIV antibodies, which cross the placenta during pregnancy. **Antibody (serological) tests, including HIV rapid tests, indicate HIV exposure and *possible* HIV infection. The HIV exposure of all infants should be known in order to diagnose HIV infection as early as possible.** To determine the HIV exposure status of a child, the mother should be tested for HIV. A positive test result for the mother indicates that the infant is HIV-exposed. If the mother's status is unknown because she is unavailable for testing or refuses to be tested, the infant should be tested with rapid testing to determine HIV exposure status.

By the age of 9 months, the majority of HIV-exposed infants (93%) no longer have maternal HIV antibodies, but the remaining 7% may carry maternal HIV antibodies until 18 months of age. **A virologic test, such as a DNA PCR, is needed to definitely determine HIV infection in children less than 18 months. Every infant born to an HIV infected mother should receive a DNA PCR test to determine their HIV infection status at 6 and 14 weeks of age.** For infants with ongoing exposure through breastfeeding, HIV rapid

test should be performed at 9 months of age and 6 weeks after cessation of breastfeeding. **If the infant is still breastfeeding, the child is still being exposed to HIV.**

The introduction of Option B+ for HIV-positive pregnant women has resulted in significant reductions in mother-to-child transmission rates. In particular, fewer infants are being infected during delivery and through breastfeeding, which were the most common periods of infection historically. As a result, more infants are being infected in utero. Performing HIV testing at birth for HIV-exposed newborns has the potential to diagnose HIV infection earlier thereby reducing the time to ART initiation and improving outcomes in these vulnerable infants. Evidence from ongoing research studies will guide future implementation of HIV testing at birth in Lesotho.

In children less than 18 months, all positive HIV rapid tests should be followed immediately by DNA PCR testing to determine the infant's HIV infection status. **A positive DNA PCR indicates HIV infection. All positive DNA PCR tests should be repeated immediately on a separate sample to confirm HIV infection. However, ART should be initiated immediately while waiting for the repeat DNA PCR test result** (see Table 3.2)**.** If the confirmatory DNA PCR result is negative giving discordant results, a third DNA PCR sample should be sent along with a HIV viral load to determine the infant's HIV infection status. ART should be continued until the results of the third DNA PCR and viral load have returned and an expert pediatric HIV clinician should be consulted.

All HIV-exposed infants with previous negative HIV tests need confirmatory rapid testing at 18 months. All HIV-infected infants need two *definitive* tests to diagnose HIV infection: either 2 positive DNA PCRs or 1 positive DNA PCR and positive HIV rapid tests at 18 months.

A positive HIV rapid test in a child less than 18 months of age means that the infant has been *exposed* to HIV and may be HIV infected. A DNA PCR test should be performed to establish the child's HIV infection status.

Rapid tests conducted in children less than 18 months should be done using parallel HIV testing. This means that two rapid tests, such as Determine and Unigold, should be done at the same time to determine HIV exposure status. **If one or both of the tests are positive, the child is HIV-exposed. Additional testing with DNA PCR is necessary to determine HIV infection status.** It is important to ensure that infants who receive DNA PCR testing are given follow-up appointments to obtain their results and be retained in HIV-exposed infant care, while awaiting results.

TABLE 3.2: INTERPRETATION OF DNA PCR TESTING IN CHILDREN < 18 MONTHS

DNA PCR Result	Test Interpretation
POSITIVE	• Definitively HIV infected ○ Send a second sample for confirmation of HIV status and initiate ART immediately
NEGATIVE**	• Definitively HIV uninfected, if outside the window period* **OR** • HIV exposed and possibly HIV infected, if still within the window period*
INDETERMINATE	• Inconclusive result, possibly due to quality of sample or error in performing DNA PCR. DNA PCR sample must be repeated as soon as possible

* Window period for DNA PCR test is 6 weeks. Repeat testing should be performed 6 weeks after the last exposure (6 weeks after cessation of breastfeeding).
** Must always consider window period when interpreting HIV negative test results

The turn-around time for DNA PCR test results is usually 2-6 weeks. While waiting for results, an infant must be managed as an HIV-exposed infant and started and maintained on co-trimoxazole prophylaxis. All infants presenting for HIV testing must be examined and those with signs suggestive of "presumptive diagnosis of severe HIV disease" initiated on ART.

Diagnosis of HIV in Infants between 0 and 9 Months of Age

Infants below the age of 9 months who have a known exposure to HIV can only be confirmed definitively HIV positive by two positive DNA PCR tests. If the HIV status of the mother is unknown or undocumented, rapid testing should be performed on either the mother or the infant to determine HIV exposure status. If the result of the rapid HIV test is positive or indeterminate, then the infant is HIV-exposed.

All HIV-exposed infants (infants born to HIV-infected mothers, or infants with positive or indeterminate rapid tests) should receive ARV prophylaxis with nevirapine for at least 6 weeks, receive DNA PCR testing at 6 weeks and 14 weeks of age for early infant diagnosis, and should be started on co-trimoxazole prophylaxis at 4-6 weeks of age and maintained until they are confirmed to be *definitively* HIV negative.

If **DNA PCR is positive**, the infant is HIV infected and should be started on ART immediately. A second specimen should be sent for DNA PCR testing to confirm HIV infection.

If **DNA PCR is negative *outside the window period***, then the infant can be declared definitively negative.

If **DNA PCR is negative *within the window period*** (i.e. infant is still breastfeeding or breastfeeding was stopped less than 6 weeks prior to the test being taken), then the baby is still HIV exposed and could still possibly be infected. The child needs to be retained into HIV-exposed infant care. See Figure 3.1 for HIV diagnostic algorithm for infants 0-9 months of age.

Diagnosis of HIV in Children between 9 and 18 Months

By 9 months, most HIV-exposed infants no longer possess maternal HIV antibodies. HIV rapid testing is performed at 9 months for HIV-exposed infants with ongoing exposure through breastfeeding. If the rapid test result is positive or indeterminate, then the infant is HIV exposed and possibly infected. DNA PCR testing is then needed to determine HIV infection status.

If the rapid HIV test is negative and the infant is outside the window period (six weeks after last exposure), then the infant can be considered definitively negative. Confirmatory HIV rapid tests should be performed at 18 months of age to verify HIV negative status.

If the test is negative and the infant is still within the window period, then the infant remains HIV exposed. Continue HIV-exposed infant care. Rapid HIV testing should be repeated 6 weeks after complete cessation of breastfeeding. Repeat sooner if clinically indicated. See Figure 3.2 for the HIV diagnostic algorithm for infants 9-18 months of age.

Repeat DNA PCR or rapid HIV testing may be done at any time if clinically indicated.

Presumptive Clinical Diagnosis of HIV in Children under 18 Months

In cases where DNA PCR is not available or results are pending, the presumptive diagnosis of severe HIV disease is essential for early initiation of antiretroviral treatment. A child diagnosed with HIV based on the clinical criteria in Table 3.3 below should be started on ART immediately even before definitive DNA PCR test results are available.

TABLE 3.3: CRITERIA FOR PRESUMPTIVE DIAGNOSIS IN CHILDREN < 18 MONTHS

A presumptive diagnosis of severe HIV disease should be made if:

A diagnosis of any AIDS-indicator condition(s) can be made	**OR**	The child is symptomatic with *two or more* of the following: • Oral thrush[a]; • Severe pneumonia[b]; • Severe sepsis[c]

Other factors that support the diagnosis of severe HIV disease in an HIV seropositive child include:

- Recent HIV-related maternal death; *or*
- Advanced HIV disease in the mother; or
- CD4 < 20% in infant.

Confirmation of the diagnosis of HIV infection should be sought as soon as possible.

NB: The presence of a positive rapid test is no longer one of the criteria for presumptive diagnosis of severe HIV disease in infants because women who are recently infected with HIV may not pass HIV antibodies to their child before delivery or in sufficient amounts through breastfeeding leading to false negative results in the infant

AIDS-defining conditions include *Pneumocystis jirovceii* pneumonia, oesophageal candidiasis, cryptococcal meningitis, cerebral toxoplasmosis, and unexplained wasting or malnutrition.

IMCI definitions:

a. Oral thrush: Creamy white to yellow soft small plaques on red or normally coloured mucosa which can often be scraped off (pseudo membranous), or red patches on the tongue, palate or lining of mouth, usually painful or tender.

b. Severe pneumonia: Cough or difficulty in breathing in a child with chest in-drawing, stridor or any of the IMCI general danger signs i.e., lethargy or unconsciousness, not able to drink or breastfeed; vomiting; and presence or history of convulsions during current illness.

c. Severe sepsis: Fever or low body temperature in an infant with any severe sign such as fast breathing, chest in-drawing, bulging fontanelle, lethargy, reduced movement, not feeding or sucking breast milk, convulsions.

FIGURE 3.1: HIV DIAGNOSIS IN INFANTS 0-9 MONTHS OF AGE

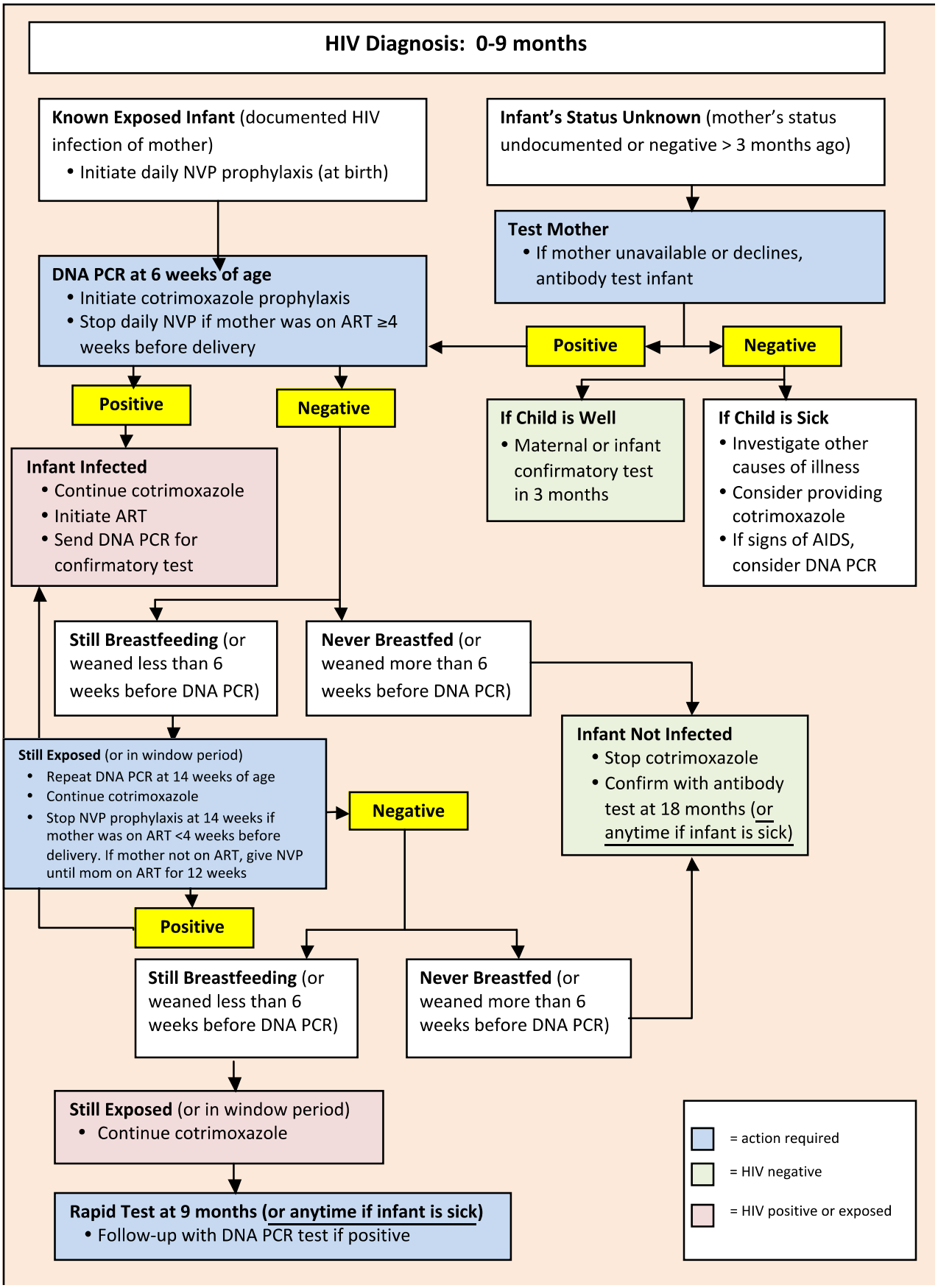
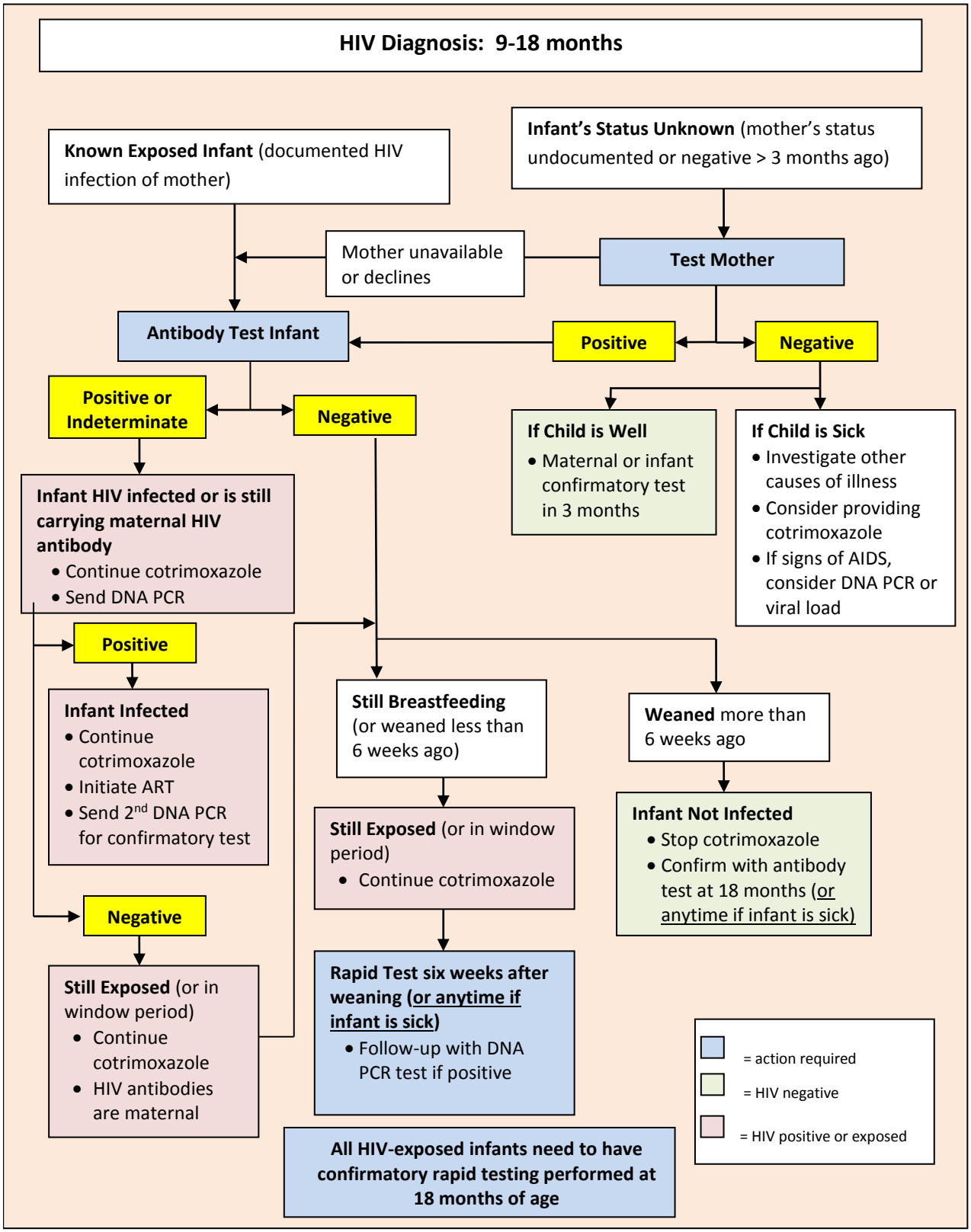


FIGURE 3.2: HIV DIAGNOSIS IN INFANTS 9-18 MONTHS OF AGE



SECTION 3.3: DIAGNOSIS OF HIV IN ADULTS, ADOLESCENTS, AND CHILDREN ≥ 18 MONTHS

By 18 months of age, all HIV-exposed children have lost their maternal HIV antibodies. Thus, serial rapid HIV testing can accurately confirm HIV infection. Serial testing is done in children over the age of 18 months, adolescents, and adults to determine HIV infection status. Children ≥ 18 months still breastfeeding should be considered to still be HIV exposed. Rapid testing should be repeated 6 weeks after cessation of all breastfeeding. All previously HIV-exposed children >18 months who did not have confirmatory rapid testing done at 18 months should have rapid HIV testing as soon as possible to confirm their HIV status.

Interpretation of HIV serial rapid testing: **(Refer to the Annex 18 and National HIV Testing Services Guidelines for the complete HIV rapid testing algorithm)**

- If the first rapid test (A1) is negative, the result is reported as **HIV negative**. Counselling on strategies to stay negative should be conducted and repeat HIV testing is recommended based on the assessment of the individual's recent potential HIV exposure and/or high risk behaviours (see Section 3.1)
- If the first rapid test (A1) is positive, a different confirmation rapid test (A2) is carried out
    - If the second rapid test (A2) is also positive, the result is reported as **HIV-positive**. **The patient should be referred for confirmatory HIV testing by a second HIV tester on a separate sample before the initiation of ART.** This repeat confirmatory testing follows the same testing algorithm (test A1 followed by A2 if A1 is positive). Confirmatory testing is recommended to ensure a correct HIV diagnosis before ART initiation.
        - If confirmatory rapid testing yields different results than the initial testing results (i.e. either A1 or A2 are negative on repeat) an additional test is needed to determine the HIV status. Refer to Annex 18 and National HTS Guidelines for full HIV rapid testing algorithm.
    - If the second rapid test (A2) is negative, a third rapid test (A3) is performed.
        - If the third rapid test (A3) is negative, the result is reported as **HIV negative**. Counselling on strategies to stay negative should be conducted and repeat HIV testing is recommended based on the assessment of the individual's recent potential HIV exposure and/or high risk behaviours (see Section 3.1)
        - If the third rapid test (A3) is positive, the result is reported as **indeterminate**. Repeat testing is recommended in 14 days. If an indeterminate result is reached again (A1+ A2- A3+), send a DNA PCR. Refer to Annex 18 and the National HTS Guidelines for full algorithm.
- If a pregnant woman has an indeterminate rapid test result, treat her as if she is HIV positive and initiate and continue her on ART until her true HIV status can be established.
- All known HIV patients who previously have not been eligible for ART (i.e. CD4 >500) should also receive confirmatory rapid testing before they are initiated on ART. Only one round of serial testing is required since the patient has previously had two positive rapid tests.
- **HIV patients already on ART should not receive repeat rapid testing. Viral suppression by ART can lead to significant declines in circulating HIV antibodies yielding a false negative rapid test result**

SECTION 3.4: DOCUMENTATION OF TEST RESULTS

Test results (Rapid HIV test, DNA PCR or RNA-based tests), are recorded in the bukana as follows.

FIGURE 3.3: RECORDING HIV STATUS IN THE BUKANA

HTC done: Y or N **Date*: _____**
Type of test (rapid, DNA PCR):

1st rapid test: P or N
2nd rapid test: P or N
DNA PCR tests*: P or N or I

Where:

P = Positive
N = Negative
I = Indeterminate
U = Unknown

**Record the date that DNA PCR test is done and the results can be filled in when they arrive.*

All HIV test results should also be recorded in the HTS Register.

If available, the Under 5 stamp should be used in the bukana and test results recorded as indicated on the stamp. Test results may also be recorded on the PMTCT stamp where available.

CHAPTER 4: HIV CARE AND TREATMENT

After a person is infected with HIV, the virus progressively weakens the immune system. Infections that do not occur in individuals with normal immune systems begin to appear and the risk of HIV-related cancers significantly increases as the CD4 count declines. TB is the most common opportunistic infection in Lesotho and is 10 times more likely to develop in HIV-positive persons. Without antiretroviral treatment, HIV infection is nearly uniformly fatal.

Antiretroviral treatment, in combination with comprehensive primary health care, is able to stop further immune destruction and allow for immune recovery through the suppression of on-going HIV replication. People with HIV successfully taking ART have been shown to have life spans almost the same as HIV-negative individuals. It is therefore crucial that all people diagnosed with HIV are linked to HIV care and antiretroviral treatment as soon as possible and retained.

- After diagnosis of HIV, people living with HIV should be linked to HIV care in order to receive the comprehensive package of HIV services.
- Assessments to determine an individual's readiness to start ART should be started immediately upon entry into HIV care.
- ART should be initiated as soon as a person is ready to commit to treatment regardless of the availability of baseline laboratory tests.

SECTION 4.1: HIV CARE AND TREATMENT PACKAGE

People living with HIV should receive the comprehensive package of services depicted in Figure 4.1 and described in the following sections after being linked to and enrolled in chronic HIV care. A complete record of care and treatment services provided should be kept in the HIV Care / ART card and the bukana.

SECTION 4.2: CLINICAL EVALUATION OF THE HIV INFECTED PATIENT

A thorough clinical evaluation must be performed on all newly-diagnosed HIV-infected patients. A comprehensive history and physical examination allow for the accurate assessment of the WHO clinical stage, screening for active TB disease, and diagnosis and management of other opportunistic infections and co-morbid conditions (see Annex 14 for a guide to performing a comprehensive history and physical examination).

Clinical Evaluation: WHO Clinical Staging

The HIV clinical stage based on the established WHO criteria should be determined based on the findings of the initial history and physical examination (see Annex 15 for WHO clinical staging criteria). Clinical staging should be based on the evaluation of current conditions. Past conditions can be considered for clinical staging only if they are well documented. A history of repeated chest infections, herpes infections, or other OIs is indicative of an advanced clinical stage. The presence or history of confirmed PCP, TB, cryptococcal meningitis, or toxoplasmosis indicates severe HIV infection. Note that the term 'AIDS' refers to the condition in which a person's immune system is severely compromised and the risk for developing serious HIV-related infections is high and is defined as WHO clinical stage 4 or the presence of severe immunodeficiency (CD4 <200 cell/mm^3) (see Table 4.1).

FIGURE 4.1: COMPREHENSIVE PACKAGE OF HIV SERVICES

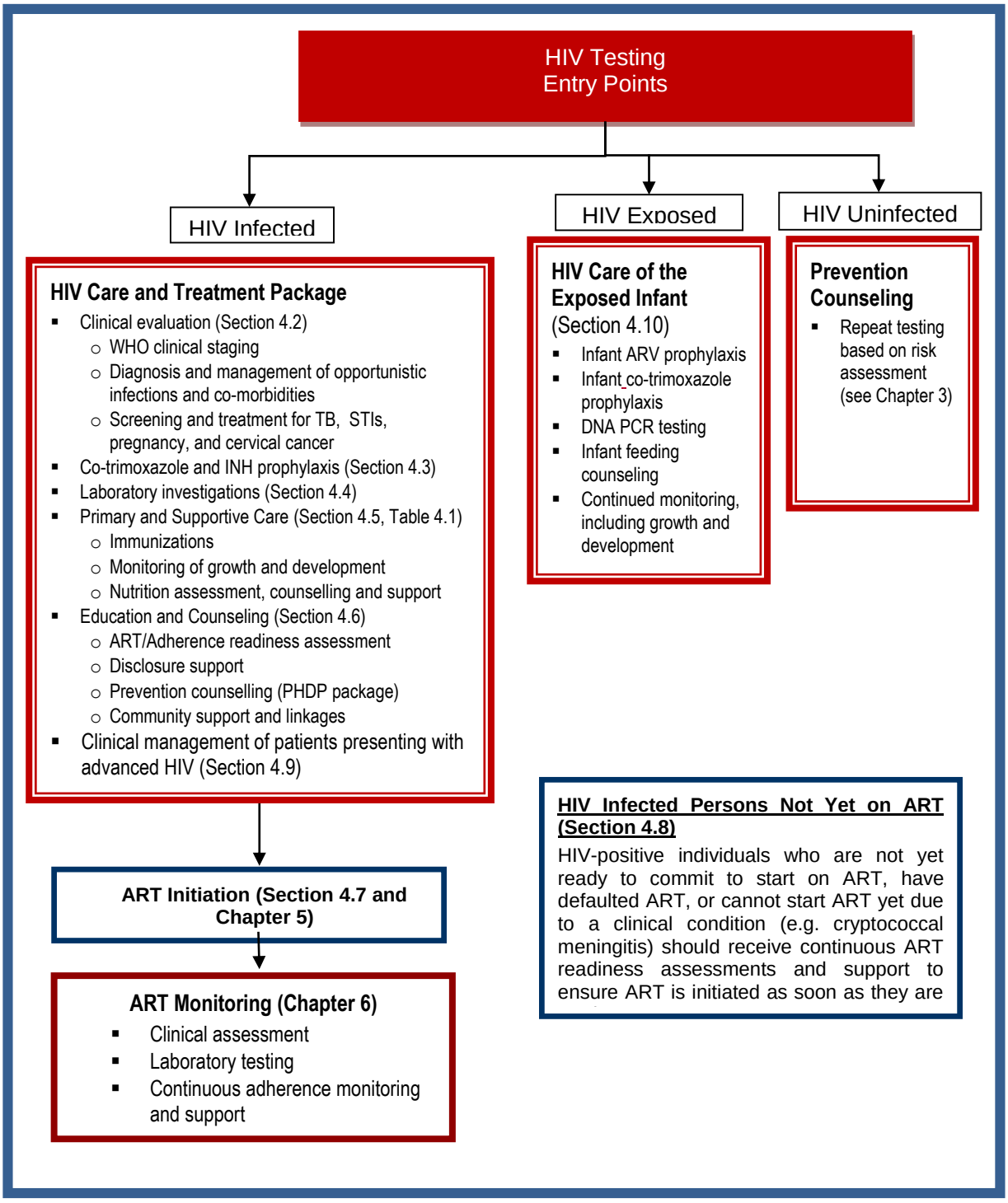


TABLE 4.1: WHO CLASSIFICATION OF HIV-ASSOCIATED CLINICAL DISEASE

WHO clinical stage	Classification of HIV-associated clinical disease
1	Asymptomatic
2	Mild
3	Advanced
4	Severe

People with HIV should be restaged at every clinical visit by conducting a focused history and physical exam. Prior to initiating ART, patients remain at their lowest ever clinical stage even after treatment for the causative opportunistic infection. For example, a person who has recovered from PCP remain stage 4 even after completion of PCP treatment. Six months after ART has been initiated, persons with HIV should be staged with a 'T' for treatment. The 'T' stage should reflect their current WHO clinical stage. For example, an adult with chronic herpes simplex infection successfully treated with acyclovir and asymptomatic after 6 months of ART should be restaged from stage 3 to stage T1.

Clinical Evaluation: Diagnosis and Management of Opportunistic Infections and Co-morbid Conditions

Opportunistic infections identified during clinical staging should be appropriately treated while the patient is being prepared for ART initiation. A thorough clinical evaluation for opportunistic infections with focused laboratory investigations is crucial to minimize the chance of immune reconstitution inflammatory syndrome (IRIS) developing after ART initiation and reduce the severity of IRIS if it does occur. See Chapter 8 for the recommended approach to the diagnosis and management of common opportunistic infections, HIV co-morbid conditions and IRIS.

Clinical Evaluation: Screening for Tuberculosis, STIs, Cervical Cancer and Pregnancy

Routine screening for tuberculosis, STIs, cervical cancer, and pregnancy are essential components of the HIV care package.

TB screening must be done during the initial assessment and during every clinical encounter for all people living with HIV. All HIV-positive patients with presumptive pulmonary TB should have sputum taken for investigations. GeneXpert MTB/RIF is the recommended first-line test for all HIV-positive presumptive TB clients (see Annex 16 for MOH TB Diagnostic Algorithm).

If active TB disease is identified, initiate TB treatment first then begin ART after 2-4 weeks.

People living HIV have increased susceptibility to TB infection and a greater risk of progression from primary TB infection to active disease and reactivation of latent TB infection. TB continues to be the most common opportunistic infection and number one cause of death among people living with HIV in Lesotho. It is important to rule out active TB disease before initiating ART due to reduce TB IRIS. **Every HIV-positive individual should be actively screened for TB at each clinical encounter using a TB screening tool** (see Annex 17). Answering 'yes' to one or more question on the screening tool makes a HIV-positive person a presumptive TB case and appropriate investigations to further examine for TB should be taken. A sputum sample for GeneXpert MTB/RIF testing is the recommended first-line TB diagnostic for all HIV-positive presumptive TB cases (see Annex 16). Clinicians should consider obtaining a CXR as part of the evaluation of HIV-positive presumptive TB patients but sending a patient for a CXR should not delay the workup and clinical decision making process given the rapid progression of TB observed in HIV patients. All people living with HIV should receive isoniazid preventive therapy (IPT) after HIV diagnosis after active TB disease has been excluded (for IPT, see Section 4.3; for further information on the presentation, diagnosis, and management of TB in people living with HIV, see Chapter 8).

The presence of STIs, such as syphilis, herpes, gonorrhoea, and chlamydia, in either a HIV-positive or HIV-negative person significantly increases the risk of HIV transmission. **Symptomatic screening for STIs and syndromic management for any STI identified should be conducted at every clinical visit for HIV-positive adults and adolescents** (see Chapter 8 and the National STI Management Protocols).

Cervical cancer is the most common cancer among Basotho women and causes the most cancer-related deaths in this group. HIV-positive women are at a higher risk of pre-cancerous lesions and invasive cervical cancers. **All HIV-infected women and sexually active adolescent girls should be screened for cervical cancer upon HIV diagnosis and annually thereafter** (visual inspection with acetic acid [VIA] is recommended for premenopausal females and Pap smears for postmenopausal women). Patients with abnormal screening results should be referred to an appropriate health facility or clinician for immediate management of pre-cancerous and cancerous lesions (see the MOH Cervical Cancer Guidelines for detailed cervical cancer screening and treatment recommendations).

Prompt identification of pregnancies among women and adolescent girls living with HIV helps to ensure that optimal care and ART is provided in order to minimize the risk of mother-to-child transmission of HIV. should be asked about their menstrual history. Family planning practices, pregnancy intentions, and menstrual history should be discussed at every clinical encounter for HIV-postive women and adolescents and urine pregnancy testing performed as indicated.

SECTION 4.3: CO-TRIMOXAZOLE PROPHYLAXIS AND ISONIAZID PREVENTIVE THERAPY

Co-trimoxazole Prophylaxis

Co-trimoxazole (CTX) prophylaxis is an inexpensive and cost-effective way to reduce morbidity and mortality among people living with HIV. It protects against:

- *Pneumocystis* pneumonia (PCP)
- Toxoplasmosis
- Diarrhoea caused by *Isospora belli* and *Cyclospora* species
- Certain bacterial infections, including bacterial pneumonia and urinary tract infections

Co-trimoxazole prophylaxis is recommended for children under the following circumstances:

- All HIV-exposed children starting at 4-6 weeks of age. CTX should be continued until:
  - HIV infection has definitively been excluded in the child *and*
  - The infant is no longer at risk of acquiring HIV through breastfeeding
- All HIV-positive children < 5 years regardless of CD4 or HIV clinical stage
- For HIV-positive children ≥5 years, follow adult and adolescent guidelines on co-trimoxazole prophylaxis

Co-trimoxazole prophylaxis is recommended for HIV-positive adults and adolescents under the following circumstances:

- All those in WHO clinical stage 3 or 4, including those with TB co-infection
- Those in clinical stage 1 and 2 where the CD4 count is ≤ 350 cells/mm3.
- All those in clinical stages 2, 3 and 4 where a recent CD4 count is not available

TABLE 4.2: INDICATIONS FOR CO-TRIMOXAZOLE PROPHYLAXIS IN ADULTS, ADOLESCENTS, AND CHILDREN ≥5 YEARS

WHO Clinical Stage	CD4 is available	CD4 is not available
4	Daily CTX	
3	Daily CTX	
2	Daily CTX if CD4 < 350	Daily CTX
1	Daily CTX if CD4 < 350	Do not give CTX

Dosing of Co-trimoxazole

TABLE 4.3: DOSE OF CO-TRIMOXAZOLE PROPHYLAXIS

Age	Suspension (200/40 mg/5 ml)	Single Strength tablet (400/80 mg)	Double Strength tablet (800/160 mg)
< 6 Months	2.5 ml	¼ tablet	--
6 mo- 5 Years	5 ml	½ tablet	--
6-14 Years	-	1 tablet	½ tablet
>14 Years	--	2 tablets	1 tablet

Co-trimoxazole should be avoided in the following situations:

- History of a severe rash with prior use of co-trimoxazole (or another 'sulfa' drug)
- Severe renal disease
- Severe hepatic disease

Patients who are unable to take co-trimoxazole should be offered dapsone 100 mg daily (children: 2 mg/kg daily) to help prevent *Pneumocystis* pneumonia (PCP). Patients with mild (Grade 1 or 2) adverse effects can be desensitized in a monitored setting. Densitization should never be attempted in a patient who developed Stevens Johnson Syndrome, anaphylaxis, or in children. The MSF HIV/TB Clinical Guide has a densitization regimen in the appendix and is free on the internet.

When to Discontinue Co-trimoxazole Prophylaxis

Co-trimoxazole prophylaxis can be discontinued in adults, adolescents and children $\geq$ 5 years who:

- Are on ART and have two consecutive CD4 counts ≥ 350 cells/mm^3
- TB co-infected patients after the completion of tuberculosis treatment if their CD4 is ≥ 350 cells/mm^3 and the patient is restaged as WHO Stage 1 or 2.
- Those with previous PCP infection if the above conditions above are met

Isoniazid Preventive Therapy (IPT)

Isoniazid preventive therapy reduces the risk of developing active TB disease in persons living with HIV by treating latent TB infection. The risk of developing TB is particularly high during the first six months after ART initiation.

Given the high prevalence of latent TB infection in Lesotho, every individual with HIV greater than 1 year of age who has no signs or symptoms of active TB should be started on IPT as soon as possible.

HIV-positive people should be screened for TB upon HIV diagnosis and at every clinical encounter using a TB screening tool (see Annex 17). Individuals who screen positive on the TB screening tool should be considered presumptive TB cases and sputum samples and further investigations should be performed. Individuals who screen negative for symptoms of active TB should be initiated on IPT regardless of CD4 count, WHO clinical stage, and ART status. IPT and ART can be safely initiated at the same time in people living with HIV. Isoniazid is safe during pregnancy and breastfeeding and IPT. The additional indications for IPT are:

- HIV-positive children <10 years exposed to TB through household contacts without signs or symptoms of active TB, including infants <1 year
- After the completion of TB treatment for all TB/HIV co-infected persons
- HIV-negative children <5 years exposed to TB through household contacts without signs or symptoms of active TB, including infants <1 year

The standard IPT regimen is:

Adults

Isoniazid (INH): 300 mg/day x 6 months

Pyridoxine (vitamin B6): 25 mg/day x 6 months

Children

Isoniazid (INH) 10 mg/kg/day (max 300 mg/d) x 6 months

Pyridoxine (vitamin B6): 12.5-25 mg/day x 6 months (12.5 mg/day for children <3 years)

Pyridoxine is given along with isoniazid to prevent the occurrence of peripheral neuropathy.

The same course of IPT can be resumed if the interruption has been less than 3 months. If the interruption in IPT has been ≥3 months, the IPT course must be restarted from the beginning.

TABLE 4.4: SIMPLIFIED WEIGHT-BASED DOSING FOR ISONIAZID

Weight (kg)	Number of 100mg 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 Tablets	150
14 – 19.9	2 Tablets	200
20 – 24.9	2 ½ Tablets	250
>25	3 Tablets	300

Adapted from WHO Guidelines of Antiretroviral Therapy for HIV infection in Infants and Children: Towards Universal Access. 2010 Revision

Patients should not be offered IPT if they report:

- Acute or chronic liver disease. Signs and symptoms suggestive of active hepatitis are: nausea, vomiting, right upper quadrant pain, jaundice, and dark urine, or
- Regular and heavy alcohol consumption or
- Symptoms of severe peripheral neuropathy or
- History of epilepsy or convulsions
- Kidney failure

The absence of baseline liver function tests should not preclude or delay the initiation of IPT. If liver function test (LFTs) results are available, the most recent LFT results should be reviewed. Table 4.5 details the recommended course of action for IPT initiation based on the baseline LFT results.

TABLE 4.5: INTERPRETATION OF LFT RESULTS IN CONTEXT OF INITIATING IPT

Baseline Liver Function Tests	Course of action
Normal up to 2x the upper limit of normal (ULN) in the absence of symptoms of hepatitis	Initiate IPT, no further LFT testing required
2-5x the ULN in the absence of symptoms of hepatitis	Initiate IPT and check ALT monthly
Greater than 5x the ULN or symptoms of hepatitis	Do not initiate IPT until LFTs normalize

Patients on IPT should be monitored through monthly clinical assessments to include:

- Screening for symptoms and signs of active TB
- Screening for possible side-effects of isoniazid (e.g. rash, peripheral neuropathy, convulsions, or any signs/symptoms of hepatitis including nausea and vomiting, jaundice, right upper quadrant pain and dark urine).
- Adherence to isoniazid.

If a patient on IPT develops symptoms of active TB:

- Discontinue IPT immediately
- Investigate for active TB disease:
    - Send sputum specimen for GeneXpert MTB/RIF and culture with DST to evaluate for isoniazid resistance
    - Refer, if needed, to ensure that investigations are completed
- If active TB is confirmed, a full TB treatment regimen should be started
- Perform other laboratory investigations as clinically indicated

SECTION 4.4: BASELINE LABORATORY INVESTIGATIONS

Laboratory investigations enhance clinical assessment, which is the primary tool for evaluating patients both before and after initiation of ART. Laboratory investigations can help inform which ART regimen to choose but are not essential for ART initiation.

The inability to perform laboratory investigations, including CD4 count, should not prevent HIV patients from being initiated on ART if they are otherwise assessed as ready to start ART

The baseline laboratory investigations in Table 4.6 are recommended for all persons newly diagnosed with HIV.

Lab tests should be taken as soon as an individual is linked to HIV care. ART can be started before results of lab tests have returned and the treating clinician's clinical assessment should guide the choice of first-line ART regimen. When lab test results are available they can be used to guide ARV substitutions required due to contraindications, such as TDF use in advanced renal disease (CrCl < 50 ml/min) or AZT use in anemia (Hb < 8 gm/dl).

CD4: Immunological Staging

While viral load monitoring is now the preferred method for assessing response to ART, assessing the CD4 count remains important for the clinical management of HIV patients to assess the degree of HIV-related immune suppression, risk for opportunistic infections, and need for co-trimoxazole prophylaxis. CD4 should not be used for determining when to start ART. Further guidance regarding viral load and CD4 testing is given in Chapter 5 on Patient Monitoring.

Table 4.6: Recommended baseline laboratory investigations for newly diagnosed HIV clients	
Test	Purpose
CD4 count	• Assess immunologic HIV stage (see Annex 15 for WHO clinical staging) • Determine need for co-trimoxazole prophylaxis • Assess risk for immune reconstitution inflammatory syndrome (IRIS) upon starting ART **NB: CD4 is no longer a criteria to be used for ART initiation**
Serum cryptococcal antigen for adolescents and adults with CD4 count <100 cells/mm^3	• Screen for asymptomatic cryptococcemia and need for fluconazole prophylaxis and possible further investigations to evaluate for cryptococcal meningitis (see Section 7.3: Management of Cryptococcal Disease)
VDRL or RPR if 12 years or above	• Screen for syphilis
Hepatitis B surface antigen (HBsAg) and hepatitis C serology	• Screen for hepatitis co-infections
FBC (haemoglobin if FBC unavailable)	• Screen for anemia and assess for contraindications to AZT (Hb < 8 gm/dl)
LFTs (ALT if full LFTs unavailable)	• Screen for liver disease and assess for contraindications to INH (ALT >5x upper limit of normal)
Serum creatinine and urine dipstick for glucose and protein	• Screen for renal disease and assess for contraindications to TDF (CrCl < 50 ml/min)
Pregnancy test	• Screen for pregnancy; enrol in PMTCT services if pregnant and offer family planning services if not pregnant
Blood glucose and fasting cholesterol and triglycerides for patients in need of protease inhibitor-based ART regimens	• Screen for diabetes and hyperlipidemia, which can be worsened by LPV/r more than other PIs, such as ATV or DRV

The CD4 count, measured in cells/mm^3, gives an approximate measure of the strength of one's immune system. The CD4 count declines with HIV disease progression and can be used to predict the risk for developing opportunistic infections (see Table 4.7 for WHO immunologic staging criteria). Conditions such as TB, severe malnutrition, and even common infections like upper respiratory tract infections can also lower the CD4 count although the CD4 count recovers quickly after minor illnesses.

TABLE 4.7: WHO IMMUNOLOGIC STAGING IN ADOLESCENTS AND ADULTS

Immunological Category	CD4 Count
No significant immunodeficiency	> 500 cells/mm^3
Evidence of mild immunodeficiency	350-499 cells/mm^3
Evidence of advanced immunodeficiency	200-349 cells/mm^3
Evidence of severe immunodeficiency	< 200 cells/mm^3

In HIV-infected children <5 years, the CD4 percentage should be used to monitor the immune status instead of the absolute CD4 count because infant's and young children's CD4 counts are higher than adults, adolescents and older children. CD4 counts decline slowly during childhood to reach adult levels by the age of 5 years but the CD4 percentage remains fairly constant throughout childhood into adulthood. If no CD4 percentage is available, then severe immunosuppression should be categorized using CD4 count (see Table 4.8). CD4 percentage can also be calculated using the following formula:

$$\text{CD4 \%} = \frac{\text{CD4 absolute count X 100}}{\text{Total Lymphocyte Count (TLC)}}$$

TLC = White Blood Count (WBC) x % Lymphocytes

The CD4 count and percentage can decline very rapidly in HIV-postive infants. Opportunistic infections can develop at any CD4 count or percentage in this population because of the immaturity of infants' immune systems.

TABLE 4.8: WHO CLASSIFICATION OF HIV IMMUNODEFICIENCY IN CHILDREN

Classification of Immunodeficiency	< 12 Months (CD4 %)	12-35 Months (CD4 %)	36-59 Months (CD4 %)	≥ 5 Years (CD4 count)
Not significant	> 35%	> 30%	> 25%	> 500
Mild	30-35%	25-30%	20-25%	350-499
Advanced	25-30%	20-25%	15-20%	200-349
Severe	< 25%, or < 1500 cells/mm^3	< 20%, or < 750 cells/mm^3	< 15%, or < 350 cells/mm^3	< 15%, or < 200 cells/mm^3
Source: WHO ART of HIV Infection in Infants and Children: Towards Universal Access				

SECTION 4.5: PRIMARY AND SUPPORTIVE CARE

People living with HIV should receive the comprehensive package of primary care services outlined in Table 4.9.

TABLE 4.9: PRIMARY HEALTH CARE SERVICES FOR HIV INFECTED PATIENTS

Recommended Service	Target Group
Treatment preparedness and adherence evaluation	All HIV infected patients
Continuous adherence assessment and support	All HIV infected patients
Routine immunizations	Children, adolescents and pregnant women
Vitamin A and micronutrient supplements	Children
Routine de-worming	Children
Monitoring of growth and development	Children and adolescents
Annual screening for cervical cancer	All HIV-positive women and adolescent girls
Family planning counselling and method provision	Adults and adolescents
Condom use counselling and provision	Adults and adolescents
Mental health screening	All HIV infected patients
Substance abuse screening	Adults and adolescents
Nutritional assessment, counselling and support (see Chapter 9)	All HIV infected patients
Hepatitis B vaccination	• HIV-positive adolescents and adults with negative HBsAg result • Newborns of mothers with chronic Hepatitis B
Safe water supply	All HIV infected patients

Immunizations

Immunizations in HIV-exposed and HIV-infected infants and children should follow the standard Lesotho immunization schedule:

TABLE 4.10: IMMUNIZATION SCHEDULE

Age	Immunizations
Birth	BCG
0-2 weeks	bOPV
6 weeks	Pentavalent vaccine (DPT, Hep B, HiB); bOPV, PCV-13, Rotavirus
10 weeks	Pentavalent vaccine (DPT, Hep B, HiB); bOPV, PCV-13, Rotavirus
14 weeks	Pentavalent vaccine (DPT, Hep B, HiB); bOPV, PCV-13, IPV
9 months	MR (Measles, Rubella)
18 months	MR, DT

Notes

- Children who have or are suspected to have HIV infection but are not yet symptomatic should be given all appropriate vaccines, including BCG, measles, and yellow fever vaccine (if indicated).
- BCG and yellow fever vaccines should not be given to a child who has symptomatic HIV infection or who is severely immunodeficient. Virtually all HIV-exposed and HIV-infected infants are asymptomatic at birth and can receive the BCG vaccine at birth.
- Consider giving measles vaccine early at 6 months and again at 9 and 18 months in children with HIV infection. Measles vaccine may be given to a child with symptomatic HIV infection as long as there are no features suggestive of severe immunodeficiency.
- All HIV-positive adults and adolescents who test hepatitis B surface antigen negative should be vaccinated against hepatitis B infection
- All health care workers, regardless of HIV status, who test hepatitis B surface antigen negative should be vaccinated against hepatitis B infection
- MR (Measles and rubella) vaccine is scheduled for introduction in late 2016; rotavirus vaccine is scheduled for introduction in 2017

Routine Oral Vitamin A Supplementation

The following dosages of vitamin A should be administered to all children every 6 months until age 5:

Age	Dose of Vitamin A
6 months	100,000 Units
12 months to 5 years	200,000 Units

Routine De-worming

HIV-positive children should be de-wormed routinely every 6 months from 1 year until age 12 (HIV-negative children are routinely de-wormed until age 5) using one of the following recommended treatments:

Age	Weight	Albendazole		Mebendazole (alternative)
12-23 months	<10 kg	200 mg once	**or**	100 mg BD for 3 days or 500 mg stat
≥2 years	>10 kg	400 mg once		500 mg once

Nutrition Assessment, Counselling, and Support

The nutritional status of people living with HIV should be assessed as part of the comprehensive care package. Children in particular should be assessed for malnutrition. See Chapter 9 and the National Guidelines for the Integrated Management of Acute Malnutrition for complete details regarding nutritional assessment, counselling, and support recommendations.

SECTION 4.6: EDUCATION AND COUNSELLING

Immediately upon HIV diagnosis, patients should begin to be prepared for ARV initiation through HIV education and counselling and the performance of a psychosocial assessment. These activities will assist future adherence counselling as well as the identification of potential barriers to successful treatment adherence and potential strategies to optimise care and treatment. Key topics to be addressed in initial education and counselling sessions include:

- Establishing a partnership with the patient and organizing a care plan
- Screening for substance abuse and mental health issues
- Support for disclosure to partners and family members
- Reinforce self-management, including looking out for key symptoms, avoidance of dangerous habits, such as substance abuse (alcohol, injection drug use, marijuana)
- Importance of preventing HIV transmission to sexual partners and children, review of key prevention methods
- Encourage testing of partners and children
- Available community-based programs and support groups/networks

Refer to Chapter 7: Adherence and Disclosure for detailed guidance on ART readiness assessments and ART adherence counselling.

Initial education and counselling sessions should reinforce the importance of preventing HIV transmission and preparation for ARV treatment.

Preventing Transmission of HIV among PLHIV

From a public health perspective, people living with HIV constitute the most important group in terms of HIV prevention. Studies have shown that HIV treatment for PLHIV is the most effective method for preventing HIV transmission in combination with the general prevention strategies detailed below. Change in the risk behaviors of an individual living with HIV can have a greater impact on the transmission of HIV than that of a HIV-negative person. Education and counselling on positive prevention strategies for PLHIV should be implemented at group and individual levels in health facilities and the community. The comprehensive package of services aimed at prevention of HIV transmission for people living with HIV is referred to as **Positive Health, Dignity and Prevention (PHDP)** and includes:

- Encourage consistent condom use through education and condom and lubricant provision
- Reduction in high risk behaviors, including unprotected sex and multiple sexual partners
- Routine screening and treatment of STIs
- Mental health and substance abuse screening with referral to appropriate services for individuals, including Blue Cross and Alcoholic Anonymous groups
- Support for disclosure of HIV status to partners and partner testing with appropriate referral to prevention services for HIV-negative partners, such as PrEP and VMMC (see Chapter 2)

- Continuous adherence monitoring and support for PLHIV on ART
- Prompt identification of pregnancy and provision of family planning services to PLHIV not currently desiring pregnancy
- Referral to and from relevant community-based programs for non-clinical support and services

SECTION 4.7: WHEN TO START ANTIRETROVIRAL THERAPY

All HIV-infected individuals are eligible to initiate antiretroviral therapy as soon as possible after HIV diagnosis.

Because antiretroviral treatment is life-long and optimal adherence is crucial to treatment success, it is important to assess every individual's (or caregiver's) readiness to start ART. **The initial ART readiness assessment should be conducted as soon as possible even on the day of HIV diagnosis.** All HIV patients should receive 1-3 counselling sessions around the time of ART initiation. **A patient's (or caregiver's) level of understanding and readiness to start ART will determine the number of adherence sessions to be done before initiation of ART. Initiation of ART on the same day of HIV diagnosis is recommended for people who demonstrate clear readiness to begin ART.** See Chapter 7: Adherence and Disclosure for detailed guidance on conducting ART readiness assessments for adults, adolescents and children.

SECTION 4.8: ADULTS AND CHILDREN NOT YET INITIATED ON ART

There are some people living with HIV who will not be ready to commit to initiating on life-long ART during initial counselling sessions and others individuals start ART and then default from treatment. Some patients have an opportunistic infection, such as TB or cryptococcal meningitis, which precludes them from starting ART immediately. Those individuals who have not yet initiated ART or have defaulted should continue to receive the complete package of HIV care outlined in this chapter in order to optimize their health while preparing to start ART.

HIV clients not yet initiated on ART should have regular clinical reviews, adherence readiness assessments and ART preparation sessions so that ART is initiated as soon as a client is ready to begin treatment.

It is recommended that people living with HIV who are not yet on ART should be reviewed at least every 3 months. This is particularly important for all HIV-infected children not on ART and adults and adolescents with advanced HIV disease because their clinical status can deteriorate rapidly. The CD4 count should be monitored every 6 months to evaluate disease progression and the need for co-trimoxazole prophylaxis for these individuals.

SECTION 4.9: CLINICAL MANAGEMENT OF PATIENTS PRESENTING WITH ADVANCED HIV

Many people living with HIV are still diagnosed at advanced stages of HIV or have been lost from HIV care and/or ART and re-present with advanced HIV. These 'late presenters' are defined as patients with CD4 count <200 cell/mm^3 or WHO stage 3 or 4. Late presenters require more intensive care and support in order to reduce the high rates of HIV morbidity and mortality seen in this group compared to asymptomatic HIV patients presenting with higher CD4s.

Late presenters should receive a package of care that includes:

- Rapid initiation on ART once any OIs have been identified and treatment begun
- Serum cryptococcal antigen screening test for all with CD4 < 100 cells/mm^3

- TB screening followed by prompt initiation of TB treatment for those co-infected with TB and start of IPT for those screening negative for TB signs and symtpoms. Clinicians can consider obtaining a CXR in patients with advanced HIV even in the absence of symptoms, such as cough, as studies have demonstrated high rates of asymptomatic, sputum culture-positive TB in 'late presenters'
- Initiation of co-trimoxazole prophylaxis
- Careful clinical examination to look for OIs, such as TB (including extrapulmonary TB), Kaposi's sarcoma lesions, CMV retinitis, cryptococcal meningitis, and disseminated MAI/MAC
- Nutritional assessment and provision of therapeutic food or nutritional support for those with moderate or severe malnutrition
- Intensive follow-up with more frequent clinical visits to rescreen for OIs and signs of IRIS

There should be a low threshold for admitting patients presenting with advanced HIV to the hospital for stabilization, nutritional support, and observation during the initial stages of ART and any needed OI treatments.

SECTION 4.10: CARE OF THE HIV-EXPOSED INFANT

Most infants with HIV infection are asymptomatic at birth. Without identification and treatment nearly 50% of HIV-infected infants will die before the age of 2. It is therefore essential that infants exposed to HIV are placed on appropriate prophylaxis and monitored closely until their final HIV status is confirmed. All efforts should be made to ensure that HIV-exposed infants are not lost to follow-up. Table 4.11 summarizes the schedule for HIV-exposed infant care. Key highlights are:

- Initiation of infant ARV prophylaxis at birth
- Initiation of co-trimoxazole prophylaxis at 4-6 weeks of life until infant is confirmed to be definitively HIV-negative (see Section 4.3)
- Monthly clinical assessments to monitor growth and development, ongoing HIV exposure through breastfeeding, and evaluate for signs of symptoms of HIV disease and other illnesses
- Provision of education and counselling on recommended Infant and Young Children Feeding Practices (see Chapter 9)
- DNA PCR testing at 6 and 14 weeks of life for all HIV-exposed infants with prompt initiation of ART for all infants with a positive DNA PCR while awaiting results of confirmatory DNA PCR testing (see Chapter 3 for recommendations for diagnosis of HIV in HIV-exposed infants and children)
- HIV rapid testing at 9 months for infants with ongoing HIV exposure through breastfeeding (see Chapter 3)
- Confirmatory HIV rapid testing at 18 months for all HIV-exposed infants (see Chapter 3)

Infant ARV Prophylaxis

HIV-exposed infants should be started on ARV prophylaxis with nevirapine at birth or as soon as HIV exposure is recognized. The duration of ARV prophylaxis is based on when the mother initiated ART (see Table 4.12 for various scenarios of maternal ART and infant ARV prophylaxis and Table 4.13 for recommended dosing of infant NVP prophylaxis):

- If the mother was on ART for ≥4 weeks prior to delivery or last viral load before delivery was <1000 copies/ml, give NVP prophylaxis from birth until 6 weeks of life
- If the mother was started on ART <4 weeks before delivery or last viral load before delivery was ≥1000 copies/ml, give NVP prophylaxis from birth until 14 weeks

- If the mother refuses to start or has defaulted ART, continue NVP prophylaxis until the mother has initiated/restarted ART and been taking ARVs for 12 weeks or 1 week after breastfeeding is stopped

TABLE 4.11: SCHEDULE FOR MONITORING VISITS FOR HIV EXPOSED INFANTS

Age	Services to be offered
At birth	○ Clinical evaluation (thorough history and physical examination) ○ Provide BCG vaccination ○ Infant feeding counselling and support ○ Ensure that infant ARV prophylaxis is started
7 days	○ Clinical evaluation (thorough history and physical examination) ○ Infant feeding counselling and support ○ Ensure that infant ARV prophylaxis is being provided
6 weeks	○ Clinical monitoring (thorough history and physical exam) ○ Infant feeding counselling and support ○ Provide vaccinations ○ Monitor growth and development ○ Send DBS for DNA PCR ○ Initiate co-trimoxazole prophylaxis ○ Stop infant ARV prophylaxis if mother was on ART ≥4 weeks before delivery or last viral load before delivery was <1000 copies/ml. ○ Continue infant ARV prophylaxis if mother is not on ART or did not initiate ART until <4 weeks before delivery or last viral load was ≥1000 copies/ml
10 weeks	○ Clinical monitoring (thorough history and physical exam) ○ Infant feeding counselling and support ○ Provide vaccinations ○ Provide DNA PCR results to caregiver; If DNA PCR positive; initiate ART and send confirmatory DNA PCR ○ Monitor growth and development ○ Continue co-trimoxazole prophylaxis ○ Ensure infant ARV prophylaxis is being provided to HIV-exposed infants of women who are not on ART or did not initiate ART until <4 weeks before delivery or last viral load before delivery was ≥1000 copies/ml
14 weeks	○ Clinical monitoring (thorough history and physical exam) ○ Infant feeding counselling and support ○ Provide vaccinations ○ Provide DNA PCR results to caregiver if not given; If DNA PCR positive: initiate ART and send confirmatory DNA PCR; ○ Repeat DNA PCR test if 6 week DNA PCR was negative ○ Monitor growth and development ○ Continue co-trimoxazole prophylaxis ○ Stop infant ARV prophylaxis for HIV-exposed infants if mother was initiated on ART <4 weeks before delivery or last viral load before delivery was ≥1000 ○ Continue infant ARV prophylaxis if mother is not on ART
Monthly visits until 12 months of age	○ Clinical monitoring (thorough history and physical exam) ○ Infant feeding counselling and support ○ Provide vaccinations, vitamin A, routine de-worming as per MOH guidelines ○ Provide DNA PCR results to caregiver if not given; If DNA PCR positive; initiate ART and send confirmatory DNA PCR ○ Check HIV rapid tests at 9 months of age for all HIV-exposed infants with ongoing HIV exposure through breastfeeding. Send DNA PCR if rapid tests positive or indeterminate to determine HIV status (see Section 3.2) ○ Monitor growth and development ○ Continue co-trimoxazole prophylaxis until confirmed as definitively negative
18 months	○ Clinical monitoring (thorough history and physical exam) ○ Provide vaccinations, vitamin A, routine de-worming as per MOH guidelines ○ Monitor growth and development ○ Check HIV rapid tests for all HIV-exposed children to confirm final HIV status

TABLE 4.12: SUMMARY OF MATERNAL AND INFANT ARV PROPHYLAXIS RECOMMENDATIONS FOR DIFFERENT CLINICAL SCENARIOS

Scenario	Maternal ARV prophylaxis	Infant ARV prophylaxis
Mother diagnosed with HIV during pregnancy and received ART for ≥4 weeks before delivery or last viral load before delivery was <1000 copies/ml	--	Give NVP until 6 weeks of age
Mother diagnosed with HIV during pregnancy and received ART but last viral load before delivery was ≥1000 copies/ml	--	Give NVP until 14 weeks of age
Mother diagnosed with HIV during labour or immediately postpartum and plans to breastfeed	Initiate maternal ART as soon as possible for mother's health and PMTCT	Give NVP until 14 weeks of age
Mother diagnosed with HIV during labour or immediately postpartum and plans replacement feeding	Initiate maternal ART as soon as possible for mother's health	Give NVP until 14 weeks of age
Infant identified as HIV exposed after birth (through infant or maternal HIV antibody testing) and is breastfeeding	Initiate maternal ART as soon as possible for mother's health and PMTCT	Give NVP until mother has been on ART for 12 weeks or until 1 week after breastfeeding is stopped
Infant identified as HIV exposed after birth (through infant or maternal HIV antibody testing) and is not breastfeeding	Initiate maternal ART as soon as possible for mother's health	Give NVP until 14 weeks of age
Mother receiving ART but interrupts ART regimen while breastfeeding (such as toxicity, stock-outs or refusal to continue)	**Toxicity or stock-out:** determine an alternative ART regimen for mother **Default:** counsel regarding continuing ART without interruptions	Give NVP until mother has been on ART for 12 weeks or until 1 week after breastfeeding is stopped

TABLE 4.13: INFANT DOSING OF NEVIRAPINE SYRUP

NVP Daily Dose Birth to 6 wks		NVP Daily Dose Birth to 2wks	
2 - 2.49 kg	1 ml	1 – 1.8 kg	0.3 ml
≥ 2.5 kg	1.5 ml	1.8 - 2 kg	0.5 ml
		NVP Daily Dose 2wks to 6 wks	
		≥ 2 to 6 wks	1 ml

Identifying Infants with Signs and Symptoms of HIV Infection

Infants may be HIV-infected but completely asymptomatic. More commonly, they present with recurrent common infections. HIV-exposed infants should be be assessed monthly and the criteria for presumptive diagnosis of severe HIV disease should be used to initiate ART in sick HIV-exposed infants awaiting DNA PCR results (see Chapter 3.2: HIV Diagnosis in Children).

CHAPTER 5: ANTIRETROVIRAL TREATMENT REGIMENS

SECTION 5.1: GENERAL PRINCIPLES OF ANTIRETROVIRAL THERAPY

Three antiretroviral drugs from two different classes are given together in order to effectively treat HIV infection because of HIV's propensity to develop resistance.

If fewer than 3 ARVs are used for treatment, resistance of HIV to individual ARVs will eventually develop, resulting in treatment failure.

The goals of antiretroviral therapy (ART) are the:

- Maximal and durable suppression of HIV replication
- Restoration and preservation of immune function
- Reduction in HIV-related morbidity and mortality
- Improvement in quality of life and prolonged survival
- Prevention of mother-to-child transmission of HIV
- Accelerated growth and normalization of development for children
- Reduction of transmission of HIV from infected to uninfected individuals through the use of ARVs ('Treatment as prevention')

First-line ART

In treatment-naïve adults, adolescents, and older chlidren, the first-line ART regimen should consist of two nucleoside reverse transcriptase inhibitors (NRTIs) plus one non-nucleoside reverse transcriptase iInhibitor (NNRTI). For treatment-naïve children younger than three years, a protease inhibitor-based regimen is the preferred first-line ART regimen (see Table 5.1).

TABLE 5.1: SUMMARY OF RECOMMENDED FIRST-LINE ART REGIMENS

First-line ART	Preferred first-line regimens	Alternative first-line regimens
Adults including pregnant and breastfeeding women and adolescents (10 to 19 years and ≥35 kg)	TDF + 3TC + EFV	AZT + 3TC + EFV *ABC + 3TC + EFV TDF + 3TC + DTG (not currently available) If severe EFV adverse effect or EFV contraindication: TDF + 3TC + LPV/r or ATV/r AZT + 3TC + LPV/r or ATV/r *ABC + 3TC + LPV/r or ATV/r
Children (3 to 9 years) and Adolescents <35 kg	ABC + 3TC + EFV	AZT + 3TC + EFV If severe EFV adverse effect or EFV contraindication: ABC + 3TC + LPV/r or ATV/r AZT + 3TC + LPV/r or ATV/r
Children < 3 years	ABC + 3TC + LPV/r	AZT + 3TC + LPV/r **ABC + 3TC + NVP **AZT + 3TC + NVP

*ABC or boosted PIs (ATV/r, LPV/r) can be used in special circumstances.
** NVP should only be substituted for LPV/r due to need for concominant TB treatment (see Table 5.3)
For all patients on emtricitabine (FTC), lamivudine (3TC) can be substituted as both drugs have the pharmacological properties and are interchangeable.

Second-line ART

Patients who fail first-line antiretroviral treatment are switched to second-line ART after any adherence issues that are present are identified and adequately addressed. Switching to second-line ART regimens will not fix ongoing adherence issues, which is the most common reason for ART failure. Chapter 6 provides the definitions, causes, and recommended evaluation and management of antiretroviral treatment failure.

The basic principle of constructing a second-line ART regimen is to introduce at least two new ARVs and at least one new class of ARV drugs that the patient has not previously taken. Obtaining a patient's *complete* antiretroviral treatment history is crucial to selecting an appropriate second or third-line regimen that will maximize the potential of suppressing their viral load. Table 5.2 summarizes the preferred second-line ART regimens. For patients failing a protease-inhibitor based first-line ART regimen, a genotypic resistance test is recommended to guide selection of the second-line ART regimen. Genotypic resistance tests should only be sent when a patient is currently taking their current ART regimen with good adherence. Consultation with a HIV expert clinican should be obtained for patients with complicated treatment histories.

SECTION 5.2: ANTIRETROVIRAL THERAPY FOR ADULTS AND ADOLESCENTS

First-line ART for Adults and Adolescents

- First-line ART for adults and adolescents should consist of two nucleos(t)ide reverse-transcriptase inhibitors (NRTIs) plus a non-nucleoside reverse-transcriptase inhibitor (NNRTI)
- TDF + 3TC + EFV as a fixed-dose combination is recommended as the preferred first-line ART regimen given its potency and its minimal side effect profile
- If TDF + 3TC + EFV is contraindicated or not available, one of the following ART regimens is recommended as an alternate first-line regimen:
    - AZT + 3TC + EFV
    - ABC + 3TC + EFV
- If a patient develops a severe adverse reaction while taking EFV (e.g. Stevens Johnson Syndrome or psychosis) or has an absolute contraindication to initiating EFV (e.g. uncontrolled mental health condition), they should be initiated on a protease inhibitor-based regimen with LPV/r or ATV/r
- Nevirapine (NVP) is no longer recommended as part of first-line ART regimens because of its lower potency and increased risk for liver toxicity when initiating NVP at CD4 counts ≥250 cells/mm^3 in women and ≥400 cells/mm^3 in men.
    - ***HIV patients who are already on NVP should continue on their NVP-based regimen***
- In addition to patients already on NVP, nevirapine can also be initiated in MDR TB co-infected patients due to drug interactions between MDR-TB medications and EFV and protease inhibitors.
- All HIV patients with hepatitis B co-infection should be given TDF/3TC to treat their hepatitis B infection. Consult an expert clinician if there are contraindications to TDF.
- A new fixed-dose formulation of TDF/3TC/EFV that contains a lower dose of EFV (400 mg instead of the current 600 mg formulation) will replace the current formulation when it is available (expected to be introduced by 2017) as the lower EFV dose has been shown to reduce EFV adverse effects. Further guidance will be released at the time of the introduction of the new formulation.

TABLE 5.2: SUMMARY OF RECOMMENDED SECOND-LINE ART REGIMENS

	Age group	First-line ART regimen	Second-line ART regimen
NNRTI-based first-line regimen	Adults and adolscents (≥10 yrs and ≥35kg)	TDF-3TC-EFV or NVP	AZT-3TC-LPV/r or ATV/r
		ABC-3TC-EFV or NVP	
		AZT-3TC-EFV or NVP	TDF-3TC-LPV/r or ATV/r
	Children <10 or <35kg	ABC-3TC-EFV or NVP	AZT-3TC-LPV/r or ATV/r*
		AZT-3TC-EFV or NVP	ABC-3TC-LPV/r or ATV/r*
	Children <3 yrs or <10kg	ABC-3TC-NVP	AZT-3TC-LPV/r
		AZT-3TC-NVP	ABC-3TC-LPV/r
PI-based first-line regimen**	Adults and adolscents (≥10 yrs and ≥35kg)	TDF-3TC-LPV/r or ATV/r	*Based on resistance test* *Preferred:* AZT-3TC-RAL or DTG *Other Alternatives:* AZT-3TC-DRV/r DRV/r-RAL or DTG AZT-3TC-NVP
		ABC-3TC-LPV/r or ATV/r	
		AZT-3TC-LPV/r or ATV/r	*Based on resistance test* *Preferred:* TDF-3TC-RAL or DTG *Other Alternatives:* TDF-3TC-DRV/r DRV/r-RAL or DTG TDF-3TC-NVP
	Children < 10 yrs or <35kg	ABC-3TC-LPV/r	*Based on resistance test* *Preferred:* AZT-3TC-DRV/r *1st Alternative:* AZT-3TC-RAL *Other Alternative:* DRV/r-RAL
		AZT-3TC-LPV/r	*Based on resistance test* *Preferred:* ABC-3TC-DRV/r *1st Alternative:* ABC-3TC-RAL *Other Alternative:* DRV/r-RAL
	Children < 3 years or <10 kg	ABC + 3TC + LPV/r	AZT-3TC-RAL if LPV/r resistance identified
		AZT + 3TC + LPV/r	ABC-3TC-RAL if LPV/r resistance identified

*ATV/r can be used in children ≥6 years and is the preferred PI in adolescents due to once daily dosing
**A genotypic resistance test is recommended for all patients failing a protease inhibitor-based first-line ART regimen in order to guide the selection of the second-line regimen
NB: Obtaining a complete history of every ARV ever taken (e.g. prior d4T use before phase out) is important in choosing the correct second or third-line ART regimen

- At the time of the finalization of these guidelines there was insufficient data to recommend the 400 mg dose of EFV for pregnant women and TB co-infected patients. Studies are currently ongoing examining the efficacy of EFV 400mg in these two populations and clear guidance will be provided at the time of introduction of TDF/3TC/EFV400.
- A new fixed-dose combination tablet containing TDF/3TC/DTG is expected to be introduced in 2018 or 2019. Dolutegravir (DTG) is an integrase inhibitor with high potency, excellent tolerability, and a high barrier to resistance. Further guidance regarding the use of TDF/3TC/DTG will be released at the time of its introduction.

First-line ART for pregnant and breastfeeding women

- **TDF + 3TC + EFV** as a fixed-dose combination 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. The recommendation applies for lifelong treatment initiated for PMTCT (Option B+).
- HIV infected pregnant women require the same care for their own health as any other infected adult (see Chapter 4 on HIV Care and Treatment). In addition, they need special education and counselling about PMTCT, family planning, care for their HIV-exposed infant(s) (see Chapter 4.10), and partner involvement.
- **Pregnant women should be 'fast-tracked' for initiation of ART to reduce the risk of mother-to-child transmission.**

Second-line ART for Adults and Adolescents

- Second-line ART regimens should continue to consist of a NRTI backbone. The following sequencing of second-line NRTI options is recommended:
    - After failure of a TDF + 3TC or ABC + 3TC based first-line regimen, use AZT + 3TC as the NRTI backbone in the second-line regimen
    - After failure on an AZT + 3TC based first-line regimen, use TDF + 3TC as the NRTI backbone in the second-line regimen or ABC + 3TC if TDF is contraindicated
- Patients failing a NNRTI-based first-line regimen should receive a PI-based second-line regimen. Heat-stable fixed-dose combinations of ATV/r and LPV/r are the preferred boosted PI options for second-line ART in adults and adolescents.
    - ATV/r is the preferred PI for patients with lipodystrophy syndrome, hyperlipidemia, or other risk factors for coronary artery disease
    - ATV/r is the preferred PI for adolesents due to its once daily dosing, which reduces a common adherence barrier in this population
- **A genotypic resistance test is recommended for patients failing a PI-based first-line ART regimen in order to guide selection of the second-line ART regimen**
    - If resistance to the first-line protease inhibitor is identified, the patient should be switched to an integrase inhibitor-based second-line regimen of either raltegravir (RAL) or dolutegravir (DTG)
    - **If no resistance to the first-line protease inhibitor is identified on the genotypic resistance test, the patient is likely not adhering to their ART regimen.** An expert HIV clinician/committee should be consulted for management recommendations.
    - If a patient is clinical deteriorating and the results of the genotypic resistance test are not yet available, an empiric switch to an integrase inhibitor-based second-line regimen containing RAL or DTG should be made
- Adults and adolescents with TB co-infection who are failing a NNRTI-based first-line regimen have 2 second-line ART regimen options (see Chapter 8.2):
    1. Switch to a PI-based second-line regimen and receive additional ritonavir boosting to counteract the drug-drug interaction between rifampin with PIs
        a. Give additional ritonavir tablets to achieve LPV/RTV dosing of 400/400mg twice daily *or*
        b. Give double dose of LPV/r (800/200mg twice daily)
    2. Switch to an integrase inhibitor-based second-line regimen for the duration of TB treatment (RAL or DTG)
        a. The dose of raltegravir and dolutegravir must be doubled during TB treatment (e.g. raltegravir 800 mg BD and dolutegravir 50 mg BD)
        b. After completion of TB treatment, RAL or DTG should be switched to an appropriate PI (LPV/r or ATV/r)

- Patients with HIV/Hepatitis B co-infection should always receive a second-line regimen that contains TDF in order to appropriately treat the hepatitis B infection
    - After failure of TDF + 3TC first-line regimen, give AZT + 3TC + TDF
    - After failure of AZT + 3TC first-line regimen, give TDF + 3TC
- Consultation with a HIV expert clinican should be obtained for patients with complicated treatment histories

SECTION 5.3: ANTIRETROVIRAL THERAPY FOR CHILDREN < 10 YEARS

First-line ART for Children

- ABC + 3TC is the preferred NRTI backbone for all children <10 years.
    - AZT + 3TC is the alternative NRTI backbone in the case of serious adverse events to ABC, such as abacavir hypersensitivity syndrome (see Chapter 6.4).
- ABC + 3TC + EFV is the preferred first-line ART regimen for HIV-infected children ⩾ 3 years and ⩾10kg
- ABC + 3TC + LPV/r is the preferred first-line ART regimen for all HIV-infected children <3 years regardless of an infant's exposure to NVP prophylaxis or maternal ARVs due to LPV/r's superiority over NVP-based regimens in this age group. NVP should be initiated only for children <3 years with TB co-infection (see next bullet) or HIV-positive infants with a corrected <2 weeks old as LPV/r cannot be used until ⩾2 weeks corrected age (corrected age = gestational age at birth + actual age)
- For children <3 years with TB co-infection, ABC + 3TC + NVP *or* a triple NRTI regimen of AZT + 3TC + ABC is recommended *during TB treatment*. Once TB treatment is completed, the regimen should be changed to the recommended first-line regimen of ABC + 3TC + LPV/r (see Table 5.3 and Chapter 8.2 for more details)
- Dosing of all ARVs in children is based on weight. Refer to Annex 4 for dosing recommendations

Second-line ART for Children

- Second-line ART regimens should continue to consist of a NRTI backbone similar to adults and adolescents. The following sequencing of second-line NRTI options is recommended:
    - After failure on an ABC + 3TC based first-line regimen, use AZT + 3TC as the NRTI backbone in the second-line regimen
    - After failure on an AZT + 3TC based first-line regimen, use ABC + 3TC as the NRTI backbone in the second-line regimen
- Patients failing a NNRTI-based first-line regimen should receive a PI-based second-line regimen. LPV/r is the preferred boosted PI although ATV/r can be given to children ≥6 years.
- **A genotypic resistance test is recommended for children failing a PI-based first-line ART regimen in order to guide selection of the second-line ART regimen**
    - If resistance to the first-line protease inhibitor is identified, the patient should be switched to an integrase inhibitor-based second-line regimen of raltegravir (RAL) or darunavir (DRV) if RAL is not available and there are no DRV-associated mutations identified on the genotypic resistance test
    - **If no resistance to the first-line protease inhibitor is identified on the genotypic resistance test, the patient is likely not adhering to their ART regimen.** An expert HIV clinician/committee should be consulted for management recommendations.
        - Resistance to protease inhibitors is uncommon and suboptimal adherence is the most common reason for treatment failure in this age group, especially children younger than 3 years

TABLE 5.3: RECOMMENDED ART REGIMENS FOR CHILDREN WHO NEED TB TREATMENT

Recommended ART regimens for HIV-infected children and infants with TB co-infection	
Younger than 3 years	• Substitute NVP for LPV/r, ensuring that dose is 200mg/m^2/dose or • Give triple NRTI (AZT + 3TC + ABC) ***Switch to preferred first-line of ABC + 3TC + LPV/r after TB treatment**
≥3 years	If the child has no history of failure of a NNRTI-based regimen: • Initiate on EFV or • If already on ART, substitute NVP or LPV/r with EFV If the child has a history of failure of a NNRTI-based regimen: • Give triple NRTI (AZT + 3TC + ABC) or • Urgent consultation with HIV expert for constructing an ART regimen ***If the child was on LPV/r before TB treatment, switch the EFV back to their original LPV/r-based ART regimen after TB treatment. If the child was on NVP prior to TB treatment they can remain on EFV**

  - If a child is clinical deteriorating and the results of the genotypic resistance test are not yet available, an empiric switch to boosted DRV or an integrase inhibitor-based second-line regimen of RAL should be made
- **Switching to a NNRTI-based second-line regimen after failure of a LPV/r-based first-line regimen is discouraged in children.** Any children switched to a NNRTI-based second-line regimen must have close viral load monitoring and prompt genotypic resistance testing performed if viral suppression is not achieved

SECTION 5.4 THIRD-LINE REGIMENS

Lesotho's ART programme is now 12 years old and although the majority of ART patients remain on first-line regimens, there are an increasing number of patients on second-line regimens. The country's goal is to maintain patients on successful first-line for as long as possible followed by second-line ART when needed. However, it is expected that as the national ART programme continues to expand, more patients will fail second-line treatment and require third-line line ART.

If there is evidence of treatment failure while a patient is on a second-line regimen, switching to a third-line regimen should be done with the same principles for patients failing first-line ART (see Chapter 6.3). **All patients failing second-line ART require a genotypic resistance test to help select an appropriate third-line regimen and should be reviewed by an expert HIV clinician/committee.**

Third-line ARVs drugs for Lesotho include: boosted darunavir (DRV), raltegravir (RAL), dolutegravir (DTG), etravirine (ETV), and recycled NRTIs based on a patient's genotypic resistance test results and complete ARV treatment history. Pediatric formulations of DRV and ETV are ready available in Lesotho through a long-term donation program from the drug manufacturer.

Patients on a failing second-line or third-line regimen with no new ARV options should continue on a tolerated ART regimen that achieves maximal viral suppression in order to slow disease progression and HIV-related morbidity and mortality. Partial viral suppression is better than uncontrolled viral replication.

CHAPTER 6: PATIENT MONITORING

Monitoring patients on ART

Clinical assessment and laboratory tests play a key role in monitoring persons with HIV before, during, and after the initiation of ART. Monitoring done before and/or at the time of initiation of ART can help guide the selection of the first-line ART regimen. After ART is started, clinical and lab monitoring will help to identify and manage possible side effects early before they become serious; assess the efficacy of treatment; and help identify treatment failure.

SECTION 6.1: CLINICAL AND ADHERENCE MONITORING

Clinical assessment should be the primary tool for monitoring HIV patients throughout the HIV care continuum. Clinical and adherence assessments should be done 2 weeks, 1 month, 3 months, and 6 months after ART initiation and at least every 6-12 months thereafter (see Table 6.1). **More frequent clinical monitoring should be conducted for patients presenting with advanced HIV disease, those with poor ART adherence and/or treatment failure, pregnant and breastfeeding women, and HIV-infected children and adolescents.**

A focused history and physical assessment should be performed during routine visit, including:

- Monitoring of:
  - Weight (measure at every visit)
  - Height (in children; measure every 3 months)
  - Blood pressure
  - Head circumference (in children < 3 years; measure every 3 months)
  - Developmental status in children
  - Nutritional status in all HIV patients (BMI or weight-for-height)
- Diagnosis and management of new illnesses
  - OIs, especially TB, which may suggest immune reconstitution inflammatory syndrome (IRIS) if they occur soon after ART initiation or treatment failure if patient has been on ART for ≥6 months
  - Other co-morbidities, including STIs, hepatitis B, hypertension, diabetes mellitus, substance abuse, psychiatric illness, etc.
- Medication review
  - Side effects
  - Adherence and dosing
  - Other medications including traditional and herbal medicines that may interact with ARVs
- Early diagnosis of pregnancy
- Provision of routine primary health care services
- Changes in the social situation that might affect adherence to ART

TABLE 6.1: MONITORING SCHEDULE FOR PATIENTS ON ANTIRETROVIRAL THERAPY

ARV Regimen	Assessment / Investigations	Baseline or day of ART initiation	Wk 2	Mo 1	Mo 3	Mo 6	Mo 12	Every 12 months
All Regimens	Rule out active TB using TB screen tool	X	X	X	X	X	X	At every visit Children & Adolescents: 3 monthly Adults: 6-12 monthly
	Adherence assessment		X	X	X	X	X	
	Clinical exam (including weight)	X	X	X	X	X	X	
	Assessment for possible ARV side effects		X	X	X	X	X	
	Treatment Supporter	X					X	If adherence concerns
TDF‡/3TC/EFV		CD4, ALT, Urine dipstick§, Cr				VL, CD4, Urine dipstick§	VL, CD4, Urine dipstick§, Cr	VL, CD4, Urine dipstick§, Cr
TDF‡/3TC/DTG		CD4, ALT, Urine dipstick§, Cr				VL, CD4, Urine dipstick§	VL, CD4, Urine dipstick§, Cr	VL, CD4, Urine dipstick§, Cr
TDF‡/3TC/NVP		CD4, ALT, FBC, Urine dipstick§, Cr	ALT+		ALT+	VL, CD4,Urine dipstick§,ALT	VL, CD4, Urine dipstick§, Cr	VL, CD4, Urine dipstick§, Cr
AZT/3TC/EFV		CD4, ALT, FBC*		Hb		VL, Hb, CD4	VL, Hb, CD4,	VL, Hb, CD4
AZT/3TC/NVP		CD4, ALT, FBC*	ALT+	Hb	ALT+	VL, Hb, ALT, CD4	VL, Hb, CD4	VL, Hb, CD4
ABC/3TC/EFV		CD4, ALT				CD4, VL	CD4, VL	CD4, VL
ABC/3TC/NVP		CD4, ALT	ALT+		ALT+	ALT, CD4, VL	CD4, VL	CD4, VL
All Pregnant women		Pregnant women should receive monthly clinical exams and extra Hb testing (at 2 weeks and monthly thereafter)						
Any regimen containing NRTIs		Check lactate level when symptoms or signs suggest high lactate (or lactic acidosis)						
Any regimen containing PI		Glucose and lipids (both done fasting) should be checked at baseline and annually thereafter						

+All adults with CD4 ≥250 (females) or ≥400 (males) cells/mm^3 are at increased risk of NVP-related hepatotoxicity, check extra ALT tests at 2 weeks and 3 months
*All patients with abnormal Hb at baseline should have repeat measurement to ensure correction
‡ Inability to perform creatinine clearance should not be a barrier to tenofovir use
§ All patients on TDF should have a urine dipstick for glucose and protein checked every 6 months. Creatinine should be sent if glucose or protein is detected on urine dipstick and annually if urine dipsticks are normal

SECTION 6.2: LABORATORY MONITORING

Guiding principles:

- Laboratory monitoring is not a prerequisite for the initiation or continuation of ART
- Viral load monitoring is the preferred lab test for monitoring the success of ART and evaluation of treatment failure
- Viral load should be measured 6 and 12 months after ART initiation and annually thereafter (see Figure 6.1: Viral Load Monitoring Algorithm)
- CD4 monitoring will continue to play a role in monitoring HIV patients to assess their need for co-trimoxazole prophylaxis and risk for opportunistic infections. However, CD4 monitoring is now de-emphasized in favor of viral load monitoring for monitoring the success of ART because of viral load's greater accuracy in identifying treatment failure
- Symptom-directed laboratory monitoring for safety and toxicity is recommended for those on ART.

Baseline Laboratory Investigations

Laboratory monitoring should complement clinical assessments. Baseline laboratory tests can help determine the ART regimen a patient should be initiated on, however, the lack of test results or the capacity to perform laboratory tests should not delay a person who is otherwise ready to start ART from initiating treatment. See Chapter 4.4 for the recommended baseline laboratory investigations.

Routine Laboratory Investigations on ART

The following laboratory tests should be performed **routinely** depending on the regimen the patient is on (See Table 6.1: Monitoring Schedule). Viral load and CD4 monitoring is discussed in the next section.

- If initiated **on TDF**, perform **urine dipstick** at baseline and every six months thereafter. If urine protein or glucose is detected, check **serum creatinine** and calculate rate of creatinine clearance every 6 months. If urine dipsticks are normal, check serum creatinine annually
    - TDF is contraindicated if creatinine clearance is < 50 ml/min (see below for creatinine clearance calculation)
- **Inability to monitor serum creatinine should not be a barrier to TDF use**. Creatinine clearance monitoring is needed in those with underlying renal disease; of older age groups; and with low body weight or other risk factors for renal disease, such as diabetes or hypertension.
- If initiated **on AZT**, **haemoglobin** (Hb) should be checked at 1 month, 6 months, and 1 year after ART initiation and annually thereafter
    - AZT is relatively contraindicated if Hb is <8 but can often be given as underlying anemia is most often due to uncontrolled HIV, which the AZT will correct
- If initiated **on NVP**, **ALT** should be checked at baseline, 2 weeks, 3 months, and 6 months after ART initiation. Thereafter, check ALT only based on clinical suspicion of hepatotoxicity.
- For individuals with HIV/HBV or HIV/HCV co-infection, it is recommended that liver enzymes be monitored 1 and 3 months after ART initiation and as indicated thereafter.

Additional laboratory tests can be requested based on clinical assessments but should only be done if the results will guide clinical management. Such tests include but are not limited to:

- Lactate assay, if the patient is on a NRTI for > 4 months and losing weight, and/or having other symptoms that suggest hyperlactatemia
- Glucose and lipid profiles annually, if the patient is taking a PI, such as LPV/r or ATV/r

Point-of-care testing equipment should ideally be available in all clinics to measure Haemoglobin (Hb) and glucose. Not only do such equipment allow for immediate results, but they also take some pressure off the district hospital laboratories, which have to cope with an ever-increasing load of specimens.

Calculation of Creatinine clearance in ml/min using Cockcroft Gault Equation

Male: $\frac{1.23 \times (140\text{-age}) \times \text{wt in Kg}}{\text{Creatinine in micromols/L}}$

Female: $\frac{1.04 \times (140\text{-age}) \times \text{wt in kg}}{\text{Creatinine in micromols/L}}$

Measuring Efficacy of Treatment

The effectiveness of ART may be monitored by assessing clinical improvement, immunologic function (CD4 count and percentage), and viral load. However, **virologic monitoring is the gold standard for monitoring ART success**.

Viral load is the preferred monitoring approach to diagnose and confirm ARV treatment failure as well as ART success. If viral load is not routinely available, use CD4 count and clinical monitoring to assess ART success and diagnose treatment failure.

Clinical monitoring

Monitoring ART in adults and adolescents

The following clinical indices suggest that a patient is responding to ART:

- The patient feels better and has more energy to perform daily tasks
- The patient is gaining weight
- There is an improvement in symptoms and signs of the original presenting illnes
- The patient is free of new WHO Stage 3 or 4 conditions

Monitoring of ART in children

In children, growth and development are important clinical monitoring indicators and are assessed using growth charts.

Clinical assessment of children on ART involves the following:

- Always assessing the child's and caregiver's understanding of ART as well as anticipated support and adherence to ART.
- Always checking for symptoms of potential drug toxicities.
- Always assessing for treatment failure through clinical staging

Important signs of infants' and children's response to ART include the following:

- Improvement in growth in children who have been failing to grow
- Improvement in neurological symptoms and development in children with encephalopathy or developmental delay/regression due to HIV
- Decreased frequency of infections (bacterial infections, oral thrush, and/or other OIs)

See Section 6.3: Treatment Failure for the definition and management of clinical treatment failure.

Virologic (HIV viral load) monitoring

The viral load usually decreases to undetectable levels in the blood (< 40 copies/ml) within six months of 95-105% adherence to ART. The viral load measurement is the most accurate method for assessing treatment failure. **Any viral load ≥ 1000 copies/ml must stimulate a thorough review, including**:

- Enhanced adherence counselling sessions to evaluate for any adherence issues and address them
- Identify any untreated opportunistic infections, co-infections, or illnesses
- Checking for any drug-drug interactions with ARVs, including assessing for traditional Sesotho or herbal medication use

Although the viral load cutoff for the definition of virologic treatment failure is ≥ 1000 copies/ml, there is clear evidence that even low levels of sustained viremia (≥100-200 copies/ml) increases the risk of developing resistance. Thus, even though it is not recommended to change to a second or third-line ART regimen for low level viremia (viral loads between 100 – 1000 copies/ml), patients with low level viremia should be thoroughly evaluated in a similar fashion to patients with viral loads ≥ 1000 copies/ml.

See Section 6.3: Treatment Failure for the definition and management of virologic treatment failure.

Frequency of viral load monitoring (See Figure 6.1: Viral Load Testing Algorithm)

- The viral load should be tested 6 and 12 months after initiating ART and then annually thereafter to detect treatment failure.
- Pregnant and breastfeeding women and children <5 years should continue to have their viral load checked every 6 months due to their higher risk of treatment failure
- Check the viral load 6 and 12 months after switching a patient to second-line or third-line ART
- Follow-up every viral load ≥1000 copies/ml with a repeat viral load approximately 8-12 weeks after initiating enhanced adherence counselling sessions once any adherence issues identified have been resolved
- Consider sending a viral load when substituting one ARV for another due to a toxicity / serious adverse effect to rule out treatment failure in the setting of a single drug substitution (does not apply when ARV substitution is made <6 months after ART initiation as the viral load is likely not fully suppressed yet)
- If viral load testing is not routinely available, CD4 count and clinical monitoring should be used to diagnose treatment failure, with targeted viral load testing to confirm virologic failure where possible.

Immunologic (CD4) monitoring

With ART, immune recovery is expected as indicated by improvement in the CD4 count and percentage. Monitoring of CD4 can serve as an important proxy of ART effectiveness, however, viral load monitoring is the preferred method of monitoring ART success. In the absence of routine viral load monitoring, a falling CD4 count may indicate intercurrent illness or an opportunistic infection, poor adherence, or treatment failure due to resistance. Such patients need a thorough review inclusive of:

- A viral load must be sent if it has not previously been done to determine if patient if truly experiencing treatment failure
- Assessment for other possible reasons for CD4 decline besides treatment failure, such as intercurrent temporary illness (e.g. respiratory tract infection), TB, or malignancy, or other OI
- If treatment failure is confirmed,
    - Conduct enhanced adherence counselling sessions to evaluate for adherence issues and address them
    - Identify any untreated opportunistic infections, co-infections, or illnesses

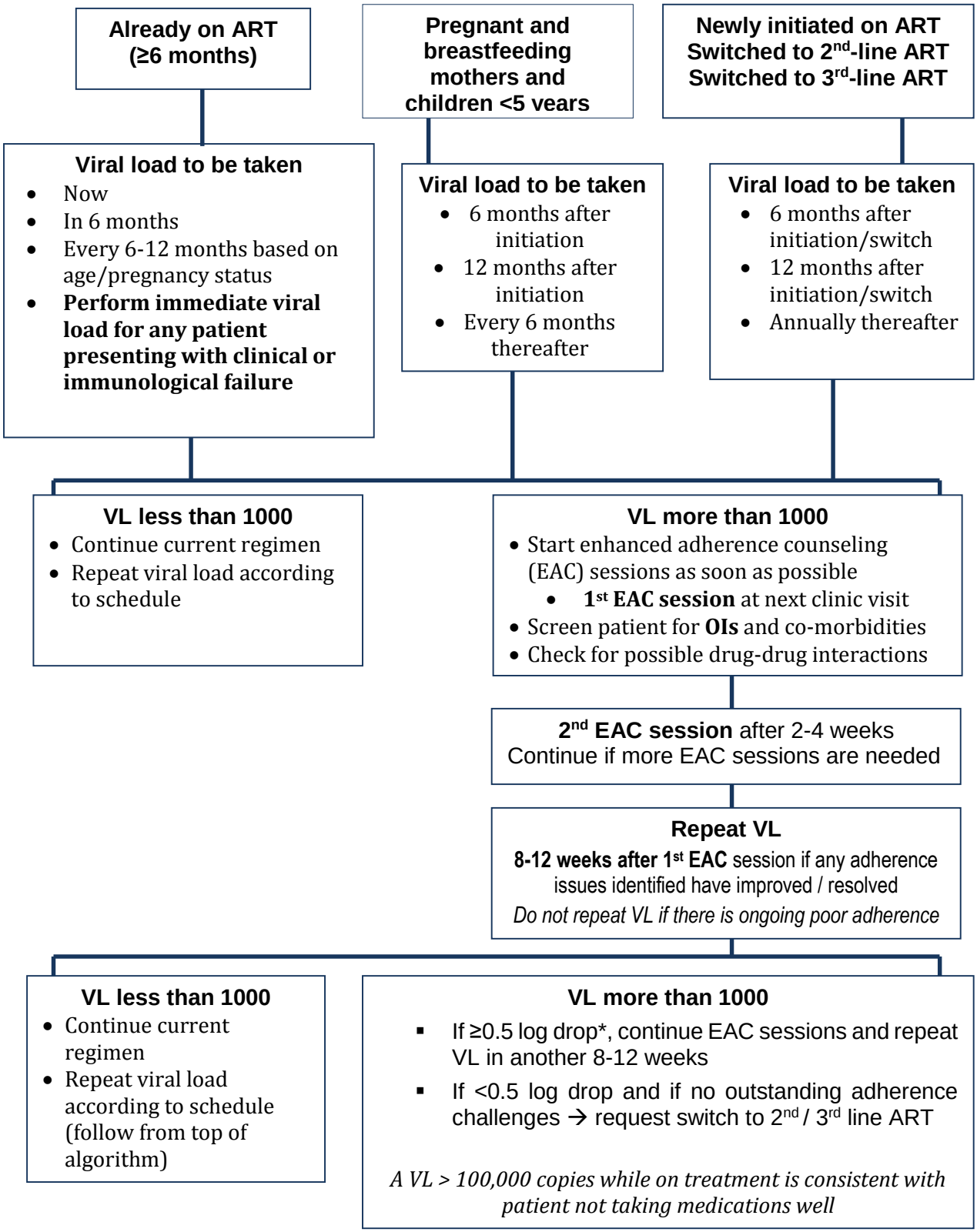
- Checking for any drug-drug interactions with ARVs, including assessing for traditional Sesotho or herbal medication use

See Section 6.3: Treatment Failure for the definition and management of immunologic treatment failure.

Frequency of CD4 monitoring

- CD4 count should be assessed at baseline and then 6 months and 12 months after ART initiation. Thereafter:
  - If a patient's viral load is <1,000 at 12 months and the CD4 count is ≥350, routine CD4 monitoring can be done annually with VL.
  - If the viral load is <1,000 but the CD4 count is < 350, continue to check CD4 every 6 months to determine need for co-trimoxazole prophylaxis
  - If the viral load is ≥1,000 copies/ml, check the CD4 count every 6 months as the patient is at risk for HIV disease progression
  - CD4 count should be checked along with a viral load if a patient develops a WHO Stage 3 or 4 condition after being on ART for ≥6 months
  - Monitor CD4 every 6 months for patients who have not yet started ART for any reason to assess for disease progression and need for co-trimoxazole prophylaxis

FIGURE 6.1: VIRAL LOAD TESTING ALGORITHM



*****Viral loads are often reported on a logarithmic scale. A drop of 0.5 log is roughly equivalent to a 2/3 reduction in viral load. For example, a viral load log of 2.3 = 2000 copies/ml. A drop of 0.5 log units to 1.8 log = 650 copies/ml. On the other hand, a decrease from 12000 copies/ml to 5000 copies/ml only represents a 0.4 log unit drop from 4.1 log to 3.7 log.*

SECTION 6.3 ANTIRETROVIRAL TREATMENT FAILURE

The majority of people living with HIV will achieve full viral suppression on their first-line ART regimen. Patients who do not achieve viral suppression on ART after 6 months of an appropriate ART regimen are considered to have treatment failure. These patients are at high risk for developing resistance to one or more of their ARV drugs and this risk increases the longer that a patient continues to take ART in the setting of a non-suppressed viral load. The prompt identification of treatment failure is important to:

- Minimize resistance and preserve other ARVs for future ART regimens
- Reduce HIV disease progression and resulting HIV-related morbidity and mortality
- Reduce onward transmission of HIV, including decreasing the risk of transmission of resistant HIV strains

There are 3 types of antiretroviral treatment failure: virologic, immunologic, and clinical (see Table 6.2). The typical progression of treatment failure is that virologic treatment failure develops first followed by immunologic failure and then clinical failure. This progression is the reason that viral load monitoring is the preferred tool for assessing ART success so that treatment failure can be detected earlier than if CD4 and clinical monitoring are used alone.

Upon recognizing treatment failure, regardless of the type of failure (virologic, immunologic, or clinical), a thorough evaluation must be initiated to determine the cause. The most common causes of antiretroviral treatment failure are:

- Suboptimal ARV adherence
- Resistance to one or more ARV drugs in the ART regimen
- Drug-drug interactions leading to suboptimal ARV drug levels
- Opportunistic infections or other medical conditions, such as cancer, though full viral suppression can usually be achieved even in the setting of an untreated OI or medical condition with good ART adherence

Suboptimal ART adherence and ARV drug resistance are the first and second most common causes of treatment failure respectively. Because of this, the main focus of the evaluation of a patient with treatment failure should be to determine whether poor adherence is the root cause. Switching a patient to second-line or third-line ART without correcting underlying adherence issues will typically result in continued treatment failure

TABLE 6.2: WHO DEFINITIONS OF CLINICAL, IMMUNOLOGICAL AND VIROLOGIC FAILURE TO SUPPORT DECISION-MAKING FOR SWITCHING ART REGIMENS.

Failure	Definition
Clinical Failure	**Adults and Adolescents** New or recurrent clinical event(s) indicating severe immunodeficiency (WHO clinical stage 4 condition) after 6 months of effective ART **Children** New or recurrent clinical event(s) indicating advanced or severe immunodeficiency (WHO clinical stage 3 and 4 clinical condition with exception of TB) after 6 months of effective ART
Immunological failure	**Adults and adolescents** CD4 count falls to the baseline before ART was initiated (or below) or Persistent CD4 levels below 100 cells/mm^3
	Children: **Younger than 5 years** Persistent CD4 levels below 200 cells/mm^3 or <10% **Older than 5 years** Persistent CD4 levels below 100 cells/mm^3
Virologic Failure	Plasma viral load ≥1000 copies/ml based on two consecutive viral load measurements after 2-3 months of enhanced adherence support

and further increases the risk of developing resistance, which can reduce a patient's future ARV drug options. HIV genotypic resistance tests can help to assess for the presence of resistance to ARVs but the high costs of these tests make them impractical for most ART patients with treatment failure in Lesotho.

Upon identifying treatment failure, enhanced adherence counselling (EAC) sessions should begin as soon as possible. EAC sessions should focus on reviewing a patient's adherence, identifying adherence issues and barriers to good adherence, and developing and implementing a plan with the patient and their treatment supporter / caregiver to address them. At least 2 EAC sessions should be conducted in a short time period (e.g. 2-4 weeks) with further EAC sessions as needed. A repeat viral load should be sent 8-12 weeks after the EAC sessions began *if* the adherence issues identified have improved or been resolved. Do not send a repeat viral load if there are ongoing adherence issues as the viral load will likely continue to be non-suppressed but a confident determination of whether the viral load is elevated due to poor adherence or viral resistance will not be able to be made. **Patients with treatment failure should be evaluated regularly at frequent intervals by a multidisciplinary team** until a conclusion is reached about the primary cause of their treatment failure and the need for a change in their ART regimen**.** Refer to Chapter 7: Adherence and Disclosure for more detailed guidance on conducting EAC sessions.

Poor adherence and/or suboptimal ARV drug levels eventually leads to HIV resistance to one or more of the ARVs in the ART regimen. As a result, a patient may be failing ART because of one or more of the reasons stated above. The primary purpose of the EAC sessions and thorough history and physical examination of patients with treatment failure is to identify those for whom there are reversible causes (e.g. poor adherence, drug-drug interaction) and determine if correction of those issues will lead to viral suppression allowing the patient to stay on their current ART regimen. Studies have shown that the highest viral suppression rates occur with first-line ART regimens compared to second-line or third-line regimens. Because of this, **changes to second-line and third-line ART should be made after a patient's care team is reasonably assured that the primary reason for treatment failu is viral resistance to a patient's ARVs**.

Unavailability of viral load monitoring for patients with treatment failure

- If a patient presents with clinical and/or immunologic treatment failure but the treating clinician does not have readily available access to viral load monitoring, EAC sessions and the evaluation of treatment failure should be started while efforts are made to check a viral load
- If access to viral load testing is interrupted after a patient is identified with virologic treatment failure, EAC sessions and treatment failure evaluation should proceed
- If viral load monitoring is unavailable or the results of viral load testing are delayed for a patient with treatment failure who is clinically deterioritating, a change to second-line ART should not be delayed if there are no unresolved adherence issues
- Similarly, a delayed response from a second-line ART committee should not prevent a clinicially deteriorating patient with treatment failure from being switched to second-line ART

The basic principle of constructing a second-line or third-line ART regimen is to introduce at least two new ARVs and at least one new class of ARV drugs that the patient has not previously taken. Obtaining a patient's *complete* antiretroviral treatment history is crucial to selecting an appropriate second or third-line regimen that will maximize the potential of suppressing their viral load. See Chapter 5 for detailed discussion of appropriate second-line and third-line ART regimens.

SECTION 6.4 MONITORING AND SUBSTITUTIONS FOR ARV DRUG TOXICITIES

- The availability of laboratory monitoring is not required for initiating or continuing ART.
- Symptom-directed laboratory monitoring for safety and toxicity can be used for those receiving ART

Most ARV adverse effects are mild to moderate in severity and transient occur during the initial weeks to months on an ART regimen. In general, ARV substitutions for toxicity should only be made for Grade 3 or 4 adverse events that are severe and/or life-threatening. Table 6.3 below summarizes the main types of toxicities associated with the first, second and third line ARVs, the risk factors associated with the toxicities, and provides suggested management. See Annex 6 for additional information.

TABLE 6.3: TYPES OF TOXICITIES ASSOCIATED WITH FIRST-, SECOND-, AND THIRD-LINE ARV DRUGS

ARV	Major types of toxicity	Risk Factors	Suggested Management
TDF	Tubular renal dysfunction, Fanconi syndrome	○ Underlying renal disease ○ Older age ○ BMI<18.5 or body wt <50kg ○ Untreated Diabetes Mellitus ○ Untreated hypertension ○ Concomitant use of nephrotoxic drugs or a boosted PI	Substitute with ABC if creatinine clearance decreases to less than 50 ml/min
	Decreases in bone mineral density	○ History of osteomalacia & pathological fractures ○ Osteoporosis or bone loss	
	Lactic acidosis or severe hepatomegaly with steatosis	○ Prolonged exposure to nucleoside analogues ○ Obesity	
ABC	Hypersensitivity reaction	○ Presence of HLA-B*5701 gene	Substitute with TDF in adults and adolescents and with AZT in children
AZT	Anaemia, neutropaenia, myopathy, lipoatrophy or lipodystrophy	○ Baseline anaemia or neutropaenia ○ CD4 count ≤200 cells/mm^3	Substitute with TDF or ABC for severe anemia (Hb < 5 or symptomatic anemia)
	Lactic acidosis or severe hepatomegaly with steatosis	○ BMI >25 (or body weight ○ >75 kg) ○ Prolonged exposure to nucleoside analogues	
	Vomiting - persistent	○ Risk factors unknown	
EFV	Hepatotoxicity	○ Underlying hepatic disease – HBV and HCV coinfection	LPV/r or ATV/r
	Convulsions	○ History of seizure	
	Hypersensitivity reaction, Stevens-Johnson syndrome	○ Risk factors unknown	
NVP	Hepatotoxicity	○ Underlying hepatic disease ○ HBV and HCV coinfection ○ Concomitant use of hepatotoxic drugs ○ CD4>250 cells/mm^3 in women; and CD4 >400 cells/mm^3 in men	Substitute with EFV, if person cannot tolerate either NNRTI, use PI (LPV/r or ATV/r)

ARV	Major types of toxicity	Risk Factors	Suggested Management
	Severe (Grade 4) skin rash and hypersensitivity reaction (Stevens-Johnson syndrome)	○ Risk factors unknown	Use boosted PIs (LPV/r or ATV/r)
ATV/r	Electrocardiographic abnormalities (PR interval prolongation)	○ Pre-existing conduction disease ○ Concomitant use of other drugs that may prolong the PR interval	Substitute with LPV/r or DRV/r. If boosted PIs are contraindicated and NNRTIs have failed in first-line ART, give integrase inhibitor (RAL or DTG)
	Indirect hyperbilirubinaemia (clinical jaundice)	○ Underlying hepatic disease ○ HBV and HCV coinfection ○ Concomitant use of ○ hepatotoxic drugs	
	Nephrolithiasis & risk of prematurity	○ Risk factors unknown	
LPV/r	Electrocardiographic abnormalities (PR and QT interval prolongation, torsades de pointes)	○ People with pre-existing conduction system disease ○ Concomitant use of other drugs that may prolong the QT interval	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/r can be used for children older than 6 years. If LPV/r is used in second-line ART for adults, use ATV/r or DRV/r. If boosted PIs are contraindicated and the person has failed on treatment with NNRTI in first-line ART, consider integrase inhibitors.
	QT interval prolongation	○ Congenital long QT syndrome ○ Hypokalaemia ○ Concomitant use of other drugs that may prolong the PR interval	
	Hepatotoxicity	○ Underlying hepatic disease ○ HBV and HCV coinfection ○ Concomitant use of hepatotoxic drugs	
	Pancreatitis	○ Advanced HIV disease	
	Risk of prematurity, lipoatrophy or metabolic syndrome, dyslipidaemia or severe diarrhea	○ Risk factors unknown	
DRV/r	Hepatotoxicity	○ Underlying hepatic disease HBV and HCV coinfection ○ Concomitant use of hepatotoxic drugs	When it is used in third-line ART, limited options are available; refer to specialist.
	Severe skin and hypersensitivity reactions	○ Sulfonamide allergy	
ETV	Severe skin and hypersensitivity reactions	○ Unknown	Limited options are available
RAL	Rhabdomyolosis, myopathy, myalgia	○ Concomitant use of other drugs that increase the risk of myopathy and rhabdomyolosis	Substitute with DTG
DTG	Insomnia, depression	○ Risk factors unknown	1st line: Substitute EFV 3rd line: Limited options are available; refer to specialist.
	Hyperglycemia	○ Risk factors unknown	
	Increased ALT	○ Hepatitis co-infections	

SECTION 6.5 DRUG-DRUG INTERACTIONS

Before initiating ART and during each clinical encounter, all current medications that a patient is taking, including traditional and herbal medicines should be reviewed. Since NVP, EFV, and LPV/r are all metabolised by the liver, drugs that induce or inhibit liver metabolism may affect drug levels. Refer to Annex 9 for further information on drug-drug interactions.

The effects of Sesotho medicines on serum levels of antiretrovirals have not been evaluated. It is therefore recommended that patients do not take traditional medicines along with antiretrovirals.

TABLE 6.4: IMPORTANT DRUG-DRUG INTERACTIONS

ARV drug	Key interactions	Suggested management
AZT	Ribavirin and peg-interferon alfa-2a	Substitute AZT with TDF
Boosted PI (ATV/r, LPV/r)	Rifampicin	Adjust the PI dose or change regimen
	Phenytoin and phenobarbital	Use alternative antiepileptic drug. Valproic acid is preferred followed by carbamazepine
	Lovastatin and simvastatin	Use an alternative dyslipidaemia agent (for example pravastatin)
	Estrogen-based hormonal contraception	Use alternative or additional contraceptive methods
	Astemizole and terfenadine	Use alternative antihistamine agent
	TDF	Monitor renal function
EFV	Amodiaquine	Use an alternative antimalarial agent
	Phenytoin and phenobarbital	Use alternative antiepileptic drug. Valproic acid is preferred followed by carbamazepine
	Estrogen-based hormonal contraception	Use alternative or additional contraceptive methods
	Astemizole and terfenadine	Use an alternative anti-histamine agent
NVP	Rifampicin	Substitute NVP with EFV
	Itraconazole and ketoconazole	Use an alternative antifungal agent (for example fluconazole)
	Phenytoin and phenobarbital	Use alternative antiepileptic drug. Valproic acid is preferred followed by carbamazepine

CHAPTER 7: ADHERENCE AND DISCLOSURE

"Drugs do not work in patients who do not take them;" *New England Journal of Medicine, 353(5), 2005.*

Excellent adherence to the first ART regimen has the best chance of long term success

SECTION 7.1: INTRODUCTION

The standard clinical definition of adherence is taking 95-105% of medications the right way at the right time (the 4 R's: **R**ight drug, **R**ight dose, **R**ight time, and **R**ight way). Over time this definition has been broadened to include more factors related to continuous care, such as following an agreed-upon care plan; attending scheduled clinic appointments; picking up medications on time; and getting regular required laboratory tests.

Adherence to ART is critical for improving a patient's clinical, immunological and virologic outcomes. Maintaining good adherence to the prescribed ARV regimen prevents or delays the onset of drug resistance, treatment failure and the need to switch to second and third-line drugs.

The ability to execute treatment adherence implies treatment literacy on the part of the patient/caregiver. This means that the patient/caregiver must understand both the disease process and necessary medications.

Health facilities should form multidisciplinary teams, consisting of clinicians (doctors, nurses), psychosocial support (counsellor, social worker, and psychologist), and pharmacy and laboratory personnel in order to assist patients to achieve excellent adherence.

SECTION 7.2: ADHERENCE PREPARATION

Assuring adherence to the prescribed regimen begins with educating and counselling patients/caregivers on HIV and AIDS care and treatment. Immediately after HIV diagnosis, all persons living with HIV should be prepared for initiating ART. 1-3 adherence counselling sessions should be conducted in group and/or individual counselling sessions to help patients/caregivers understand basic HIV knowledge as well as the importance of excellent adherence to ART and care plans.

A patient's/caregiver's level of understanding will determine the number of adherence sessions to be done before initiation of ART.

Topics to be covered during the ART preparation/adherence counselling sessions include:

Basic HIV knowledge	▪ Modes of transmission of HIV and how HIV is not transmitted ▪ Signs and symptoms of HIV ▪ The difference between HIV and AIDS ▪ Significance of CD4 count/percentage and viral load
ART	▪ Names of ARVs (including brand names) ▪ Side effects of ARVs including the possibility of IRIS ▪ How and when to take ARVs ▪ Importance of bringing all medications to clinic visits ▪ Anticipated monitoring schedules; both clinical and laboratory, ▪ Importance of adherence; taking 95-105% (up to 110% of syrups, such as Kaletra syrup) of prescribed doses to suppress viral load and prevent resistance ▪ The fact that treatment is lifelong even when one is feeling well
Other relevant and practical issues	▪ Demonstration to caregivers how to draw syrups into syringes and applying other measures, such as marking of syringe to indicate proper dose measurement

	▪ Teaching caregivers how to mask the flavour of Kaletra syrup (e.g. mixing with multivitamin and/or co-trimoxazole syrups) ▪ Importance of proper nutrition, safe water, immunizations, and primary care ▪ Re-assessment of understanding of basic HIV knowledge and antiretroviral therapy ▪ Discouraging use of unauthorized medical and herbal therapies for HIV, including Sesotho medicines ▪ Provision of medicines for management of common OIs, especially TB ▪ Encouragement of disclosure to family, partners, and other caregivers who can support the treatment plan ▪ Referrals to community based care support groups

Issues to consider in initiating ART in children

Psychosocial factors: It is important to identify and counsel at least one dedicated caregiver who can supervise and/or give medicines. Disclosure to another adult in the same household (secondary caregiver) is encouraged to assist with medication administration.

Disclosure: The process of disclosure to the child should be initiated as early as possible, usually from as early as 5-7 years of age. ART adherence is improved in children who know their HIV status and are supported to adhere to medicines.

Barriers to Adherence

Barriers to adherence should be discussed with the patient/caregiver prior to initiation of ART. Adherence does not depend solely on the patient's or caregiver's ability to remember to take medications. Possible barriers include:

- Patient/caregiver medical/mental health
- Patient/caregiver's workload
- Lack of transportation; distance from the health facility; lack of access to refills
- Medication side effects
- Number of pills to take (pill burden)
- Unavailability of food
- Migration
- Inability to afford associated medical costs
- Inconsistent caregiver
- Alcohol or other substance use that impairs patient or caregiver
- Domestic violence
- Living alone; lack of social support from family and/or friends
- Lack of disclosure of HIV status
- Illiteracy
- Poor understanding of the relationship between non-adherence and resistance
- Inadequate understanding of ARV regimen or effectiveness
- Lack of confidence in ability to adhere
- Belief in alternative medicines or religious healings
- Work or school schedule

Strategies to address Barriers to Adherence

Once potential barriers have been identified, attempts should be made to help patients/caregivers overcome them. Interventions and strategies include:

- Referral to community health workers; support groups; Community ART Groups (CAGS) (once eligible to join a CAG)
- Identifying supportive family/community members

- Linkage to social support services – transportation, food
- Use of pill boxes, reminder calendars or written schedules
- Referral for assistance with substance abuse problems
- Repeat adherence sessions to ensure appropriate understanding of key issues
- Use of pictorial education materials to assist with understanding
- Frequent clinic visits to monitor adherence closely
- Identification of treatment buddies or second caregivers for backup
- Use of tablets or capsules instead of syrups where applicable
- Incorporating taking of ARVs into the patient's lifestyle.
- Keeping medications in places where they are easily seen
- Planning ahead if overnight travel is anticipated
- Encouraging patients to attend facilities that are geographically closest to them
- Disclosure of HIV status to supportive family / community members
- Mobile ART services
- Linkage to adolescent-friendly services for adolescents
- Home visits
- Moonlight services (providing services after normal working hours)
- Use of mobile technologies (e.g. sending of mobile SMS messages to remind clients of visits)

Both group and individual counselling should be provided for caregivers of children. When appropriate, children should be included in counselling sessions. Adolescents should be included in counselling sessions once they have been fully disclosed to.

Readiness Assessment

ART should be started once readiness has been agreed between the patient (or caregiver) and the health care provider.

The health care team needs to assess a patient's/caregiver's readiness to initiate ART. ART readiness assessments should consider the following:

- General understanding of HIV, AIDS, ARVs, CD4 count/percentage, viral load, and their relationship with health status
- Understanding importance of keeping appointments and adhering to care plan
- When applicable, successful adherence to co-trimoxazole, TB therapy, IPT, or any other chronic medication
- Presence of support network in family/community to assist with treatment adherence and medication reminder
- Understanding roles of different household members in drug administration and relevant household members have been counseled
- Discussion of adherence strategy, including medication schedule and methods for remembering
- Patient's/caregiver's desire and commitment to taking lifelong therapy
- Household conditions of drug storage met

For children and adolescents, collaboration between the child, caregiver and the multidisciplinary team is paramount. The following should be considered during readiness assessment:

- Disclosure status of child
- Commitment of the caregiver(s)
- Cooperation of the child
- Skills for monitoring and supporting adherence by treatment supporter and/or Community Health Worker
- Provision of linkages to community support structures

ARV treatment for children is complicated by:

- Developmental stage and age of the child
- Caregiver-child interaction
- Psychosocial issues
- Use of syrups/inability to swallow pills/tablets
- Caregiver factors
- Disclosure status, particularly for older children and adolescents

A supporter or treatment buddy is strongly encouraged for adults but is not a pre-requisite for the initiation of treatment. The health facility can assist the client to identify a supporter who should live within a walking distance of the patient's home and be older than 12 years. For children, a reliable, consistent caregiver should be identified to give medicines to the child and bring the child for clinic visits. If possible a second caregiver should also be identified to assist with medications when the primary caregiver is unavailable. Older siblings who are not yet adults should not be given the primary responsibility for administering ARVs to younger siblings. Older children and young adolescents should still be supervised by their caregiver in taking their ART.

The patient's readiness to start ART should be documented prior to initiation of therapy. It is important to thoroughly assess and address the patient's psychosocial and economic issues as part of adherence counselling. An adherence contract, including consent for home visits for future adherence assessments should be signed by patients (or caregivers) prior to starting ARV treatment.

SECTION 7.3: MAINTAINING ADHERENCE

Adherence is a lifelong process and continued assessment and education must be done at every opportunity to ensure the success of ART. At each visit, adherence must be assessed using the following parameters:

- ARV pill count or suspension return:
  - In order to perform pill counts, the pharmacy must document the date ARVs were dispensed and the # of pills dispensed. Adherence calculation should be document in the patient's bukana and their file at every visit.

% Adherence = $\frac{\text{(\# Pills taken)}}{\text{(\# Pills prescribed)}} = \frac{\text{(\# Pills given) - (\# Pills remaining)}}{\text{(Daily dose) x (\# Days since refill)}} \times 100$

Example:
On January 1, a patient received 60 pills of AZT/3TC/NVP. Her prescribed dose was 1 tablet of AZT/3TC/NVP in the morning and 1 in the evening (2 per day).
The patient returns for a refill on January 27th (26 days since prescription filled). You count 10 pills left in the bottle. Therefore, she has taken a total of 50 pills (60-10 = 50). She was supposed to take 2 pills per day multiplied by 26 days. She should have taken 52 pills. She missed 2 doses of medication (4%).

$$\% \text{ Adherence} = \frac{\text{(60 Pills given) – (10 Pills left)}}{\text{(2 Pills/day) x (26 Days since refill)}} \times 100 = 96\%$$

- Quantitative questioning:
  - "How many doses of ARVs have you missed over the past 3 days?"
  - "How many doses of ARVs have you missed over the past month?"
- Qualitative questioning:
  - "How well do you take your ARV's?" (can use patient/caregiver to rate adherence on visual analogue scale or rate between 1 [0% adherence] and 10 [100% adherence])
  - "What are the names of your medications?"
  - "How often do you take/give the ARVs?"
  - "What time do you take/give the ARVs?"
  - "How many tablet/pills do you take/give for each dose?"
  - "How much syrup do you take/give for each dose?"

Remember to use a multidisciplinary team approach: Doctor, nurse, counsellor, social worker, laboratory technician, pharmacist, family, friends, support groups, community or village health workers, caregivers, and the PATIENT need to be involved to maintain adherence.

Help the patient/family with adherence by:

- Providing education at every opportunity
- Discussing the importance of adherence at every visit
- Asking the patient/family to name or describe the specific medications (colour, #, size, or amount given)
- If any doses have been missed or adherence is too high (too much medication has been taken) (>105% for pills or >110% for syrups) ascertain the reason
- Asking the patient/family to update you on living conditions and location
- If you expect problems and non-adherence; plan and schedule follow-up

Dealing with Poor Adherence

If adherence is questionable (< 95% for pills and syrups or >105% for pills and >110% for syrups):

- Repeat adherence counselling
- Increase frequency of monitoring
- Identify barriers to adherence and assist with interventions/strategies
- Emphasize the importance of honest reporting of poor adherence (normalize imperfect adherence) in order to explore for pill tossing (e.g. adherence calculations are good clinical status or lab tests suggest poor adherence)
- Performing home visits

In addition to considering the barriers to adherence discussed in Section 7.2, other factors that may contribute to poor adherence and should be investigated include:

- Caregiver illness
- Mental illness (in the child, adolescent, or caregiver)
- Presence of multiple caregivers
- Holiday/vacation travel for patient or caregiver
- Disruptions in the home environment (e.g. visits from extended family who are unaware of patient's positive HIV status)
- Poor communication among family members or between parents regarding the child's HIV status and/or ART schedule
- Treatment fatigue

Other adherence considerations for children include:

Infants and young children:

- Emotional and physical support for caregivers
- Have at least 2 people knowledgeable about the child's medication and available to administer
- Help the family to create a realistic medication schedule
- School-age children:
- Teach them how to count / measure medication
- Help them discover foods that make medications more palatable

Older Children and Adolescents:

- Caregiver's control over the child's treatment should be subtler (one to one; not a public issue)
- Ongoing supervision of medication by caregiver
- Individual counseling with adolescents

TABLE 7.1: UNDERSTANDING AND MONITORING ADHERENCE AND TOOLS TO IMPROVE IT

Reason for non-adherence relating to drugs	Poor palatability and unpleasant flavour
	Amount of pills/solution volume
	Frequency of dosing
	Nausea
	Fear of adverse effects (particularly if prior bad experience)
	Child's refusal
Reason for non-adherence relating to the family or individual	Lack of disclosure in the family and to the child
	Strangers or visitors in the house
	Parental/caretaker illness, mental health, drug/alcohol abuse
	Lack of belief in the value of the treatment
	Cultural, traditional or spiritual beliefs
	Responsibility for giving the medication residing with a specific member of the family
	Poor understanding/knowledge
	Denial
	Lack of food security
	Lack of funding/transport to return to the clinic
Tools for the patient or caregiver	Colour coded bottles and syringes
	Pillboxes
	Diary cards to use as memory aid
	Encourage use of alarms (i.e. in cellular phones)
	Use of modern technologies, such as mobile SMS messages
	Link medication to specific times e.g. meals or television programmes
	Make use of treatment supporters in the community
	Regular visits to therapeutic counsellors
	Early switch to pills from syrups/suspensions
	Treatment buddies
Methods to measure adherence	Calculate pill count adherence at every visit and document in the patient's file and bukana (see above for how to calculate)
	Check for late returns to both the clinic and the pharmacy (use ART card and Appointment Book)
	Ask about problems with specific drugs
	Look at diary cards
The clinic should:	Emphasize adherence at every visit
	Assist with disclosure within the family and to the child
	Help explain to children why they must take the drugs
	Provide or refer the caregiver for psychosocial support
	Assist with financial and food security through grants and referral to appropriate NGOs and departments, such as Social Development and Agriculture
	Support groups; tracing for missed appointments
	Involve Department of Social Development or CGPU in special circumstances, such as child neglect or abuse

- Identify friends/ peer support groups/ older children willing to help
- Provide discreet pill boxes for social events
- Use role play for problem solving

If adherence continues to be poor despite adherence interventions, stopping ART in order to reduce the risk of resistance developing can be considered as a last resort but should only be done in consultation with an experienced HIV physician. Remember not to stop all ARVs at once if using an NNRTI-based regimen; stop NVP or EFV first while continuing the NRTI backbone (e.g. AZT/3TC, ABC/3TC, or TDF/3TC) for one more week in order to reduce the risk of NNRTI resistance due to their long half-life. Re-start ART once barriers have been identified and accordingly addressed.

Adherence Counseling must be:

- Continuous and repetitive; at every visit
- Personalised: Tailored to the needs and situation of each patient
- Universal: Reinforced by all health care providers

SECTION 7.4: ENHANCED OR INTENSIVE ADHERENCE COUNSELLING

ART patients experiencing treatment failure (clinical, immunologic, or virologic) must receive enhanced adherence counselling (EAC) sessions to assess if suboptimal adherence is the primary reason for ART failure. As discussed in Chapter 6.3, poor adherence is the most common reason for treatment failure followed by viral resistance. As a result, EAC sessions should thoroughly investigate a failing patient's adherence and explore for potential barriers to optimal adherence as discussed in Section 7.2 above.

Any member of the health care team who is knowledgeable in ART adherence, adherence counseling, and treatment failure can conduct EAC sessions. This includes, but is not limited to, clinicians (physicians and nurses), counselors (professional and lay), pharmacists and pharmacy technicians, social workers, psychologists, expert patients, and peer leaders. Lower-level cadres also involved in the care of ART patients, such as community health workers, can also participate in the enhanced adherence counselling process.

EAC sessions should begin as soon as treatment failure is identified and a minimum of 3 EAC sessions are recommended over a period of 8-12 weeks. Patients with treatment failure should have close follow-up with visits at the health facility and possibly the home.

The suggested topics to be covered in EAC sessions include:
Explanation of treatment failure and resistance and review of the relationship between viral load, CD4 and clinical status
Inquire about the home situation (who administers the medication, do they do directly observed therapy)
Develop enhanced adherence plan (e.g. re-involve or identify new treatment supporter)
Discuss strategies to mask taste of medications with unpleasant taste
Institute directly observed therapy by an agreed upon person, such as caregiver, treatment supporter, or community health worker
Conduct psychosocial assessment of patient and/or caregiver
Complete a depression screening tool for the patient and/or caregiver
Complete a substance abuse screening tool

If viral load monitoring is available, a repeat viral load should be taken after any adherence issues have been addressed and good adherence has been documented at 2 or more visits.A viral load should not be repeated in the setting of continued poor adherence as it will likely continue to be non-suppressed but a confident determination of whether the viral load is elevated due to poor adherence or viral resistance will not be able to be made (see Figure 6.1 for Viral Load Testing Algorithm and Chapter 6.3 on Treatment Failure).

SECTION 7.5: DISCLOSURE

Disclosure is a situation where information about a client's HIV status is shared with one or more people (spouse, children, parents, friends, caregiver, employer, or other person). A counsellor can help a client develop a plan to share information about his/her HIV status. This involves exploring the options of whom and when to tell. Disclosure is important for promoting the client's adherence to treatment, prevention and care plan.

All patients should be encouraged to disclose their status to family, sexual partners, household members and community members. Appropriate disclosure can help a patient develop a

reliable support network, which can be crucial to successful adherence. Furthermore, disclosure can help fight stigma and encourage others within the family and community to know their HIV status.

Benefits of Disclosure

Disclosure can help reduce stigma and discrimination, as it:

- Enables an individual to begin with the issue of reducing transmission and getting support
- Promotes easy access to care, support and treatment services as well as adoption of safer behaviour to protect family and partners
- Creates a sense of empowerment and control over the HIV infection since the person is able to talk with friends or counsellors for advice and support
- Client can feel confident and no longer has to worry about having to disclose
- Client may be able to influence others to test and get appropriate services
- Openness about HIV status can stop rumours and suspicion.

Skills for supporting clients to disclose include assessing the client's readiness for disclosure:

- Make sure that it is what the client wants to do and assist him/her to plan
- Help the client to take time to make a decision

Assist clients to disclose by encouraging them to:

- Take time to accept their status
- Ensure that they are ready and comfortable to disclose
- Choose someone they can trust and who is likely to support them.
- Choose a time when the person to be disclosed to has enough time to listen and is in a good mood
- Choose a place that is comfortable and private
- Think about how the person will react and plan for their possible response

Empower the client to disclose appropriately and safely by:

- Providing the client with information and support that can help him/her live positively
- Emphasising the need for discussing with sexual partners who need protection against infection.
- Facilitating role plays such as 'empty chair' rehearsals where the individual client practices disclosure alone but pretending that the person is sitting next to him/her in an empty chair
- Emphasising the importance of speaking calmly and clearly

For further details on disclosure, refer to the National HIV Testing Services Guidelines.

Disclosure in Children

Informing HIV-positive children about their status should be age-appropriate and is recommended for all children. Partial disclosure should start gradually from the age of 5 years. Full disclosure to adolescents $\geqslant$10 years old regarding their positive HIV status prior to initiation of treatment is especially important to ensure adherence.

- Ensure that the child's HIV status is known. The child should hear about HIV from the caregiver. The healthcare worker should support the caregiver to provide timely disclosure and appropriate information.
- Honesty is important in child-caregiver relationship
- Children often know the truth before we expect or think they do
- Children often cope with the truth better than we anticipate
- Secrecy may be associated with increased behavioural problems
- Provide the child with a sense of control over his/her life
- The child should know why he/she goes to the clinic and has blood taken regularly
- Remember that it is a child's right to know their status

- Give the child permission to talk openly about HIV with caregivers

Children informed about their diagnosis have better coping mechanisms and higher self-esteem than children who are not disclosed to. In addition, children and adolescents who have been disclosed to tend to have better adherence.

Source: Committee on Pediatric AIDS. Disclosure of illness status to children and adolescents with HIV infection. Pediatrics. Jan 1999.

Disclosure and discussion of the child's illness forms an essential part of regular follow up. An age-appropriate disclosure process and plan should be established for all children. Disclosure is a process and not a single event. Disclosure should be done by the caregiver with assistance from the clinical team.

Process of Disclosure

"Disclosure of HIV infection status to children and adolescents should take into consideration their age, psychosocial maturity, the complexity of family dynamics and the clinical context."

Committee on Pediatric AIDS. Disclosure of illness status to children and adolescents with HIV infection. Pediatrics. Jan 1999.

What the caregiver says during the process of informing a child depends on the following:

- Age of the child
- Maturity of the child
- What the chlid already knows
- Personality of the child
- Illnesses the child has had
- Whether the child is on ART or not
- Health of others in family
- Recent stressors

How disclosure should be done:

- Private location
- Planned in advance
- Guide the child regarding who they can talk to about their status
- Progressive disclosure is preferable to "all at once."
- Provide follow-up support

Disclosure Guidelines by Age

For young children (5-9 years):

- Simple information in a language they can understand
- Discuss:
- Nature of illness
- How they can care for themselves
- The near future

Note that diagnosis and prognosis are not a priority at this stage.

For older children and adolescents (10-19 years old):

- It is recommended that they should be informed of their status
- Discuss and plan disclosure with parents
- First determine what they already know; may ask if they know why they are coming to clinic/getting blood drawn
- Need for correct child assessment
- Information should be specific
- Provide moderate amount of information instead of all at once
- Assist in developing coping mechanisms
- Talk about who/what they can tell others
- Should be informed of their status

Discuss all aspects of the disease:

- Basic nature of the HIV virus and disease progression
- Transmission and Prevention
- Diagnosis and Prognosis
- Self-care and self-medication
- Drug Resistance
- Living Positively and Normality
- Sexual health education

Expect the following possible feelings after disclosure:

- Shock
- Anger
- Sadness/Depression
- Fear
- Confusion
- Rejection
- Isolation
- Relief
- Acceptance

It is important to help children cope with their diagnosis, care and treatment. Ways to help children cope include:

- Problem-solving with the patient
- Empowering them
- Help the child/adolescent take one step at a time
- Reassurance
- Comfort

See Annex 5 for further details on disclosure.

CHAPTER 8: OPPORTUNISTIC INFECTIONS, CO-INFECTIONS & CO-MORBIDITIES

SECTION 8.1: MANAGEMENT OF OPPORTUNISTIC AND CO-INFECTIONS

Introduction

People living with HIV and AIDS are at a higher risk of developing infections and cancers due to their immunocompromised status. The term **co-infection** is used to refer to infections that can interact with HIV to alter its natural history and vice versa.

The term **opportunistic infection** refers to an infection caused by a pathogen that is typically harmless to a normal host but causes severe disease in patients with HIV infection. Opportunistic infections are often associated with advanced or severe immunodeficiency and usually represent WHO clinical stage 3 or 4. Due to an infant's immature immune system, opportunistic infections may occur despite a high CD4 count or CD4 %. Hence HIV-infected children are more susceptible and vulnerable to severe life threatening opportunistic diseases and must be monitored closely and treated aggressively.

Due to an infant's immature immune system, opportunistic infections may occur despite a high CD4 count or CD4%.

Common HIV-associated illnesses are often the presenting clinical manifestations that may lead to the diagnosis of HIV. Although TB is the most common co-infection and is responsible for the highest number of deaths, there are other diseases that should be considered and monitored in patients with HIV. Diagnosis and treatment of opportunistic infections in HIV-infected patients is an essential component of their package of care. Table 8.1 below presents common adult and paediatric OIs; their major presenting signs and symptoms; diagnostic investigations; and subsequent management. Specific infections are discussed in more detail in the remainder of the chapter.

TABLE 8.1- COMMON OPPORTUNISTIC INFECTIONS AND CO-INFECTIONS

Opportunistic Infection	Major Presenting Symptoms	Prophylaxis	Diagnosis	Management	Comments
Oral candidiasis (thrush)	White spots or plaques in the mouth, painful	None	Clinical	Nystatin suspension 100,000 IU 5x daily Miconazole oral gel Fluconazole 200-400 mg stat	Nystatin troches may be used but can be less effective than a single dose of fluconazole or Miconazole
Vaginal candidiasis	Vaginal itching, white creamy discharge	None	Clinical KOH prep	Nystatin or clotrimazole pessaries Fluconazole 200-400 mg stat	Nystatin pessaries are used but can be less effective than a single dose of fluconazole
Oesophageal candidiasis	Retrosternal pain and/or vomiting Difficulty in swallowing	None	Clinical	Fluconazole 200-400 mg daily for 14-21 days (6 mg/kg daily for children)	

Opportunistic Infection	Major Presenting Symptoms	Prophylaxis	Diagnosis	Management	Comments
Pneumocystis jirovecii pneumonia (PCP)	Sub-acute shortness of breath; dry cough; fever; hypoxia; auscultation – normal or rales	CTX (see Section 3.2)	Clinical; Chest x-ray	Adults: Cotrimoxazole two 960 mg tablets tds for 21 days + folic acid Pediatric: 120 mg/kg/day divided QID	If dyspnoea is severe and the patient's clinical status critical, add prednisone 1 mg/kg/day x 5 days then taper to 0.5 mg/kg/day for 16 days
Bacterial pneumonia	Fever, cough, fast breathing, acute onset	CTX	Clinical; chest x-ray	Amoxicillin 500mg TDS for 7-10 days (50 mg/kg/day) Erythromycin 500mg QID for 7-10 days (add pediatric dose)	Admit and give IV antibiotics if severe respiratory distress (see Section 7 or hypoxia
Lymphocytic interstitial pneumonia (LIP), Chronic lung disease	Chronic cough, lymphadenopathy, finger clubbing	None	CXRSputum culture for routine bacteria; GeneXpert to rule out TB	ART Antibiotics as for bacterial pneumonia and salbutamol for symptomatic flares Rule out TB	LIP is a paediatric disease Reticulonodular patter on CXR CLD → bronchiectasis, cystic changes
Mycobacterium avium complex (MAC)/Mycobacterium other than TB (MOTT)	Varied: Abdominal pain; cough; malaise	Azithromycin	AFB culture	Rifampicin Ethambutol Clarithromycin	Associated with very low CD4 (usually < 50) Initiate ART at same time of MAC treatment initiation
Toxoplasmosis	Headache, fever, seizure, focal neurologic signs (facial palsy, hemiparesis), confusion	CTX	Clinical Head CT: ring-enhancing lesions with oedema	Cotrimoxazole 1920 mg BD (60mg/kg/day) for 6 weeks plus folic acid 5mg daily	Consider steroids to reduce oedema
Bacterial meningitis	Fever, headache, confusion, stiff neck, vomiting, bulging fontanelle	CTX	Lumbar puncture Head CT for focal neurologic signs	Ceftriaxone IV/IM 1-2 gm daily (100mg/kg daily) or Chloramphenicol 25 mg/kg QID	Consider head CT if no improvement or continued fevers and evaluation for TB meningitis
Isospora Crypto-sporidium Microsporidium	Persistent diarrhoea	CTX	Stool iodine stain	ART	Ensure good nutrition and rehydration
Giardia	Diarrhoea, bulky, foul-smelling stool, flatulence	CTX	Stool iodine stain	Metronidazole 400mg (10mg/kg) TDS x 5 days	

Opportunistic Infection	Major Presenting Symptoms	Prophylaxis	Diagnosis	Management	Comments
Typhoid	Fever without a focus, abdominal pain, diarrhoea or constipation		Blood or stool culture	Ciprofloxacin 500mg twice daily x 7 days	Complications – peritonitis, perforation
Dysentery	Bloody diarrhoea, abdominal pain, fever, vomiting		Clinical Stool culture	Ciprofloxacin 500mg twice daily x 5 days	Additional antibiotics based on stool culture Ensure hydration
Orolabial HSV	Painful oral or pharyngeal ulcers	Acyclovir	Clinical Tzanck smear	Acyclovir 400mg (25mg/kg) TDS x 10 days	Consider suppresive therapy for recurrent/severeepi sodes (>6/year)
Parotitis	Swelling of parotid gland; pain with mouth movement		Clinical	Analgesics	Associated with LIP and untreated HIV
Acute tonsillitis or otitis media or gingivitis	Fever, pain, swollen tonsils, purulent drainage	CTX	Clinical	Amoxicillin 500mg (50-90 mg/kg/day divided TDS x 5-7 days	If suspect epiglottitis, admit for IV antibiotics
Acute necrotizing ulcerative gingivitis	Ulcerative gingivitis with soft tissue loss of cheek and gums, teeth		Clinical	Ampicillin IV 25mg/kg QID *plus* Gentamycin 7.5 mg/kg daily *plus* Flagyl 10mg/kg TDS	Refer for urgent admission for debridement and reconstruction by Dental
Pruritic papular eruption (PPE)	Itchy papules, 2mm to 2cm		Clinical	Antihistamine Topical steroids if no response	Resolves with immune reconstitution with ART
Scabies	Itchy rash Burrows and papules in webs of fingers, wrists		Clinical KOH prep	Benzyl benzoate applied from neck down overnight and repeated in 1 week (dilute 1:1 with water for children 6 months – 5 years) Infants <6 months: Sulfur ointment nightly for 3 days	Boil clothing and bedclothes Treat family
Varicella (chickenpox)	Itchy popular rash in crops		Clinical Tzank smear	Severe cases: Acyclovir 20mg/kg/dose QID x 7-10 days	Isolate away from other immune suppressed children
Herpes Zoster	Painful vesicles,		Clinical Tzank smear	Acyclovir 800mg (20mg/kg/dose QID x 7-10 days	Monitor for post-herpetic neuralgia

Opportunistic Infection	Major Presenting Symptoms	Prophylaxis	Diagnosis	Management	Comments
	dermatomal distribution			Analgesics	Refer for urgent ophthalmologic exam if rash is near eye or on nose
Molluscum	Umbilicated lesions		Clinical	ART	
Tinea (ringworm)	Round scaly itchy lesions with raised edges		Clinical KOH prep	Clotrimazole cream twice daily (body) 6 wks Griseofulvin 20mg/kg daily (scalp) x 6 wks	Monitor ALT if on griseofulvin and ART and/or ATT Give cloxacillin for superinfected lesions
Kaposi Sarcoma	Reddish-purple or hyperpigmen-ted dark flat or raised lesions on skin or mucous membranes		Clinical Biopsy	ART Chemotherapy (Bleomycin, Thalidomide, Vincristine)	Refer all patients with KS to oncology
Syphilis	Painless genital lesions, rash		Clinical VDRL, RPR	Benzathine pencillin 2.4 MU IM weekly x 3	Treat partner and reinforce condom use
Gonorrhoea, Chlamydia	Burning urethral discharge, Vaginal discharge		Clinical	Ciprofloxacin 500mg po stat **plus** azithromycin 1gm stat *or* Erythromycin 500mg QID x 7 d **plus** metronidazole 400mg BD x 7 days Substitute ceftriaxone 250mg IM stat for Cipro if pregnant	Treat partners and reinforce condom use Do not use ciprofloxacin or doxycycline if pregnant
Genital HSV	Painful anal or genital ulcers		Clinical	First episode: Acyclovir 400mg TID x 10 days Recurrence: acyclovir 400 mg TID x 5 days	Consider suppresive therapy for recurrent/severe episodes (>6/year)
HPV/genital warts	Painless, raised fleshy lesions	HPV vaccine	Clinical	Podophyllin 0.5% twice daily on 3 consecutive days weekly x 4 weeks	If no response to podophyllin, refer for surgical excision or curettage evaluation
Cervical cancer	Vaginal bleeding	HPV vaccine	PAP smear orVIAC Biopsy	Colposcopy Hysterectomy	Early diagnosis improves outcomes

Opportunistic Infection	Major Presenting Symptoms	Prophylaxis	Diagnosis	Management	Comments
HIV advanced nephropathy (HIVAN)	Sub-acute (high blood pressure or oedema rare)		Protein-uria Elevated creatinine	ART Enalapril 2.5mg twice daily	Avoid TDF if CrCl < 50 ml/min or clinical signs of renal failure
CMV	Variable Malaise, visual loss, bloody diarrhoea; Vision loss		Clinical	ART Gancyclovir	Refer for urgent ophthalmology evaluation if concern for CMV retinitis Associated with CD4 < 50
Lymphoma	Malaise, swollen lymph nodes, weight loss		Biopsy	Chemotherapy	

SECTION 8.2: TUBERCULOSIS

TB and HIV are closely interrelated. TB is the leading cause of morbidity and mortality in HIV-infected patients. HIV is the single most important factor fueling the TB epidemic in settings with a high prevalence of HIV infection. Patients infected with HIV infection have a 10% annual risk of developing active TB disease compared to the 10% *lifetime* risk of HIV-negative persons. TB disease occurs through two mechanisms in HIV patients:

1. Reactivation of latent TB infection to cause TB disease due to HIV-related immunodeficiency
2. Rapid progression from recent TB infection (including TB re-infection) to TB disease (this occurs much more frequently in HIV-positive individuals as well as infants and young children regardless of HIV status)

Early diagnosis of TB in HIV-infected patients is critical to ensure prompt treatment and cure of TB, to minimize the negative effects of TB on HIV progression, and halt the TB transmission in the community. Proper case management of TB can prolong the survival of PLHIV. Likewise, early diagnosis of HIV in TB patients will enable early initiation of HIV care and treatment, which has been shown to reduce morbidity and mortality of TB/HIV co-infected patients.

Reducing the Burden of TB in PLHIV

The integration of TB/HIV services is essential for addressing this challenge. The following 3 activities are the pillars of TB control:

- Intensified Case Finding (ICF) and prompt initiation of TB treatment
- Isoniazid Preventive Therapy (IPT) for Latent TB Infection
- Infection Control (IC) for TB in congregate settings

Integration of TB services in the HIV care and treatment settings is key for delivering these services. Providers in HIV services should routinely screen for TB among all PLHIV receiving HIV services and promptly provide TB treatment for identified cases. In settings where integration is not yet implemented, effective referral mechanisms must be established and maintained between the HIV and TB services so that patients are able to access the dual services with ease.

Intensified Case Finding (ICF)

TB cases are routinely detected through passive case-finding, when symptomatic patients present to health services for diagnosis and treatment. Intensified case finding for TB (ICF) differs from passive case finding in that screening and the diagnostic work up for TB are initiated by the provider, leading to earlier TB detection and reducing morbidity and mortality of TB.

HIV-infected persons are at a higher risk of developing TB disease and may present with varied atypical features making the diagnosis difficult, thus the need to implement ICF. This should be done routinely for all HIV-infected patients using the approved national TB screening tool.

HIV-infected patients should be screened for signs and symptoms of active TB at every clinical encounter, including on the day of HIV diagnosis (see Annex 17). Answering 'yes' to one or more question makes a HIV-positive client a presumptive TB case. Diagnosis of TB should be seamlessly integrated into HIV care. Diagnostic tests and procedures to evaluate for active TB disease should be initiated in the HIV clinic for all patients with a positive TB screen. Collection of a sputum sample for GeneXpert MTB/RIF testing is the recommended first-line diagnostic test for all people with HIV with presumptive pulmonary TB. Clinicians should also consider obtaining a CXR although this process should not delay the prompt evaluation and clinical decision making for presumptive TB clients with HIV (see Annex 16 for MOH TB diagnostic algorithm).

ICF should be intimately linked to prompt provision of TB treatment services for people found to have active TB and comprehensive registration of all TB cases and contact tracing of household contacts.

Isoniazid Preventive Therapy (IPT)

Isoniazid preventive therapy has been shown to reduce the risk of active TB disease in persons infected with HIV. It is used to treat latent TB infection and reduce the risk of progression to active TB disease. The risk of developing active TB disease is particularly high during the first six months after ART initiation due to the immune reconstitution that occurs as a result of viral suppression by ART. Given the high prevalence of latent TB infection in Lesotho, every individual with HIV greater than 1 year of age who has no signs or symptoms of TB at the time of HIV testing and/or entry into care should be started on IPT as soon as possible so long as there are no contraindications to IPT present. See Chapter 4.4 for a detailed description of ART.

Infection Control

Persons with undiagnosed, untreated and potentially contagious TB are often seen and managed in health care settings; such frequent exposure to patients with infectious TB disease puts the health worker and other patients at risk of TB infection. Furthermore, HCW and staff may be immunosuppressed themselves and be at higher risks of developing TB disease after TB infection.

Nosocomial transmission of *M. tuberculosis* has been linked to close contact with persons with TB disease during aerosol-generating or aerosol-producing procedures, which include bronchoscopy, endotracheal intubation, suctioning, other respiratory procedures, open abscess irrigation, autopsy, sputum induction, and aerosol treatments that induce coughing.

All health facilities should be made aware of the need for preventing transmission of *M. tuberculosis* especially in settings where persons infected with HIV might be encountered or might work. All HCWs should be sufficiently informed regarding the risk of developing TB disease after being infected with *M. tuberculosis*.

All health care settings should implement a TB infection control plan designed to ensure prompt detection, airborne precautions, and treatment of persons with TB disease. TB infection control

measures can be divided into three categories: managerial/administrative, environmental (or engineering), and personal respiratory protection controls. Healthcare workers should use N95 respirator masks when working with TB patients and TB patients should wear surgical masks while in health facilities. See Chapter 11: Infection Control for additional details.

TB/HIV Co-Infection: Clinical Presentation and Comprehensive Evaluation

The clinical picture of TB varies with the level of immunity of the patient. PLHIV are more likely to present with sputum smear-negative pulmonary TB, disseminated TB, or extrapulmonary TB (EPTB), especially as the immunosuppression from HIV progresses. Therefore, a high index of clinical suspicion is needed to avoid misdiagnosis or delays in TB diagnosis, which may lead to increased morbidity and mortality.

One of the major focuses of the initial history and physical examination of an individual with HIV is to identify signs and symptoms of active TB disease before initiating ART. TB is the most common cause of IRIS after ART initiation; in fact, IRIS can occur in HIV-negative individuals with TB after initiation of TB treatment. TB IRIS can be life-threatening if not recognized promptly and treated appropriately. Evaluating for and excluding TB is especially important in HIV patients presenting with advanced disease (see Chapter 4.9). See below for a more detailed description of TB IRIS.

Signs and symptoms of possible TB infection among people with HIV include (see Table 8.3 for detailed description of common presenting signs and symptoms of various forms of TB):

- History of TB contact
- Cough
- Hemoptysis
- Fever
- Night sweats
- Weight loss
- Failure to gain weight appropriately in children
- Lymphadenopathy
- Poor appetite or anorexia
- Cachexia
- Anemia and, occasionally, pancytopenia

Possible investigations include:

- Sputum for GeneXpert MTB/RIF (first-line diagnostic test in PLHIV with presumptive TB) and acid-fast bacilli (AFB) smear
- Chest x-ray (CXR) – Clinicians can consider obtaining a CXR upon entry into care for all people living with HIV, especially those with advanced HIV given the significant rates of asymptomatic, culture-positive TB observed during surveillance studies. A baseline CXR also allows for comparison at a later point if an initially asymptomatic patient develops TB symptoms at a later time.
- AFB smear or GeneXpert MTB/RIF of non-sputum samples (e.g. lymph node aspirate)
- Culture and drug-susceptibility testing (DST) of sputum, blood, other specimens
- If extrapulmonary TB is suspected, further investigations should be pursued to confirm the diagnosis if possible, including: fine needle aspirates of enlarged lymph node, lumbar puncture, thoracentesis, paracentesis, abdominal ultrasound, spinal x-ray, etc. Specific investigations will depend upon the site of disease. **See National TB Guidelines for details.**

In children, TB disease is difficult to confirm as they typically have fewer TB bacteria present and are unable to expectorate sputum. There should be a low threshold to start TB treatment among children with moderate to high suspicion of TB disease (see Table 8.2). Sputum samples obtained by sputum induction or gastric aspirates should be obtained from all infants and children with presumptive TB for GeneXpert MTB/RIF testing. Adolescents should be coached to produce a quality sputum sample.

TABLE 8.2: DIAGNOSING TB IN CHILDREN

Clinical Suspicion	CXR Findings	Management
High ▪ TB contact and ▪ Clinical signs and/or symptoms	Suspicious	Initiate TB treatment
	Not suspicious	Initiate TB treatment
Moderate ▪ Clinical signs and/or symptoms	Suspicious	Initiate TB treatment
	Not suspicious	Monitor and consider initiating TB treatment if no response to antibiotics; consider other diagnoses
Low ▪ Intermittent clinical symptoms	Suspicious	Monitor and consider initiating TB treatment if no response to antibiotics; consider other diagnoses
	Not suspicious	No TB treatment needed
NB: Due to high morbidity and mortality from untreated TB in children, the unavailability of CXR and/or lab investigations should not prevent a clinician from making a clinical diagnosis of TB in a child and initiating TB treatment		

TABLE 8.3: MANIFESTATIONS AND CLINICAL FEATURES OF TUBERCULOSIS

Form of TB	Symptoms	Signs
Pulmonary	Infants and Children: fever, cough, dyspnea, poor appetite, weight loss Adolescents and adults: fever, cough, sputum production, anorexia, weight loss, night sweats, hemoptysis	Crackles, wheezing, decreased breath sounds
Pleural	Chest pain, cough, dyspnea, fatigue, anorexia, weight loss, night sweats	Decreased breath sounds, dullness to percussion, asymmetric chest movement, pleural rub, decreased vocal resonance and fremitus, bronchial breathing and egophony above the effusion
Peripheral lymphadenitis	Painless, slowly enlarging lymph nodes over weeks to months without erythema or warmth, fever, weight loss, fatigue, night sweats	
Intrathoracic lymphadenopathy	Usually none; rarely causes symptoms associated with extrinsic airway compression or trachea-esophageal fistula formation	
Disseminated, including miliary	Fever, cough, dyspnea, weight loss, anorexia, night sweats, rigors	Fever, cachexia, tachypnea, hypoxemia, abnormal lung exam, hepatosplenomegaly, lymphadenopathy, erythematous macular or papular skin lesions, choroid tubercles
Pericardial	Fever, chest pain, cough, dyspnea, orthopnea, weight loss	Hepatomegaly, jugular venous distension, pulsus paradoxus, pericardial friction rub/knock, ascites, pedal edema
Meningitis	Adults and adolescents: headache, fever, neck stiffness, lethargy, confusion Children: headaches, nausea, abdominal complaints, lethargy, irritability, fevers, convulsions Infants: lethargy, irritability, poor feeding, fevers, convulsions	Stage I (early): nonfocal signs Stage II (intermediate): Brudzinski's and Kernig's signs, tripod phenomenon, cranial nerve palsies Stage III (advanced): hemiplegia or paraplegia, hypertonia, hypertension, hemodynamic instability, decerebrate posturing, seizures, coma

Form of TB	Symptoms	Signs
Tuberculous brain abscess (tuberculoma)	Headache, fever, delirium	Cranial nerve palsies, papilledema, hemiparesis, seizures
Laryngeal	Cough, hemoptysis, odynophagia, hoarseness, pain or weakness with speaking	Laryngeal edema and/or hyperemia; nodular swelling of interarytenoid space, aryepiglottic folds and/or epiglottis; vocal cord paralysis; laryngeal stenosis
Otologic	Painless, persistent and/or recurrentotorrhea, hearing loss, and/or ear pain	Tympanic perforations, thickened tympanic membrane, facial nerve paralysis, bony labyrinthitis
Abdominal (enteritis, peritonitis)	Abdominal pain, weight loss, fever, weakness, nausea, vomiting, anorexia, abdominal distension, night sweats, constipation, diarrhea	Cachexia, abdominal mass, abdominal distension, "doughy" abdomen, ascites, rebound tenderness
Hepatobiliary	Abdominal pain, fever, malaise, fatigue, night sweats, anorexia, weight loss	Right upper quadrant tenderness, hepatosplenomegaly, jaundice, ascites
Kidney, ureters, and bladder	Fever, night sweats, weight loss, dysuria, flank pain, hematuria, urinary frequency/urgency, nocturia	Hematuria, costovertebral tenderness
Fallopian tubes, endometrium, and ovaries	Pelvic pain, infertility, amenorrhea, dysmenorrheal, abnormal uterine bleeding, fever, weight loss, fatigue	Adnexal masses, uterine enlargement
Spinal (Pott's) disease (typically thoracolumbar)	Back and neck pain, weakness, numbness, changes in gait	Flank mass, paraparesis, paraplegia, spinal deformity
Adrenal gland	Fatigue, anorexia, nausea, abdominal pain, diarrhea, arthralgias, myalgias	Orthostatic hypotension, hyperpigmentation
Mastitis	Unilateral breast lump/swelling	

Treatment of TB in PLHIV

TB treatment is similarly effective for both HIV-positive and HIV-negative persons. The same TB regimens used for HIV-negative persons should be used for HIV-positive patients for the the same duration. There is a need for prompt initiation of TB treatment because of the increased morbidity and mortality associated with TB/HIV co-infection.

Enhanced DOTS (support for TB and HIV by same treatment supporter) should be provided to patients with TB/HIV co-infection and comprehensive adherence preparation needs to be provided to both the patient and treatment supporter. This is in view of the increased morbidity and mortality (especially in the initial two months of TB and HIV treatment), increased pill burden, and potential overlapping side effects from concurrent ARVs and TB medications.

Cotrimoxazole

In all HIV-positive TB patients, co-trimoxazole prophylaxis should be initiated as soon as possible after TB diagnosis and given throughout TB treatment. Co-trimoxazole prophylaxis substantially reduces mortality in HIV-positive TB patients. The criteria for stopping co-trimoxazole prophylaxis after the completion of TB treatment are the same as HIV-positive adults, adolescents, and children without TB (see Chapter 4.3).

HIV treatment for TB/HIV co-infected patients

TB/HIV co-infected patients have an increased risk of death before TB treatment is completed; mortality primarily occurs during the first two months of TB treatment. Prompt initiation of both TB and HIV care and treatment is key to reducing mortality rates in TB/HIV

co-infected patients. Even though simultaneous treatment of TB and HIV is associated with drug-drug interactions, overlapping toxicities, greater pill burden with risk of poor adherence, and increased frequency of immune reconstitution inflammatory syndrome (IRIS), the reductions in morbidity and mortality achieved from early initiation of ART far outweigh any adverse events.

When to start ART in TB/HIV co-infected patients

All TB/HIV co-infected patients should be started on ART within 2-4 weeks of TB treatment initiation, irrespective of the CD4 cell count. Similar to HIV patients without TB, clinical assessment is the primary tool used in evaluating TB/HIV co-infected patients; clinical assessments are supported by laboratory tests. The absence of baseline lab results should not delay initiation of TB treatment or ART.

Comprehensive patient preparation should be provided in view of the need for optimal adherence to both TB and HIV treatments. Adherence counselling should be offered on an ongoing basis after initiation of TB and HIV treatments.

What ART regimens to use for TB/HIV co-infected patients

TB/HIV Co-infected Patients Not Yet Initiated on ART

Adults and adolescents (≥10 years and ≥35kg), including pregnant and breastfeeding women

- The preferred 1st-line ART regimen for TB/HIV co-infected adults and adolescents is **TDF + 3TC + EFV**. Efavirenz is the preferred NNRTI in patients on RHZE TB treatment due to the least drug-drug interactions with TB medications

Children 3-9 years or ≥10 years but <35kg

- The preferred 1st line ART regimen for TB/HIV co-infected children 3-9 years old or ≥10 years but <35kg is **ABC + 3TC + EFV**

Children <3 years or ≥3 years but <10kg

- The preferred 1st line ART regimen for TB/HIV co-infected children <3 years or ≥3 years but <10kg is **ABC + 3TC + NVP**. Nevirapine is given instead of lopinavir-ritonavir due to drug-drug interactions between rifampin and lopinavir-ritonavir. Nevirapine must be dosed at the maximum dose of 200 mg/m^2/dose given twice daily due to interactions with rifampin (see Annex 4).
- An alternative regimen for this group is a triple NRTI regimen of AZT + 3TC + ABC, which should be used if the child has a history of failing a NNRTI-based regimen in the past
- After the completion of TB treatment, patients should be switched to ABC + 3TC + LPV/r and children ≥3 years and now ≥10kg should be switched to ABC + 3TC + EFV.

HIV-Positive Patients who Develop TB while already on ART

While TB is common in Lesotho even among HIV-negative persons, HIV clinicians should investigate for ART treatment failure for HIV-positive clients who develop TB after they have been on ART for more than 6 months.

Adults and adolescents, including pregnant and breastfeeding women

- HIV clients already on nevirapine at the time of TB diagnosis should be switched to efavirenz. The NRTIs should not be changed.
- Patients already on efavirenz at the time of TB diagnosis should remain on their ART regimen.
- Protease inhibitors, such as lopinavir-ritonavir, have significant drug-drug interactions with rifampin. HIV-positive adults and adolescents currently taking LPV/r or another

protease inhibitor who develop TB should be assessed for whether their ART regimen can be changed during TB treatment. If there is a history of previous ART failure on a NNRTI-based regimen (NVP or EFV), the protease inhibitor should be continued but additional ritonavir given to provide additional boosting.

- Give additional ritonavir tablets to achieve LPV/RTV dosing of 400/400mg twice daily *or*
- Give double dose of LPV/r (800/200mg twice daily)
- An alternative regimen is to switch to an integrase inhibitor-based second-line regimen for the duration of TB treatment (RAL or DTG)
  - The dose of raltegravir and dolutegravir must be doubled during TB treatment (e.g. raltegravir 800 mg BD and dolutegravir 50 mg BD)
  - After completion of TB treatment, RAL or DTG should be switched to an appropriate PI (LPV/r or ATV/r)

Children 3-9 years or ≥10 years but <35kg

- Children in this age group already on nevirapine-based ART regimen at the time of TB diagnosis should be switched to efavirenz.
- Patients already on efavirenz at the time of their TB diagnosis should remain on the same ART regimen.
- Children in this age group on LPV/r or another protease inhibitor-based ART regimen who develop TB who previously failed NVP or EFV should be switched to a triple NRTI regimen of AZT + 3TC + ABC and an expert HIV clinican should be consulted
  - An alternative ART regimen is to switch the PI to raltegravir for the duration of TB treatment but this should only be done in consultation with an HIV expert

Children <3 years of ≥3 years but <10kg

- Children in this age group on LPV/r at the time of TB diagnosis should be switched to NVP, which should be dosed at the maximum dose of 200 mg/m^2/dose given twice daily due to interactions with rifampin (see Annex 4)
- An alternative ART is a triple NRTI regimen of AZT + 3TC + ABC
- Children in this age group already on NVP at the time of TB diagnosis should remain on their ART regimen and the clinician should ensure the maximum NVP dose of 200 mg/m^2/dose twice daily is given
- After the completion of TB treatment, patients previously on LPV/r should be switched from NVP or the triple NRTI regimen back to LPV/r.

Drug-Resistant TB and HIV

Drug-resistant forms of TB (such as MDR-TB and XDR-TB) have been reported to be more common among HIV-infected populations in some studies. Thus, any patient not clinically or bacteriologically responding to TB treatment after two months who is receiving good DOT should have a culture sent for drug susceptibility testing (DST). For management of patients with suspected or confirmed drug-resistant TB, please refer to the National TB Guidelines.

Immune Reconstitution Inflammatory Syndrome (IRIS)

Following the initiation of ART, the immune system is reconstituted and begins to respond to antigens more vigorously, which may result in a paradoxical reaction with worsening symptoms and signs of an opportunistic infection despite appropriate treatment. This is situation is referred to as immune reconstitution inflammatory syndrome (IRIS). IRIS most commonly occurs in TB/HIV co-infected patients after the initiation of TB and HIV treatment.

IRIS can present in two ways:

- Paradoxical IRIS – a patient is diagnosed with an opportunistic infection, most commonly TB, starts appropriate OI treatment followed by ART, and then develops worsening or new signs and symptoms of their opportunistic infection.

- Unmasking IRIS – a patient is screened for opportunistic infections before initiation of ART and no signs or symptoms of OI are found. The patient then starts ART, followed by onset of new symptoms and signs of an opportunistic infection (most commonly TB).

IRIS usually occurs within the first 2-12 weeks of initiating ART but occur up to 6 months after ART initiation.

The key risk factors for IRIS include the following:

- Severe immune suppression (CD4 count <50)
- High viral load (>100,000 copies/ml)
- Early initiation of ART
- Marked rise of CD4 count and fall of viral load following ART initiation
- Presence of subclinical opportunistic infections

The management of IRIS is to continue treatment for the opportunistic infection as well as HIV and provide supportive management with non-steroidal anti-inflammatory drugs (NSAIDs). Corticosteroids may be used in cases with severe signs. Admit all patients with danger signs. Neither the OI treatment nor ART should not be stopped unless a patient has severe, life-threatening symptoms despite proper IRIS management. Clinicians should explain the possibility of IRIS to HIV patients when initiated them on ART even if they do not have any signs or symptoms of opportunistic infection (i.e. if symptomatic already, developing brief worsening of symptoms before becoming better or, if asymptomatic, developing new symptoms). The presence of IRIS does not mean a patient is failing ART.

Danger signs include, but are not limited to:

- Respiratory distress (RR > 30)
- Fever ($T>39^0$)
- Tachycardia (HR > 120)
- New or worsening adenitis, with obstructive symptoms

IRIS is a diagnosis of exclusion and particular attention should be paid to assess/exclude the following:

- TB treatment failure or drug resistant TB
- ART treatment failure, especially due to poor adherence
- Other opportunistic infections
- Side effects of TB treatment and/or ART
- Drug fever
- Other HIV-related diseases (lymphoma, Kaposi's sarcoma)

SECTION 8.3 MANAGEMENT OF CRYPTOCOCCAL DISEASE

Prevention of Cryptococcal Disease

Patients initiating ART with undiagnosed cryptococcal disease are at higher risk of early mortality than patients who are diagnosed and treated for cryptococcal disease. All patients initiating ART should be clinically screened for evidence of symptomatic cryptococcal disease – headache, neck stiffness, fever, focal neurologic signs, confusion, altered mental status, vomiting. All those who screen positive should be referred for further diagnostic work up for meningitis. Screening of asymptomatic ART naïve individuals with CD4 count <100 cells/mm3 is recommended and should be done with a *Cryptococcus neoformans* antigen test (CrAg) on serum, plasma or CSF. A lumbar puncture should be offered to individuals who screen positive for cryptococcal antigen, as a positive cryptococcal antigen may precede the onset of clinical cryptococcal meningitis by many weeks (see Table 8.4).

Initiate ART 2-4 weeks after initiation of antifungal therapy in individuals who screen positive for serum CrAg without any evidence of disseminated cryptococcal meningitis.

TABLE 8.4: TREATMENT DECISIONS FOR ASYMPTOMATIC CRYPTOCOCCAL DISEASE

Serum CrAg negative	No LP necessary. No fluconazole required. Initiate ART.
Serum CrAg positive	Perform LP.
	If CSF CrAg positive, manage for cryptococcal meningitis (Table 8.6)
	If CSF CrAg negative, treat with Fluconazole 800mg orally once daily for 2 weeks, then Fluconazole 400mg orally daily for 8 weeks, followed by maintenance therapy with Fluconazole 200mg orally daily until CD4>200 cells/mm^3 for 6 months

Treatment of Cryptococcal Meningitis

Cryptococcal meningitis remains a major cause of death in HIV infected patients. Early diagnosis and prompt treatment is critical to improve clinical outcomes. The mainstay of treatment is rapid diagnosis, prompt initiation of appropriate antifungal therapy and management of raised intracranial pressure. Patients at greatest risk of cryptococcal meningitis are those with very low CD4 counts, and clinical suspicion must be high for all patients presenting with headaches, confusion, altered mental status.

Diagnosis of cryptococcal meningitis is made by lumbar puncture. Lumbar puncture is both diagnostic and therapeutic. Elevated opening pressure is characteristic of cryptococcal meningitis. If a manometer is not available, intravenous tubing and a tape measure may be used to measure the column of CSF fluid. CSF samples can be tested for cryptococcus by India ink staining and/or CSF cryptococcal antigen test. Sensitivity and specificity for India ink staining are not as high as cryptococcal antigen testing, and a negative test does not exclude cryptococcal meningitis in the right clinical setting.

Treat cryptococcal disease with amphotericin B based regimens. Combination therapy with amphotericin B and fluconazole is strongly recommended. In the absence of amphotercin B, high dose fluconazole can be used as alternative therapy (See Table 8.5). Therapy is characterized by a 2-week induction phase, followed by an 8-week consolidation phase, and maintenance therapy which is continued until adequate immune reconstitution is achieved.

Management of Raised Intracranial pressure

Mortality and morbidity from cryptococcal meningitis is high with a significant proportion attributable to raised intracranial pressure. Management of raised ICP is critical to ensure good clinical outcomes. If the intracranial pressures is >25cm of water, remove 10-30ml of CSF and continue with daily lumbar punctures until CSF pressures have normalized (<25cm of water). Lumbar puncture should be performed even if manometer is not available. Doctors can monitor pressure clinically. Failure to adequately manage intracranial pressures can result in persistent headache, cranial nerve abnormalities which include hearing loss, vision loss, and death.

TABLE 8.5: RECOMMENDED THERAPY FOR CRYPTOCOCCAL MENINGITIS

	Treatment phase	Regimen	Duration of therapy
Preferred	Induction phase	Amphotericin B 0.7-1mg/kg/day IV + Fluconazole 800mg orally once daily	2 weeks
	Consolidation phase	Fluconazole 800mg orally once daily	8 weeks
	Maintenance/Secondary prophylaxis	Fluconazole 200mg orally once daily	Until CD4 count >200 cells/mm^3 for 6 months
Alternate	Induction Phase	Fluconazole 1200mg orally once daily	2 weeks
	Consolidation Phase	Fluconazole 800mg orally once daily	8 weeks
	Maintenance/Secondary prophylaxis	Fluconazole 200mg orally once daily	Until CD4 count >200 cells/mm^3 for 6 months

Management of Amphotericin B associated toxicities

Amphotericin B is associated with renal tubular toxicities and can lead to electrolyte abnormalities such as hypokalemia and hypomagnesemia. It can also result in anaemia and administration-related febrile reactions.

- Amphotericin B is often provided as a powder and should be mixed with 5% dextrose water. **It should never be mixed with normal saline or half normal saline as this will result in precipitation of the amphotericin B.** To minimize renal toxicities, administer slowly over 4 hours.
- Prehydration with 500ml-1L of normal saline with 20mEq of potassium chloride is recommended based on the volume status of the patient.
- Provide oral potassium supplementation – e.g. 1200mg twice a day. The potassium supplementation minimizes the extent of hypokalemia that can develop. Where available, supplementation with magnesium trisilicate 500mg orally twice daily is also recommended. Potassium and magnesium replacement should be started along with amphotericin instead of waiting until electrolyte deficiencies occur.
- Renal function must be monitored at baseline. Monitor renal function (urea & electrolytes) twice weekly.

If the creatinine doubles, a dose of amphotericin B can be omitted, and prehydration increased to 1L of normal saline every 8 hours and creatinine rechecked. If creatinine normalizes, prehydrate with IL normal saline with 20mEq KCL and restart at amphotericin B (0.7mg/kg/day) given over 4 hours.

If repeat creatinine remains elevated or continues to increase, amphotericin B should be discontinued and high dose fluconazole 1200mg orally once daily initiated. Monitoring of haemoglobin at baseline and weekly is also recommended.

Timing of ART in Cryptococcal Meningitis

Early initiation of ART is recommended for all OIs, except for intracranial OIs such as TB meningitis and cryptococcal meningitis. In cryptococcal meningitis ART can be initiated 2- 4 weeks after initiation of antifungal therapy with amphotericin B based regimens. In patients who are predominately treated with fluconazole monotherapy, ART should be initiated at least 4 weeks after initiation of antifungal therapy.

ART should not be commenced at the same time that amphotericin B and/or fluconazole therapy is commenced for cryptococcal meningitis as the risk for IRIS is extremely high and can be fatal with intracranial infections due to excessive swelling leading to herniation.

SECTION 8.4 *PNEUMOCYTIS JIROVECII* PNEUMONIA (PCP)

Pneumocystis jirovecii pneumonia is caused by a fungus, *Pneumocystis jirovecii*, which is common in the environment and does not cause disease in immunocompetent people.

Clinical presentation and diagnosis

Diagnosis of PCP is mainly clinical, and patients commonly present with sub-acute onset and progression of shortness of breath, non-productive cough and chest pain. Fever is not always present but can be high. PCP is common in HIV-infected children and may be the presenting condition. The peak age for PCP in children is six months, and any exposed infant with presumptive PCP disease needs an immediate DNA PCR to confirm HIV infection status.

Patients commonly have severe immunosuppression, CD4 <200 cells/mm^3, or CD4% <15% in infants and young children. Physical examination shows tachycardia, increased respiratory rate ± rales. Hypoxia is common, and cyanosis may be present. Auscultation may be normal in many cases and in the presence of hypoxia should raise the suspicion of PCP.

Chest X-ray findings: often bilateral symmetrical interstitial infiltrates ("ground-glass" appearance) but may be normal in up to 30% of cases.

Treatment

High dose cotrimoxazole: 120mg/kg/day in 3 divided doses for 21 days (typical adult dose is 2 double –strength tablets three times a day).

Alternatives: Dapsone 100mg once daily + Trimethoprim 5mg/kg/day TID for 21 days or Primaquine 15-30mg once daily + clindamycin 600mg IV 6 hourly for 21 days.

Patients with severe disease (PaO_2 < 70 mmHg at room air) should receive corticosteroids (prednisolone 40mg twice daily for 5 days, then 40 mg once daily for 5 days, then 20 mg once daily for the remaining 11 days of antibiotic therapy).

Secondary prophylaxis with cotrimoxazole 960mg once daily should be given until the patient is stable on ART with immune recovery - CD4 > 350 cells/mm^3 for six months.

SECTION 8.5 OTHER HIV-ASSOCIATED ILLNESSES

Hepatitis B

TDF-3TC based regimen is preferable for patients with HIV/HBV co-infection as both drugs are also active against hepatitis B. All patients need baseline screening for hepatitis B (HBsAg) and vaccination if no infection is detected. When switching patients with hepatitis B infection to second-line regimens, close monitoring for worsening of hepatitis B status should be done. Start ART in all HIV/HBV-coinfected individuals irrespective of the CD4 cell count or WHO clinical stage.

Syphilis

Syphilis is a common sexually transmitted disease that can occur in the presence of HIV infection. All HIV-infected patients over 12 years of age should have a baseline RPR or VDRL test done and be treated with benzathine penicillin 2.4 MU IM every week for 3 consecutive weeks if the test is positive. Patients with presumed neurosyphilis need additional investigation and treatment with aqueous Penicillin G 3-4 MU IV q4 hours x 14 days. Point-of-care tests for syphilis are now available and should enable timely treatment.

Human papilloma virus

HPV has been linked to cervical cancer; a major cause of morbidity and mortality among women with HIV. For this reason, all sexually active HIV-infected women should undergo yearly cervical cancer screening. The HPV vaccine is given to all girls from 9-15 years as part of cervical cancer primary prevention.

Other Sexually Transmitted Infections

Patients with HIV are at an increased risk of contracting other STIs. Conversely, other STIs (especially ulcerative ones such as HSV) may increase the risk of HIV transmission. Patients should therefore be asked a series of screening questions at each encounter regarding the presence of genital ulcers and/or discharge and managed accordingly. Refer to National Guidelines for Syndromic Management of STIs for more details.

SECTION 8.6 MENTAL HEALTH PROBLEMS IN RELATION TO HIV

Mental health problems such as depression, anxiety, substance abuse and confusion are more common in PLHIV and can be a significant contributor to poor adherence to treatment.

DEPRESSION

Depression is linked to the psychological impact of HIV status on the patient or from a close relative (child, parent, spouse) and may impair adherence to treatment. Symptoms of major depression are chronic (at least 2 weeks) and impact the patient's life.

The main criteria are a pervasive sadness and a lack of interest in daily activities. Additional symptoms include:

- Significant loss of appetite. If depression is untreated, patients will also lose weight.
- Insomnia, with early waking
- Psychomotor retardation or agitation (uncommon)
- Significant fatigue
- Difficulty concentrating or making decisions
- Feeling guilty, worthless, despair
- Suicidal ideation

Treatment involves a combination of cognitive/behavioural therapy and medication. Exclude any other causes of depression: hypothyroidism, Parkinson syndrome, Efavirenz intolerance (associated with insomnia, nightmares, loss of memory), recent family death, etc.

Pharmacological treatment is often needed and speeds recovery. Many patients benefit from 3-6 month courses of therapy, but some will need longer-term treatment. Medication is encouraged for those with suicidal ideation, repeat episodes of depression and insufficient response to psychological support alone. All patients on anti-depressant medication also benefit from psychological support, and combination therapy is highly recommended.

Selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine are the drugs of choice. Dosage is 10-20mg daily initially but can be titrated up to 60mg daily. Older anti-depressants such as amitriptyline may also be considered. Dosage is 25mg initially but may be titrated up to 100mg daily. Lower doses should be used in older patients. In patients with combination depression and anxiety, diazepam 5 to 10 mg/day in 2 divided doses can be added during the first two weeks of anti-depressive treatment.

Weekly consultations the first month are necessary, to follow the symptoms, the side-effects and to refill medications. It is recommended to not prescribe too many tablets initially due to risk of suicide. The treatment should always be stopped gradually, over a 2-week period for fluoxetine and a 4-week period for amitriptyline.

GENERALISED ANXIETY DISORDER

Symptoms: feeling tense; nervous with poor concentration; restlessness; agitation; termers; sleep disturbances; palpitations; dry mouth or dizziness.

Mostly anxiety is associated with depression.

Management:

- Detailed history taking and physical examination.

- Mental state assessment.
- Rule out medical condition mimicking symptoms like Thyroid disorders; adrenal tumours; hypertension or cardiac dysrhythmias.

Drug treatment:

- Treat underlying medical condition if found.
- SSRI- Fluoxetine/ paroxetine 20mg daily for 3-4 months; night time if insomnia Diazepam 2-5 mg at night for a week.
- Alternatively, amitriptyline 25mg – 75mg daily in divided doses.

Provide counselling and support. Treatment is based on psychosocial support and counseling. Involvement in support groups is also helpful. Some patients will benefit from medication like diazepam.

SUBSTANCE ABUSE DISORDERS

Use of alcohol or other drugs is a common reason for poor adherence. Management involves regular support counseling. Co-morbid depression or anxiety should be diagnosed and treated.

Acute Psychosis:

Symptoms include: restlessness, agitation, shouting, aggressive and violent behaviour, running away, destructive to property, setting fire to house and property, illogical, irrational and irrelevant talk, sees and hears voice from nowhere, and poor hygiene.

Management:

- Brief history taking from relative/ escortee.
- Physical examination if possible.
- Look and note injuries.

Drug Treatment:

- Inj. Haloperidol 5mg I/M.
- Inj. Diazepam 5-10mg I/M; repeat inj if necessary after 4-6 hrs.

Once patient is calm and cooperative do thorough physical examination and laboratory investigations including radiological investigation.

Start Oral treatment:

- Haloperidol 5mg twice daily or Risperidone 2mg – 4mg daily orally in divided doses.
- Watch for extra pyramidal symptoms like termers, stiffness in lounge, rolling of eye balls and excessive salivation. If there are extrapyramidal side effects, give Artane 2mg twice a day or Akineton 2mg twice a day.

Patients with organic brain syndrome are very prone to develop severe side effects like EPS, tardive dyskinesia and neuroleptic malignant syndrome

CONFUSION

Confusion, disorientation in time and space, impaired consciousness, concentration problems, may all be associated with HIV infection. The cause is often organic: cerebral toxoplasmosis, meningitis or encephalitis, or medication side-effect: Efavirenz (rare). Identification and treatment of the underlying cause is essential. Direct HIV effects will improve with ART.

HIV/AIDS related Dementia:

Symptoms: Memory impairment in abstract thinking and judgement; loss of attention and concentration; restlessness, agitation and wandering around; suspicious and accusing people around; motor imbalance, lack of coordination or urinary incontinence.

Management:

- Detailed history and previous medical record and medications

- Medical examination/neurological examination
- Lab investigations: urea and electrolytes, thyroid functions, L F T, Serum B12 and folic acid level, Lumber puncture if indicated, CT / MRI of brain.
- Treatment of medical conditions: urinary or respiratory tract infection, cardio pulmonary dysfunctions, R/out sub dural haematoma.

Drug treatment:

- INJ. haloperidol 2.5 – 5mg I/M; Inj Diazepam 5mg. I/M.
- Start oral treatment when pt. is calm and co-operative: Haloperidol 2.5 – 5mg twice a day or Risperdal 2mg- 4mg daily orally.
- Watch for extra pyramidal symptoms if it appears then Artane 2mg twice a day orally.

Other measures: frequent reminders of time and place to patient to reduce confusion; assess ability to perform daily task; reduce stress in care givers in long term management.

SECTION 8.7 MALIGNANCY AND HIV

Kaposi's sarcoma

Kaposi's sarcoma (KS) is the most common malignancy in patients with HIV infection. HIV-associated KS does not have a preferential pattern of localization and may affect all skin and mucous membranes. Lymph nodes and internal organs such as stomach, gut, lung or liver may also be involved. The progression of HIV-associated KS is variable: the tumors can remain unchanged for months to years, or grow rapidly within a few weeks and disseminate.

Typical findings at manifestation are a few asymptomatic purple macules or nodules. Rapid growth can lead to localized pain and a discoloration of the area around the tumor as a result of hemorrhage. Further progression of the tumor can lead to central necrosis and ulceration. The tumors may bleed easily. Plaque-like and nodular KS lesions often become confluent and can be accompanied by massive lymphoedema. In the oral cavity, the hard palate is frequently affected. Lesions begin with purplish erythema and progress to plaques and nodules that ulcerate easily. KS lesions may also involve the external genitalia including the foreskin and glans penis.

Diagnosis

Diagnosis of cutaneous KS is usually made based on clinical findings. However, in all inconclusive or questionable cases a histologic diagnosis is recommended. Differential diagnosis includes other neoplasia such as cutaneous lymphomas or angiosarcoma, but also infectious diseases such as syphilis and bacillary angiomatosis. Histological findings include spindle-shaped cells with vascular channels lined by abnormal endothelial cells.

In all cases of KS, clinical staging procedures are recommended, including:

- Complete inspection (oral and genital mucous membranes)
- Abdominal ultrasound
- Gastroduodenoscopy and colposcopy (both procedures obligatory when mucous membranes are involved)
- Chest radiography (exclusion of a pulmonary KS)

Treatment

If KS is newly diagnosed in an HIV-infected patient naïve to antiretroviral therapy, ART should be initiated: in early KS, additional chemotherapy is only required in 20% of adult cases. With viral suppression and immune reconstitution, many KS lesions stabilize or even resolve completely without specific treatment. In contrast, children with KS almost always need chemotherapy in addition to ART. Patients with KS should be referred to an oncologist to determine regimen and timing of chemotherapy.

Cervical intraepithelial neoplasia (CIN) and cervical cancer

In Sub-Saharan Africa, cervical cancer is the most common cancer in women aged below 35 years. Worldwide, however, cervical cancer is the second most common cancer in women. The incidence of some HIV-associated cancers, including Kaposi sarcoma and non-Hodgkin lymphoma, has fallen markedly in populations who have been treated with ART. In contrast, the incidence of cervical cancer has not changed significantly. Women with HIV infection are more likely to have infection with HPV 16 or 18 and to have a higher prevalence and incidence of CIN than HIV-negative women.

Diagnosis and management

Women with HIV and invasive cervical cancer should be managed in the same manner as HIV-negative women, according to specialized guidelines. Diagnosis is based on histopathological examination of cervical biopsies, and clinical staging. Regular screening allows for early diagnosis and treatment of cervical cancer. See National Guidelines for Cervical Cancer Screening for additional information.

Malignant lymphomas

Malignant lymphomas are neoplastic diseases of the lymphatic system that grow rapidly and aggressively, and lead to death within a few weeks or months if left untreated. Hodgkin's lymphoma (HL) is distinguished from the large group of non-Hodgkin's lymphomas (NHL). In comparison to the general population, HIV-infected patients are affected significantly more frequently by all types of lymphoma. Aggressive non-Hodgkin's lymphomas of B-cell origin are particularly frequent. The incidence of lymphomas has been markedly reduced by the introduction of ART.

Malignant lymphomas in HIV-infected patients are also biologically very heterogeneous and differ in several aspects. The extent of immunodeficiency also varies significantly. Burkitt's lymphoma and Hodgkin's lymphoma frequently occur even when immune status is good. In contrast, immunoblastic and primary CNS lymphoma (PCNSL) are almost always associated with severe immunodeficiency. It has also been noted that HIV-associated lymphomas – both NHL and HL – have numerous common clinical features. Characteristics include the usually aggressive growth, diagnosis in advanced stages with frequent extranodal manifestations, poorer response to treatment, high relapse rates and an overall poor prognosis. The treatment of such cases should follow the recommendations for HIV-negative patients in specialized centers.

Systemic non-Hodgkin lymphomas (NHL)

A close association between systemic NHL and AIDS has been described for a long time. More than 90% of HIV-associated NHLs are of B-cell origin. They are almost always of high-grade malignancy. Two main histological types dominate: Burkitt's lymphomas, which comprise 30–40% of cases, and diffuse large-cell B cell lymphomas, comprising 40–60%.

Prevention and early detection

There is no data supporting specific therapies or diagnostic procedures for prevention or early detection of malignant lymphomas. Antiretroviral therapy seems to be the best protection against lymphoma. ART not only improves the immune status but it also reduces chronic B-cell stimulation, a risk factor for the development of lymphoma. Viral suppression is important as cumulative HIV viremia is an independent and strong predictor of AIDS-related lymphoma among patients receiving ART.

Signs and symptoms

The main symptom is lymph node enlargement. Lymphomas are firm, immobile or barely mobile and painless. A large proportion of patients have advanced-stage lymphoma at the time of diagnosis. B symptoms with fever, night sweats and/or weight loss are found in the

majority of cases (60–80%). General asthenia, significant malaise and rapid physical deterioration are also frequently seen.

Diagnosis

Rapid histological diagnosis is essential. If bone marrow biopsy cannot secure the diagnosis, then excision lymph node (e.g., cervical, axillary or inguinal) biopsy is recommended. All patients with suspected NHL should be staged. Basic diagnostic tests for staging include chest radiography; abdominal ultrasound; CT scans of the neck, thorax and abdomen; and bone marrow biopsy; aspiration alone is not enough. In addition to an updated immune status and viral load, the following should be determined at the very least: blood count, ESR, CRP, uric acid, LDH, liver and kidney parameters and electrolytes. ECG and echocardiography are also important right away.

Therapy

Due to extremely rapid generalization, even "early stages" move quickly. Every HIV-associated lymphoma is considered aggressive and requires systemic chemotherapy with a curative intent. Surgery or radiation therapy alone is not sufficient. Treatment should be started rapidly due to the aggressive nature of these lymphomas.

Special entities of lymphoma

Burkitt's lymphomas: the particularly high proliferative capacity and aggressiveness of Burkitt's lymphomas is a problem even in HIV-negative patients. Specific chemotherapy regimens are recommended.

Plasmablastic lymphomas: are relatively "new" entities in HIV-infected patients. Plasmablastic lymphomas probably belong to the diffuse large cell NHLs, but display a completely characteristic immune phenotype. The oral cavity is the site of involvement, although extra-oral manifestations do occur. Like Burkitt's lymphoma, plasmablastic lymphomas have a very high rate of proliferation and are extremely aggressive. Prognosis remains poor.

Primary effusion lymphoma (PEL): a relatively rare entity, also called body cavity lymphoma. These lymphomas are often very difficult to diagnose histologically. A visible tumor mass is usually absent, and malignant cells can only be found in body cavities (e.g., pleural, pericardial, peritoneal). Every pleural or pericardial effusion occurring in an HIV-infected patient and containing malignant cells is suspicious of PEL. The involved pathologist should always be informed about this suspicion. Recent reports indicated encouraging results with a combined chemotherapy with high-dose methotrexate.

Primary CNS lymphoma

Primary CNS lymphomas (PCNSL) are a late complication of HIV-infection and were previously seen in up to 10% of AIDS patients. Histologically, findings are consistent with diffuse large cell non-Hodgkin's lymphomas. CD4 is almost always below 50cells/mm^3 at the time of diagnosis. In the pre-HAART era, PCNSL had the poorest prognosis of all the AIDS-defining illnesses, with a median survival of less than three months. In more recent years, this bleak picture has changed significantly. In the ART era, survival may be several years and complete remission has become possible.

Signs and symptoms

Different neurological deficits occur depending on the location. Epileptic seizures may be the first manifestation of disease. Personality changes, changes in awareness, headaches and focal deficits such as paresis are also frequent. Fever is usually absent. As patients are almost always severely immunocompromised, constitutional symptoms may mask the real problem.

Diagnosis

Cranial CT or (better) MRI should be performed rapidly. The most important differential diagnosis is cerebral toxoplasmosis. A solitary mass is usually more indicative of PCNSL. However, 2–4 lesions may be present, which are usually fairly large at more than 2 cm in diameter. More than four lesions of a PCNSL are rarely found. In addition to the physical examination, a minimal diagnostic program (chest radiography, abdominal ultrasound) should clarify whether the CNS involvement is secondary to systemic lymphoma. This should always include fundoscopy to exclude ocular involvement (up to 20%).

Treatment

Cranial radiation therapy is only option for patients with PCNSL, independent of HIV status. All patients with PCNSL should be treated intensively with antiretroviral therapy, to achieve the best possible immune reconstitution.

Hodgkin's disease (HD)

The incidence of HD is elevated in HIV-infected patients by a factor of 5–15 compared to the HIV-negative population. Worrisome data indicate that the incidence of HIV-related HD is increasing in the setting of improved immunity. An advanced stage of disease at diagnosis is typical, as is frequent extranodal involvement and a trend towards prognostically poorer subtypes. Mediastinal disease is significantly less frequent than in HIV-negative patients.

Signs and symptoms

B symptoms occur in the majority of cases. Extranodal and advanced stages are almost always the rule. Lymphomas are firm, immobile or hardly mobile and painless, and the distinction from HIV-related lymphadenopathy or tuberculous lymphadenitis is not always possible.

Diagnosis

Staging is necessary as for non-Hodgkin lymphomas. Diagnostic lymph node excisional biopsy is even more important here than with NHL. As with NHL, specimens should be sent to reference laboratories if possible.

Treatment

Risk-adapted treatment strategy in patients with HIV-related HD in accordance with standard treatment procedures established for HIV-negative patients is recommended.

Non-AIDS-defining malignancies

HIV-infected patients have an increased risk of cancer. The risk for non-AIDS-defining malignancies is approximately two to three times higher in HIV-infected patients than in the non-infected population.

Anal carcinoma

Infections with human papilloma virus (HPV) are among the most frequently sexually transmitted virus infections. HIV-infected patients have a 2-to 6-fold higher risk for anal HPV infection, independent of gender and sexual practices.

Testicular tumors

Testicular tumors are the most frequently occurring cancer in men between 20 and 35 years of age. The relative risk factor for HIV-infected patients in the same age group is 2.5-fold. HIV-infected patients should be treated with the standard regimens that are also recommended for negative patients. Treatment should be performed in cooperation with a urologist experienced in oncology and an HIV specialist.

Lung cancer

In the general population, lung cancer is the most frequent cancer disease that leads to death in male patients. This tendency is increasing in women and already ranks third. The risk seems to be rising with HIV-infected patients. Overall risk seems to rise as immunodeficiency worsens.

CHAPTER 9: NUTRITION AND HIV

Introduction

The *2013 Mid-Term Review of the Lesotho National HIV and AIDS Strategy* revealed that food insecurity was increasingly becoming an important driver of the HIV epidemic. Poverty and food insecurity in Lesotho are further fuelled by high HIV prevalence. The link between HIV and nutrition is often described as a vicious cycle: both malnutrition and HIV weaken the immune system. HIV infection increases nutrient requirements and at the same time impairs nutrient intake and absorption. On the other hand, poor nutrition increases the risk of opportunistic infections and accelerates the progression of HIV and AIDS.

Good nutrition is an important component in the comprehensive care of people living with HIV. Additional intake enhances immune rehabilitation and adherence to ART. PLHIV will therefore benefit from referral to supplementary food programmes.

Macronutrients

The major cause of HIV related weight loss and wasting is a combination of low energy intake and increased energy demands as a result of HIV and related infections. Energy requirements increase by 10% to maintain body weight and physical activity in asymptomatic HIV-infected adults and growth in asymptomatic children.

Symptomatic HIV-infected adults have to increase their energy intake by 20 to 30% whereas children experiencing weight loss need an additional 50% to 100% energy intake on top of their normal requirements.

Micronutrients

PLHIV should consume diets that ensure micronutrient intake meets the recommended daily allowance (RDA) levels. Multivitamin and mineral supplementation should be considered for those at risk of vitamin or mineral deficiencies.

HIV-Infected Children

HIV-infected children should be routinely assessed for nutritional status, including weight and height at scheduled visits. Nutritional assessment and support should be an integral part of the care plan for any HIV-infected infant or child, irrespective of whether the child is on ART. Several anthropometric indices are used to assess nutritional status in children: weight for age (underweight), weight for height (wasting), and height for age (stunting). All indices are compared against a reference population of healthy children.

Poor growth is reported in as many as 50% of HIV-infected children. HIV infection adversely affects pregnancy outcome; infants born to HIV-infected women have significantly lower mean birth weight and length, regardless of the infants' HIV status, compared with infants born to uninfected women. Pediatric HIV further reduces birth weight. Progressive stunting, that is, proportionately decreased linear and ponderal growth, appears to be the most common abnormality in perinatally infected children and is accompanied by preferential decreases of fat-free or lean body mass. Although data are inconsistent, deficiencies of several micronutrients with the potential to affect growth adversely have been identified, including that of vitamin A.

To define malnutrition in a clinical setting, wasting is a commonly-used indicator. It is defined by weight (kg) for height (cm) in standard deviations from the median (Z-score) or percentage of the median, as indicated below. In addition, mid-upper arm circumference (MUAC) may be used for assessment of nutritional status of infants and children 6-59 months of age (see below). A child who falls into moderate malnutrition should be enrolled on supplementary feeding (super cereal), while the one who falls into severe malnutrition should be enrolled on therapeutic feeding based on the following: if there are no complications give Plumpynut

(RUTF), in case there are complications admit and give F75 or F100. See Annex 12 for reference values for weight for length/height Z-scores (to assess the degree of malnutrition) and Annex 13 for the dosing of RUTF in children. Refer to the National Guidelines for the Integrated Management of Acute Malnutrition for further details.

TABLE 9.1: Z-SCORE AND MUAC INTERPRETATIONS

Definition	Z Score Range	MUAC (cm)	Comment
Normal	Median to -1 SD		
Mild wasting	-1 to -2 SD ≤1 SD to ≤ 2 SD (Between -1SD and 2SD)	-	
Moderate wasting	≤-2 to ≤-3 SD (Between -2SD and -3SD)	11.5 – 12.5	Supplementary feeding (CSB/super cereal)
Severe wasting	Below -3 SD	< 11.5	Inpatient if complications (loss of appetite, oedema) If no complications give RUTF (plumpynut)

Infant Feeding and Maternal Nutrition in the context of HIV

The nutrition of children is critically important. Safe Infant feeding practices can reduce the likelihood of MTCT and the risk of infant death from malnutrition and other childhood infections. Furthermore, women have the right to full information to help them decide how to feed their children and to appropriate support.

Infant feeding counselling should begin during pregnancy to enable HIV-infected pregnant women to make informed infant feeding decisions. Every HIV-infected mother should receive counselling which includes general information about the risks and benefits of the various infant feeding options and specific guidance on selecting the option most suitable for her particular situation including her health status and home environment.

Feeding for Infants ≤ 6 Months of Age

- **Exclusive breastfeeding is recommended for the first six months of life.**
- As life-long ARVs will be given to HIV-infected lactating women, the infant should be given daily Nevirapine (NVP) from birth until 6 weeks of age
- Replacement feeding (with commercial infant formula) should only be given to HIV-exposed infant if **all** of the following conditions are met:
  - Safe water and sanitation can be assured at the household level and in the community
  - The mother or other caregiver can reliably provide sufficient infant formula milk to support normal growth and development of the infant
  - The mother or caregiver can prepare the milk cleanly and frequently enough so that it is safe and carries a low risk of diarrhoea and malnutrition
  - The mother or caregiver can exclusively give infant formula milk for the first six months
  - The family is supportive of the practice
  - The mother or caregiver can access health care that offers comprehensive child health services
- For details on how to assess whether the mother meets the above conditions please refer to the National PMTCT Guidelines.
- All mothers should be counselled on the management of breast conditions such as

nipple cracks, fissures, etc., and on how to cope with breastfeeding difficulties.

HIV can be transmitted from the mother to the infant during breastfeeding. However, the risk can be reduced to a minimum by providing antiretrovirals to the mother and infant and by feeding the baby **exclusively** with breast milk for the first 6 months. **Exclusive breastfeeding means that nothing else (i.e. water, porridge, etc.) should be given to the infant.** Prescribed medications can be given.

Benefits of Exclusive Breastfeeding

- Breast milk provides complete nutrition for the infant for the first six months of life
- Colostrum, the milk produced during the first few days of the infant's life, is rich in vitamins and antibodies. It has other anti-infective properties as well.
- Breast milk contains antibodies from the mother which are beneficial to the infant as the infant's own immune system is not yet completely developed during the early months of life.
- Breast milk provides vital protection against deadly childhood illnesses such as diarrhoea and respiratory infections.
- Breast milk is easily digested and its composition changes to meet the developmental needs of the growing infant.
- Breast milk contains enzymes that help in the digestion of fat.
- Breast milk is natural and does not add extra costs.
- Breastfeeding promotes bonding between mothers and their babies.
- Breastfeeding helps the uterus to contract after delivery and reduce the risk of post-partum haemorrhage.
- Breast milk is always available and no special preparation is needed.

Challenges of Exclusive Breastfeeding

- Exclusive breastfeeding can be difficult, particularly for mothers working away from home
- It may be difficult to withstand family or community pressure to give other liquids or foods
- The mother requires additional calories to support breastfeeding

Benefits of Replacement Feeding with Commercial Infant Formula

- There is no risk of HIV transmission to the baby
- Commercial infant formula contains most of the nutrients an infant needs
- Other people (besides the mother) can feed infant

Challenges of Replacement Feeding with Commercial Infant Formula

- The infant does not benefit from the protective effects of colostrum
- Infant formula does not contain the antibodies found in breast milk
- There is an increased risk of diarrhoeal illnesses and respiratory infections with an increased risk of infant mortality, particularly in the first 6 months of life.
- There is an increased risk of malnutrition due to inadequate supply of infant formula or inappropriate feeding
- Commercial infant formula is expensive (and a regular supply must be assured)
- Requires a regular supply of fuel and clean water for preparation
- Infant formula cannot be stored; it must be freshly prepared each time it is needed

Although exclusive breastfeeding is recommended for the first six months of life for infants born to HIV-infected mothers, each mother should be informed of all available options and taken through an assessment of her individual circumstances to identify her best infant feeding option. A mother should be supported whatever choice she makes, with emphasis on the importance of exclusively practicing the option taken.

Mothers should be warned against mixed feeding (breast milk plus other foods or liquids) during the first six months of life as this is associated with a **higher risk** of HIV transmission than breastfeeding exclusively.

Infant Feeding from Six to Twelve Months of Age

- HIV-infected mothers (and those whose infants are HIV-uninfected or with unknown HIV status) should continue breastfeeding for the **first 12 months of life,** while antiretrovirals are provided to the mother for her own health and for reducing the risk of MTCT of HIV.
- After six months, all infants should start receiving complementary foods in addition to breast milk (or replacement milk). This is a high-risk time for all infants as it is often associated with growth faltering, illness, and increased risk of malnutrition. HIV-exposed infants must be monitored closely since they are at an increased risk of these complications. HIV-infected mothers should therefore receive regular support and counselling for appropriate complementary feeding.
- Health care providers should promote and encourage responsive (active) feeding, applying the principles of psychosocial care as well as supporting the maintenance of food safety and hygiene to avoid food borne diseases. Food demonstrations should be used to introduce mothers to safe and nutritious meals for their infants. Guidance should focus on the quantity, quality and frequency of feeding.

Infant Feeding from Twelve to Twenty-Four Months

- After 12 months of age, breastfeeding for all infants **should only** stop if a nutritionally adequate and safe diet can be provided to the infant.
    - Appropriate complementary foods should still be provided during this time.
- Studies indicate improved survival among HIV-infected infants who are breastfed. All HIV-infected infants should therefore be breastfed exclusively for the first six months and continue breastfeeding for as long as possible while receiving complementary foods.
- Adequate feeding practices around the weaning period are crucial to achieving optimal child growth. HIV-infected women should turn to early cessation of breastfeeding only when they are counseled properly to provide adequate complementary feeding to take over breast milk

When Mothers Decide to Stop Breastfeeding

- When HIV-infected mothers stop breastfeeding, they should do so gradually within one month as stopping breastfeeding abruptly is not advisable.
- If the infant is younger than six months of age when breastfeeding ceases:
    - Commercial infant formula milk should be provided exclusively
    - Note that modified animal milk is not recommended for children under 6 months.
- If the infant is older than six months when breastfeeding ceases, feeding options include:
    - Commercial infant feeding formula milk
    - Animal milk, which should be boiled for infants under 12 months

Interim Feeding Strategies

- HIV-infected mothers may consider expressing and heat-treating breast milk as an interim feeding strategy under the following conditions:
    - In the neonatal period if the infant is born with low birth weight or is otherwise ill

and unable to breastfeed
    - The mother is unwell and temporarily unable to breastfeed or has a temporary breast health problem such as mastitis or
    - Antiretroviral drugs are temporarily not available
- Some mothers may also consider using expressed and heat-treated breast milk as a step towards stopping breastfeeding if the baby is younger than six months of age.
- Mothers choosing to utilize these interim feeding strategies should receive appropriate instructions from health care providers describing the appropriate procedure for heat-treating breast milk in order to ensure that the milk retains its full nutritional benefits.

Maternal Nutritional Support

Good nutrition for pregnant and breastfeeding mothers is important for the survival and well-being of the developing baby. In addition, an HIV-positive mother's nutrition before, during and after pregnancy can influence her own health and the risk of transmitting HIV to her child. HIV-positive mothers are at a higher risk of malnutrition and illness while pregnant and breastfeeding. During pregnancy or lactation, the mothers' need for energy and other nutrients increases to meet the demands of:

- Adequate weight gain due to pregnancy
- Development of the baby
- Milk production

In order to maintain good health, HIV-positive mothers therefore need additional food to meet the extra demands associated with HIV, pregnancy and lactation. Food intake for pregnant women includes a variety of macro and micronutrients. For further management of diet and related conditions refer to the Lesotho Food Based Dietary Guidelines for people living HIV and AIDS.

HIV-Infected Adults

Nutritional assessment and management is a central component to the comprehensive care of PLWHIV. Numerous studies have shown the association between indices of nutritional states such as body mass index (BMI) and mortality. Body mass index is the main indicator for malnutrition in adults along with MUAC for pregnant and breastfeeding women. Defined as body weight in kilograms divided by the height in meters squared [Weight (kg)/ Height (m^2)], BMI interpretations are as follows:

TABLE 9.2: BMI AND MUAC INTERPRETATIONS

MAM	SAM Outpatient Care	SAM Inpatient Care
BMI: 16 – 18.5 OR MUAC: Men: 22.5 to 23cm; Women: 21.5 to 22cm Pregnant Women: 21.0 to 23.0cm Adolescent Pregnant Women; 19.0 to 21.0cm **AND** No recent weight loss	BMI: < 16.0 OR MUAC: Men: < 22.5cm; Women: < 21.5cm; Pregnant Women: < 21.0cm Adolescent Pregnant Women; <19.0cm **AND** 5 – 10% recent weight loss	BMI: < 16 OR MUAC: Men: < 22.5cm; Women: < 21.5cm; Pregnant Women: < 21.0cm Adolescent Pregnant Women; <19.0cm **AND** More than 10% recent weight loss

Source: Lesotho IMAM protocol 2015

BMI Range	Interpretation
≥30.0	Obese
25.0 – 29.9	Overweight
18.5 – 24.9	Normal
16.0 – 18.4	Moderately undernutrition (MAM)
< 16.0	Severely undernutrition (SAM)

When BMI below 18.5 is diagnosed, therapeutic food supplementation is recommended *(*refer to the National Guidelines for the Integrated Management of Acute Malnutrition and Lesotho NACS Manual*)*. A BMI of 30 or greater is considered obese; obese clients should be referred to a nutrionist for education on an appropriate diet, exercise, and weight loss strategies.

TABLE 9.3: LIST OF MACRONUTRIENTS

Nutrient	Sources	Functions
Protein	▪ Meat-chicken, pork, beef, fish ▪ Dairy-milk, yoghurt, cheese ▪ Egg ▪ Nuts/grains-peanuts, bread ▪ Legumes-beans	▪ Provide necessary materials for building and repairing worn-out tissues ▪ Develops the immune systems and resistance to infections
Carbohydrates	▪ Vegetables ▪ Papa, samp, potatoes ▪ Fruits - peaches, bananas, apples ▪ Grains - bread, rice, cereal	▪ Provide energy for the body ▪ Fibre (a non-digested type of carbohydrate found in grains, fruits and green vegetables) prevents constipation, coronary heart disease and diabetes ▪ Soluble fibre is used in diarrhoea treatment
Fats	▪ Cooking oil, butter and animal fats	▪ Provide energy and heat; important for weight gain ▪ Aid in the absorption of and transportation of fat-soluble vitamins

TABLE 9.4: LIST OF MICRONUTRIENTS

Nutrient	Source	Function
Vitamin A	Carrots, spinach, pumpkin, peaches, tenane, sepaile, milk eggs, liver, fish, oils	▪ Good for white blood cells, vision and bone development ▪ Anti-oxidants needed for immune function and resistance to infections
VitaminB1 (thiamine)	Milk, eggs, beans, liver, fish, Likhobe tsa poone, tsa mabele, tsa koro, pork	▪ Used in energy production ▪ Supports heart, muscles, and central nervous system
Vitamin B2 (riboflavin)	Milk, eggs, beans, nuts, dairy, nama ea khoho, fish, likhobe	▪ Energy production, good vision, making blood cells
Vitamin B3 (niacin)	Milk, eggs, red meat, poultry, peanuts, likhobe	▪ Energy production, healthy skin, supports the nervous system
Vitamin B6	Likhobe, potatoes, bananas, beans, poultry, green vegetables, tomatoes, liver, fish, watermelon	▪ Breakdown protein and fat, production of antibodies ▪ Assists in production of red blood cells and supports function
Vitamin B12	Fish, liver, poultry, kidneys, sardines, milk, cheese, yoghurt, eggs	▪ Formation of red blood cells ▪ Maintains nerve and digestive tissues
Vitamin C (ascorbic acid)	Oranges, tenane, lshoabe, theepe, spinach, tomatoes, bell peppers, apples	▪ For healthy teeth, gums and bones ▪ Fights infection ▪ Helps iron absorption ▪ An anti-oxidant

Nutrient	Source	Function
Vitamin E	Sunflower oil, likhobe, beans, peas, lentils, cabbage, tenane, leshoabe, eggs	▪ An anti-oxidant that helps prevent cells from damage, increase disease resistance, and aids healing of scar tissue
Folate (folic acid)	Poultry, liver fish, beans, peas, green leafy vegetables, oranges	▪ Builds new cells, especially red blood cells
Calcium	Milk, mafi, yoghurt, spinach, cabbage, sepaile, beans, peas, lentils	▪ Builds strong bones and teeth ▪ Necessary for normal muscle function and blood clotting
Iodine	Fish, iodized salt, meroho ea Sesotho (e.g. theepe, tenane, leshoabe, seruoe)	▪ Development and proper thyroid function ▪ Important for normal growth and development, and prevent goiter
Zinc	Theepe, sepaile, pumpkin, likhobe, nuts, beans, corn, milk, cheese, liver, eggs, garlic, poultry, fish, red meat	▪ Important for growth and development ▪ Supports the immune system and improves wound healing
Selenium	Fish, red meat, likhobe, eggs, rice, sepaile	▪ An anti-oxidant ▪ Helps prevent breakdown of cells
Magnesium	Beans, peas, lentils, likhobe, spinach, sepaile	▪ Supports muscle and nerve function ▪ Releases energy from fats, proteins and carbohydrates ▪ Build strong bones and teeth
Iron	Red meat, pork, liver, eggs, green leafy vegetables, beans, peas, lentils, mangangajane	▪ Needed for the production of red blood cells and the delivery of oxygen to body tissues

DIETARY MANAGEMENT OF HIV AND AIDS RELATED CONDITIONS

People living with HIV experience conditions, which make the process of eating and digestion of food, absorption and utilization of nutrients difficult. The person might have many other illnesses or conditions such as fever, oral thrush, nausea and vomiting, which reduce appetite and make eating difficult. As a result, nutrient stores are diminished and the immune system is further weakened. The individual thus loses weight and fails to fight opportunistic infections. In order to manage weight loss and opportunistic infections, it is necessary to prepare nutritious meals for PLHIV in such a way that they can be easily eaten to provide the body with sufficient nutrients. This will enable the body to boost its immunity and maintain desirable body weight; hence help patient stay well for longer periods of time. In addition, choosing food ingredients, modification of food preparations, eating practices and other behaviours can help to manage these complications.

Remember

Different complications associated with HIV and AIDS may require different nutritional management approaches; and recommendations given for one condition can create problems to another condition. Seek advice from a qualified health worker whenever necessary. Consider food and drug interactions when giving dietary advices.

CHAPTER 10: WELLNESS INFORMATION

Introduction

Many people living with HIV and AIDS need education, counselling and support in order to learn how to care for themselves and lead healthy, positive lives. A healthy lifestyle can help to slow disease progression and promote safer sexual practices, which in turn will reduce the risk of transmitting HIV to others. Some aspects of a 'Wellness' Program include:

10.1 Healthy diet (see Chapter 9)

- PLHIV should eat healthy foods
- Eat a balanced diet, which includes many fresh fruits and vegetables

10.2 Consider nutritional supplements

- The use of nutritional supplements can be of value if the patient is unable to eat a balanced diet.

10.3 Avoid smoking

- Tobacco smoke (first or second-hand) harms lung immunity
- Since respiratory infections account for a large proportion of opportunistic infections, a healthy respiratory system is important.
- Patients should be encouraged and assisted to stop smoking.

10.4 Avoid alcohol intoxication

- Too much alcohol is harmful to one's health
- Since many drugs used in HIV disease are potentially toxic to the liver, a healthy liver is important.
- Advise patients to minimize alcohol intake, which among other things, will have a negative effect on adherence to ARVs and other important medications.

10.5 Keep fit and exercise regularly

- Exercise helps to keep the body in good physical shape and can help patients to better well and strong
- Advise patients not to over-stress the body, especially when symptoms of illness are present (diarrhoea, cough, fever, etc.).

10.6 Avoid taking unnecessary drugs

- Any drug has potential side effects.
- The potential risk of medication must always be weighed against the potential benefit.
- Patients should only take medication which has been prescribed by a trained health care provider.

10.7 Get a lot of rest and sleep

- Rest regularly and get enough sleep.
- If at all possible, patients should avoid too much stress.

10.8 Have a positive mental attitude

- A positive mental attitude promotes well-being, and helps to keep patients well for longer.

10.9 Alternative therapies

- The value of alternative therapies such as herbal and traditional medication has not been proven. In addition, the effects of these medications on ARVs has not been evaluated. Therefore, it is **recommended that patients *do not* take herbal and traditional medications in conjunction with ARVs** to prevent possible development of resistance and severe adverse effects, such as liver failure.

10.10 Seek treatment early for medical problems

- It is important to seek treatment for medical problems as soon as symptoms appear.
- Many HIV-related conditions can be effectively treated if they are diagnosed early enough.
- Encourage patients to come for assessment as soon as they notice any problems.

10.11 Safer sexual practices

- It is important for patients to prevent spreading HIV infection to their partners
- Condoms are recommended for all sexual encounters

10.12 Illegal drugs (including marijuana)

- These should be discouraged as they can have a negative impact on adherence and influence people to make unwise and unsafe decisions for their health

10.13 Advice on vaccines

- All HIV-positive people are advised to have an annual Influenza vaccine.
- Hepatitis B vaccination should be given to all people with HIV who are hepatitis B surface antigen negative
- Live vaccines should be avoided in those with weakened immune systems (particularly if CD4 < 200 cells/mm^3). The effectiveness of vaccines in HIV patients is greater when CD4 cell count is > 200 cells/mm^3.

CHAPTER 11: INFECTION CONTROL

An effective infection control program includes several components that work to prevent healthcare providers and patients from being exposed to infectious fluids, including avoidance of needle stick and other sharps-related injuries. Avoidance of occupational exposure should be given top priority. Each health facility in Lesotho should have an Infection Control focal person and Infection Control plan. Measures to be undertaken include universal precautions, such as the use of gloves when exposed to potentially infectious fluids or waste in all settings and proper disposal of sharps and other contaminated materials in approved containers

A model of quality improvement for a prevention program and operational processes should foster a culture of safety, reporting injuries and accessing care and treatment. Surveys of health care providers indicate that 50% or more do not report their occupational percutaneous injuries.

Universal precautions are designed to prevent transmission of human immunodeficiency virus (HIV), hepatitis B virus (HBV) and other blood borne pathogens when providing health care. Under universal precautions, blood and certain body fluids of all patients are considered potentially infectious for HIV, HBV and other blood-borne pathogens.

Universal precautions involve the use of protective barriers such as gloves; gowns; aprons; masks or protective eyewear; which reduce the risk of exposure to potentially infective fluids and materials. Universal precautions are applied in a two-way fashion: healthcare provider to patient and patient to healthcare provider. They include:

- Hand-washing before and after patient contact
- Decontaminate equipment and devices
- Use and disposal of needles and sharps safely (avoid recapping of needles)
- Wear protective gear
- Promptly clean up blood and body fluid spills
- Use safe disposal systems for waste collection and disposal

All health care providers should routinely take appropriate barrier precautions to prevent skin and mucous membrane exposure during contact with any patient's blood or body fluids.

Hand Hygiene

Hand-washing is the **single most important measure** to reduce the risks of transmitting microorganisms from one person to another. Washing hands as promptly and thoroughly as possible between patient contacts and after contact with potentially infectious material is an important component of infection control. In addition to hand-washing, gloves play an important role in reducing transmission of microorganisms.

- Use soap and water for hand washing under running water for at least 15 seconds.
- Use alcohol-based hand rubs (or antimicrobial soap) and water for routine decontamination

Basic personal protective equipment:

- Gloves of correct size
- Aprons as waterproof barriers
- Eye wear to avoid accidental splashes
- Foot wear such as rubber boots or clean leather shoes

Gloves should be worn:

- When touching blood and body fluids, mucous membranes or non-intact skin of all patients.
- When handling items or surfaces soiled with blood or other body fluids.

Change gloves after contact with each patient. Wash hands and other skin surfaces immediately if contaminated with blood or other body fluids. Immediate hand washing is also

recommended on removal of gloves. Routine use of gloves should reduce the incidence of blood contamination of hands during phlebotomy but cannot protect against penetrating injuries caused by needles or other sharp instruments. Gloves should never be washed for reuse. Use of gloves is obligatory when the health care provider has cuts, scratches, or other breaks in his/her skin. Performing finger and/or heel sticks on children requires gloves.

Airborne Precautions

Airborne precautions are designed to reduce the risk of airborne transmission of infectious agents. Airborne transmission occurs by dissemination of nuclei of evaporated droplets that may remain suspended in the air for long periods of time. N95 masks (N category at 95% efficiency) should be used by health care providers in situations where exposure to TB is probable. TB infection control has 3 components:

Administrative controls

- Prompt identification of infectious TB cases
- Physical isolation of patients known or suspected to have TB
- Coughing patients should be separated from other outpatients in waiting areas
- Physical separation of TB suspects from HIV-positive people (patients and staff) is especially important

Note: These controls are most effective but least expensive.

Environmental (or engineering) controls

These are important in waiting rooms, consultation rooms, counselling rooms, and other places within health facilities where TB patients (suspected or confirmed) receive services, including inpatient and outpatient settings

- Natural ventilation, which can be as simple as opening windows.
- Mechanical ventilation such as using extraction fans.
- Ultraviolet irradiation
- Air filtration

N 95 Respirator Mask

Personal respiratory protection

- Use of N95 or any other respirator masks
- The masks must be properly fitted in order to protect against

Note that surgical masks **do not** protect against TB. Health care workers should wear N95 masks when serving TB patients; TB patients (presumptive or confirmed) should be given surgical masks to wear while in a health facility and educated on proper cough hygiene.

Handling and Disposal of Sharps

- Use syringe and needle once only.
- Do not recap the needle after use.
- Do not bend or break needles.
- Use puncture-proof containers for disposal.
- Clearly label container: “SHARPS”.
- Never overfill or reuse sharps containers.
- Dispose of sharps according to hospital guidelines.
- Do not recap a needle before disposal nor use the one-hand technique; it is high risk behaviour. If necessary, use needle removers which remove the needle from the syringe by cutting the hub of the syringe and/or the needle.
- Use auto-disable syringes or automatically retractable syringes: The advantage is that they cannot be re-used and they save time for health care providers from the

burden of sterilization.

Sterilization and disinfection of medical devices

In general, medical devices or equipment for patient use that enters sterile tissue or the vascular system or through which blood flows should be sterilized before each use. Sterilization means the use of a physical or chemical procedure to destroy all microbial life, including highly resistant bacterial endospores.

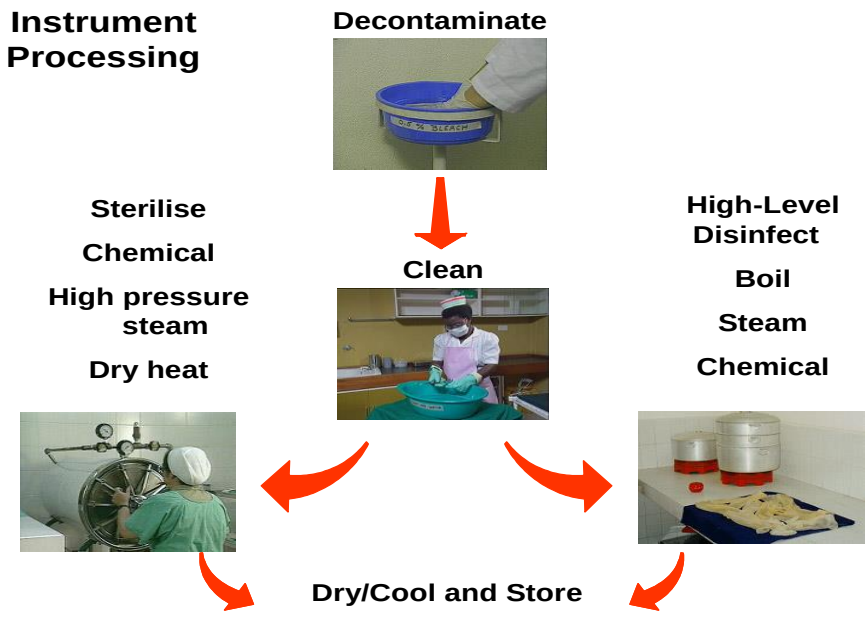
Disinfection means the use of a chemical procedure that eliminates virtually all recognized pathogenic microorganisms but not necessarily all microbial forms (i.e. bacterial endospores) on inanimate objects.

There are three levels of disinfection: high, intermediate and low. High-level disinfection kills all organisms, except high levels of bacterial spores. It is accomplished with a chemical germicide cleared for marketing as a sterilant. Intermediate disinfection kills mycobacterium, most viruses, and bacteria with a chemical germicide (e.g. Sidex). Low-level disinfection kills some viruses and bacteria with a chemical germicide registered as a hospital disinfectant. **Gloves should always be worn during the sterilization process.**

Apply risk reduction strategies:

- Assess condition of protective equipment
- Safely dispose waste materials
- Avail appropriate cleaning and disinfecting agents
- Decontaminate instruments and equipment
- Monitor skin integrity

Ongoing education for health care providers in infection prevention is essential to make all staff aware of established infection control policies.



Favero MS, Bond WW. Sterilization, disinfection, and antisepsis in the hospital. In: Manual of Clinical Microbiology, 1991; chapter 24:183-200. American Society for Microbiology. Washington, DC; Rutala WA. APIC guideline for selection and use of disinfectants. Am J Infect Control 1996;24: 313-342.

Management of Occupational Exposure

- Provide immediate care to the exposed site
- Evaluate the exposure
- Give post exposure prophylaxis (PEP) for exposures posing risk of HIV transmission.
- Perform follow up testing and counselling as necessary

Glossary

Blood-borne pathogens: Pathogenic microorganisms that are present in human blood and can cause disease in humans. These pathogens include but are not limited to hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV).

Occupational exposure: Means reasonably anticipated skin, eye, mucous membrane, or parenteral contact with blood or other potentially infectious materials that may result from the performance of a health care provider's duties.

Percutaneous: Effected or performed through the skin.

Phlebotomy: The sampling of blood for transfusion, pheresis, diagnostic testing or experimental procedures.

Recapping: The act of replacing a protective cap on a needle

Seroconversion: The development of antibodies in the blood of an individual following exposure to an infectious agent.

Sharps Injury: An exposure that occurs when any sharp medical instrument penetrates the skin

Standard precautions: An approach to infection control recommended by the Center for Disease Control and Prevention since 1996. Standard precautions synthesize the major features of universal precautions and apply to blood and all moist body substances, not just those associated with blood borne virus transmission. Standard precautions are designed to prevent transmission of infectious agents in the health care setting.

Universal Precautions: Designed to prevent transmission of human immunodeficiency virus (HIV), hepatitis B virus (HBV), and other blood borne pathogens when providing health care. Under universal precautions, blood and certain body fluids of all patients are considered potentially infectious for HIV, HBV and other blood borne pathogens. (www.cdc.gov)

Note that Universal Precautions do not apply to faeces, nasal secretions, sputum, sweat, tears, urine, saliva and vomitus unless they contain visible blood.

CHAPTER 12: OPERATIONAL AND SERVICE DELIVERY

This chapter provides guidance on some key operational and service delivery issues that need strengthening to ensure comprehensive delivery of HIV prevention, care and treatment services. The following areas are covered:

- Retention across the decentralization of HIV treatment and care
- Retention across the continuum of care
- Service integration and linkages
- Human resources
- Laboratory and diagnostic services
- Procurement and supply management system.

SECTION 12.1 DECENTRALIZATION OF HIV CARE AND TREATMENT

Decentralization can be defined as the transfer of authority and technique or dispersal of power, in public planning, management and decision making from the national level to the sub-national levels or more generally from higher to lower government levels in a country[1]. With approximately 60% of people in Lesotho residing in rural areas, the country adopted decentralization as a public health approach to improve access to ART and increase the health and survival of PLHIV.

Possible benefits of decentralization include[2]:

- Integrated health service delivery at lower levels, particularly for primary health care
- Integration of public and private entities and improved inter-sectoral coordination
- Empowerment of health care professionals at all levels for decision making
- Reduction in inequalities and promotion of equity between different geographic settings and between urban and rural areas.
- Cost containment and reduction in duplication of services at secondary level of health care delivery
- Greater community involvement in management of their own health thus leading to more appropriate health plans in relation to local health needs and problems
- Greater community ownership, participation and willingness to contribute to financing of their health needs through local government structures
- Overcoming problems and delays due to factors such as long distances, inadequate communication and poor road networks/terrain
- Some models of decentralization, such as Community ART Groups (CAGs), demonstrate increased levels of retention in care
- Decentralization also helps to decongest hospitals and health centers so that clinicians can focus on managing more acute and/or complicated health conditions and patients

HIV patients can be initiated and maintained on ART at all levels (hospitals, health centers, health posts, and in the community at health facility outreach clinics) by the following appropriately trained cadres:

- Physicians
- Nurse clinicians
- Registered nurse midwives
- Registered nurses
- Trained nursing assistants (after completion of an accredited HIV training)
- Pharmacists and pharmacy technicians (after completion of an accredited HIV training; are allowed to re-prescribe ART for stable patients only)

[1] RONDINELLI, D. A (1981). Government decentralization in comparative theory and practice in developing countries. International review of administrative sciences, 47 (2): 133- 145

[2] Zimbabwe Guidelines for the Decentralization of HIV and AIDS Care and Treatment Services, 2009, MOHCW

- Expert patients (after completion of an accredited HIV training; are allowed to re-prescribe ART for stable patients only)

Patients no longer have to travel long distances to access ART services unless faced with complications that may require specialized medical services at hospital level. HIV testing services should be offered at all health facilities and in the communities through trained community-based cadres, including trained lay and professional counsellors and village health workers.

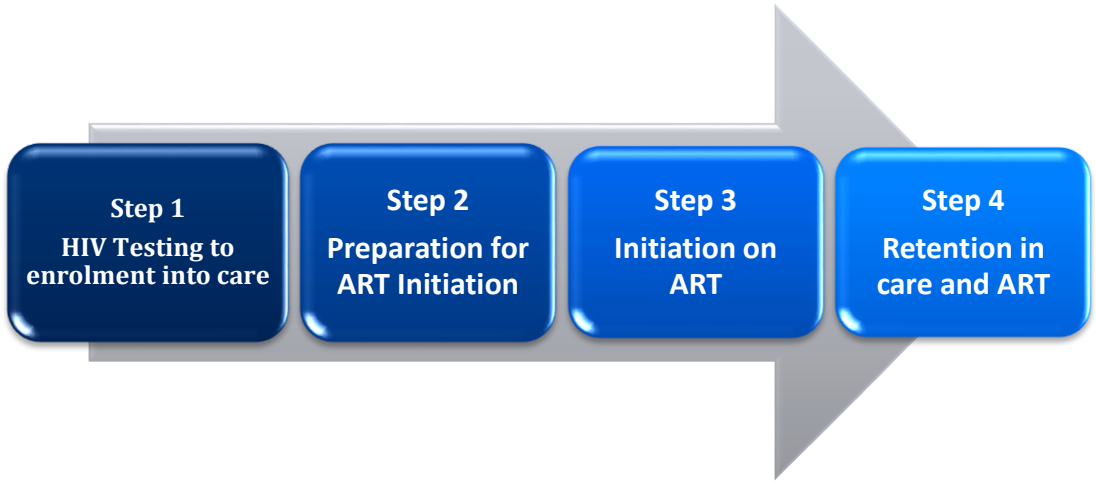
Patients who are stable on ART can receive follow up care and ARV refills at community level by trained community-based cadres between regular clinical visits at health centres. The follow up care package may include adherence counselling and support, supply of pre-packed ARVs, simplified clinical assessments and recording patient information.

Patients who are clinically stable (WHO stage 1 or 2) on ART for ≥6 months with good adherence, suppressed viral load (<1000 copies/ml) and CD4 > 200 cell/mm^3 should be given ARV refills to last 3-6 months to decongest health facilities. Stable patients should be encouraged to join a CAG to further decentralize care to the community level.

SECTION 12.2 RETENTION ACROSS THE CONTINUUM OF CARE

The HIV care cascade includes: HIV testing, linkage to and retention in care, initiation of ART and retention on ART with good adherence, and viral suppression. Losses along the care cascade must be minimized in order to realize the full benefits of HIV care and treatment in improving the health outcomes of PLHIV and reducing HIV transmission. Literature from sub-Saharan Africa has shown that 54% of those who are not yet eligible for ART based on CD4 or clinical stage were lost to follow up. Another 32% of PLHIV who were already eligible for ART were lost from care before ART could be initiated[3].

FIGURE 12.1 FACTORS AFFECTING RETENTION AND POSSIBLE INTERVENTIONS



A variety of interventions at different levels of care are required to optimize patient retention. It is important to identify specific barriers to retention and address them. Several factors that can impact patients' retention in care by affecting their ability to access services include the direct costs of accessing services, stock-outs of ARVs, lack of effective referral systems, lack of monitoring system, co-morbidities, and forgetfulness.

[3] Fox MP, Rosen S. Patient retention in antiretroviral therapy prorammes up to three years on treatment in sub-Saharan Africa, 2007-2009: systematic review. *Tropical Medicine and International Health*, 2010, 15(Suppl.1):1-16.

TABLE 12.1- FACTORS AFFECTING RETENTION AND POSSIBLE INTERVENTIONS	
Factors affecting retention	**Possible Interventions**
High costs of receiving care	• Continue to decentralize ART services, including scaling up of health posts • Provide family-centred care • Provision of 3 to 6 month supply of ARVs to stable patients with good adherence • Scaling up CAGs • Community and facility ART refills by trained nursing assistants (health extension workers), pharmacists/pharmacy technicians, and expert patients
Weak systems for monitoring patient retention	• Implement patient tracking systems including cohort monitoring and electronic patient monitoring systems • Reinforce the appointment system for patients • Scaling up provision of moonlight services
Weak patient referral system	• Strengthen patient referral system, such as use of duplicated patient referral forms and revised HTS registers for documentation of patient linkage • Use of unique patient identifiers to track patients across different points of care
Adherence support	• Strengthen community health workers and other support groups to provide adherence support • Peer support
Forgetfulness	• Linking to support groups and CAGs • Identifying a treatment supporter • Using technology, such as mobile phone text message reminders • Provision of pill boxes and medication calendars

SECTION 12.3 SERVICE INTEGRATION AND LINKAGES

The programs of HIV, TB, SRH, and maternal and child health need to collaborate so as to minimize missed opportunities while at the same time provide more comprehensive health care to patients. Potential areas of collaboration, include training, supervision and mentorship, supply chain management, resource mobilization, and monitoring and evaluation.

Delivering ART in ANC and MNCH Settings

Studies have shown that provision of ART within ANC and RMNCH settings increases the uptake of ART among HIV infected pregnant women. Since many women access maternity services during pregnancy, this serves as an opportunity to also provide HIV testing services to all pregnant women and offer life-long ART for those found to be HIV-positive. Nurses and midwives should be trained, mentored, and supervised to provide ART initiation and follow up care within the MNCH settings and refer the mother-baby pair at 24 months to an ART clinic for follow up care. Where possible partners of HIV–positive pregnant and breastfeeding women should also be offered PITC and HIV services within the RMNCH settings.

Delivering ART in TB treatment settings and TB treatment in HIV care settings

Collaboration between TB/HIV services is crucial to address the impact from the two diseases. This should span all the key levels from the national program through the district health system and facilities to the communities.

This collaboration should focus on the following thematic areas:

- Establishing mechanisms for collaboration between HIV and TB services
- Reducing the burden of TB in PLHIV and
- Reducing the burden of HIV in TB patients

For efficient coordination of TB/HIV activities the following areas are being addressed:

- Coordinating body at central level (HIV/TB Technical Advisory Committee), at district level (HIV/TB Coordination Meetings), at facility level (Multidisciplinary Teams) to manage HIV/TB services.
- Surveillance of HIV prevalence among TB patients. All presumptive and confirmed TB patients are offered HIV testing services upon diagnosis.
- Family-centered approach in TB screening, including diagnosis in children, contract tracing and provision of TB treatment for all patients, including children, at all health facilities
- Joint TB/HIV planning; joint resource mobilization (both financial and human); capacity development (including training); and HIV/TB advocacy, communication and social mobilization (ACSM)
- Joint operational research activities to inform national policy and strategy development so as to improve service delivery.
- Joint monitoring & evaluation of collaborative HIV/TB activities. This ensures timely assessment of quality, effectiveness, coverage and delivery of collaborative HIV/TB activities.
- Joint enhancement of community involvement in collaborative HIV/TB activities through support groups for PLHIV, DOT supporters, and community-based organizations. Communities can also be mobilized to help implement collaborative HIV/TB activities.

Strengthening integration of TB and HIV services at the facility level is necessary for ensuring effective HIV/TB collaboration. TB and HIV interventions should be introduced at all levels within the district health system.

TABLE 12.2: TB AND HIV INTERVENTIONS AT LEVELS OF THE HEALTH SYSTEM

LEVEL OF HEALTH CARE	HIV/TB INTERVENTIONS
HOME AND COMMUNITY Community based organizations, NGOs, faith based organizations, government community health programmes, CAGs	• IEC activities regarding TB, HIV, and STI Condom promotion • Nutritional advice and support • Psychological support • Community HTC • Intensified community screening and DOT for TB • Community-based palliative and terminal care
PRIMARY CARE Government health centres or clinics, mission health centres, NGO health centres, private health centres	• HTS and HIV prevention • TB case finding and treatment • Intensified case finding • Isoniazid and co-trimoxazole provision • Condom promotion • STI syndromic management • Management of HIV related opportunistic infection and palliative care • Prevention of mother to child transmission • ART
SECONDARY CARE Government hospitals, mission hospitals, private hospitals	• Diagnosis and treatment of HIV-related diseases • Inpatient palliative care • Diagnosis and management of complications or severe presentations of HIV/TB disease • Referral back to primary facility after stabilization of complicate cases

SECTION 12.4 HUMAN RESOURCES

Human resources are a critical component of the health system in the delivery of HIV services.

Service delivery:

- Integrated approach at all facilities to allow for increased patient load due to early ART initiation
- Coordination/interaction of all services such as sample collection, laboratory services, and all relelvant stakeholders
- Requires efficient and effective management of human resources to manage anticipated increased patient load
- Considerations around including other cadres of staff at health centres i.e. pharmacy technicians, laboratory personnel for POC, data clerks, lay counsellors, psychosocial support
- Greater inclusion and involvement of private practitioners for consistency, to reduce the burden on public sector, and increase efficiency of services
- Increased services for men at all service points; novel approaches like workplace programs

Capacity building:

Both pre-and in-services training for health workers play a key role in building competences and skills to support rapid scale up of ART services. In addition, mentorship and supervision of health workers and community-based care providers is necessary to ensure high quality HIV care services. Newer approaches to learning, including distance learning and online courses, should be used to support the classroom-based learning which may be costly and more time-consuming. Suggested approaches include:

- Decentralising training/capacity building exercises to district level and increase localized trainings (e.g. cluster model approaches)
- Develop training database that can be used at district level to track HR across different cadres who have been trained.
- Develop certified online module with respect to ART initiation and continued care
- Provide facility/individual certification for relevant trainings to improve skills

The increase in the burden of chronic care for PLHIV requires adequate numbers of care providers to provide life-long care to ensure good treatment outcomes. The situation demands proactive human resource strategies such as task-shifting to meet the current challenges. Task-shifting involves the rational redistribution of tasks among health workforce such that specific tasks are reassigned as appropriate from highly qualified to lesser qualified health workers to improve efficiencies and effectiveness in the use of available workforce. Task-shifting helps to improve access to services at health centres where there are no physicians. On the other hand, physicians are able to devote more time managing complicated cases. It is important to establish and maintain mentoring and supportive supervision to ensure quality is not compromised by task-shifting.

- Physicians, nurses, midwives, and trained nursing assistants should initiate first-line ART
- Physicians, nurses, midwives, trained nursing assistants, pharmacists, pharmacy technicians, and expert patients should maintain ART
- Trained and supervised community health workers can supply stable patients pre-packed ARVs between regular clinical visits

SECTION 12.5 LABORATORY AND DIAGNOSTIC SERVICES

Laboratory and diagnostic services are an essential component of comprehensive ART service package. Since HIV diagnostic services occur at health facility and community level by different health workers, the need for strengthening relevant quality assurance systems is

paramount. The 2016 WHO ART guidelines continue to recommend the use of viral load monitoring as a better tool for monitoring HIV treatment response; this recommendation is reflected in these guidelines as well. Consequently, laboratory services must support the expansion of viral load testing capacity to meet the country requirements.

In order to strengthen the network of laboratory and diagnostic services, it is important to consider the following:

- Strengthen transport logistics for sample transportation and delivery of results at all levels
- Expand laboratory networks to support and monitor decentralization and integration of testing services or to provide effective referral system for laboratory services
- Strategic deployment of diagnostics platforms to optimize utilization
- Standardize testing methods to streamline procurement, quality assurance, maintenance and training
- Use of high quality and evaluated diagnostics before introduction into the system
- Strengthen supply chain management system for laboratory commodities and equipment maintenance
- Integrate electronic tracking of samples to reduce loss of samples, reduce TAT
- Mobilize sufficient resources to support laboratory services (e.g. genotypic resistance testing, improved viral load transport networks)
- Integration of lab commodities delivery with ARVs up to the last mile delivery
- System that tracks expenditure and resources invested in ART scale up.

In addition to the above considerations, laboratory services should build an efficient system for sample – results transportation and expedited result reporting and data management to reduce turnaround time for EID and viral load tests. There is need to leverage on existing EID networks. It is recommended that dried blood spots are used as a tool to increase access to viral load testing. A regionalized laboratory services model for viral load testing is currently being introduced.

Quality management systems for laboratory services need to be in-built including external quality assessments and internal controls. Testing sites should be supported to enrol into external quality control programme for proficiency testing. Tools for standard operating procedures should be set up and used at all levels. Service agreements for equipment should be in place and equipment serviced according to service contracts.

SECTION 12.6 PROCUREMENT AND SUPPLY MANAGEMENT (PSM) SYSTEM

The need to ensure continuous availability of quality and affordable medicines cannot be over emphasized. The PSM system should be strengthened to cope with an increasing volume of patients that require medicines as the ART program scales up. With decentralization and integration of ART services with other services such TB and MNCH, more should be done to ensure uninterrupted supply of ARVs and OI medicines at peripheral health centres and in multiple care settings. The entire PSM cycle including selection, procurement, storage and distribution, use and monitoring, should be well managed.

Table 12.3 - Checklist of pharmaceutical and laboratory supply chain management issues	
Phase	**Activities**
Planning and Product Selection	• Update National Medicines List to include newer ARV regimens (2nd line and 3rd line), OI medicines and diagnostics • Quantify and forecast medicine requirements considering ART scale up plan
Procurement	• Procure medicines from pre-qualified suppliers • Procure generic medicines to reduce medicines costs (Maintain a system that fosters openness and transparency in engaging potential suppliers) • Implementation of a robust system for testing quality of medicines before use • Ensure sufficient buffer stock of medicines and laboratory commodities at central and service delivery level
Storage, distribution, rational use and monitoring	• Secure appropriate medicines storage capacity at central and facility levels (docking system and increased delivery frequency) • Establish/strengthen effective distribution mechanism for medicines and related commodities ('informed push' system) • Implement effective monitoring and management systems for PSM including logistics management information system (LMIS) and electronic medicine dispensing system • Institute a pharmaco-vigilance system to monitor adverse drug events

CHAPTER 13: PROGRAMME MONITORING AND EVALUATION

SECTION 13.1: DEFINITIONS

What is Patient Monitoring?

Patient monitoring is the routine collection; compilation; analysis and use of individual patient data or a *group (cohort)* of patients for decision making. Data is collected over time and across service delivery points. The information can be paper based or electronic. This is also called "patient tracking" and it provides important information for *patient management.*

What is Patient Management?

Based on the relationship between providers on a clinical team and the *individual patient*, this is generating, planning, organizing, and administering medical and nursing care services for patients, assisted by written records. It is also called "clinical management" or "clinical monitoring."

What is Programme Monitoring?

This is ongoing collection of priority information about a programme to determine if it is operating according to plan. It provides ongoing information on programme implementation and functioning**.** It is done at facility, district and national levels.

Purpose of patient monitoring

Patient monitoring is an important part of high quality patient care. Monitoring involves documenting all patient encounters by keeping regular and accurate records of key aspects of the care and treatment that is offered. This makes it possible to capture the history of a patient or group of patients over time and across different clinical sites and to collect data for reporting on and evaluating patient care at regular intervals.

In the context of facility-based HIV care, monitoring offers three major benefits:

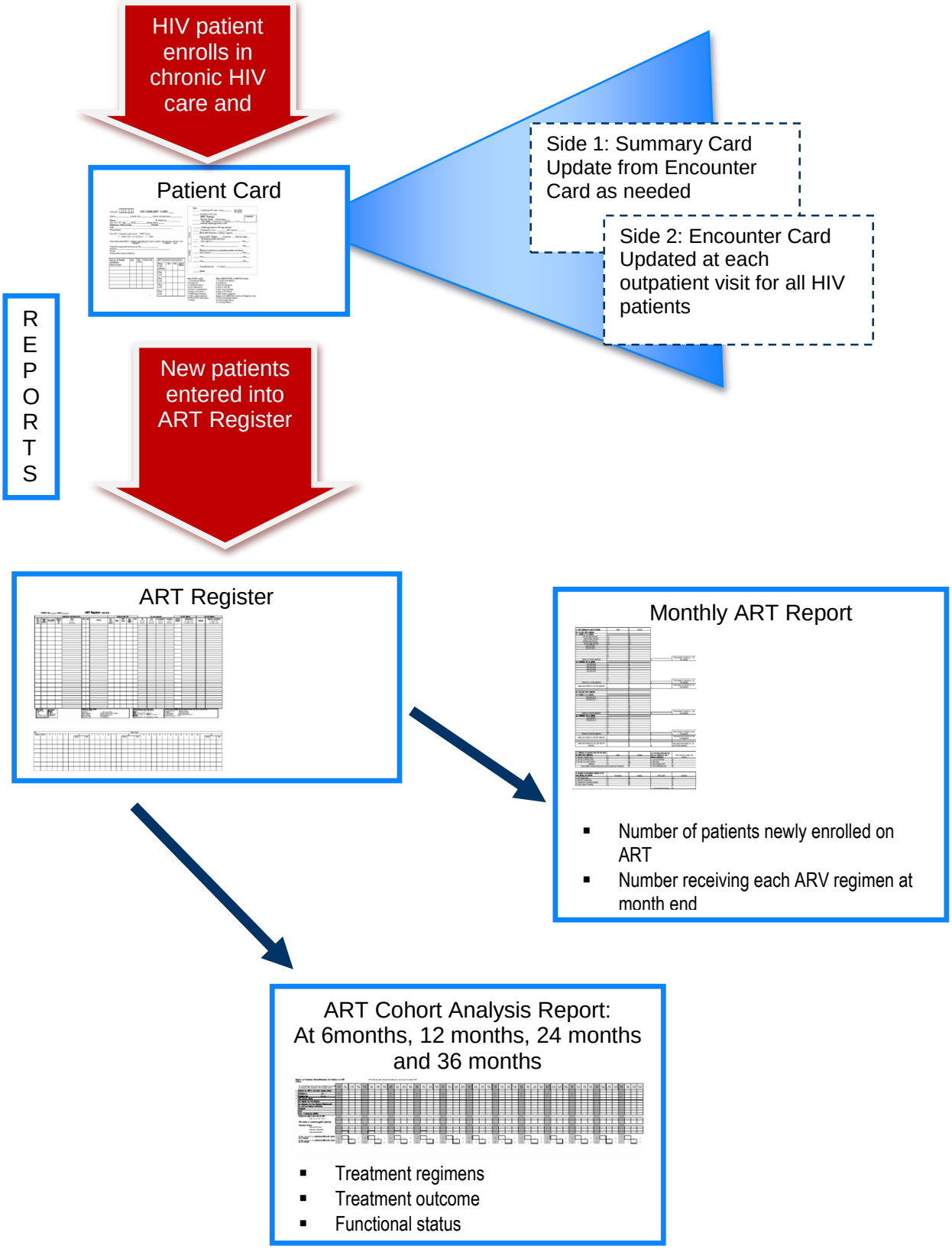
1. It provides essential information for individual case management.
2. It provides key information for managing the health facility (e.g. for ordering drugs and supplies or for making quality improvements).
3. It provides information for operating and improving an HIV/AIDS program at the facility, district, national, and international levels.

SECTION 13.2: OVERVIEW OF THE PATIENT MONITORING SYSTEM

The paper-based patient monitoring system includes the following tools:

1. A short patient-held card (Bukana)
2. HIV Care / ART card (which is kept at the facility)
3. HIV Testing Services (HTS) register
4. ART register
5. Viral load monitoring register
6. PrEP register
7. ART monthly report book
8. Cohort analysis report
9. Appointment book
10. ART Referral form
11. CAG register
12. CAG community card
13. CAG quarterly report

FIGURE 13.1: OVERVIEW OF DATA FLOW FROM PATIENT CARD TO THE TWO REGISTERS AND TWO REPORTS



SECTION 13.3: MONITORING IMPLICATIONS OF 2016 RECOMMENDATIONS

TABLE 13.1: IMPLICATIONS FOR MONITORING OF THE KEY RECOMMENDATIONS

Summary of new recommendation	Implications for monitoring
HIV testing services	• Monitor the uptake of community-based and facility-based HIV testing strategies and testing services for all key populations, including systems for linkages to care
ART	• 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 • Review the monitoring system to assess what disaggregation is needed for what purpose (such as CD4 counts ≤200 cells/mm^3 to routinely monitor late diagnosis/presentation) and how to best collect the relevant data, and age disaggregation for children and adolescents
Which ART regimen to start	• Monitor the first-, second-, and third-line ART regimens received by clients • Monitor the phasing out and/or introduction of specific drugs • Monitoring tools will be adjusted to reflect new regimen
Response to ART and diagnosing treatment failure	• Monitor the percentage of people receiving ART who had a viral load test and received the results • Monitor the reasons for switching ART regimen • Which other clinical evaluations are used to assess patient's response to ART
Service Delivery	• Monitor retention and adherence among various populations • Monitor the integration of ART into facilities providing maternal and child health services, TB services and drug dependence services, if planned, by documenting the facilities providing ART • Monitor whether the initiation and maintenance of ART has been decentralized as planned at various facilities by documenting the expansion of ART facilities and service points • Monitor the functionality of linkages from maternal and child health services, TB services and drug dependence services to HIV care and ART and linkages between communities, peripheral facilities and hospitals by documenting transfers
Task shifting	• Monitor the number of non-physician clinicians, midwives, nurses, and trained nursing assistants who are trained on ART • Monitor the number of non-physician clinicians, midwives, nurses, and nursing assistants who are initiating first-line ART and retaining patients on ART and the number of people they have initiated and retained on ART • Monitor the number of pharmacists, pharmacy technicians, and expert patients who are trained and are dispensing/represcribing ART to stable ART patients, and capture the number of people to whom they dispense ART

SECTION 13.4: OTHER MONITORING CONSIDERATIONS

HIV drug resistance poses a significant threat to the success of the national HIV program. Drug resistance results in more rapid virologic failure among people receiving ART and increases the need for second and third-line regimens, which may be associated with greater toxicity, adverse events, poorer adherence and higher costs. Drug resistance may also negatively affect the ability to prevent HIV transmission using ARV-based pre- or post-exposure prophylaxis or topical microbicides. Surveillance of drug resistance should be an integral component of national HIV programme.

Surveillance data should inform the selection of first- and second-line regimens for ART, as well as ARV drugs for PMTCT, to optimize treatment outcomes within a public health approach.

Monitoring early warning indicators for HIV drug resistance

Early warning indicators use existing clinic and pharmacy records to assess the factors associated with the emergence of HIV drug resistance at the level of ART programmes and clinics. These factors include ART prescribing practices; drug supply continuity; adherence to ARV drug regimens measured by on-time pick-up of ARV drugs; retention in care; and viral load suppression, when available.

The monitoring of early warning indicators will be integrated into a national monitoring and evaluation system and provides the information needed to address practices that may lead to poor outcomes and HIV drug resistance.

Surveys to monitor acquired HIV drug resistance and associated factors in populations receiving ART

The WHO generic protocol for monitoring acquired HIV drug resistance uses a standardized survey methodology to assess population-level virologic suppression at the national level and the emergence of HIV drug resistance among populations receiving treatment. Performed regularly at representative sites, these surveys provide evidence for action at the programme and clinic level to minimize HIV drug resistance. They also provide evidence to optimize the selection of first- and second-line ART regimens.

Surveys to monitor pre-treatment HIV drug resistance

The WHO generic protocol for surveillance of pre-treatment HIV drug resistance provides a nationally representative estimate of HIV drug resistance in populations initiating ART. Performed regularly at representative ART clinics, these surveys support national, regional and global decision-making regarding the choice of first-line regimens.

Surveillance of transmitted HIV drug resistance among individuals recently infected with HIV

The WHO generic protocol for surveillance of transmitted HIV drug resistance provides estimates of transmitted HIV drug resistance in recently infected populations, and the results should contribute to ART policy decisions, including guidelines on ART regimens and HIV prophylaxis.

Surveys to monitor HIV incidence and prevalence of suppressed viral load

MOH will conduct the PHIA study; the goal of the survey is to examine the distribution of HIV disease, to assess the coverage and impact of HIV services at the population level, and to measure HIV-related risk behaviours using a nationally-representative sample of adults and children.

ANNEXES

ANNEX 1: DEVELOPMENTAL MILESTONES IN INFANTS AND YOUNG CHILDREN

Age	Psychosocial	Gross Motor	Fine Motor/Visual	Communication / Hearing
1 month	▪ follows faces to the midline	▪ moves all extremities equally ▪ lifts head when lying on stomach	▪ opens hands spontaneously	▪ startled by loud sounds ▪ cries ▪ quiets when fed and comforted
2 months	▪ follows faces past midline ▪ smiles responsively	▪ lifts head up 45 degrees when on stomach	▪ looks at own hand	▪ makes baby sounds (cooing, squealing, gurgling)
3 months	▪ recognizes mother ▪ smiles responsively	▪ supports head for a few seconds when held upright	▪ opens hands frequently	▪ responds to voices ▪ laughs
4 months	▪ follows an object with eyes for 180 degrees ▪ regards own hand ▪ anticipates food on sight	▪ bears weight on legs ▪ good neck control when pulled to sitting ▪ lifts chest and supports self on elbows when pulled to sit	▪ brings hands together in midline (clasps hands) ▪ grabs an object (such as a rattle) ▪ reaches for objects	▪ turns head to sound
6 months	▪ reaches for familiar people	▪ rolls from stomach to back or back to stomach ▪ sits with anterior support	▪ plays with hands by touching them together ▪ sees small objects such as crumbs	▪ responds to name ▪ babbles
9 months	▪ indicates wants/desires ▪ waves bye-bye ▪ stranger anxiety	▪ can sit without support ▪ creeps or crawls on hands and knees	▪ looks for a toy when it falls from his/her hand ▪ takes a toy in each hand ▪ transfers a toy from one hand to the other	▪ responds to soft sounds such as whispers
12 months	▪ has separation anxiety ▪ social interactions ▪ intentional and goal-directed	▪ pulls self up to standing position ▪ walks with support	▪ points at objects with index finger	▪ says at least one word ▪ makes “ma-ma” or “da-da” sounds ▪ locates sounds by turning head
15 months	▪ imitates activities ▪ finds a nearby hidden object	▪ can take steps by himself ▪ can get to a sitting position from a lying position	▪ can stack one cube on top of another	▪ able to say mama and dada to respective parents
18 months	▪ initiates interactions by calling to adult	▪ walks without help	▪ takes off own shoes ▪ feeds self	▪ says at least 3 words
2 years	▪ does things to please others ▪ parallel (imitative) play	▪ runs without falling	▪ looks at pictures in a book ▪ imitates drawing a vertical line	▪ combines two different words

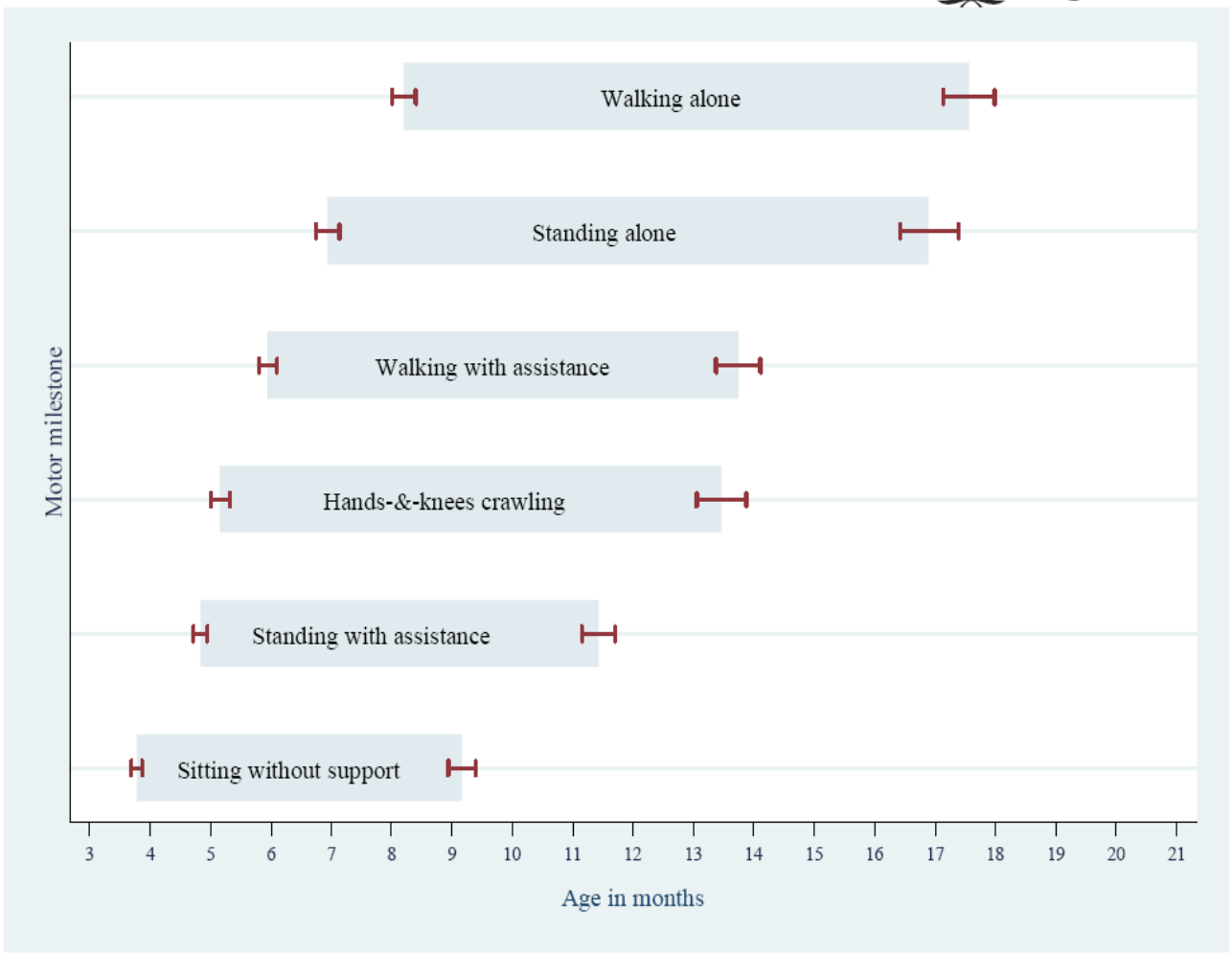
ANNEX 2: DEVELOPMENTAL RED FLAGS

Birth to 3 months	▪ Failure to respond to environmental stimuli ▪ Rolling over before 2 months (hypertonia) ▪ Persistent fisting at 3 months
4-6 months	▪ Poor head control ▪ Failure to smile ▪ Failure to reach for objects by 5 months
6-12 months	▪ No baby sounds or babbling ▪ Inability to localize sounds by 10 months
12-24 months	▪ Lack of consonant production ▪ Hand dominance prior to 18 months (contralateral weakness) ▪ No imitation of speech and activities by 16 months
Any age	▪ Loss of previously attained milestones

ANNEX 3: GROSS MOTOR MILESTONES IN INFANTS AND YOUNG CHILDREN

Windows of achievement for six gross motor milestones

World Health Organization



Reference: WHO Multicentre Growth Reference Study Group. WHO Motor Development Study: Windows of achievement for six gross motor development milestones. Acta Paediatrica Supplement 2006;450:86-95.

ANNEX 4: WEIGHT-BASED DOSING OF ANTIRETROVIRALS AND PROPHYLACTICS

Ministry Of Health - Lesotho
Weight-Based Dosing Chart for Antiretroviral Drugs and Prophylactics

	Medication	Strength	Medication dosages by weight band					Strength	Dosages by weight band	Strength	Dosages 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		>35 kg
Once Daily ART	ABC/3TC	60/30 mg	2	3	4	5	6	600/300 mg	1	600/300 mg	1
	EFV	200 mg	-	-	1	1.5	1.5	200 mg	2	600 mg	1
	ATV/r		-	-	-	-	-		-	300/100mg	1

	Medication	Strength	3-5.9 kg		6-9.9 kg		10-13.9 kg		14-19.9 kg		20-24.9 kg		Strength	25-34.9 kg		Strength	>35 kg	
			AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM		AM	PM
Twice Daily ART	ABC/3TC	60/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	600/300 mg	-	1	600/300 mg	-	1
	LPV/r	80/20 mg/ml	1 ml	1 ml	1.5 ml	1.5 ml	2 ml	2 ml	2.5 ml	2.5 ml	3 ml	3 ml	100/25 mg	3	3	200/50 mg	2	2
	LPV/r	100/25 mg	-		-		2	1	2	2	2	2						
	AZT/3TC	60/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300/150 mg	1	1	300/150 mg	1	1
	AZT/3TC/NVP	60/30/50 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300/150/200	1	1	300/150/200	1	1
	NVP	10 mg/ml	5 ml	5 ml	8 ml	8 ml	10 ml	10ml	-		-		200 mg	1	1	200 mg	1	1
	NVP	200 mg	-		-		0.5	0.5	1	0.5	1	0.5						
	RAL		-		-		-		-		-			-		400mg	1	1

	Medication	Strength	3-5.9 kg	6-9.9 kg	10-13.9 kg	14-19.9 kg	20-24.9 kg	Strength	25-34.9 kg	Strength	>35 kg
Prophylaxis	CTX	240 mg/5ml	2.5 ml	5 ml	5 ml	-	-	960 mg	1	960 mg	1
	CTX	480 mg	-	0.5	0.5	1	1				
	INH	100 mg	0.5	1	1.5	2	2.5	300 mg	1	300 mg	1

Weight-based ART Dosing for Children < 3 yrs and < 10kg on Concomitant Anti-Tuberculosis Therapy**

Weight (kg)	Paediatric Zidovudine/Lamivudine/Nevirapine (AZT/3TC/NVP) 60/30/50mg tabs (maintenance)		Additional Nevirapine (NVP) 10mg/ml Syrup to add	
	AM Dose	**PM Dose**	**AM Dose**	**PM Dose**
3-3.9	1	1	0	0
4-4.9	1	1	1ml	0
5-5.9	1	1	1.5ml	1.5ml
6-6.9	1.5	1.5	0	0
7-7.9	1.5	1.5	1ml	0
8-8.9	1.5	1.5	1.5ml	1.5ml
9-9.9	1.5	1.5	2ml	2ml
10-10.9	2	2	0	0

***Note that since Rifampicin is known to reduce levels of NVP, lead-in (once-daily) dosing of NVP for the first 2 weeks is not necessary when initiating NVP-containing ART with concomitant TB treatment.*

ANNEX 5: TALKING ABOUT HIV TO HIV-INFECTED CHILDREN

<6 Years: Most children will not understand HIV or be able to keep it private
Suggestions for explaining HIV:
• You have a germ in your blood
• The germ hurts the healthy parts of your blood
• When the health parts are hurt, you get sick with coughing or diarrhoea or other things that make you feel bad
• The medicine will kill the germs so that your blood can become healthy again
• If you take your medicine every day you can stay healthy and stop the germ from making you sick
• You can always talk to your family (indicate which members) and to your doctors and nurses about being sick
Some questions that may come up with answers:
• Q: How did I get this germ?
• A: You were born with it, you have had it since you were a baby
• Q: Can you get rid of this germ?
• A: The medicine can get rid of most of it so you can stay healthy, but we cannot get rid of all of it.
• Q: When can I stop taking my medicine?
• A: You have to take your medicine everyday so that you can stay healthy, maybe one day doctors will be able to get rid of all the germs, but for now you have to take your medicine everyday.
7-11 Years: Not all children seek the same amount for information. Take your lead from the child as to how much information to provide. You can and should explain infection, immune depletion and the reason for taking drugs - without mentioning HIV in children where the child or the family is not ready for full disclosure. Keep information simple.
Suggestions for explaining HIV:
• You have come to the doctor because you have an illness-you may get sick some times
• You have a germ (virus) that lives in your blood – Ask what the child knows about germs and illness and correct misinformation
• Viruses make you sick and the doctors visits and medicines are needed to help you stay healthy
• The virus (HIV) kills the cells in your blood that helps you stay healthy
• The name of these cells are T- cells – the virus (HIV) kills T cells
• Without T-cells your body struggles to stay well and you get sick with coughing or other things that make you feel bad
• The medicine kill the virus (HIV) so that your T-cells can grow back and they can help you stay healthy
• If you stop taking your medicine the virus (HIV) will get stronger again and kill your T-cells then you will get sick again.
• We take blood so that we can measure the T-cells and as well as how much virus is in your blood.
• When you are doing well, we see lots of T-cells and very little virus
Explaining transmission:
• You got this virus when you were born. Your mother has the same virus. You got this virus from your mother
• You cannot get this virus by being friends or hugging or touching. It is ok to play and go to school. If you hurt yourself, you must not let other people touch your blood
Regarding privacy:
• We are explaining all this to you so that you can take better care of yourself
• This is private information. Indicate the person the child can discuss this with.
Some questions that may come up with answers:
• Q: Can you get rid of this virus?

• A: The medicine can get rid of most of it, so you can stay healthy, but cannot get rid of all of it. Currently there is no cure.
• Q: When can I stop taking medicine?
• A: You have to take your medicine everyday so that you can stay healthy. Maybe one day doctors will be able to cure HIV, but for now you have to take your medicine everyday
• Q: Am I going to die?
• A: If you take medicines everyday, you can stay healthy for a long time.
• Q: How did my mom get HIV? – ALWAYS DEFER TO THE MOTHER

ANNEX 6: GRADING OF ARV TOXICITIES

Symptom *(and diagnoses to consider, plus likely ARV responsible)*	Grade 1	Grade 2	Grade 3	Grade 4
Abdominal pain +/- nausea	▪ Mild and transient (<24 hr)	▪ Food intake decreased (24 - 48 hrs)	▪ Minimal food intake (> 48 hrs)	▪ Patient too sick for outpatient treatment
▪ NRTI-associated pancreatitis or lactic acidosis ▪ NVP-related hepatitis	▪ No treatment needed, but have patient return early if pain worsens	▪ Encourage frequent small meals ▪ Give Metoclopramide 10 mg every 12 hours prn ▪ Take blood for ALT and Lipase (or Amylase) and reassess in 2-3 days	▪ Consider stopping all ARVs* if lipase or amylase > 4 times normal, or ALT > 400 ▪ Also, check lactate level if patient has been on d4T for more than 4 months, to rule out high lactate as the cause	▪ Stop all ARVs and refer to hospital*
Vomiting	▪ Once per day and/or lasting < 3 days	▪ < 4 episodes per day and not dehydrated	▪ Vomits > 3 times per day, and dehydrated	▪ Dehydrated and too sick for outpatient treatment
▪ NRTI-associated pancreatitis or lactic acidosis ▪ NVP-related hepatitis	▪ Reassure patient, but have patient return early if worsens ▪ Consider giving Metoclopramide 10 mg every 12 hours prn	▪ Give ORT ▪ Encourage frequent small meals ▪ Give Metoclopramide 10 mg every 12 hours prn ▪ Take blood for ALT and Lipase (or Amylase) and reassess in 2-3 days	▪ Give ORT ▪ Give Metoclopramide 10 mg every 12 hours prn ▪ Consider stopping all ARVs* until blood results (Lipase and ALT) are available ▪ Check lactate level if patient has been on d4T for more than 4 months, to rule out high lactate as the cause	▪ Stop all ARVs and refer to hospital* ▪ Rehydrate with intravenous (IV) normal saline ▪ Check lactate level to rule out high lactate as the cause
Psychological	▪ Dizziness	▪ Vivid dreams	▪ Mood changes or persistent disturbing dreams	▪ Acute psychosis, hallucinations, confused behaviour
▪ EFV	▪ Reassure patient ▪ Confirm EFV is being taken at night	▪ Reassure patient ▪ Symptom will go away after few weeks	▪ Give Chlorpromazine 50 mg at night as needed	▪ Stop all ARVs and refer to hospital* ▪ Perform Lumbar Puncture to rule out meningitis ▪ Only restart ARVs when symptoms have fully resolved (use NVP instead of EFV)
Skin rash	▪ Red, itchy	▪ Maculo-papular rash or dry scales	▪ Blisters or moist loss of skin	▪ Rash involves mucous membranes or eyes +/- sloughing of skin

Symptom *(and diagnoses to consider, plus likely ARV responsible)*	Grade 1	Grade 2	Grade 3	Grade 4
▪ NVP (more commonly) ▪ EFV (but also consider TB meds or Co-trimoxazole as possible causes)	▪ Reassure, but have patient return early if worsens ▪ Consider giving Chlorpheniramine 4 mg every 8 hours prn, if itch is significant	▪ Give Aqueous cream +/- 0.1% Betamethasone ▪ Consider giving Chlorpheniramine 4 mg every 8 hours prn ▪ Check ALT, and reassess in 2-3 days ▪ Patient to return early if rash worse, or abdominal pain	▪ Stop all ARVs*, check ALT, and refer to doctor ▪ Give Chlorpheniramine 4 mg every 8 hours as needed ▪ When symptoms have resolved, restart ARVs using EFV (if rash was due to NVP)	▪ Stop all ARVs and refer to hospital ▪ ARVs can be restarted once patient is stable but avoid NVP or EFV in the future (instead, use Kaletra in the first-line regimen)
Elevated ALT *(in U/L)*	▪ 50 - 100	▪ 100 - 200	▪ 200 - 400	▪ > 400
▪ NVP (more commonly) ▪ EFV	▪ Continue ARVs, but recheck ALT in 1 month	▪ Continue ARVs if no other problem ▪ Recheck ALT again after 2 weeks	▪ Switch NVP to EFV (unless patient is in the first trimester of pregnancy) ▪ Monitor ALT weekly to ensure a fall in ALT	▪ Stop all ARVs and refer to hospital* ▪ Check ALT frequently to ensure it returns to normal ▪ Restart ARVs with EFV (unless in the first trimester of pregnancy)
Anaemia *(low Haemoglobin, in gm/dl)*	▪ 8 - 9,4	▪ 7 - 7,9	▪ 6,5 – 6,9	▪ < 6,5
▪ AZT	▪ Examine patient to rule out bleeding, or serious problem (including active TB) ▪ If no problem, continue ARVs ▪ Recheck Hb in 2 weeks	▪ Examine patient to rule out bleeding, or other serious problem (including disseminated TB) ▪ If no problem, continue ARVs ▪ Recheck Hb in 7 days	▪ Examine patient to rule out bleeding, and refer to doctor for assessment ▪ If no problem, switch AZT to ABC (or TDF, if contraindication to ABC) ▪ Recheck Hb weekly, to ensure rise in Hb ▪ Consider sending blood to lab for FBC (to rule out coexistent Neutropenia)	▪ Examine patient to rule out bleeding, and refer to hospital ▪ Consider blood transfusion ▪ Switch AZT to ABC (or TDF), or consider stopping all ARVs*
Neutropenia *(low absolute neutrophil count)*	▪ 1 - 1,5 x 106	▪ 0,75 - 1,0 x 106	▪ 0,5 - 0,75 x 106	▪ <0,5 x 106

Symptom *(and diagnoses to consider, plus likely ARV responsible)*	Grade 1	Grade 2	Grade 3	Grade 4
▪ AZT	▪ Continue ARVs ▪ Recheck FBC (+ differential) in 2 weeks	▪ Examine patient for any signs of infection ▪ Continue ARVs ▪ Recheck FBC (+ diff) in 2 weeks	▪ Examine patient for any signs of infection ▪ If no serious infection, switch AZT to d4T (or TDF, if d4T contraindicated) ▪ Recheck FBC (+ diff) weekly to ensure rise in absolute neutrophil count	▪ Examine patient for any signs of infection ▪ If serious infection, refer to doctor for assessment ▪ Switch AZT to d4T (or TDF), or consider stopping all ARVs*
Hyperlactatemia = High Lactate *(which will progress to lactic acidosis if not identified early, or managed appropriately!)*	▪ Asymptomatic ▪ and/or Lactate < 2.5	▪ Symptomatic hyperlactatemia ▪ (weight loss, fatigue, peripheral neuropathy, nausea, etc) ▪ Lactate between 2.5 – 3.5	▪ Symptomatic hyperlactatemia with risk of progression to lactic acidosis ▪ (Think of lactic acidosis if symptoms of hyperlactatemia, plus abdominal pain, vomiting, shortness of breath, and ketones on urine dipstick.) ▪ Lactate between 3.6 – 4.9	▪ Lactic acidosis (note that this condition can be fatal, if not managed appropriately and immediately!) ▪ Lactate 5.0 or greater, or RR > 20 (even if lactate level is < 5.0)
▪ AZT *(less commonly)*	▪ Continue ARVs	▪ Examine patient to rule out new infection ▪ Check urine for ketones (using dipstick) to rule out acidosis ▪ Monitor lactate level weekly until lactate normalizes	▪ Examine patient to rule out new infection and/or acidosis ▪ Check urine for ketones (using dipstick) to rule out acidosis ▪ Monitor lactate level weekly until lactate normalizes ▪ If lactate does not improve, stop all ARVs (and consider giving Kaletra 4 tabs BD for one week to prevent resistance to NNRTI) ▪ When lactate level is normal, use TDF (avoid AZT)	▪ Admit to hospital ▪ Rehydrate with intravenous fluid (+/- bicarbonate) ▪ Investigate for new infection (pneumonia, sepsis, TB, etc) ▪ Consider giving i.v. Ceftriaxone for 3 days ▪ Monitor lactate level frequently until normal ▪ When lactate level is normal, restart ARVs with Tenofovir (TDF) ▪ Avoid d4T, ddI, and all other NRTIs in the future

**Whenever possible, use 'tail protection' to prevent the development of resistance to NVP or EFV. This means stopping NVP or EFV first, and continuing 2 NRTIs (TDF/3TC, AZT/3TC or d4T/3TC, as appropriate) for one week*

ANNEX 7: HIV CHRONIC CARE/ART REFERRAL FORM

Referral From: ……

Referral to: ……

Name:……Age:……

Physical Address:…… ……sex:…… ……

Date confirmed HIV positive: dd [ ] mm[ ] yy [ ]

Pre-ART information(if client is referred before starting ARVs)
HIV Chronic Care no: ……
Date Enrolled in Chronic Care: ……
Recent CD4 Count & Clinical Stage: [CD4]……Clinical stage: ……
Date of last assessment: ……
ART information: (if client is referred already on ARVs)
ART Unique number:……Date started ART: dd[ ] mm [ ] yy [ ]
COHORT: mm [ ] yy [ ]
At Start of ART: Weight: :……Functional status: ……
Clinical Stage: [1] [2] [3] [4] (please tick)
CD4 Count: ……Date done: ……
Initial regimen: ……
Current regimen (During transfer): ……

Laboratory Investigations:

Date	Hb/FBC	ALT/LFT	CD4	Creatinine	HBs(AG)	HCV

Comments:……
……
……
Name of referring Doctor: ……Date……
Signature:……Phone no:……

ANNEX 8: ADHERENCE CONTRACT

ADHERENCE PLAN:

Please tick after each statement once it has been reviewed with the applicable individual(s):

1. I understand that antiretroviral drugs (ARVs) against HIV stop the virus from multiplying, leading to a better quality of life, although they are not a cure for HIV. HIV is a lifelong infection and ARVs are a lifelong treatment. Therefore, even if I/my child feels better after starting the ARVs, I understand that if the ARVs are stopped, sickness will resume.

[ ] Primary Caretaker [ ] Patient (if disclosed to) [ ] Caretaker #2, if applicable [ ] Caretaker #3, if applicable

2. I understand that taking all of the ARV medications together as prescribed is critical to treatment success, and that even missing 1 dose may result in permanent drug failure and sickness. I will not miss any doses. If I do miss doses, I will ask the clinic for help since it is so important.

[ ] Primary Caretaker [ ] Patient (if disclosed to) [ ] Caretaker #2, if applicable [ ] Caretaker #3, if applicable

3. I understand that I/my child cannot miss any doses. Therefore, I will return on time for each clinic appointment for ARV refills. If I run out of ARVs in advance of my/mychild's appointment due to an accident/spill, then I will return to the clinic immediately for a refill on a clinic day.

[ ] Primary Caretaker [ ] Patient (if disclosed to) [ ] Caretaker #2, if applicable [ ] Caretaker #3, if applicable

4. I understand that since all the ARVs must be taken together to work, I will not stop any one of the medications without consultation with a doctor. I will not give away or sell the ARVs to anyone since this will be hurtful to me/my child and to the other person. I understand that if I stop one or more ARVs without the advice of a doctor, I may seriously hurt my/my child's future treatment options because of HIV resistance. The first ARV regimen is the most important/effective. If it fails, the options are limited.

[ ] Primary Caretaker [ ] Patient (if disclosed to) [ ] Caretaker #2, if applicable [ ] Caretaker #3, if applicable

5. I understand that the ARVs must be taken at the same time of day every day. However, should I forget to administer/take a dose, I should administer/take it as soon as I remember. However, if it is 6 hours past the time that the dose was due (for twice daily ARVs) or 12 hours past the time the dose was due (for once daily ARVs), then skip the missed dose and continue your regular dosing schedule. Do not take a double dose to make up for a missed one.

[ ] Primary Caretaker [ ] Patient (if disclosed to) [ ] Caretaker #2, if applicable [ ] Caretaker #3, if applicable

6. I understand that all medications may have associated side effects. These may include temporary weakness, rash, tiredness or lack of blood, loose stools, tingling sensation in the feet, vivid dreams, or others. I will come to the clinic if any side effects occur and will not stop any medications unless directed to do so by a doctor.

[ ] Primary Caretaker [ ] Patient (if disclosed to) [ ] Caretaker #2, if applicable [ ] Caretaker #3, if applicable

7. If I/my child vomits within 30 minutes of taking the medication, or if I can see the ARVs in the vomit itself, then I will repeat the dose.
[ ] Primary Caretaker [ ] Patient (if disclosed to) [ ] Caretaker #2, if applicable [ ] Caretaker #3, if applicable

8. I will bring my/my child's ARVs and/or pill box to every visit.

[ ] Primary Caretaker [ ] Patient (if disclosed to) [ ] Caretaker #2, if applicable [ ] Caretaker #3, if applicable

9. For caretaker(s): I am fully committed to making certain that the child I am caring for receives his/her ARVs. If I can no longer care for the child, I will let the clinic counselor know in as far advance as possible, so that another adult may be counseled to do so.

[ ] Primary Caretaker [ ] Caretaker #2, if applicable [ ] Caretaker #3, if applicable

10. For caretaker(s) of children only: I understand that I should encourage my child to be responsible for taking their ARVs; however, I understand that children must be directly monitored while swallowing the ARVs and I will closely supervise them successfully taking them.

[ ] Primary Caretaker [ ] Caretaker #2, if applicable [ ] Caretaker #3, if applicable

For all patients if disclosed to: I understand that since ARVs are not a cure, it is still possible for me to pass on the virus to someone else through my blood or through sexual intercourse. I understand how to avoid passing the virus to others, and I understand that it is possible for me to contract another strain of HIV, such that it is also in my best interest to protect myself from further infection.

[ ] Patient (if disclosed to)

12. For all female patients if disclosed to: I understand that it is still possible for me to transmit HIV mother-to-child during pregnancy, delivery, or breastfeeding even while on ARVs, although this risk is lower than among HIV-positive women not on ARVs. Since some ARVs may harm the developing fetes, I will inform my doctor if I am or plan to become sexually active or pregnant.

[ ] Patient (if disclosed to)

ADHERENCE COMMITTMENT:

By signing below, I commit to adhering to each and every dose of ARV medication for the rest of my/the child I care for's life:

Primary Caretaker Name	Primary Caretaker Signature	Date
Patient's Name (*if disclosed to)*	Patient's Signature	Date
Caretaker #2 Name *(if applicable; required, if High Risk)*	Caretaker #2 Signature	Date
Caretaker #3 Name *(if applicable)*	Caretaker #3 Signature	Date
Counselor Name	Counselor Signature	Date

TUMELLANO KAPA BOITLAMO BA HO NOA LITLHARE KA NEPO

Letsatsi:_____ Nomoro ea Faele:_____

U koptjoa ho ts'oaea ka mor'a hoba polelo ka 'ngoe e hlahlojoe le motho /batho ba lokelang.

1. Kea utloisisa hore litlhare tsa li ARV khahlanong le HIV, li thibela kokoana-hloko ho ikatisa, e leng ho lebisang bophelong ba boleng bo betere, leha e se pheko ea HIV. HIV ke ts'oaetso ea bophelo bohle 'me li ARV ke kalafo ea bophelo bohle. Kahoo, leha eba 'na kapa ngoan'aka a ikutloa a le betere kamor'a ho qala li ARV, kea utloisisa hore ha li ARV li khaotsoa, bokuli botla tsoela-pele hape.
[ ] Mohlokomeli oa mathomo [ ] Mokuli (haeba a se a boleletsoe boemo)
[ ] Mohlokomeli oa bobeli, haeba a le teng [ ] Mohlokomeli oa boraro haeba a le teng.

2. Kea utloisisa hore ho noa li ARV hammoho, joalo ka ha ho boletsoe, ho bohlokoa bakeng sa kalafo e atlehileng, 'me le hore leha ele ho fosa ho noa le se le seng sa litlhare ho ka baka ho hlolehela ruri hoa litlhare le bokuli. Nkeke ka fosa ho noa litlhare leha e le ha 'ngoe. Ha nka fosa, ke tla kopa cliniki hore e nthuse ka ha hoo ho le bohlokoa.
[ ] Mohlokomeli oa mathomo [ ] Mokuli (haeba a se a boleletsoe boemo)
[ ] Mohlokomeli oa bobeli, haeba a le teng [ ] Mohlokomeli oa boraro haeba a le teng.

3. Kea utloisisa hore 'na kapa ngoana'ka a keke a fosa ho noa litlhare, kahoo ke tla khutlela cliniking ka nako bakeng sa matsatsi ao ke a behetsoeng ho lata litlhare. Haeba litlhare li mphella pele ho nako e behiloeng ka baka la tsietsi kapa ho qhalana, ke tla khutlela cliniking hang-hang, ka letsatsi la cliniki la ts'ebetso.
[ ] Mohlokomeli oa mathomo [ ] Mokuli (haeba a se a boleletsoe boemo)
[ ] Mohlokomeli oa bobeli,haeba a le teng [ ] Mohlokomeli oa boraro haeba a le teng.

4. Kea utloisisa hore ka ha li ARV li lokela ho nooa kaofela, hammoho hore li tle li sebetse, nke ke ka khaotsa ho noa kapa ho noesa ngoana setlhare sefe kapa sefe ntle le ho botsa ngaka. Nke ke ka fana kapa ka rekisa li ARV ho mang kapa mang, ka ha hoo ho ba kotsi ho 'na kapa ngoana'ka le ho motho eo e mong. Kea utloisisa hore ha ke khaotsa ho noa kapa ho noesa ngoana'ka setlhare se le seng, kapa ho feta, ntle le boeletsi ba ngaka, nka baka kotsi kalafong ea kamoso ea ka kapa ea ngoana'ka, ka lebaka la manganga a HIV. Mokhahlelo oa pele oa kalafo ke 'ona o bohlokoahali. Ha o hloleha, menyetla ea kalafo e se e fokola.
[ ] Mohlokomeli oa mathomo [ ] Mokuli (haeba a se a boleletsoe boemo)
[ ] Mohlokomeli oa bobeli, haeba a le teng [ ] Mohlokomeli oa boraro haeba a le teng.

5. Kea utloisisa hore li ARV li lokela ho nooa ka nako e le 'ngoe letsatsi le letsatsi. Leha ho le joalo, ha nka lebala ho noa kapa ho noesa ngoana litlhare, ke lokela ho noa kapa ho mo noesa lithlare tseo hang ha ke hopola. Empa haeba ke hopola kamor`a lihora tse ts'eletseng (bakeng sa litlhare tse nooang habeli ka letsatsi), ke tla tlola litlhare tseo tse fetiloeng ke nako, ke tsoele-pele ka nako ea mehla. Nke ke ka noa kapa ka noesa ngoana litlhare habeli ele ho lefa tse fetiloeng ke nako kapa tseo nako ea tsona e fositsoeng.
[ ] Mohlokomeli oa mathomo [ ] Mokuli (haeba a se a boleletsoe boemo)
[ ] Mohlokomeli oa bobeli, haeba a le teng [ ] Mohlokomeli oa boraro haeba a le teng.

6. Kea utloisisa hore litlhare tsohle li ka ba le litla-morao. Litla-morao tsena li ka kenyeletsa ho fokolloa ke matla ha nakoana, lekhopho, mokhathala kapa khaello ea mali, ho choachoasela ha maoto, litoro tse matla, le tse ling. Ke tla tla cliniking haeba se seng sa litla-morao se iponahatsa, 'me nke ke ka khaotsa ho noa kapa ho noesa ngoana litlhare, ntle le ha ngaka e bolela joalo.
[ ] Mohlokomeli oa mathomo [ ] Mokuli (haeba a se a boleletsoe boemo)
[ ] Mohlokomeli oa bobeli, haeba a le teng [ ] Mohlokomeli oa boraro haeba a le teng.

7. Haeba ‘na kapa ngoana’ka a hlatsa nakong ea metsotso e mashome a mararo a ho noa litlhare, kapa haeba nka ka bona li ARV ka bo tsona mahlatseng, ke tla pheta ho noa kapa ho noesa ngoana litlhare.
[ ] Mohlokomeli oa mathomo [ ] Mokuli (haeba a se a boleletsoe boemo)
[ ] Mohlokomeli oa bobeli, haeba a le teng [ ] Mohlokomeli oa boraro haeba a le teng.

8. Ke tla tla le lebokose la ka kapa la ngoana’ka la litlhare nako eohle ha ke khutlela cliniking.
[ ] Mohlokomeli oa mathomo [ ] Mokuli (haeba a se a boleletsoe boemo)
[ ] Mohlokomeli oa bobeli, haeba a le teng [ ] Mohlokomeli oa boraro haeba a le teng.

9. Bakeng sa bahlokomeli: ke itlama ka botlalo ho netefatseng hore ngoana eo ke mo hlokomelang o fumana li ARV. Haeba ke se ke sitoa ho tsoela-pele ho mo hlokomela, ke tla bolella mohlabolli oa cliniki kapele kamoo ho ka khonahalang, ele hore motho e mong e moholo a tle a hlabolloe ho etsa joalo (ho hlokomela ngoana).
[ ] Mohlokomeli oa mathomo [ ] Mokuli (haeba a se a boleletsoe boemo)
[ ] Mohlokomeli oa bobeli, haeba a le teng [ ] Mohlokomeli oa boraro haeba a le teng.

10. Bakeng sa bahlokomeli ba bana feela: kea utloisisa hore ke lokela ho khothaletsa ngoana’ka ho ba le boikarabello ba ho noa li ARV; leha ho le joalo, kea utloisisa hore bana ba lokela ho supisoa ka kotloloho ha ba e-noa kapa ba koenya li ARV, ‘me ke tla ba tataisa ka hloko ho li noeng.
[ ] Mohlokomeli oa mathomo [ ] Mokuli (haeba a se a boleletsoe boemo)
[ ] Mohlokomeli oa bobeli,haeba a le teng [ ] Mohlokomeli oa boraro haeba a le teng.

11. Bakeng sa bakuli bohle, haeba ba boleletsoe boemo ba bona: kea utloisisa hore kaha li ARV hase pheko, ho ntse ho khonahala hore nka fetisetsa kokoana-hloko ho ba bang, ‘me kea utloisisa hore hoa khonahala hore nka fumana mofuta o mong oa HIV, hoo ho molemong oa ka ho its’ireletsa khahlanong le ts’oaetso e `ngoe. [ ] Mokuli (haeba a boleletsoe boemo ba hae).

E tekennoe ke: Mohlokomeli oa mathomo: _____
Mohlokomeli oa bobeli kapa mots’ehetsi: _____
Mokuli (haeba a le kaholimo ho lilemo tse 12): _____

ANNEX 9: DRUG-DRUG INTERACTIONS

(Modified from WHO Recommendations Aug 2006)

	NVP	EFV	LPV/r
Anti-mycobacterium/Antibiotics			
Rifampin	↓ NVP by 20-58%. Per Lesotho Guidelines, ok to coadminister for concurrent ATT/ART in children < 3yrs or < 10kg	↓ EFV by 25%	↓ LPV by 75% Double lpv/r dose while on concurrent ATT/ART. Do not forget to change dose once ATT completed.
Clarithromycin	None	↓ clarithro by 39% Monitor efficacy or use alternative drugs	↑ clarithro by 75% Adjust clarithro dose if renal impairment
Antifungals			
Ketoconazole	↑ ketoconazole by 63% ↑ NVP by 15-30% DO NOT COADMINISTER	No significant change in ketoconazole or EFV levels	↑ LPV ↑ ketoconazole 3x Do not exceed 200mg/day ketoconazole
Fluconazole	↑ NVP Cmax, AUC, Cmin by 100% No change in fluc level Possible increase in hepatotoxicity	No data	
Oral Contraceptives			
Ethinyl estradiol	↓ ethinyl estradiol by 20% USE ALTERNATIVE OR ADDITIONAL METHODS	↑ ethinyl estradiol by 37% USE ALTERNATIVE OR ADDITIONAL METHODS	↓ ethinyl estradiol by 42% USE ALTERNATIVE OR ADDITIONAL METHODS
Lipid lowering agents			
Simvastatin, lovastatin	No data	↓ simvastatin by 58% EFV unchanged	Potential large ↑ statin DO NOT COADMINISTER
Anti-epileptics			
Carbamazepine **Phenytoin**	USE WITH CAUTION	USE WITH CAUTION	↑ levels when coadministerd with RTV USE WITH CAUTION
Phenytoin	USE WITH CAUTION	USE WITH CAUTION One case report showed low EFV with phenytoin	↓ levels of LPV/r and ↓ levels of phenytoin DO NOT COADMINISTER
Phenobarbital	USE WITH CAUTION	USE WITH CAUTION	USE WITH CAUTION
Other			
Cisapride		↑ cisapride DO NOT COADMINISTER	↑ cisapride DO NOT COADMINISTER
Midazolam	Potential interaction, may require close monitoring	DO NOT COADMINISTER	DO NOT COADMINISTER
Methadone	Methadone ↓ significantly; opiate withdrawal common; increase methadone dose often necessary	Methadone ↓ 60% opiate withdrawal common; increase methadone dose often necessary	Methadone ↓ 53% opiate withdrawal may occur; may require increase in methadone dose

ARV-ARV Interactions

NVP – LPV/r	NVP lowers LPV/r level ▪ Dose of LPV/r must be increased to 600/150 BD (3 tabs) for treatment experienced. ▪ Standard dose of LPV/r can be used for treatment naïve.
EFV – LPV/r	EFV lowers LPV/r level ▪ Dose of LPV/r must be increased to 600/150 BD (3 tabs) for treatment experienced. ▪ Standard dose of LPV/r can be used for treatment naïve.
LPV/r – ddI	LPV/r requires an acidic environment (with meals), ddI requires an antacid for buffering; ▪ LPV/r and ddI should not be coadministered at the same time. ▪ ddI should be taken before meals (30-60 minutes) and ▪ LPV/r should be taken with the meal.
TDF – ddI	TDF increases the levels of ddI; for body weight < 60kg, dose of ddI may be lowered ▪ This combination should be avoided.
ddI – d4t	▪ This combination should be avoided due to overlapping toxicities
d4t – AZT	▪ This combination should never be used due to overlapping mechanism of action.

If patient is taking other ARV drugs or other traditional medicines consult with HIV specialist

ANNEX 10: HOW TO ANALYSE INDICATORS AND IDENTIFY PROBLEMS

Calculating and analysing the indicators listed in the chart below will help to monitor chronic HIV care and ART in your district.

Indicators related to ART at the district level

Indicator	Time frame for cohort	Which number or formula for calculating *(numerator / denominator)*[a]	Sources of data
1. Indicators related to patients accessing HIV care and ART			
1a. Number enrolled in HIV care	Last quarter	- New in last month - Cumulative number of persons enrolled in HIV care	Quarterly report form—Table 1
1b. Number started on ART	Last quarter	- New in last month - Cumulative number of persons ever started on ART at this facility	Quarterly report form—Table 2
1b. Number currently on ART	Cross-sectional—at end of last quarter	Total and disaggregated by sex, adult /child	Quarterly report form—Table 4
1c. Number of persons who are enrolled and eligible for ART but have not been started on ART	Cross-sectional—at end of last quarter	Total number enrolled and eligible but not on ART (S1 + S2)	Quarterly report form—Table 1
1d. Proportion of those eligible for ART in clinic who have been started on ART	Cross-sectional—at end of last quarter	Cumulative number of persons ever started on ART at this facility --- Total number enrolled and eligible but not on ART (S1 + S2) plus cumulative number of persons ever started on ART at this facility	Quarterly report form
1e. Proportion of people with advanced HIV infection receiving ARV combination therapy (UNGASS core indicator)	Cross-sectional	Number currently on ART --- Denominator is an estimate based on HIV prevalence and expected proportion with AIDS (not from register data)	Quarterly report form --- Estimate, HIV prevalence data
2. Indicators related to success of ART			
2a. Core indicator 9 Survival at 6, 12, 24, 36 months etc after initiation of ART	6 months on ART, 12 months on ART, 24 months, 36 months etc on ART	H + I + J --- N	Cohort analysis form --- Cohort analysis form
2b. Core indicator 8	6 months on ART, 12 months on ART, 24 months on ART	6 months on ART, 12 months on ART, 24 months, 36 months etc on ART ---	Cohort analysis form ---

Indicator	Time frame for cohort	Which number or formula for calculating *(numerator / denominator)*[a]	Sources of data
Continuation of first-line ARV regimen at 6, 12 and 24 months after initiating treatment		Persons who started 1st-line ART for the first time during the time period under consideration.	Cohort analysis form
2c. Proportion of people on ART at 6, 12 and 24 months whose functional status is working	6 months on ART, 12 months on ART, 24 months, 36 months etc on ART	Working --- Working + Ambulatory + Bedridden	Cohort analysis form
2d. Median CD4 and increase at 6 and at 12 months on ART compared to baseline.			Cohort analysis form
3. HIV drug resistance early warning indicators			
3a. Proportion of patients who started ART 6 or 12 months ago who picked up ARV medications 6/6 or 12/12 months.	Cross-sectional—at end of last quarter	Persons who started ART 6 or 12 months ago who picked up ARV medications 6/6 or 12/12 months. --- Persons who started ART 6 or 12 months ago and are still prescribed ART at the end of the time period.	Cohort analysis form
3b. Proportion of patients with (good) adherence to ART			Patient encounter form

Other indicators for facility-level programme monitoring

Indicator	Rationale
a. Number on cotrimoxazole, fluconazole, INH prophylaxis at end of month	Drug supply orders
b. Distribution of entry points of patients enrolled in HIV care	Identifies linkages between programmes and activities
c. Distribution of reasons for regimen substitution, switching, termination, interruption, and poor adherence	Helps clinical team to identify and respond to poor adherence; assists with quality assurance related to regimen substitutions, switches and interruptions.
d. Distribution of patients not yet on ART by clinical stage	May help estimate resources to care for patients, drug supply for OI prophylaxis and treatment.
e. Percentage of patients referred	Monitoring referral rates may enable facilities to manage referral systems more efficiently
f. Side effects, OIs, other problems	Facilitates individual patient management and allows review of side effects and new OIs

Calculating indicators or other aggregated data

Agreed minimum essential data elements	What happens to the data	Indicators or other aggregated data
At baseline, 6, 12 months then yearly; disaggregated by sex and child/adult: On ART and: ALIVE DEAD LOST/DROP/Transfer out Current regimen Original 1st-line Substituted to alternative 1st-line 2nd-line or higher CD4 test results Functional status Regimen collected in last quarter	Transfer to ART register then to Cohort Analysis Report	Based on cohort analysis form, at 6, 12 months then yearly and compared to baseline: Indicators related to success of ART Proportion alive and on ART/Mortality on ART Proportion still on a first-line regimen Proportion working, ambulatory, bedridden Median or mean CD4 counts (optional) HIV drug resistance early warning indicators: Proportion switched to a second-line (or higher) regimen Proportion collected ARV drugs 6/6 or 12/12 months
B. When registered for HIV care When medically eligible for ART When medically eligible and ready for ART When ART started Dead before ART Lost or Transfer out before ART	Transfer to pre-ART or ART register then to Quarterly Report	Indicators related to patients accessing HIV care and ART: Disaggregated by adult, child, sex, pregnancy status: Number enrolled in HIV care: new and cumulative ever at the facility Number started on ART: new and cumulative ever started at the facility Number currently on ART at the facility Not disaggregated: Number eligible for ART but not yet started
C. Entry point Why eligible for ART Reasons for: Substitution within first-line Switch/Substitution to or within second-line Stop ART Number and weeks of each ART treatment interruption Pregnancy status Start/stop dates of prophylaxis: Co-trimoxazole Fluconazole INH TB treatment	Transferred to Pre-ART or ART Register but used only by clinical team /district ART coordinator not transferred to quarterly report or cohort analysis	Indicators for patient and programmeme management at the facility/district level: Distribution of entry points in patients enrolled in HIV care Why eligible for ART: clinical only, CD4 or TLC Distribution of patients not yet on ART by clinical stage Distribution of reasons for substitute, switch, stop to investigate problems; whether substitutions and switches are appropriate (use in context reviewing medical officer log) ART treatment interruptions: Number/Proportion of patients Number weeks

Agreed minimum essential data elements	What happens to the data	Indicators or other aggregated data
Adherence on ART		Proportion of pregnant patients linked with PMTCT interventions (or simply use to generate lists to assure linkage) Number on co-trimoxazole, fluconazole, INH prophylaxis at end of quarter (for ordering prophylaxis drugs) Number/Proportion of patients on both TB treatment and ART % patients with good adherence to ART
D. Date of each encounter Weight (each visit; % wt gain or loss) Adherence on CTX Adherence on INH Potential side effects New OI, other problems TB status (other than treatment or prophylaxis) Referred or consulted with MD Number inpatient days If poor adherence on ART, reasons (coded)	Patient Card only. Not transferred to register	Indicators for patient management at the facility level or special studies: % patients referred to MD Common side effects, OI, other problems: Patients with special problems Identify patients for review at clinical team meetings # or proportion patients hospitalized; number days Reasons for poor adherence

National core indicators

These are used both for individual patient management and for medical officer or clinical mentor review on site visits. For potentially serious side effects which result in a consultation or referral, medical officer needs to put in log and do further adverse even reporting. Tabulations for special studies

ANNEX 11: WEIGHT-BASED DOSING OF ANTI-TB FIXED-DOSE COMBINATION MEDICATIONS

Weight-based dosing of anti-TB medications using pediatric formulations (2-25 kg body weight)

Weight (kg)	Intensive phase (2 months)		Continuation phase (4 months)
	RHZ (pediatric) 60/30/150 mg	Ethambutol 100 mg	RH (pediatric) 60/60 mg
2 - 3.9 kg	1/2 tablet	1/2 tablet	1/2 tablet
4 - 5.9 kg	1 tablet	1 tablet	1 tablet
6 - 7.9 kg	1.5 tablets	1.5 tablets	1.5 tablets
8 - 10.9 kg	2 tablets	2 tablets	2 tablets
11 - 14.9 kg	3 tablets	2 tablets	3 tablets
14 - 19.9 kg	4 tablets	3 tablets	4 tablets
20-24.9 kg	5 tablets	4 tablets *(or 400mg tablet)*	5 tablets

* Follow adult dosing for children weighing 25kg or above.

Recommended treatment regimen and dosages for new adult TB cases

Phase of treatment	Drugs	Weight in kg			
		30-39	40-54	55-70	>70
Intensive phase of 2 months	**RHZE*** 150mg/75mg/400mg/275mg	2 tabs daily	3 tabs daily	4 tabs daily	5 tabs daily
Continuation phase of 4 months	**RH 150mg/75mg**	2 tabs daily	3 tabs daily	4 tabs daily	5 tabs daily

***Fixed-dose combination (FDC) drugs

Dosing for INH prophylaxis for children

Weight (kg)	Daily Dosage (mg) 10 mg/kg/day for 6 months	Number of 100mg Tablets of INH given daily
< 5.0	50 mg	½ tab
5.1-9.9	100 mg	1 tab
10-13.9	150 mg	1.5 tabs
14-19.9	200 mg	2 tabs
20-24.9	250 mg	2.5 tabs
>25	300 mg	3 tabs

ANNEX 12: REFERENCE VALUES FOR WEIGHT-FOR-HEIGHT AND WEIGHT-FOR-LENGTH

Weight-for-Height Reference Table (WHO)

Boys weight (kg)						Girls weight (kg)				
-4SD	-3SD	-2SD	-1SD	Median	Length (cm)[a]	Median	-1SD	-2SD	-3SD	-4SD
1,7	1,9	2,0	2,2	2,4	**45,0**	2,5	2,3	2,1	1,9	1,7
1,8	1,9	2,1	2,3	2,5	**45,5**	2,5	2,3	2,1	2,0	1,8
1,8	2,0	2,2	2,4	2,6	**46,0**	2,6	2,4	2,2	2,0	1,9
1,9	2,1	2,3	2,5	2,7	**46,5**	2,7	2,5	2,3	2,1	1,9
2,0	2,1	2,3	2,5	2,8	**47,0**	2,8	2,6	2,4	2,2	2,0
2,0	2,2	2,4	2,6	2,9	**47,5**	2,9	2,6	2,4	2,2	2,0
2,1	2,3	2,5	2,7	2,9	**48,0**	3,0	2,7	2,5	2,3	2,1
2,1	2,3	2,6	2,8	3,0	**48,5**	3,1	2,8	2,6	2,4	2,2
2,2	2,4	2,6	2,9	3,1	**49,0**	3,2	2,9	2,6	2,4	2,2
2,3	2,5	2,7	3,0	3,2	**49,5**	3,3	3,0	2,7	2,5	2,3
2,4	2,6	2,8	3,0	3,3	**50,0**	3,4	3,1	2,8	2,6	2,4
2,4	2,7	2,9	3,1	3,4	**50,5**	3,5	3,2	2,9	2,7	2,4
2,5	2,7	3,0	3,2	3,5	**51,0**	3,6	3,3	3,0	2,8	2,5
2,6	2,8	3,1	3,3	3,6	**51,5**	3,7	3,4	3,1	2,8	2,6
2,7	2,9	3,2	3,5	3,8	**52,0**	3,8	3,5	3,2	2,9	2,7
2,8	3,0	3,3	3,6	3,9	**52,5**	3,9	3,6	3,3	3,0	2,8
2,9	3,1	3,4	3,7	4,0	**53,0**	4,0	3,7	3,4	3,1	2,8
3,0	3,2	3,5	3,8	4,1	**53,5**	4,2	3,8	3,5	3,2	2,9
3,1	3,3	3,6	3,9	4,3	**54,0**	4,3	3,9	3,6	3,3	3,0
3,2	3,4	3,7	4,0	4,4	**54,5**	4,4	4,0	3,7	3,4	3,1
3,3	3,6	3,8	4,2	4,5	**55,0**	4,6	4,2	3,8	3,5	3,2
3,4	3,7	4,0	4,3	4,7	**55,5**	4,7	4,3	3,9	3,6	3,3
3,5	3,8	4,1	4,4	4,8	**56,0**	4,8	4,4	4,0	3,7	3,4
3,6	3,9	4,2	4,6	5,0	**56,5**	5,0	4,5	4,2	3,8	3,5
3,7	4,0	4,3	4,7	5,1	**57,0**	5,1	4,6	4,3	3,9	3,6
3,8	4,1	4,5	4,9	5,3	**57,5**	5,2	4,8	4,4	4,0	3,7
3,9	4,3	4,6	5,0	5,4	**58,0**	5,4	4,9	4,5	4,1	3,8
4,0	4,4	4,7	5,1	5,6	**58,5**	5,5	5,0	4,6	4,2	3,9
4,1	4,5	4,8	5,3	5,7	**59,0**	5,6	5,1	4,7	4,3	3,9
4,2	4,6	5,0	5,4	5,9	**59,5**	5,7	5,3	4,8	4,4	4,0
4,3	4,7	5,1	5,5	6,0	**60,0**	5,9	5,4	4,9	4,5	4,1
4,4	4,8	5,2	5,6	6,1	**60,5**	6,0	5,5	5,0	4,6	4,2
4,5	4,9	5,3	5,8	6,3	**61,0**	6,1	5,6	5,1	4,7	4,3
4,6	5,0	5,4	5,9	6,4	**61,5**	6,3	5,7	5,2	4,8	4,4
4,7	5,1	5,6	6,0	6,5	**62,0**	6,4	5,8	5,3	4,9	4,5
4,8	5,2	5,7	6,1	6,7	**62,5**	6,5	5,9	5,4	5,0	4,6
4,9	5,3	5,8	6,2	6,8	**63,0**	6,6	6,0	5,5	5,1	4,7
5,0	5,4	5,9	6,4	6,9	**63,5**	6,7	6,2	5,6	5,2	4,7
5,1	5,5	6,0	6,5	7,0	**64,0**	6,9	6,3	5,7	5,3	4,8
5,2	5,6	6,1	6,6	7,1	**64,5**	7,0	6,4	5,8	5,4	4,9
5,3	5,7	6,2	6,7	7,3	**65,0**	7,1	6,5	5,9	5,5	5,0
5,4	5,8	6,3	6,8	7,4	**65,5**	7,2	6,6	6,0	5,5	5,1
5,5	5,9	6,4	6,9	7,5	**66,0**	7,3	6,7	6,1	5,6	5,1
5,5	6,0	6,5	7,0	7,6	**66,5**	7,4	6,8	6,2	5,7	5,2
5,6	6,1	6,6	7,1	7,7	**67,0**	7,5	6,9	6,3	5,8	5,3
5,7	6,2	6,7	7,2	7,9	**67,5**	7,6	7,0	6,4	5,9	5,4
5,8	6,3	6,8	7,3	8,0	**68,0**	7,7	7,1	6,5	6,0	5,5
5,9	6,4	6,9	7,5	8,1	**68,5**	7,9	7,2	6,6	6,1	5,5
6,0	6,5	7,0	7,6	8,2	**69,0**	8,0	7,3	6,7	6,1	5,6
6,0	6,6	7,1	7,7	8,3	**69,5**	8,1	7,4	6,8	6,2	5,7
6,1	6,6	7,2	7,8	8,4	**70,0**	8,2	7,5	6,9	6,3	5,8
6,2	6,7	7,3	7,9	8,5	**70,5**	8,3	7,6	6,9	6,4	5,8
6,3	6,8	7,4	8,0	8,6	**71,0**	8,4	7,7	7,0	6,5	5,9
6,4	6,9	7,5	8,1	8,8	**71,5**	8,5	7,7	7,1	6,5	6,0
6,4	7,0	7,6	8,2	8,9	**72,0**	8,6	7,8	7,2	6,6	6,0
6,5	7,1	7,6	8,3	9,0	**72,5**	8,7	7,9	7,3	6,7	6,1
6,6	7,2	7,7	8,4	9,1	**73,0**	8,8	8,0	7,4	6,8	6,2
6,7	7,2	7,8	8,5	9,2	**73,5**	8,9	8,1	7,4	6,9	6,3
6,7	7,3	7,9	8,6	9,3	**74,0**	9,0	8,2	7,5	6,9	6,3
6,8	7,4	8,0	8,7	9,4	**74,5**	9,1	8,3	7,6	7,0	6,4
6,9	7,5	8,1	8,8	9,5	**75,0**	9,1	8,4	7,7	7,1	6,5
7,0	7,6	8,2	8,9	9,6	**75,5**	9,2	8,5	7,8	7,1	6,5
7,0	7,6	8,3	8,9	9,7	**76,0**	9,3	8,5	7,8	7,2	6,6
7,1	7,7	8,3	9,0	9,8	**76,5**	9,4	8,6	7,9	7,3	6,7
7,2	7,8	8,4	9,1	9,9	**77,0**	9,5	8,7	8,0	7,4	6,7
7,2	7,9	8,5	9,2	10,0	**77,5**	9,6	8,8	8,1	7,4	6,8
7,3	7,9	8,6	9,3	10,1	**78,0**	9,7	8,9	8,2	7,5	6,9
7,4	8,0	8,7	9,4	10,2	**78,5**	9,8	9,0	8,2	7,6	6,9
7,4	8,1	8,7	9,5	10,3	**79,0**	9,9	9,1	8,3	7,7	7,0
7,5	8,2	8,8	9,5	10,4	**79,5**	10,0	9,1	8,4	7,7	7,1
7,6	8,2	8,9	9,6	10,4	**80,0**	10,1	9,2	8,5	7,8	7,1
7,6	8,3	9,0	9,7	10,5	**80,5**	10,2	9,3	8,6	7,9	7,2
7,7	8,4	9,1	9,8	10,6	**81,0**	10,3	9,4	8,7	8,0	7,3
7,8	8,5	9,1	9,9	10,7	**81,5**	10,4	9,5	8,8	8,1	7,4
7,9	8,5	9,2	10,0	10,8	**82,0**	10,5	9,6	8,8	8,2	7,5
7,9	8,6	9,3	10,1	10,9	**82,5**	10,6	9,7	8,9	8,2	7,5
8,0	8,7	9,4	10,2	11,0	**83,0**	10,7	9,8	9,0	8,3	7,6
8,1	8,8	9,5	10,3	11,2	**83,5**	10,9	9,9	9,1	8,4	7,7
8,2	8,9	9,6	10,4	11,3	**84,0**	11,0	10,1	9,2	8,5	7,8
8,3	9,0	9,7	10,5	11,4	**84,5**	11,1	10,2	9,3	8,6	7,9

Weight-for-Height Reference Table (WHO)

Boys weight (kg)						Girls weight (kg)				
-4SD	-3SD	-2SD	-1SD	Median	Height (cm)[a]	Median	-1SD	-2SD	-3SD	-4SD
8,4	9,1	9,8	10,6	11,5	**85,0**	11,2	10,3	9,4	8,7	8,0
8,5	9,2	9,9	10,7	11,6	**85,5**	11,3	10,4	9,6	8,8	8,0
8,6	9,3	10,0	10,8	11,7	**86,0**	11,5	10,5	9,7	8,9	8,1
8,7	9,4	10,1	11,0	11,9	**86,5**	11,6	10,6	9,8	9,0	8,2
8,9	9,6	10,4	11,2	12,2	**87,0**	11,9	10,9	10,0	9,2	8,4
9,0	9,7	10,5	11,3	12,3	**87,5**	12,0	11,0	10,1	9,3	8,5
9,1	9,8	10,6	11,5	12,4	**88,0**	12,1	11,1	10,2	9,4	8,6
9,2	9,9	10,7	11,6	12,5	**88,5**	12,3	11,2	10,3	9,5	8,7
9,3	10,0	10,8	11,7	12,7	**89,0**	12,4	11,4	10,4	9,6	8,8
9,3	10,1	10,9	11,8	12,8	**89,5**	12,5	11,5	10,5	9,7	8,9
9,4	10,2	11,0	11,9	12,9	**90,0**	12,6	11,6	10,6	9,8	9,0
9,5	10,3	11,1	12,0	13,0	**90,5**	12,8	11,7	10,7	9,9	9,1
9,6	10,4	11,2	12,1	13,1	**91,0**	12,9	11,8	10,9	10,0	9,1
9,7	10,5	11,3	12,2	13,2	**91,5**	13,0	11,9	11,0	10,1	9,2
9,8	10,6	11,4	12,3	13,4	**92,0**	13,1	12,0	11,1	10,2	9,3
9,9	10,7	11,5	12,4	13,5	**92,5**	13,3	12,1	11,2	10,3	9,4
9,9	10,8	11,6	12,6	13,6	**93,0**	13,4	12,3	11,3	10,4	9,5
10,0	10,9	11,7	12,7	13,7	**93,5**	13,5	12,4	11,4	10,5	9,6
10,1	11,0	11,8	12,8	13,8	**94,0**	13,6	12,5	11,5	10,6	9,7
10,2	11,1	11,9	12,9	13,9	**94,5**	13,8	12,6	11,6	10,7	9,7
10,3	11,1	12,0	13,0	14,1	**95,0**	13,9	12,7	11,7	10,8	9,8
10,4	11,2	12,1	13,1	14,2	**95,5**	14,0	12,8	11,8	10,8	9,9
10,4	11,3	12,2	13,2	14,3	**96,0**	14,1	12,9	11,9	10,9	10,0
10,5	11,4	12,3	13,3	14,4	**96,5**	14,3	13,1	12,0	11,0	10,1
10,6	11,5	12,4	13,4	14,6	**97,0**	14,4	13,2	12,1	11,1	10,2
10,7	11,6	12,5	13,6	14,7	**97,5**	14,5	13,3	12,2	11,2	10,3
10,8	11,7	12,6	13,7	14,8	**98,0**	14,7	13,4	12,3	11,3	10,4
10,9	11,8	12,8	13,8	14,9	**98,5**	14,8	13,5	12,4	11,4	10,4
11,0	11,9	12,9	13,9	15,1	**99,0**	14,9	13,7	12,5	11,5	10,5
11,1	12,0	13,0	14,0	15,2	**99,5**	15,1	13,8	12,7	11,6	10,6
11,2	12,1	13,1	14,2	15,4	**100,0**	15,2	13,9	12,8	11,7	10,7
11,2	12,2	13,2	14,3	15,5	**100,5**	15,4	14,1	12,9	11,9	10,8
11,3	12,3	13,3	14,4	15,6	**101,0**	15,5	14,2	13,0	12,0	10,9
11,4	12,4	13,4	14,5	15,8	**101,5**	15,7	14,3	13,1	12,1	11,0
11,5	12,5	13,6	14,7	15,9	**102,0**	15,8	14,5	13,3	12,2	11,1
11,6	12,6	13,7	14,8	16,1	**102,5**	16,0	14,6	13,4	12,3	11,2
11,7	12,8	13,8	14,9	16,2	**103,0**	16,1	14,7	13,5	12,4	11,3
11,8	12,9	13,9	15,1	16,4	**103,5**	16,3	14,9	13,6	12,5	11,4
11,9	13,0	14,0	15,2	16,5	**104,0**	16,4	15,0	13,8	12,7	11,5
12,0	13,1	14,2	15,4	16,7	**104,5**	16,6	15,2	13,9	12,8	11,6
12,1	13,2	14,3	15,5	16,8	**105,0**	16,8	15,3	14,0	12,9	11,8
12,2	13,3	14,4	15,6	17,0	**105,5**	17,0	15,5	14,2	13,0	11,9
12,3	13,4	14,5	15,8	17,2	**106,0**	17,1	15,6	14,3	13,1	12,0
12,4	13,5	14,7	15,9	17,3	**106,5**	17,3	15,8	14,5	13,3	12,1
12,5	13,7	14,8	16,1	17,5	**107,0**	17,5	15,9	14,6	13,4	12,2
12,6	13,8	14,9	16,2	17,7	**107,5**	17,7	16,1	14,7	13,5	12,3
12,7	13,9	15,1	16,4	17,8	**108,0**	17,8	16,3	14,9	13,7	12,4
12,8	14,0	15,2	16,5	18,0	**108,5**	18,0	16,4	15,0	13,8	12,6
12,9	14,1	15,3	16,7	18,2	**109,0**	18,2	16,6	15,2	13,9	12,7
13,1	14,3	15,5	16,8	18,3	**109,5**	18,4	16,8	15,4	14,1	12,8
13,2	14,4	15,6	17,0	18,5	**110,0**	18,6	17,0	15,5	14,2	12,9
13,3	14,5	15,8	17,1	18,7	**110,5**	18,8	17,1	15,7	14,4	13,1
13,4	14,6	15,9	17,3	18,9	**111,0**	19,0	17,3	15,8	14,5	13,2
13,5	14,8	16,0	17,5	19,1	**111,5**	19,2	17,5	16,0	14,7	13,3
13,6	14,9	16,2	17,6	19,2	**112,0**	19,4	17,7	16,2	14,8	13,5
13,7	15,0	16,3	17,8	19,4	**112,5**	19,6	17,9	16,3	15,0	13,6
13,8	15,2	16,5	18,0	19,6	**113,0**	19,8	18,0	16,5	15,1	13,7
14,0	15,3	16,6	18,1	19,8	**113,5**	20,0	18,2	16,7	15,3	13,9
14,1	15,4	16,8	18,3	20,0	**114,0**	20,2	18,4	16,8	15,4	14,0
14,2	15,6	16,9	18,5	20,2	**114,5**	20,5	18,6	17,0	15,6	14,1
14,3	15,7	17,1	18,6	20,4	**115,0**	20,7	18,8	17,2	15,7	14,3
14,4	15,8	17,2	18,8	20,6	**115,5**	20,9	19,0	17,3	15,9	14,4
14,6	16,0	17,4	19,0	20,8	**116,0**	21,1	19,2	17,5	16,0	14,5
14,7	16,1	17,5	19,2	21,0	**116,5**	21,3	19,4	17,7	16,2	14,7
14,8	16,2	17,7	19,3	21,2	**117,0**	21,5	19,6	17,8	16,3	14,8
14,9	16,4	17,9	19,5	21,4	**117,5**	21,7	19,8	18,0	16,5	15,0
15,0	16,5	18,0	19,7	21,6	**118,0**	22,0	20,0	18,2	16,6	15,1
15,2	16,7	18,2	19,9	21,8	**118,5**	22,2	20,1	18,4	16,8	15,2
15,3	16,8	18,3	20,0	22,0	**119,0**	22,4	20,3	18,5	16,9	15,4
15,4	16,9	18,5	20,2	22,2	**119,5**	22,6	20,5	18,7	17,1	15,5
15,5	17,1	18,6	20,4	22,4	**120,0**	22,8	20,7	18,9	17,3	15,6

[a] Using this table, length should be measured from 45 to 86,9 cm and height should be measured from 87 to 120 cm.

ANNEX 13: READY-TO-USE THERAPEUTIC FOOD (RUTF) DOSING

Weight (kg)	Sachets per Day	Sachets per Week
3.5-3.9	1.5	11
4.0-5.4	2	14
5.5-6.9	2.5	18
7.0-8.4	3	21
8.5-9.4	3.5	25
9.5-10.4	4	28
10.5-11.9	4.5	32
≥ 12	5	35

ANNEX 14: COMPONENTS OF A COMPREHENSIVE HISTORY AND PHYSICAL EXAMINATION

1. The **history** should consist of the following components:
   a. Current symptoms
   b. Past medical history:
      - Birth history in children
      - Growth and developmental history in children (Annexes 1,2,3)
      - Obstetrics/gynaecology history in adolescent girls and women
      - History of STIs, diabetes, hepatitis, renal insufficiency, peripheral neuropathy, hyperlipidemia, lipodystrophy, hypertension
      - Mental health and substance abuse history
      - Past hospital admissions
   c. Assessment of TB symptoms, prior TB treatment history, and TB exposure history
   d. Nutritional assessment, including a feeding history and date of last breastfeeding (in children)
   e. Immunization assessment
   f. Medications, including:
      - Current medications
      - Prior exposure to ARVs, including those for PrEP, PEP, or PMTCT(obtaining details of all ARVs previously taken is crucial in order to select the correct ART regimen for a patient)
      - Any traditional or herbal medicines
      - Known food or medication allergies
   g. Family history
      - HIV status of current household members and sexual partners
      - Possible TB contacts
      - Other medical conditions
   h. Social history, including:
      - Initial assessment for potential barriers to adherence (familial, financial, medical and mental status)
      - Work history
      - School attendance
      - Functional ability
      - Family planning
      - Substance use, including alcohol, tobacco, marijuana, and other drug use
   i. Review of symptoms
2. **Physical examination** should proceed from head to toe, and include the following:
   a. Anthropometric measurements:
      - Weight (to be repeated at <u>every</u> visit)
      - Baseline length or height for all (repeated every 3 months in children)
      - Head circumference for children <u>≤</u> 3 years of age (repeated every 3 months until 3 years of age)
      - Assess weight-for-height Z score for children <5 years
      - Body mass index (BMI) for children ≥5 years, adolescents, and adults (determine BMI for age for children 5-18 years old)
      - Mid upper arm circumference (MUAC)
   b. Vitals signs (temperature, heart rate, blood pressure, respiratory rate, oxygen saturation measured by pulse oximeter if available)
   c. General appearance (wasting, respiratory distress, pallor, jaundice, cyanosis, parotid enlargement, generalized oedema, signs of dehydration)

d. Scalp (tinea, sores, signs of malnutrition)
e. Conjunctivae (paleness, kerato conjunctivitis, jaundice)
f. Ears (discharge)
g. Mouth, oropharynx (thrush, ulcers, dental caries, gingivitis, Kaposi's sarcoma lesions)
h. Lymphadenopathy (submandibular, cervical, axillary, inguinal)
i. Lung sounds (wheeze, crackles, rhonchi); respiratory distress (tachypnea, nasal flaring, chest in-drawing)
j. Heart sounds (murmur, gallop, tachycardia, irregular rhythm, extra heart sounds) and peripheral pulses
k. Abdomen (hepatomegaly, splenomegaly, distension, tenderness)
l. Genital area:
    - Tanner staging in older children
    - Evidence of STIs (ulcers, warts, discharge)
m. Extremities:
    - Fingers (paronychia, clubbing, paleness)
    - Peripheral oedema
    - Musculoskeletal (joint swelling, joint pain, back pain, muscle tenderness)
n. Skin lesions
o. Neurological (sensory abnormalities, hypotonia, hypertonia, decreased strength, developmental milestones)
p. Mental status

ANNEX 15: WHO CLINICAL STAGING

WHO Clinical Stages of HIV disease in adults, adolescents and children	
Adults and adolescents	**Children**
Clinical Stage 1 (Asymptomatic)	
• Asymptomatic • Persistent generalized lymphadenopathy	• Asymptomatic • Persistent generalized lymphadenopathy
Clinical Stage 2	
• Moderate unexplained weight loss (<10% of presumed or measured body weight) • Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis) • Herpes zoster • Angular cheilitis • Recurrent oral ulceration (≥2 episodes in 6 months) • Papular pruritic eruption (PPE) • Fungal nail infections • Seborrhoeic dermatitis	• Unexplained persistent hepatosplenomegaly • Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis) • Herpes zoster • Lineal gingival erythema • Recurrent oral ulceration (≥2 episodes in 6 months) • Papular pruritic eruption (PPE) • Fungal nail infections • Extensive wart virus infection (verruca planus) (facial or ≥5% body surface) • Extensive molluscum contagiosum (facial or ≥5% body surface) • Unexplained persistent parotid enlargement
Clinical Stage 3	
• Unexplained severe weight loss (>10% of presumed or measured body weight) • Unexplained chronic diarrhoea for longer than 1 month • Unexplained persistent fever (intermittent or constant for longer than 1 month) • Persistent oral candidiasis • Oral hairy leukoplakia • Pulmonary tuberculosis • Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia) • Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis • Unexplained anaemia (<8 g/dl), neutropaenia (<0.5 x 10^9/l) and/or chronic thrombocytopaenia (<50 x 10^9/l)	• Unexplained moderate malnutrition not adequately responding to standard therapy • Unexplained persistent diarrhoea (14 days or more) • Unexplained persistent fever (above 37.5°C, intermittent or constant, for longer than one 1 month) • Persistent oral candidiasis (after first 6 weeks of life) • Oral hairy leukoplakia • Lymph node tuberculosis • Pulmonary tuberculosis • Severe recurrent bacterial pneumonia • Acute necrotizing ulcerative gingivitis or periodontitis • Unexplained anaemia (<8 g/dl), neutropaenia (<0.5 x 10^9/l) or chronic thrombocytopaenia (<50 x 10^9/l) • Symptomatic lymphoid interstitial pneumonitis • Chronic HIV-associated lung disease, including bronchiectasis

Clinical Stage 4	
• HIV wasting syndrome • Pneumocystis (jirovecii) pneumonia • Recurrent severe bacterial pneumonia • Chronic herpes simplex infection (orolabial, genital or anorectal of more than 1 month's duration or visceral at any site) • Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) • Extrapulmonary tuberculosis • Kaposi sarcoma • Cytomegalovirus infection (retinitis or infection of other organs) • Central nervous system toxoplasmosis • HIV encephalopathy • Extrapulmonary cryptococcosis, including meningitis • Disseminated nontuberculous mycobacterial infection • Progressive multifocal leukoencephalopathy • Chronic cryptosporidiosis • Chronic isosporiasis • Disseminated mycosis (extrapulmonary histoplasmosis, coccidioidomycosis) • Lymphoma (cerebral or B-cell non-Hodgkin) • Symptomatic HIV-associated nephropathy or cardiomyopathy • Recurrent septicaemia (including nontyphoidal Salmonella) • Invasive cervical carcinoma • Atypical disseminated leishmaniasis	• Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy • Pneumocystis (jirovecii) pneumonia • Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia) • Chronic herpes simplex infection (orolabial or cutaneous of more than 1 month's duration or visceral at any site) • Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) • Extrapulmonary tuberculosis • Kaposi sarcoma • Cytomegalovirus infection (retinitis or infection of other organs with onset at age more than 1 month) • Central nervous system toxoplasmosis (after the neonatal period) • HIV encephalopathy • Extrapulmonary cryptococcosis, including meningitis • Disseminated nontuberculous mycobacterial infection • Progressive multifocal leukoencephalopathy • Chronic cryptosporidiosis (with diarrhoea) • Chronic isosporiasis • Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidioidomycosis, penicilliosis) • Lymphoma (cerebral or B-cell non-Hodgkin) • HIV-associated nephropathy or cardiomyopathy

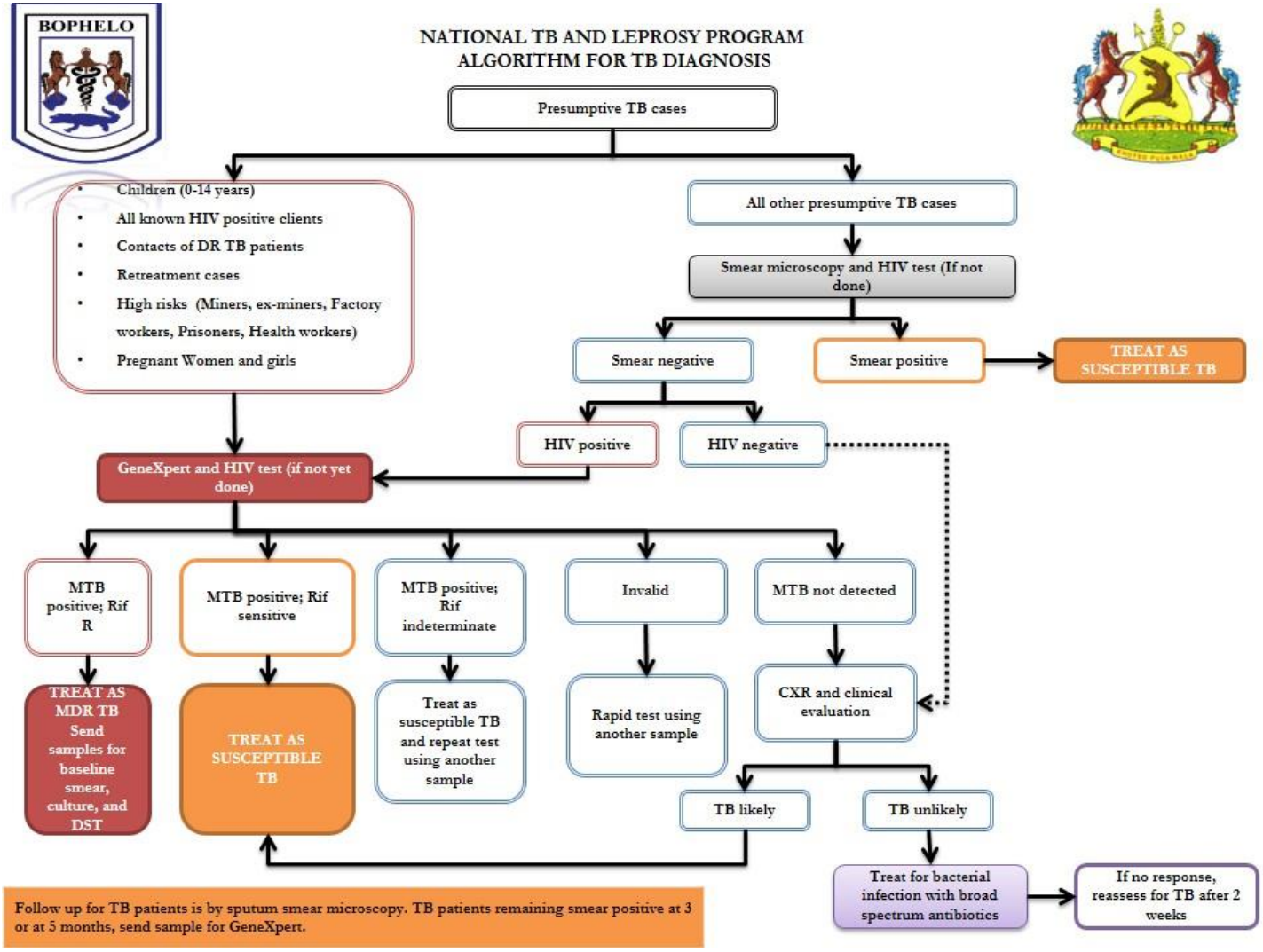
a In the development of this table, adolescents were defined as 15 years or older. For those aged less than 15 years, the clinical staging for children should be used.

b For children younger than 5 years, moderate malnutrition is defined as weight-for-height < –2 Z-score or mid-upper arm circumference ≥115 mm to <125 mm.

c Some additional specific conditions can be included in regional classifications, such as penicilliosis in Asia, HIV-associated rectovaginal fistula in southern Africa and reactivation of trypanosomiasis in Latin America.

d For children younger than 5 years of age, severe wasting is defined as weight-for-height < –3 Z-score; stunting is defined as length-for-age/height-for-age < –2 Z-score; and severe acute malnutrition is defined as either weight for height <–3 z-score or mid-upper arm circumference <115 mm or the presence of oedema.

ANNEX 16: NATIONAL TB DIAGNOSTIC ALGORITHM



ANNEX 17: TB SCREENING TOOL

Screening date (day / month / year) _____ / _____ / _____

District _____ Health Facility _____

Client Name _____ Sex (circle) Male Female

Age _____ DOB _____ / _____ / _____

Pregnant (circle) No Yes If yes, gestational age _____ weeks

HIV status (circle) Positive Negative Indeterminate Unknown

Adults / Adolescents YES NO
1. Are you coughing?
2. Have you lost weight (without trying)?
3. Do you have drenching/soaking sweats at night?
4. Do you have fevers?

Infants / Children YES NO
5. Has the child been coughing?
6. Has the child had a fever?
7. Failure to thrive / faltering growth1 or signs of severe malnutrition2?
8. Has the child been in contact with someone with TB disease?

[__] If "Yes" to any question above, then the patient is a TB suspect.

Record patient details in the TB suspect register, record TB suspect ID number below, and collect 3 sputum specimen for smear examination ± TB culture or GeneXpert testing.

TB suspect ID number: _____
Sputum collected for smear microscopy x 3 [__] Yes [__] No
Sputum sent for TB culture [__] Yes [__] No
Sputum sent for GeneXpert testing [__] Yes [__] No

[__] If "No" to all questions above, then the patient is not a TB suspect.

Educate HIV-infected patients and child contacts under the age of 5 years about the benefits of IPT.

IPT ID number: _____

ANNEX 18: NATIONAL HIV RAPID TESTING ALGORITHM