Guidelines for

HIV Prevention, Testing and Treatment of HIV in Zimbabwe

National Medicines and Therapeutics Policy Advisory Committee (NMTPAC)

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The AIDS and TB Directorate, Ministry of Health and Child Care, Zimbabwe

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Foreword

Zimbabwe continues to make remarkable progress as it inches closer towards HIV epidemic control. Hard work, effective leadership, consistent funding, strategic partnerships and implementation of evidence-based innovative interventions have significantly contributed towards this progress. As a country, we always strive towards responding directly to new trends in the HIV epidemic and ensuring that we have client-centric approaches that meet the needs of our clients and communities in their journey to good health.

Results of 'The Zimbabwe Population-based HIV Impact Assessment (ZIMPHIA 2020)' indicate that 86.8% of people living with HIV in Zimbabwe now know their status, a 10% increase from the previous survey in 2015. 97% of people living with HIV are now on lifelong antiretroviral therapy (ART), signifying yet another improvement from the previous 88.4% recorded in the last ZIMPHIA. For those on antiretroviral therapy, 90.3% of them have achieved viral load suppression, compared to 85.3% in the previous survey.

As a country, we are currently rolling out recency testing to track and trace where the recent infections are emerging from in terms of geographic location as well as other demographics such as age, sex and other key factors. This innovation gives us a clear bird's eye view and perspective of incident HIV infections and how we can collaboratively work together with other line ministries, private sector, partners, funders as well as our communities and curb the new infections.

Guided by our new 'Zimbabwe Health Sector HIV and STI Strategy: 2021 – 2025', the Ministry of Health and Child Care will continue to strengthen integration of our HIV prevention, treatment and care initiatives to strive towards an HIV-free generation. Part of this will be achieved through aligning our approaches with global standards and adapting to the recommended World Health Organization (WHO) Guidelines.

As we transition from the 2016 National Guidelines to these 2022 National Guidelines, it is our sincere hope and aspiration that both public and private sectors make deliberate effort to align their initiatives to these guidelines to provide the best care and attention to our clients and communities which will lead to our goal of ending AIDS by 2030.

Air Commodore Dr Jasper Chimedza
Secretary for Health and Child Care

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Abbreviation	Meaning
ART	Antiretroviral therapy
ANC	Antenatal clinic
AHD	Advanced HIV disease
ADR	Adverse drug reaction
CATS	Community Adolescent Treatment Supporter
CD4	Cluster of differentiation 4
CLHIV	Children living with HIV
CMDs	Common mental health disorders
DNA	Deoxyribonucleic acid
DPS-MOHCC	Directorate pharmacy services-Ministry of Health and childcare
DVR	Dapivirine vaginal ring
ED-PrEP	Event driven Pre-exposure Prophylaxis
EID	Early infant diagnosis
eMTCT	Elimination of maternal to child transmission of HIV and syphilis
e-PV	Electronic- pharmacovigilance
FDCs	Fixed dose combinations
HBV	Hepatitis B Virus
HIVST	HIV self-testing

Acronyms / Abbreviations (cont)

Abbreviation	Meaning
HTS	HIV Testing Services
INSTI	Integrase strand transfer inhibitors
INSTIs	Integrase strand transfer inhibitors
LEEP	Loop Electrical Excision
LLETZ	Large Loop Excision of the Transformation Zone
LF-LAM	Lateral flow lipoarabinomannan
LPV/r	Lopinavir/ritonavir
MCAZ	Medicines Control Authority of Zimbabwe
MOHCC	Ministry of Health and Child Care
MTCT	Maternal to child transmission
NAT	Nucleic acid testing
NCDs	Non-communicable diseases
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor
NtRTI	Nucleotide reverse transcriptase inhibitor
OI	Opportunistic infections
OSDM	Operation and service delivery manual
PEP	Post-exposure prophylaxis
PI	Protease Inhibitor
PITC	Provider initiated testing and counselling
PLHIV	People living with HIV
PMTCT	Prevention of maternal to child transmission
PNC	Postnatal clinic
POC	Point of care
PrEP	Pre-exposure prophylaxis
RAL	Raltegravir
RNA	Ribonucleic acid
RTRI	Rapid tests for recent HIV infection
SRH	Sexual and reproductive health
STI	Sexually transmitted infections
SSQ14	Shona symptom questionnaire 14
SVI	Single visit approach
TAF	Tenofovir Alafenamide
TaSP	Treatment as prevention
VIA	Visual inspection with acetic acid
VMMC	Voluntary medical male circumcision
WLHIV	Women living with HIV

Chapter 1 Executive Summary

1.1 HIV Testing Services

HIV testing service (HTS) remains a critical entry point to prevention, care, and treatment programs. HTS are guided by the 6 core principles (6Cs): consent, confidentiality, counselling, correct and accurate results, comfort and connection to HIV prevention, treatment, care, and support. HTS can be provided at health facilities, in communities and through HIV self-testing. National HTS algorithms for different population groups have been developed and adopted for use in Zimbabwe.

Everyone tested must be appropriately linked to HIV prevention or treatment services and other important health services (Screening for noncommunicable diseases, mental health, and sexual and reproductive health services).

Re-testing of all people newly and previously diagnosed with HIV before they initiate anti-retroviral therapy (ART) is recommended. Rapid Testing for Recent Infection (RTRI) is performed on newly diagnosed clients after retesting to verify status.

1.2 HIV Treatment Services

Zimbabwe has adopted the “Treat ALL” recommendation where, all individuals with confirmed HIV diagnosis are eligible for ART irrespective of WHO clinical stage or CD4 count. The country uses simplified guidelines using the public health approach for treating HIV. Dolutegravir based regimens are preferred for first line use in children, adolescents, and adults.

Efavirenz is now reserved for alternative first line therapy. Protease inhibitors are used for second- and third-line regimens. HIV drug resistance testing must be done in all patients failing second-line treatment before switching to third-line ART

1.3 Treatment Monitoring

- Routine viral load monitoring is the gold standard to assess the effectiveness of ART and must be done at 6 months and at 12 months after ART initiation, and then annually thereafter.
- A CD4 test is recommended at baseline to assess for the presence of Advanced HIV Disease (AHD) and to inform differentiated service delivery approaches.
- A stable patient on ART should be seen for a clinical assessment every 6 months.

- A stable patient is defined as someone who:
  Has no current OIs, has a VL<50 copies/ml and is at least 6 months on ART
  Where viral load is not available the client should have no current OIs, a CD4 > 200 copies/ml and be at least 6 months on ART

1.4 PMTCT

The Ministry of Health and Childcare (MoHCC) is committed to the elimination of maternal to child transmission of both HIV and syphilis.

- All pregnant and breastfeeding women must receive lifelong effective ART
- Pregnant women not yet on ART or those newly diagnosed to be HIV positive on the first ANC booking should be initiated on ART on the same day of first booking and should get a viral load after 3 months of starting ART, at 34-36 weeks gestation and 6 monthly during pregnancy and breastfeeding
- HIV exposed infants are stratified into either high or low risk categories depending on maternal viral load during pregnancy and breastfeeding

High risk infants are defined as follows:

- An infant whose mother has a high maternal viral load >1000copies/ ml during the last 4 weeks before delivery
- An infant born to HIV infected woman who has received less than 4 weeks of ART at the time of delivery
- An infant born to a newly diagnosed HIV infected woman during labor, delivery and postpartum (Incident HIV infection)

All HIV exposed infants should receive prophylaxis for at least 12 weeks with AZT + 3TC plus Nevirapine.

1.5 Early Infant Diagnosis

Diagnosis of HIV infection in children less than 18 months requires testing for the virus itself (called virologic testing, or PCR testing).

- Nucleic acid testing (NAT) at birth is recommended for all HIV exposed infants
- For babies who test HIV positive at birth ALWAYS retest and confirm results with repeat PCR, but retesting should not delay ART initiation.
- Repeat NAT testing is recommended for negative babies at 6 weeks and 9 months
- Antibody testing is recommended in children older than 18 months

1.6 Managing opportunistic infections, comorbidities, and advanced HIV disease

ART has reduced mortality and morbidity associated with HIV and transformed HIV into a chronic disease requiring lifetime care. Comprehensive HIV care includes the promotion of general health and well-being, maintaining quality of life, screening, the prevention and management of coinfections and comorbidities The following key issues are addressed in these guidelines

- Use of cotrimoxazole prophylaxis for prevention of several infections
- Prevention, screening, and management of Tuberculosis among people living with HIV
- Screening and management of cryptococcal disease
- Screening for noncommunicable diseases including cervical cancer and mental health conditions
- Nutritional care and support for people living with HIV

1.7 Combination HIV Prevention

- These guidelines recommend use of oral Pre-Exposure Prophylaxis (PrEP), TDF and FTC, which should be offered as an additional prevention choice for people at substantial risk of HIV infection.
- TLD is recommended for use in adolescents and adults for post exposure prophylaxis
- The Dapivirine vaginal ring is recommended for women who are unable to take oral PrEP

1.8 Reporting Adverse Medicine Events

Emphasis is made on recording and reporting all suspected adverse drug reactions to MCAZ

Chapter 2 HIV Testing Services (HTS) for Children, Adolescents and Adults and Linkage to Prevention and Treatment

2.1 Introduction

HIV testing remains a critical entry point to prevention, care, and treatment programs. The services (HTS) package includes pre-test Information giving, conducting the test, post-test counselling with linkage to appropriate post-test services for prevention, treatment, care and support. Strong coordination with the laboratory to support quality testing is essential to ensure correct and accurate results are delivered. Accurate documentation and reporting of HTS data are a critical component of programme monitoring and evaluation. HTS should always be conducted in accordance with the best interest of the client. HTS is voluntary except in unique situations such as court orders pertaining to rape and blood or tissue donors.

The goal of the Ministry of Health and Child Care (MOHCC) is to reduce HIV-related morbidity and mortality, through early diagnosis and linkage to treatment for those who test HIV positive and to HIV prevention and Sexual Reproductive Health (SRH) services for those who test HIV negative. According to the global fast track targets, the aim of the HTS programme is that 95% of people living with HIV should know their HIV status by 2025, 95% of those who know their status should be initiated on ART and 95% of those on ART should achieve viral suppression by 2025, with the vision of ending AIDS as a public health threat by 2030. As we reach epidemic control, there is need to strengthen targeted testing through index case testing, HIV self-testing (HIVST) and use of the HTS Screening tools for children and adolescents as well as that for adults. HTS is guided by the 6 core principles (6Cs): consent, confidentiality, counselling, correct and accurate results, comfort and connection to HIV prevention, treatment, care, and support. These fundamental principles for HTS are described in detail below:

Consent – All clients should receive sufficient information to understand the testing process and possible consequences of being tested. Clients receiving HTS must give informed consent, which can be either written or verbal. They should be informed of the process of HTS and their right to defer HIV testing. Consent for children and adolescents below the age of 16 years is obtained from parents or caregivers, except for mature and emancipated minors.

Confidentiality – discussions between the service provider and the client should not be disclosed to anyone without the permission of the client.The client must be informed about shared confidentiality.

Counselling – Pre-test information may be given to a group, couple or individual depending on the setting. Pre-test information should include option for HIVST, or provider delivered HIV test. Children below the age of 16 years are given pre-test information together with their parents or caregivers. Clients who opt for HIVST should be given clear messages on how to perform the test, interpretation of results, what to do with each result and the post-test services that they can access. Post-test counselling should always be given to an individual or to a couple and never to a group.

Comfort: Among pregnant women, HTS should be offered during the early stages of labour in cases where the HIV status is unknown. The health worker should assess the woman's stage of labour, comfort level, and need for analgesics. The pre-test information should be short, to the point, and explained based on the comfort level of the woman, between contractions. The health worker should ask the woman to signal for a pause when a contraction is starting

Correct and accurate HIV test - The HIV testing procedure is performed following the current national testing algorithm and standard operating procedures by trained service providers to deliver correct and accurate results.

Connections to HIV Prevention, Treatment, Care and Support services
Clients who test HIV negative should be linked to HIV prevention and sexual reproductive health services, whilst those testing positive are linked to appropriate HIV treatment services

2.2 Recency Testing

Rapid tests for recent HIV infection (RTRI) can help differentiate between recent (i.e., in the past 12 months) and long-term HIV infections. Use a RTRI for recent infection helps to provide continuous epidemiological data on person, place, and time of newly diagnosed individuals to inform HIV prevention and control strategies. RTRIs pave the way for a HIV recent infection surveillance system as part of routine HIV testing services (HTS) to detect and characterize recent HIV infection among newly diagnosed HIV cases. Identifying areas with on-going transmission is critical to steer national efforts to reach those that need care the most.

2.3. HIV Testing Services (HTS) Package

Components of the HTS package include the pre-test information, conducting the HIV test, post-test counselling and follow up counselling and referrals as highlighted in figure 2.1 below. With the introduction of the "Treat all" strategy, three key messages must be given in the post-test counselling session for those testing HIV positive:

- Treatment is available for all people living with HIV
- Starting treatment as soon as possible will prevent your health from worsening and prevent transmission to others
- Taking ART properly will allow you to live a long and fulfilling life

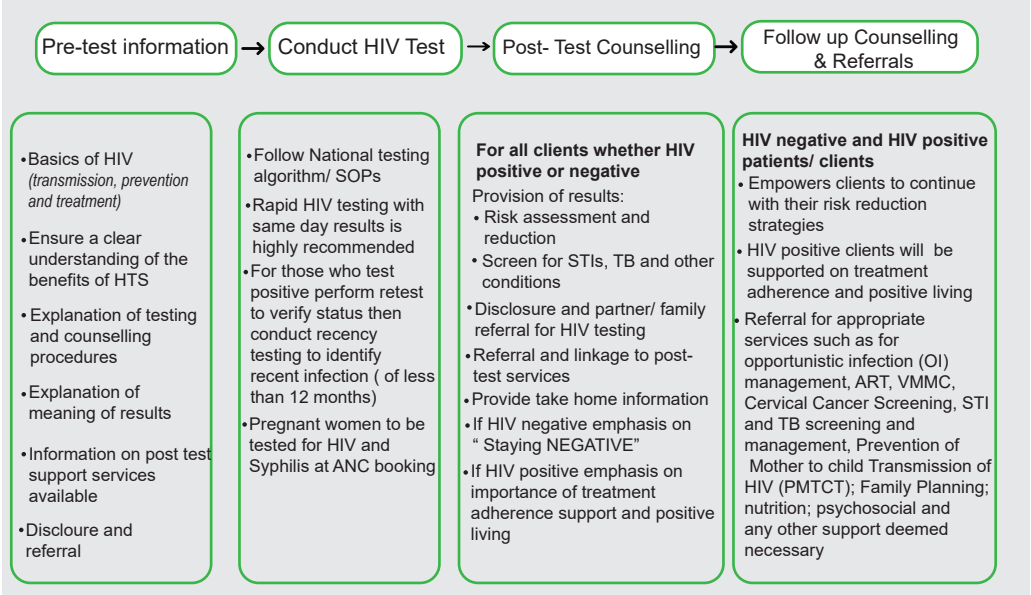


Figure 2. 1: Primary Components of HIV Testing Services (HTS) Package

2.4 Service Delivery Approaches For HTS

Facility Based HTS: Scale up targeted HIV testing to all clients using Provider Initiated Testing and counselling (PITC) for children, adolescents, and adults in all clinical settings irrespective of the reason for presenting at a health facility. PITC should be offered routinely within malnutrition and paediatric clinics, STI, viral hepatitis and TB services, inpatient and outpatient settings, antenatal clinic (ANC) settings and in health services for vulnerable groups that include children, adolescents, and key populations. Facilities can also distribute HIVST kits for both primary and secondary distribution

Community-based HTS: approaches include door-to-door / home-based testing (including index case testing) and mobile outreach campaigns in identified hot spot areas that may include growth points, mining and farming areas workplaces, parks, bars, places of worship and educational establishments. HIVST kits can be distributed through community- based distributors.

2.5 Algorithms for HIV testing

2.5.1 HIV Self-Testing (HIVST)

This refers to a process in which a person collects his or her own specimen (oral fluid or blood) and then performs a test and interprets the result, often in private or with someone he or she trusts. HIVST kits are distributed both at facility and community level and used by individuals who are 16 years and above. Secondary distribution of HIVST kits is encouraged for partner testing especially in ANC and postnatal clinic (PNC) and index case testing. HIV self-testing should be offered as an additional approach to HIV testing since it increases access to HTS while limiting physical contact.HIVST positive result should always be confirmed by a trained service provider using the national HIV testing algorithm.

Figure 2.2 below summarizes the HIV self-testing algorithm

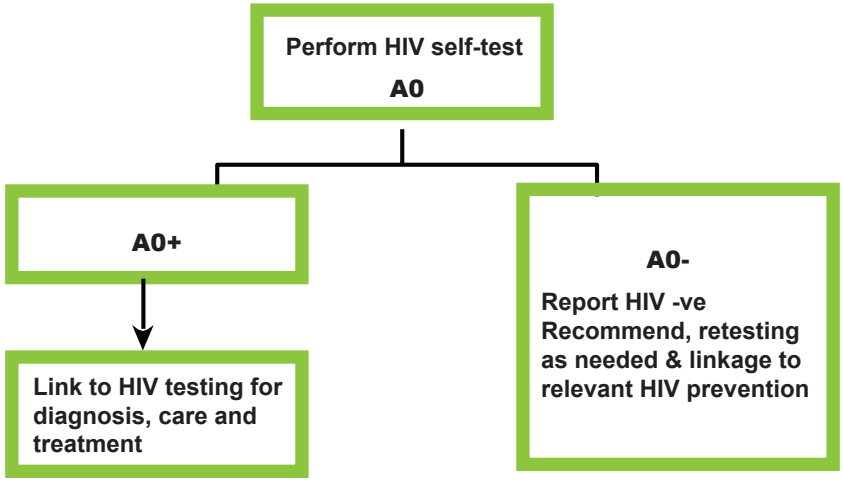


Figure 2. 2: HIV Self Testing (HIVST) Algorithm

The national testing algorithms for the general population and pregnant women are highlighted in figures 3 and 4 below. Figure 2.2 below summarizes the HIV self-testing algorithm

2.5.2 HIV Testing in the general population

Zimbabwe has adopted the WHO recommendation to use three consecutive reactive tests to provide an HIV-positive diagnosis. This is because of declines in HIV prevalence among those untreated (treatment-adjusted prevalence) and decreasing HIV positivity in HIV testing services programmes. Figure 3 below highlights the national algorithm for HIV testing for people older than 18 months

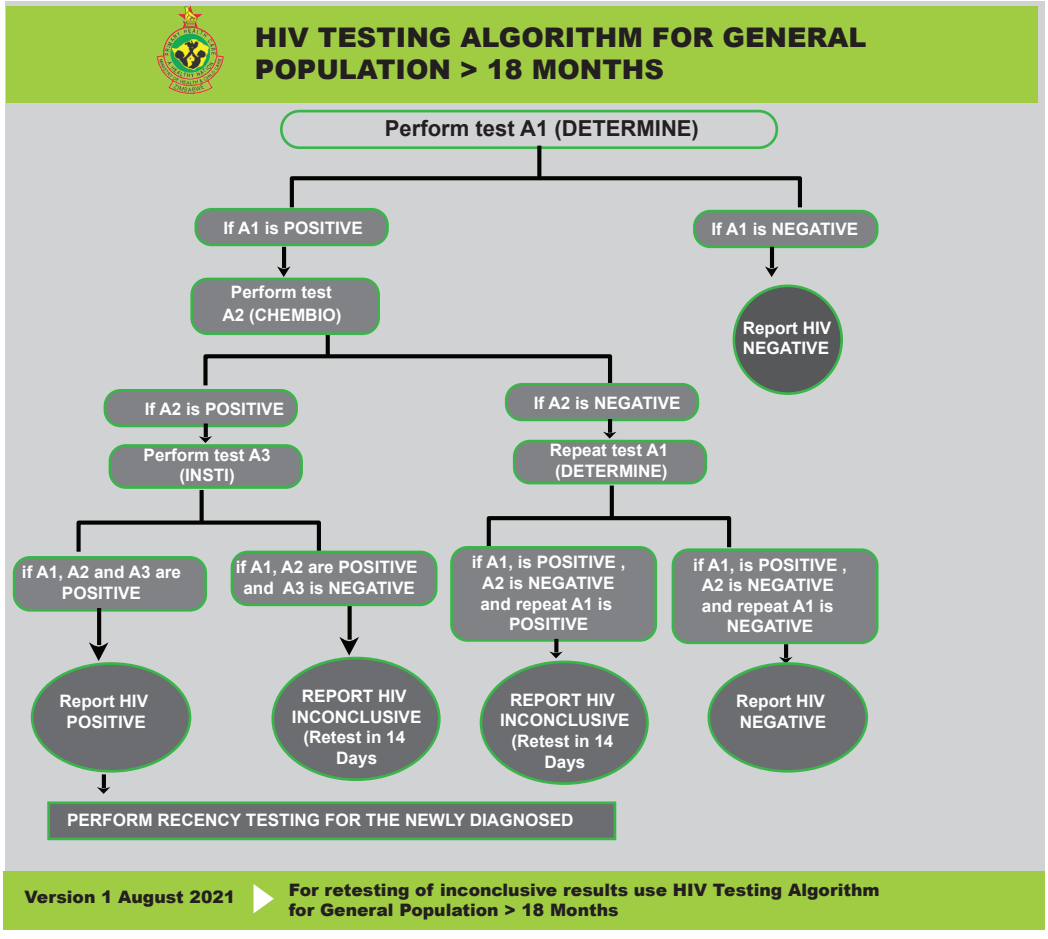


Figure 2. 3: HIV testing algorithm for General Population (>18 months)

Source: National Rapid HIV Testing Manual (2021)

2.5.3 HIV Testing among pregnant women

In all settings, dual HIV and syphilis rapid diagnostic tests should be offered as the first test in antenatal care to increase testing and treatment coverage. It is important not to use the rapid dual HIV and syphilis test for:

- women with HIV taking ART
- women already diagnosed with and treated for syphilis during their current pregnancy; and
- retesting for HIV.

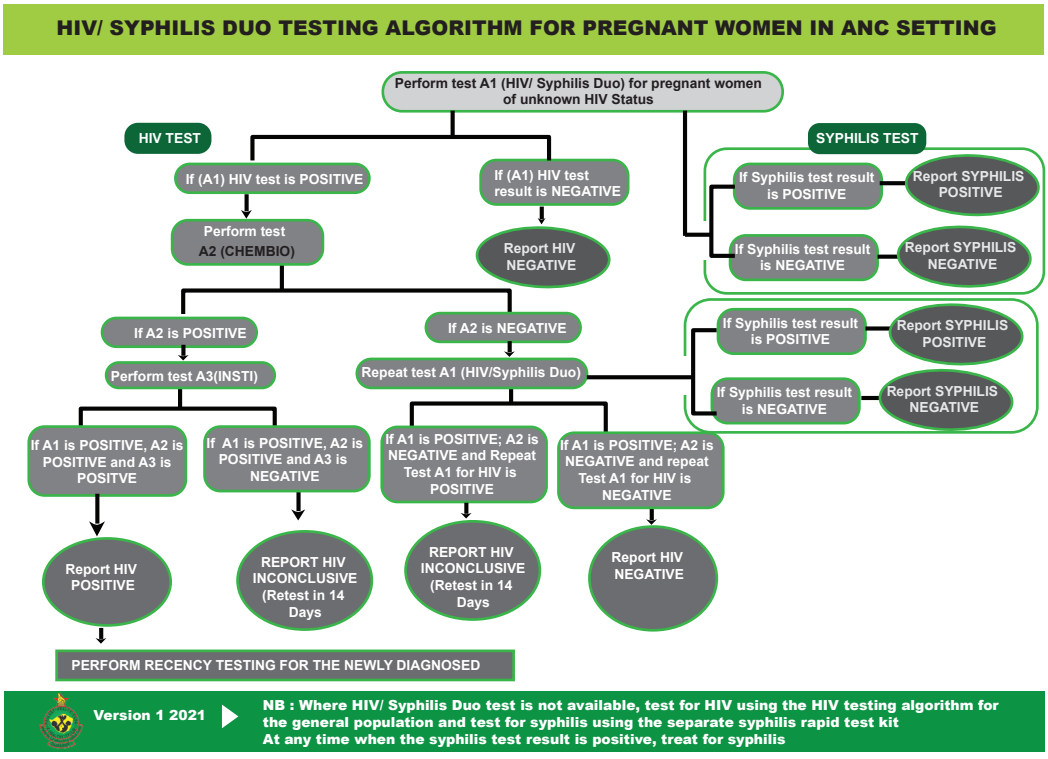


Figure 2. 4: HIV/Syphilis Duo Testing algorithm for Pregnant Women in ANC Setting

Source: National Rapid HIV Testing Manual (2021)

2.6 Retesting to Verify HIV Status

Retesting refers to using the same testing algorithm on a second specimen from the same individual.

Most individuals do not require retesting to verify an HIV negative status particularly with no on-going HIV risk. However, retesting is required for individuals with on-going risk of contracting HIV where annual retesting is recommended.

Retest all people newly and previously diagnosed with HIV before they initiate ART. Retesting should ideally be conducted by a different service provider with a different specimen. If there is only one provider, retesting can be done by the same provider after waiting at least an hour from the initial test. Recency testing is performed after retesting the client to verify status before ART initiation.
Retesting people on ART is NOT recommended as there are potential risks of incorrect diagnosis. The effect of ART in suppressing viral replication may extend to suppression of the immune response and thus of antibody production leading to inaccurate HIV diagnosis.

Table 2. 1: Recommendations for HIV retesting

Population	Recommendations
General population not at on-going risk	Offer retesting at least annually
Individuals with Inconclusive HIV test results	Retest after 14 days
Individuals on PEP	Retest at 3 months and 6 months after the initial test
Individuals on PrEP	Retest after every 3 months
Key populations	Retesting according to risk assessment (suggest three months)
HIV-negative pregnant women and lactating women	Retest previously HIV-negative women in the first trimester of pregnancy and at third trimester/ or at delivery. 6 weeks post-natal and 6 monthly during the breastfeeding period. Visits to EPI and 6 weeks (DTP) and at 9 months (measles) should be time points where maternal HIV status is reassessed
HIV positive individuals before initiation of ART	Retest all people newly and previously diagnosed with HIV before they initiate ART. Retesting should ideally be conducted by a different service provider with a different specimen. However, if there is only one health worker at the facility, they can take another blood sample an hour apart and retest

2.7 Linkage to HIV Prevention, Treatment and Support Services

Linkage is defined as a process of actions and activities that support people testing for HIV and people diagnosed with HIV to engage with prevention, treatment, and care services as appropriate for their HIV status.

For people with HIV, it refers to the period beginning with HIV diagnosis and ending with ART initiation. Those who test HIV-negative, if at continuing high risk, need linkage to prevention services. Individuals must be linked to the following services:

- HIV prevention (PrEP, PEP, VMMC etc.)
- HIV treatment, care, and support
- SRH service (STI Screening and Management, family planning and cervical cancer screening)
- Other support services (TB screening, mental health, post gender-based violence services)

Chapter 3 Principles of Antiretroviral Therapy

3.1 Background

The guiding principles for effective antiretroviral therapy (ART) include potency of regimens chosen, minimum adverse events, reduced pill burden, and accessibility and affordability of the medicine combinations. The reduced pill burden will be achieved by using fixed dose combinations (FDCs) of antiretroviral medicines. Although the potency (efficacy) of the regimen is important, adherence to a simple regimen will ensure that the ongoing viral replication is maximally suppressed, thus allowing the immune system to recover

Health-care personnel will need to receive continuing medical education to remain up to date on ART recommendations. Guidelines change as new evidence emerges from clinical trials and lessons are learnt from programme experiences. The need for those involved in managing patients on ART to undergo frequent retraining and evaluation cannot be overemphasized. ART requires in-depth knowledge about antiretroviral medicines, their side effects, and issues such as immune reconstitution inflammatory syndrome (IRIS). Being able to detect and manage opportunistic infections (OIs), knowing when to initiate ART, and knowing when to switch medicines as toxicities occur or when to switch to second-line or third-line therapy, as well as counselling abilities, are necessary skills. Such skills can be acquired through the relevant training and experiential learning. Clinical attachments and clinical mentoring are tools to improve health-care worker skills in all disciplines, including ART delivery.

Adherence to treatment regimens and schedules is crucial to the success of this therapy. Without high adherence rates, viral resistance to the medicines emerges readily. Hence, there is need to be vigilant and monitor patients during ART for adherence rates, side effects and treatment failure. Treatment failure should alert the health-care worker on the need to switch to second- line or third-line therapy.

The MOHCC is progressively increasing access to viral load testing therefore switching to second- or third-line treatment should be based on viral load testing.

3.2 Characteristics of Available ARVs

Medicines in use in most of our programmes belong to the following classes:

- Nucleoside reverse transcriptase inhibitors (NRTIs).

These medicines block the HIV reverse transcriptase enzyme and prevent the copying of the viral RNA into HIV reverse transcriptase enzyme and prevent the copying of the viral RNA into the DNA of infected host cells by imitating the building blocks of the DNA chain. The resulting DNA chain is incomplete and cannot create new viruses.

- Nucleotide reverse transcriptase inhibitors (NtRTIs) e.g., Tenofovir. These medicines act at the same stage of the viral life cycle as do NRTIs.
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs). These medicines also block the HIV reverse transcriptase enzyme but have a different mechanism of action than the NRTIs and the NtRTIs.
- Protease inhibitors (PIs). These medicines block the enzyme protease and prevent the assembly and release of HIV particles from infected cells.
- Integrase strand transfer inhibitors (INSTIs). These medicines target HIV's integrase protein, blocking its ability to integrate its genetic code into human cells.

These additional classes of ARVs are not yet in use in Zimbabwe:

- Fusion inhibitors (FIs). These work by preventing HIV from entering healthy CD4 cells by blocking proteins on the surface of CD4 cells.
- CCR5 inhibitors. These block the CCR5 co-receptor that HIV uses to enter and infect the cell. CCR5 works specifically against CCR5-tropic HIV. Before treating a patient with a CCR5 inhibitor, a test to determine the strain of virus is necessary

Table 3.1 summarizes the available antiretroviral medicines by class in Zimbabwe

Nucleoside/tide Reverse Transcriptase Inhibitors (NRTI)	Non-nucleoside Reverse Transcriptase Inhibitors (NNRTI)	Protease Inhibitors (PI)	Integrase Strand Inhibitors (INSTIs)
Tenofovir Disoproxil Fumarate (TDF) / Tenofovir alafenamide (TAF)	Nevirapine (NVP)	Lopinavir/ ritonavir (LPV/r)	Raltegravir (RAL)
Zidovudine (AZT, ZDV)	Efavirenz (EFV	Atazanavir/ ritonavir (ATV/r)	Dolutegravir (DTG)
Lamivudine (3TC)	Etravirine	Darunavir/ritonavir	Cabotegravir
		(DRV/r)	
Emtricitabine (FTC)	Rilpivirine	Ritonavir (RTV)	Bictegravir
Abacavir (ABC)	Dapivirine		Elvitegravir

3.3 Efficacy and safety

Preferred regimens are based on two NRTIs plus an integrase strand inhibiter such as Dolutegravir which are efficacious, less expensive, have generic formulations, and available as fixed dose combinations. PIs should be preserved for second-line or third-line therapy. NNRTIs are no longer part of preferred ART regimens.

The preferred first line regimen of TDF, 3TC and DTG has relatively fewer adverse effects and is taken once daily.

All ARVs have class-specific side effects, and medicine specific side effects (see Table 8.1 in Chapter 8). In addition, significant medicine interactions and toxicities may occur when using some ARVs in combination with each other and with other medicines such as TB medicines (See table 5.4 in Chapter 4).

3.4 Monitoring of patients on ART

All patients receiving ART must be routinely monitored for the following:

- Adherence to medication
- Toxicities of medication
- Treatment efficacy / success

3.5 Stopping antiretroviral therapy

Antiretroviral therapy should not be stopped unless the patient's life is in danger. In most cases where medicine toxicities develop, switching the suspected medicine(s) should be attempted first. It is recommended to ensure that the VL is suppressed before substituting a single medicine for toxicity. Otherwise, resistance may develop to the new medicine, consequently compromising future regimens. However, single-medicine substitutions can be done in the first few months of ART without measuring the VL, as the VL may take up to 6 months to become suppressed.

Chapter 4 Initiation of Antiretroviral Therapy in Adults and Adolescents

Key Issues addressed in this chapter

- Goals of ART
- Evaluating and preparing adolescents and adults for ART
- Supporting adherence for patients receiving ART
- Principles of ART in adolescents

4.1 Goals of ART

The aims of ART are as follows:

- Maximal and durable suppression of replication of HIV
- Restoration and/or preservation of immune function
- Reduction of HIV-related infectious and non- infectious morbidity
- Prolong life expectancy and improve quality of life
- Prevention of mother-to-child transmission of HIV (vertical transmission)
- Reduction of HIV transmission risk in the communities
- Minimize adverse effects of the treatment

Prior to starting ART, patients should be assessed for readiness to take ARVs; the ARV regimen; dosage; and scheduling; the likely potential adverse effects; and the required monitoring must be discussed. Both medical and psychosocial issues need to be addressed before initiating ART. Patients should be adequately counselled about adopting appropriate lifestyle measures such as use of condoms, and any other psychosocial problems that may interfere with adherence (e.g., alcohol, psychiatric disorders) should be addressed. Rapid ART initiation is recommended within seven days of HIV diagnosis and the offer of same-day ART start unless there are specific reasons to defer treatment such as active TB and cryptococcal meningitis.

At each clinic visit, always screen for tuberculosis using a TB symptom checklist, assess nutrition and the importance of medicine adherence and regular follow-up care. People taking ARVs should also be regularly asked about whether they are taking other medications including herbal remedies that may interfere with the efficacy of ARVs. The ART programme should promote treatment literacy for people living with HIV (PLHIV) including information on the benefits of early treatment,the risks of delaying treatment and the required life-long commitment to treatment adherence.

Early treatment initiation is associated with clinical and HIV prevention benefits, improving survival, and reducing the incidence of HIV infection at the community level. Increasing evidence also indicates that untreated HIV may be associated with the development of severe non-AIDS defining conditions including cardio-vascular disease, kidney disease, liver disease and neurocognitive disorders.

4.2 Medical Criteria for Initiating ART in Adults and Adolescents

All individuals with a confirmed HIV diagnosis are eligible for ART irrespective of WHO clinical stage and CD4 count level i.e., TREAT ALL.

Health workers should retest all people newly and previously diagnosed with HIV before they initiate ART to ensure correct diagnosis of HIV infection. Retesting should ideally be conducted by a different service provider with a different specimen

Once an individual is confirmed to be HIV positive; health workers should provide adequate counselling and start ART within a week. However, for those patients who are not ready yet to start ART, they should receive on-going counselling and support. EXCEPTIONS: Pregnant and breast-feeding women should be started on ART on the same day of HIV diagnosis.

Evaluating patients before commencing ART

Aim to do the following before commencing a patient on ART:

1. Screen for and treat active opportunistic infections especially cryptococcal meningitis and tuberculosis
2. Do a baseline CD4 cell count to rule out or confirm advanced HIV disease
3. If available, do liver and renal function tests (absence of tests should NOT be a barrier to initiating ART)
4. Clinical assessment must include Weight, temperature, and blood pressure measurements

Patients with CD4 cell count <200
Patients with low CD4 below 200 should be fast-tracked for treatment initiation. They should be screened for symptomatic TB and cryptococcal disease (see Chapter 10).

They should receive cotrimoxazole prophylaxis and TB preventive therapy like all other patients and should be closely monitored for 3 months as this is their highest risk period for bacterial infections and TB or cryptococcal IRIS. Health workers should educate them and their families to report immediately to a health facility if they are unwell whilst their CD4 cell count is < 200 copies/mm3.

See the WHO clinical staging system (Annex 1)

A CD4 cell count should be taken when ART starts to determine whether the person has advanced HIV disease or not, but ART should not be delayed by waiting for the CD4 test result. People starting treatment and their caregivers should be informed that the first ART regimen offers the best opportunity for effective suppression of viral loads, immune recovery and consequently,clinical benefit and that successful ART requires taking all medications as prescribed.

4.3 Psychosocial Criteria for Initiating ART

Consider the following psychosocial criteria when initiating ART:

- Has the patient been adequately counselled and informed about ARVs?
- Is a treatment partner available and/or has disclosure been made to the partner?
- Is there an easy method of following up on the patient?
- Is the patient ready and willing to start ART and take medications indefinitely?

4.4 Reasons for Deferring ART

A patient may be deferred (delayed) from starting therapy if the patient

- has cryptococcal meningitis (defer for at least a month)
- needs further psychosocial counselling (e.g., for substance use),
- has TB Meningitis (defer starting ART for at least a month)
- needs further information on HIV and AIDS,
- is terminally ill and unable to swallow oral medication (palliative care is then offered to such a patient).

Such patients should be offered continued monitoring and close follow-up as well as counselling so that ART can be commenced at an appropriate time.

4.5 Adherence to ART

WHO defines treatment adherence as 'the extent to which a person's behavior- taking medications, following a diet and/or executes lifestyle changes corresponds with agreed recommendations from a health care provider.

It should be noted that motivation to start and adhere to treatment may be more difficult for people who feel well and have higher CD4 counts than for people who are ill. Therefore, health workers should put special emphasis on adherence counselling for this group of patients. Efforts to support adherence should start before ART initiation and should include basic information about HIV, the ARV medicines, expected adverse events, preparations for long-term ART. Many factors affect adherence to treatment. Patients may just forget to take their ARVs, be away from home, mental health problems or the abuse of alcohol. Non-disclosure and negative stigma from household members may lead to poor adherence to treatment as well. Medication factors may include adverse events, pill burden, dietary restrictions. Health care factors include medicine stock outs, long distances to health facilities and costs related to care.

Effective adherence support interventions include client-centred counselling and support, support from peer educators trained as "expert patients," community treatment supporters and mobile text messaging. Other interventions involve providing patients with adherence tools such as pill boxes, diaries, and patient reminder aids.

4.6 ART in Adolescents

4.6.1 Who is an Adolescent?

The WHO defines an adolescent as a child between the ages of 10 and 19 years. This period of life encompasses many physiological and psychological changes that should be considered.

Adolescence is characterized by rapid physical, neurodevelopmental, emotional, and social changes. They have significantly worse access to ART services than adults, high risk of loss to follow-up, sub-optimal adherence, and require comprehensive health care and support services.

Perinatally infected adolescents are likely to experience chronic diseases and neuro-developmental growth and pubertal delays. However, adolescents who acquire HIV behaviorally may not face the same clinical problems, however, they may potentially have challenges relating to stigma and lack of support to access care.

4.6.2 Principles of ART in Adolescents

The principles of therapy are like those in adults and children. However, one should bear in mind specific issues when monitoring and treating HIV positive adolescents, which are discussed in the following sections.

Dosage of ART

Decisions regarding dosage for adolescents should consider the following factors:

- The age at which to start adult dosing can be difficult to determine.
- Stunting and wasting are common among HIV-positive adolescents.
- It is recommended that those under the weight of 25 kg should use paediatric dosing guidelines. Thus, all adolescents— regardless of age—should be weighed before commencing ART and at each visit.

4.6.3 Staging HIV-Positive Adolescents

HIV-positive adolescents are at risk not only of HIV associated infections but also of chronic non-infective complications. These include chronic lung disease, lymphoid interstitial pneumonitis and HIV-associated cardiomyopathy/nephropathy and stunting. Such conditions should be considered when staging HIV-positive adolescents

4.6.4 Monitoring of HIV Disease

In monitoring adolescents, remember the following:

- Stunting and pubertal delay are common.
- As well as CD4 count and Viral load monitoring, clinical monitoring should include measurement of height and weight at every clinic visit
- Girls should specifically be asked about menstruation, including age of menarche and timing of menstrual cycles.

4.6.5 Chronic Complications

As well as looking for and treating OIs, clinicians should monitor patients for chronic complications such as heart failure, lung, and skin infections.

4.6.6 Disclosure

Non-disclosure is associated with virological failure among adolescents on ART. Adolescents should be involved in the discussion about HIV testing and their status should be disclosed to them. Do not assume that adolescents are aware of their HIV status. Unless exceptional circumstances make it difficult for an adolescent to understand his or her HIV status (e.g., severe mental conditions), it is strongly recommended that HIV status be disclosed before the patient starts ART. Disclosure is a gradual process and should be done with the involvement of the guardian, a counsellor, and the clinician.

4.6.7 Adherence

Adherence is particularly problematic in adolescents. Particular attention should be paid to assessing adherence at every visit and to providing adherence support. Counselling on adherence should include exploring specific reasons that may contribute to poor adherence. Adolescents face many psychosocial issues that can affect their adherence, and these should be assessed:

- Ways of supporting attendance at clinic appointments and taking medicines while at school should be addressed (especially for those at boarding schools)
- Patients should be encouraged to identify a family member who will support their treatment.
- A package of peer-led child and adolescent mental health and psychosocial support services should be integrated within HIV treatment and care
- Counselling should be adolescent-friendly, and counselling patients on their own without the presence of guardians/parents is recommended whenever possible. This ensures that patients can talk about personal issues that affect their ability to take medicines.

4.6.8 Education, Information and Services on Sexual and Reproductive Health

Education about sexual and reproductive health should be part of the counselling and treatment of HIV-positive adolescents. Education and information should be tailored according to the patient's own knowledge and maturity. This clearly varies across the age group and should be assessed during counselling.

Specific information/services that should be given to adolescents include information on.

- Avoiding onward HIV transmission, including delaying sexual relationships, and using condoms.
- Specific modes of HIV transmission and
- Where to access family planning services and STI services and how to seek help in cases of sexual assault.
- HPV vaccine should be administered to young girls and boys before sexual debut

4.6.9 Transitioning from Adolescence into Adulthood:

Transitioning from adolescence to adulthood can be a difficult period even for those without HIV. Changes in their bodies may affect their emotions and their behavior. HIV is an added burden and adolescents who have previously adhered to therapy from childhood may start to default treatment. Health Care workers should anticipate this and discuss it with adolescents and caregivers as part of the treatment plan.

Health workers should prepare and encourage adolescents to take control of their own treatment and be less dependent on caregivers. Service providers should encourage mature adolescents (in consultation with caregivers) to attend clinic visits alone where appropriate. As a final step before transitioning to adult care, adolescents should be familiarized with the adult care setting and procedures.

Chapter 5 Recommended Treatment Regimens for Adults and Adolescents

This chapter discusses the following key recommendations

- ART regimens for use in 1st ,2nd and 3rd line treatment for adolescents and adults
- Key considerations for the management of TB / HIV co-infected patients

5.1 Introduction

The choice of medicine regimen is based on the "essential medicine" concept and the rational use of medicines. To maximize adherence, use of FDC medicines is strongly encouraged.

Essential medicines are defined as those medicines that satisfy the health needs of most of the population, at a price they and the community can afford; they should therefore be always available and in adequate amounts, and in appropriate dosage forms (WHO Expert Committee on Essential Medicines, December 1999). On the other hand, rational use of medicines requires that patients receive medicines appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period, and at the lowest cost to them and the community. (WHO Conference of Experts, Nairobi, 1985)

The National ART programme uses simplified and user friendly FDCs for ARVs. The following FDCs will be used for the first line regimens:

Dual combinations:

- Tenofovir (TDF) 300mg + Lamivudine (3TC) 300mg
- Tenofovir (TDF) 300mg + Emtricitabine (FTC) 200mg
- Tenofovir Alafenamide (TAF) 25mg + FTC 200mg
- Tenofovir Alafenamide (TAF)25mg +Lamuvudine 3TC 300mg

- Zidovudine (AZT) 300mg + Lamivudine (3TC) 150mg
- Abacavir (ABC) 300mg + Lamivudine (3TC) 300mg

The above dual FDC should be used in combination with single formulation of:

- Dolutegravir (DTG) 50mg
- Efavirenz (EFV) 400mg
- Atazanavir/r 300/100

Triple combinations:

- TDF 300mg + 3TC 300mg + DTG 50mg
- TDF 300 mg + 3TC 300 mg + EFV 400mg
- TAF 25mg + FTC 200mg + DTG 50mg
- TAF 25mg +3TC 300mg +DTG 50mg

5.2 First-line Regimen for Adults and Adolescents

- DTG in combination with an NRTI backbone is recommended as the preferred first line regimen for adults and adolescents living with HIV
- EFV (400mg) in combination with an NRTI backbone is recommended as the alternative first line regimen for adults and adolescents living with HIV

The following table 5.1 details the recommended preferred and alternative first line ART regimens for Zimbabwe

Table 5. 1: First line ARV regimens for adults and adolescents

Population	Preferred 1st line regimen	Alternative 1st line regimen
Adults and adolescents including women of childbearing potential	TDF + 3TC + DTG (Once daily FDC) (TLD1)	TDF (TAF) + 3TC (FTC) + EFV 400 TDF (TAF) + 3TC (FTC) + ATV/r ABC (AZT) + 3TC + DTG (EFV400)

- TB patients on Rifampicin to receive DTG 50mg twice daily
- ABC/3TC/DTG may be administered to patients weighing at least 20kg
- TAF may substitute TDF as part of preferred or alternative 1st line regimen
- AZT/3TC backbone may be used in special circumstances (for example where TDF is contraindicated and TAF is unavailable)

Main Considerations

- DTG is a safe and efficacious medicine with a rapid viral suppression, low potential for medicine interactions and a high genetic barrier to developing ARV resistance. It should be given as a preferred first line regimen for all populations unless where contraindicated
- DTG use has been associated with weight gain especially in women and when co-administered with TAF and 3/FTC. Prior to initiating DTG, clinicians should advise patients on this potential side effect and advise on the importance of adopting healthy lifestyles including exercising, taking healthy diets and avoidance of smoking.
- The potential signal of neural tube defects for women of childbearing potential receiving DTG has been examined extensively; the risk is lower than initially observed and does not affect its use for women of childbearing potential.

- DTG cannot be simultaneously administered with cation containing products such as antacids (such as calcium and magnesium), laxatives, zinc, iron, and multivitamin supplements because of the risk of chelation resulting in subtherapeutic DTG blood levels.
- DTG should not be used with certain anticonvulsants such as phenytoin and phenobarbitone
- In patients with diabetes mellitus on metformin, receiving DTG, there is risk of hypoglycemia, therefore regular blood sugar levels should be done, and total daily dose of metformin should not exceed 1g/day
- TAF a derivative of TDF has less renal and bone toxicity compared to TDF. For this reason, TAF should be considered in elderly patients above 50 years patients with Creatinine Clearance of 30 — 60 mmol/min and Hepatitis B Virus (HBV) co-infected. However, TAF should NOT be used in HIV/TB co-treatment; among HIV infected pregnant women and patients with renal impairment with Creatinine Clearance below 30 mmol/min.
- An alternative to 3TC is FTC; these medicines are considered pharmacologically equivalent

Caution! Tenofovir (TDF)

TDF may be associated with acute kidney injury or chronic kidney disease and reduced bone mineral density

Clinical Considerations when using TDF

- Routine blood pressure monitoring may be used to assess for hypertension.
- Urine dipsticks may be used to detect glycosuria or severe TDF nephrotoxicity in individuals without diabetes using TDF-containing regimens.
- Ideally creatinine test should be performed, use the estimated glomerular filtration rate at baseline before initiating TDF regimens. Calculation of GFR is detailed below:

Table 5. 4: Managing interactions between ARVs and TB Medicines

Calculation of GFR or Creatinine clearance in ml/min using (for adults)
Cockcroft Gault Equation
Male: 1.23 X (140 minus Age) x body wt. in Kg/ Creatinine (in micromols/L)
Female: 1.04 X (140 minus Age) x body wt. in kg/Creatinine (in micromols/L)

- Do not initiate TDF when the estimated glomerular filtration rate is <60ml/ min, or in long term diabetes, uncontrolled hypertension, and renal failure.

5.3 Second-line Treatment Recommendation for Adults and Adolescents

Second-line ART regimens depend on what the patient received at the time of failing first-line treatment as detailed in table 5.2 below:

Table 5. 2: Second line regimens for adults and adolescents including pregnant and breastfeeding women

Failing 1st line regimen	Preferred 2nd line regimen	Alternative 2nd line regimen
TDF (or TAF) + 3TC + DTG or ABC + 3TC -F DTG	AZT + 3TC+ ATV/r	AZT +3TC +LPV/r (or DRV/r)
TDF (or TAF) +3TC (or FTC) + ATV/r TDF (or TAF) + 3TC (or FTC) + EFV	AZT + 3TC + DTG	AZT +3TC +LPV/r (or DRV/r)
AZT +3TC (or FTC) + EFV	TDF (or TAF) + 3TC (or FTC) + DTG	TDF (or TAF) + 3TC (or FTC) + ATV/r (or DRV/r)

- Those patients with HBV infection will always need Tenofovir/TAF and Lamivudine/FTC among their medicines.
- For adults who cannot tolerate both TDF and AZT, use ABC/3TC
- DRV/r should not be used for children younger than three years and should be combined with appropriate dosing of RTV
- Use of DRV/r for 2nd line regimen should be done in consultation with an experienced HIV clinician

5.4 Third-line Treatment Recommendations for Adolescents, Adults, Pregnant and Breast-feeding Women

Those failing second-line therapy will need to be referred for specialist assessment which includes viral load and genotype testing prior to recommending the third-line medicines. Adherence needs to be reinforced all the time. In adolescents >12 years and adults, the preferred 3rd line ART regimen should include Dolutegravir (50mg) and Darunavir (600mg)/Ritonavir (100mg) twice daily (for PI-experienced patients).The NRTI backbone will be determined by results of genotype resistance testing.

The dose of dolutegravir is DOUBLED in patients who have previously been exposed during 1st or 2nd line ART. Table 5.3 summarizes 1st, 2nd, and 3rd line ART regimens.

Table 5. 3: Summary of sequencing options for first-line, second-line and third-line ART regimens and preferred and alternative first-line regimens for adults, adolescents

1st line Regimen	2nd line Regimen	3rd line Regimen
Two NRTIs + DTG	Two NRTIs + ATV/r (or LPV/r or DRV/r)	DRV/r + 1–2 NRTIs + DTG* Optimize the regimen using a genotype profile
Two NRTIs + EFV	Two NRTIs + DTG (or ATV/r or LPV/r or DRV/r)	Two NRTIs + (ATV/r, DRV/r or LPV/r) + DTG* Optimize the regimen using a genotype profile

** 50mg twice daily*

5.5 Key Considerations for ART in TB/HIV Co-infected Populations

5.5.1 Patients with TB who are not yet on ART

All people with presumptive and or diagnosed TB should be tested for HIV at first contact with a health care worker and those who test negative should be linked with other HIV preventive services

All TB patients who test HIV positive should be started on ART within 2– 8 weeks of commencement of TB treatment regardless of CD4 status, with the ART PREFERABLY GIVEN IN THE TB SETTING and clients should be linked with HIV prevention, treatment, and care at the end of the TB treatment.

All clients co-infected with TB and HIV should be managed for both conditions concurrently with TB treatment taking precedence over ART initiation.

TB/HIV co-infected patients without involvement of the central nervous system should receive ART after at least 2 weeks of receiving TB treatment. Cotrimoxazole prophylaxis should be provided with the commencement of the TB therapy if the patient is not on it already

All HIV infected persons with intracranial TB should be initiated on anti-TB treatment promptly and have their ART initiation delayed until after 4 weeks of commencement of TB treatment to reduce the risk of intracranial TB – Immune Reconstitution Inflammatory Syndrome (IRIS) which could end fatally.

RECOMMENDATIONS FOR ART IN HIV INFECTED CHILDREN BEING TREATED FOR TB REMAIN THE SAME AS THOSE IN ADULTS.

5.5.2 Patients who develop TB when already on ART

Manage the TB as per national TB guidelines (See national TB management guidelines)

5.6 Managing Interactions between ARVs and TB Medicines

Medicine interactions can complicate TB and HIV treatment. The rifamycins used in TB treatment (Rifampicin, Rifabutin and Rifapentine) are hepatic enzyme inducers and will lower the serum concentration of many medicines that are used to treat HIV. The following table 5.4 details the recommendations for adjusting treatment in patients receiving rifampicin.

Table 5. 4: Managing interactions between ARVs and TB Medicines

1st line Regimen	What to do when TB treatment is started
DTG based regimen	DTG dose is doubled (Should be taken 12hrly)
LPV/r regimen	Transition to DTG-based regimen (with appropriate dose adjustment) is preferable, and if not possible, LPV/r dose is doubled
ATV/r regimen	Change of regimen needed: replace ATV/r with DTG if DTG naïve (with appropriate dose adjustment) with LPV/r if DTG experienced with appropriate dose adjustment
TAF-containing regimen	Change of regimen needed: TAF to be replaced by ABC or TDFt
DRV/r-based regimen	Change of regimen needed: replace DRV/r with DTG if DTG naive, with LPV/r if DTG experienced with appropriate dose adjustment. For patient on third line ART, substitute rifampicin with rifabutin
EFV-400 based regimen	No dose adjustment is necessary

For interactions between ARVs and second line TB medicines, refer to national TB management guidelines.

Chapter 6 Prevention of Mother to Child Transmission of HIV

6.1 Introduction

Mother to child transmission (MTCT) of HIV is an important contributor of HIV transmission. The MoHCC is committed to the elimination of MTCT of both HIV and syphilis and as such efforts should be intensified to reach this goal. The aim of elimination' is to have an EMTCT rate of HIV of less than 5% in breast-feeding communities.

The national PMTCT programme therefore aims to achieve the following targets:

- Antenatal care coverage of ≥ 95%
- Coverage of HIV and syphilis testing of pregnant women ≥ 95%
- ART coverage of HIV positive pregnant women of ≥95%
- Treatment of syphilis sero-positive pregnant women of ≥95%

The Zimbabwe PMTCT programme is anchored on the United Nations four pillars (prongs) for comprehensive PMTCT:

- Primary prevention of HIV infection among women of reproductive age
- Prevention of unintended pregnancies in HIV infected women.
- Prevention of HIV transmission from infected women to their infants during pregnancy, labour, childbirth and breast-feeding through HIV counselling and testing, ARV prophylaxis, ART for life for all pregnant and breast-feeding women and safer infant feeding practices
- Provision of comprehensive care to mothers living with HIV, their children, and families.

Figure 6.1: below summarizes the synergistic purposes of providing ART to all pregnant and breast-feeding women

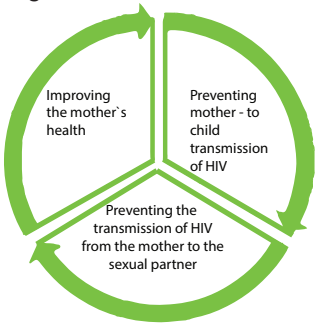


Figure 6. 1: Synergistic Purposes of Providing ART To All Pregnant and Breast-Feeding Women

Primary prevention

Several strategies for preventing HIV infection in pregnant and breastfeeding women are well established. These are based on the WHO eight elements of comprehensive HIV prevention in antenatal and postnatal care which are.

- HIV testing services (HTS): to identify women who are HIV-negative and may benefit from HIV prevention services, or who are HIV-positive and require treatment. (Refer to Chapter 2, figure 4, the HIV Testing Algorithm for Pregnant and Breastfeeding Women).
- HTS should be offered for all sexual and drug injecting partners: offer through passive or assisted partner notification approaches. Service providers offering partner notification services should discuss potential risk for harm before providing these services.
- Partner referral for ART if HIV-positive: establish referral mechanism for partner ART.
- Male partner referral for voluntary medical male circumcision (VMMC) if HIV-negative: establish referral mechanism for VMMC.
- STI screening and treatment: manage STIs, syphilis, at all antenatal and postnatal visits.
- Condom promotion: offer male and female condoms with education on their correct and consistent use.
- Risk reduction counselling: following a discussion of risk or a risk assessment, provide women with appropriate risk reduction counselling at HTS visits.
- Offer to start or continue PrEP: based on individual risk with discussion of benefits and risks. An increasing body of evidence has demonstrated that TDF-containing oral PrEP is safe during pregnancy and breastfeeding. Monthly use of the dapivirine vaginal ring has been shown to be safe and effective for HIV prevention among non-pregnant women of childbearing potential. However, data on how dapivirine affects pregnancy outcomes and infants are limited.

6.2 HIV testing services in pregnant and breastfeeding women

PITC for women should be considered a routine component of the package of care in all antenatal, childbirth, postpartum and paediatric care settings. All pregnant women should be tested for HIV and syphilis (with the inclusion of hepatitis B surface antigen (HBsAg) in settings where the seroprevalence is >2%) at least once and as early as possible. The dual HIV and syphilis rapid diagnostic test is recommended as the first test in the HIV testing algorithm for pregnant women in antenatal care. In our setting, where breastfeeding is the norm, lactating mothers who are HIV negative should be retested periodically throughout the period of breastfeeding.

Health workers should retest previously HIV-negative pregnant and breastfeeding women as follows:

- first trimester of pregnancy
- third trimester/ or at delivery
- 6 weeks post-natal and
- 6 monthly during the breastfeeding period.

In antenatal care settings, couples and partners should be offered voluntary HIV testing services with support for mutual disclosure.

Service package for pregnant women whose test result is HIV positive (including those already on ART) should include the following:

- Discussion of childbirth plans and encouragement to deliver in a health facility for health reasons and to ensure access to services for PMTCT
- Use of ARV medicines both for the mother's own health and to prevent transmission to the infant
- Importance of partner testing and information on the availability of couples testing services
- Screening for TB and testing for other infections, such as syphilis and hepatitis B
- Counselling on maternal nutrition, including iron and folic acid supplementation
- Advice on infant-feeding and support to carry out the mother's infant- feeding choice
- HIV testing for the infant and necessary follow up for HIV-exposed infants
- Counsel on sexual and reproductive health including family planning and the need for dual contraception (reliable hormonal contraceptives plus barrier methods i.e., male, and female condoms)
- Service package for pregnant adolescent girls and young women whose test result is HIV positive should include peer support if available, as they are at higher risk of delivering a positive baby and research data speak to the effectiveness of peers.

Acquisition of HIV infection in pregnancy or during the breastfeeding period is associated with peak viremia and increased risk of HIV transmission to the baby. As such women at risk of new infections (sero-discordant couples), should be provided with PrEP during pregnancy and breast feeding (Refer to Chapter 11 of these guidelines).

6.3 When to start Lifelong ART in HIV Positive Pregnant and Lactating Women

All HIV positive pregnant and breastfeeding women should initiate lifelong ART as soon as possible after their HIV positive status is confirmed irrespective of their CD4 count or WHO clinical stage; and continue ART throughout the breastfeeding period and beyond.

Health workers should conduct rapid assessment of a person's readiness for ART. In the context of pregnancy and breastfeeding and to minimize risk of MTCT, same day initiation is recommended.

Table 6. 1: 1st and 2nd line ART regimens for pregnant and lactating women

Pregnant and Lactating women	1st line therapy	2nd line therapy
Preferred Option	TDF + 3TC+ DTG	If TDF was used as first line, use AZT plus 3TC plus ATV/r or LPV/r If AZT was used as first line, use TDF plus 3TC plus ATV/r or LPV/r
Alternative Options	AZT + 3TC + EFV400	If TDF was used as first line, use AZT plus 3TC plus DTG If AZT was used as first line, use TDF plus 3TC plus DTG

- DTG in combination with an NRTI backbone is recommended as the preferred first-line regimen for pregnant and breastfeeding women with HIV initiating ART
- The benefits of DTG for women of childbearing potential newly initiating ART (more maternal suppression of viral loads, fewer maternal deaths, fewer sexual transmissions, and fewer mother-to-child transmissions) outweigh the risks.
- All women of childbearing potential or any pregnant or breastfeeding woman should receive full information and medical guidance that is appropriate to her situation. Health workers should provide support in making voluntary choice around medical therapy initiation, continuation and adherence or retention in care, as applicable.

6.4 Use of viral load testing in pregnancy

Whenever possible, utilize same-day point-of-care (POC) testing for viral load testing in pregnant and breastfeeding women to expedite result return and clinical decision-making. If not available, viral load specimens and results for pregnant and breastfeeding women should be prioritized across the laboratory referral process (including specimen collection, testing, and results return). Enhanced adherence counselling should be provided at all ANC and post-natal visits to ensure viral suppression is maintained throughout pregnancy and breastfeeding

Figure 6.2 below details VL monitoring and recommended action for pregnant and breastfeeding women.

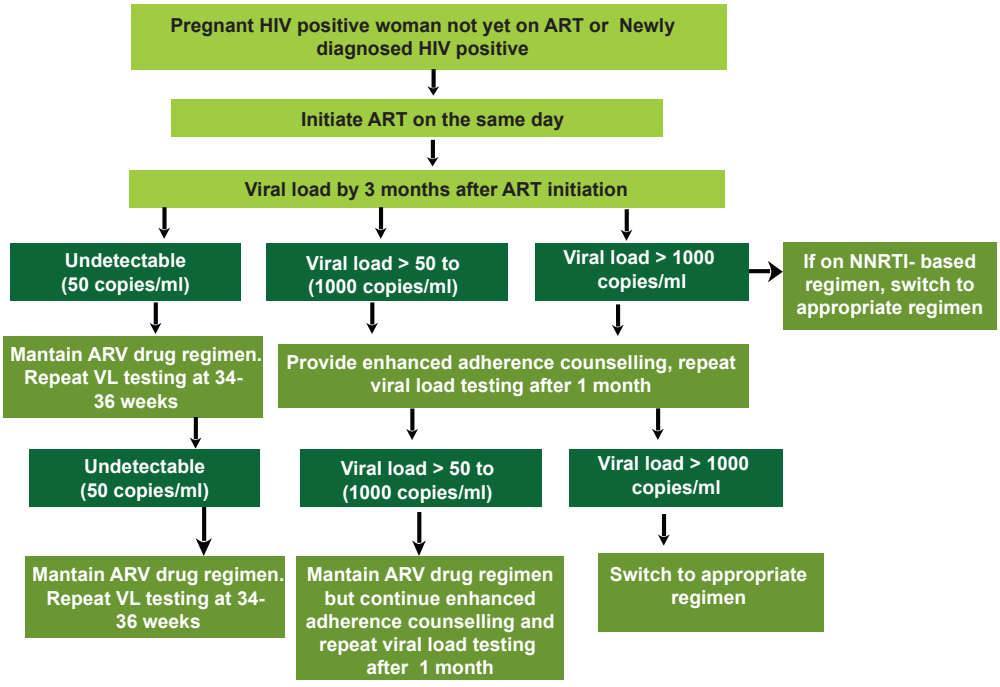


Figure 6. 2: Algorithms for VL monitoring in HIV positive pregnant and breastfeeding women

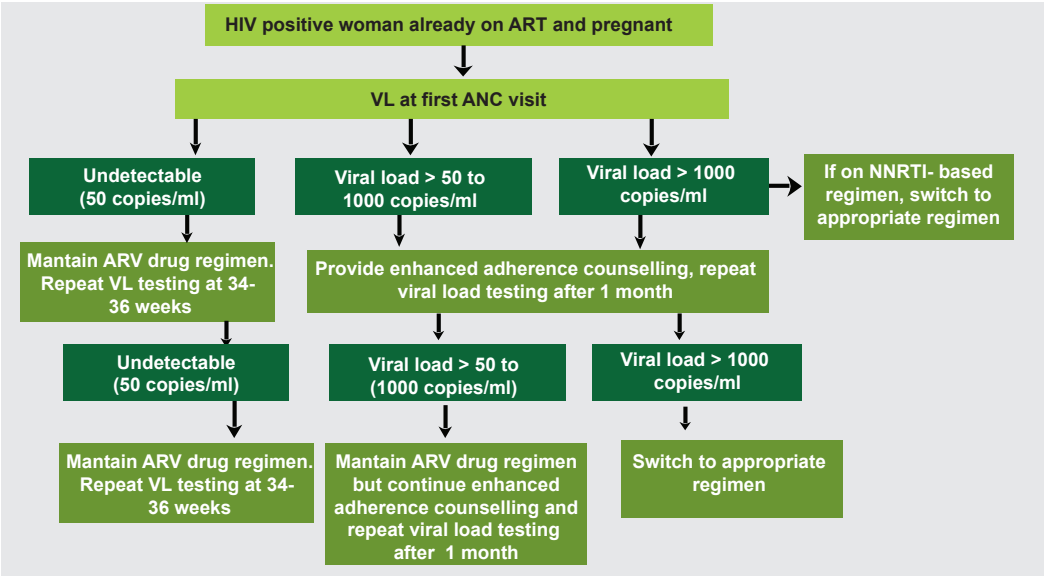


Figure 6. 3: Algorithm for risk assessment at the time of delivery to help identify infants at high and low risk of infection

Viral load at first ANC Visit maybe deferred if woman has a documented most recent VL <50 copies /ml within the previous 3 months

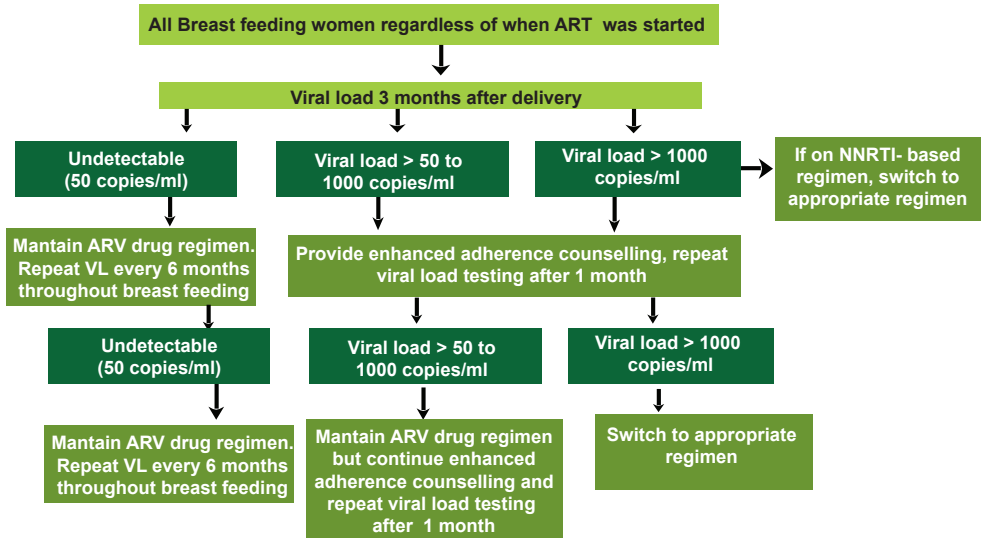


Figure 6. 5: Infant Diagnosis Algorithm

Important consideration:

- Appropriate ART regimen switch is recommended in pregnant and breastfeeding women who have a second (repeat) VL >50 to 1000 copies/ml after enhanced adherence support especially if the VL is rising

6.5 HIV Exposed Infant Prophylaxis

Important consideration:

VL testing during pregnancy and breastfeeding period and the duration of maternal ART is needed to stratify HIV exposed infants as either high risk or low risk. It is important not to use a “one size fits all” for infant prophylaxis as infants are not all at the same risk for HIV transmission.

A high-risk infant is defined as follows:

- An infant whose mother has a high viral load >1000copies/ml during the last 4 weeks before delivery
- An infant born to HIV infected woman who has received less than 4 weeks of ART at the time of delivery

- An infant born to a newly diagnosed HIV infected woman during labor, delivery and postpartum (Incident HIV infection)
- An infant whose mother has advanced HIV disease (in the absence of a VL result)

All infants who do not meet the criteria for 'high-risk' infants are classified as 'low-risk' infants. The figure below highlights algorithm for infant risk assessment

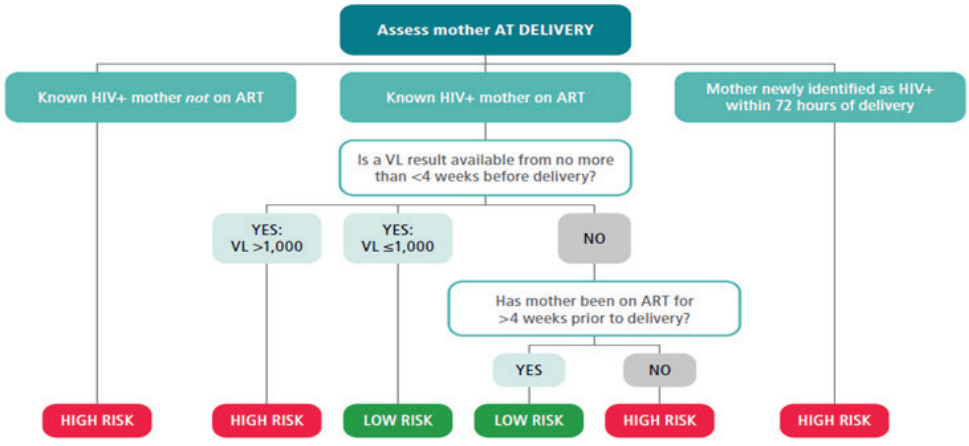


Figure 6. 3: Algorithm for risk assessment at the time of delivery to help identify infants at high and low risk of infection

Due to on-going challenges with supply chain for single formulations of AZT and Nevirapine suspension, and concerns regarding use of AZT or NVP mono or dual prophylaxis in HIV exposed infants who then test HIV positive later, the recommendation is to offer triple ARVs for post-partum prophylaxis in all HIV exposed infants. Other countries in high HIV prevalence settings such as Malawi, Zambia and Botswana have already moved in this direction.

It is important to perform a NAT prior to starting the triple regimen, and if the result is not available immediately, at least collect a specimen as interpretation of later testing will be difficult. The results of any future tests will be influenced by the ARVs on board.

Regimen for triple ARVs for post-natal prophylaxis will be AZT+3TC+NVP
In case of non-availability of triple ARVs for post-natal prophylaxis, infant prophylaxis should be provided as indicated in the figure below:

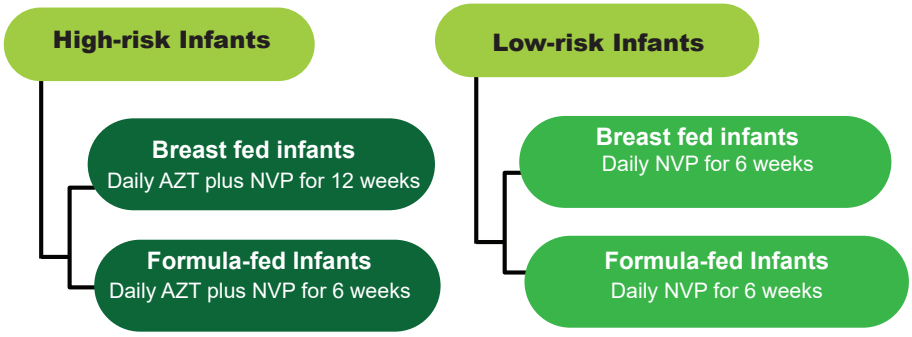


Figure 6. 4: Infant ARV prophylaxis regimens

N.B. Infants born to mothers who are newly identified or sero-convert during the postnatal period are eligible to receive infant ARV prophylaxis as indicated above.

Use of cotrimoxazole prophylaxis

In addition to ARV prophylaxis, all HIV-exposed infants born to mothers living with HIV should receive cotrimoxazole prophylaxis from 6 weeks (or at their first encounter with the health system if this happens after age 6 weeks) and stopping after the period of risk and final confirmation of a negative HIV status, defined as a negative 18-month test or testing after breastfeeding ends if breastfed longer than 18 months. See Chapter 7, table 7.7 for cotrimoxazole dosing in infants.

6.6 Infant feeding in the context of HIV

The MOHCC promotes, supports, and protects breastfeeding because it is the first and best investment for a child's nutrition and health.
Appropriate feeding methods including their advantages and disadvantages should be explained to all mothers to allow them to make an informed decision.
Mothers who choose to breastfeed are advised to

- Exclusively breastfeed their infants for the first 6 months of life, introducing appropriate complementary foods at 6 months, and continue breastfeeding up to 24 months and beyond
- Avoid mixed feeding (feeding infants with breast milk and other fluids, and semi-solid or solid foods).

HIV-infected mothers may consider expressing breast milk as an interim feeding strategy:

- In special circumstances such as when the infant is born with low birth weight or is otherwise ill in the neonatal period and unable to breastfeed.
- When the mother is unwell and temporarily unable to breastfeed or has a temporary breast health problem such as mastitis.

Expressing breastmilk should also be taught to mothers to assist mothers to stop breast-feeding.

- Breastfeeding mothers who decide to stop breastfeeding at any time should stop gradually within one month. Abrupt cessation of breastfeeding is not advised.
- Breastfeeding mothers should be counselled on how to solve common difficulties, such as sore nipples, perceptions of "insufficient milk," breast engorgement, manual expression, and storage of breast milk.
- Breastfeeding mothers are advised to immediately seek treatment for mastitis, cracked nipples, infant mouth lesions, and thrush to decrease the risk of MTCT.
- Breastfeeding mothers should be counselled on appropriate complementary foods that must be introduced to the infants' diet beginning at 6 months as per the Zimbabwe Infant and Young Child Feeding Guidelines.

For HIV infected mothers who choose not to breastfeed, they can adopt exclusive formula feeding for the first six months, introducing appropriate complementary foods at 6 months, and continue formula feeding up to 12 months and beyond if they choose. It is important to support the mother in the feeding option they may choose. The following conditions must be met in their entirety for safe exclusive replacement feeding.

- Safe water and sanitation are assured at the household level and in the community, and
- The mother, or other caregiver can reliably provide sufficient infant formula milk to support normal growth and development of the infant, and
- The mother or caregiver can prepare it cleanly and frequently enough so that it is safe and carries a low risk of diarrhoea and malnutrition, and
- The mother or caregiver can, in the first six months, exclusively give infant formula milk, and
- The family is supportive of this practice, and
- The mother or caregiver can access health care that offers comprehensive child health services.

6.7 Early Infant Diagnosis of HIV

All infants with unknown or uncertain HIV exposure being seen in health-care facilities at or around birth or at the first postnatal visit (usually 4–6 weeks) or other child health visit should have their HIV exposure status ascertained. This can be done by:

- Asking if the mother knows she is HIV positive or is on ART
- Checking the handheld child health card for information on maternal HIV status
- Performing a rapid HIV test on the mother
- Performing a rapid HIV test on the baby- N.B. this can be used to assess HIV exposure only in infants less than 4 months of age. HIV-exposure status in infants and children 4–18 months of age should be ascertained by undertaking HIV serological testing in the mother

6.8 Testing of HIV Exposed Infants

All babies of HIV-infected mothers are born with maternal anti-HIV antibodies that are passed on to them transplacentally. These antibodies start to wane from about 4 months, and by 18 months have cleared off completely.

Due to the presence of these maternal antibodies, HIV antibody tests in infants under the age of 18 months cannot be used to definitively diagnose HIV infection. Diagnosis of HIV infection in children less than 18 months requires testing for the virus itself (called virologic testing, or nucleic acid testing). Infants with an initial positive virological test result should be commenced on ART without any delay and, at the same time, a second specimen should be collected to confirm the initial positive virological test result. Immediate initiation of ART saves lives and should not be delayed while waiting for the results of the confirmatory test. In case of a confirmatory negative NAT, a third NAT should be performed before considering ART interruption.

In case the 3rd NAT is negative some factors should be considered when assessing patient for ART interruption:

- The child should NOT have signs/symptoms suggestive of HIV infection
- Follow-up plan should be agreed upon with caregiver(s) and HCW

The infant should be followed up for a minimum of 8 months after interruption of ART. Where possible, both early infant diagnosis (EID) (qualitative) and VL (quantitative) tests should be performed at 4 weeks, 4 months, and 8 months after ART interruption. Figure 5 below details the algorithm for diagnosing HIV in exposed infants.

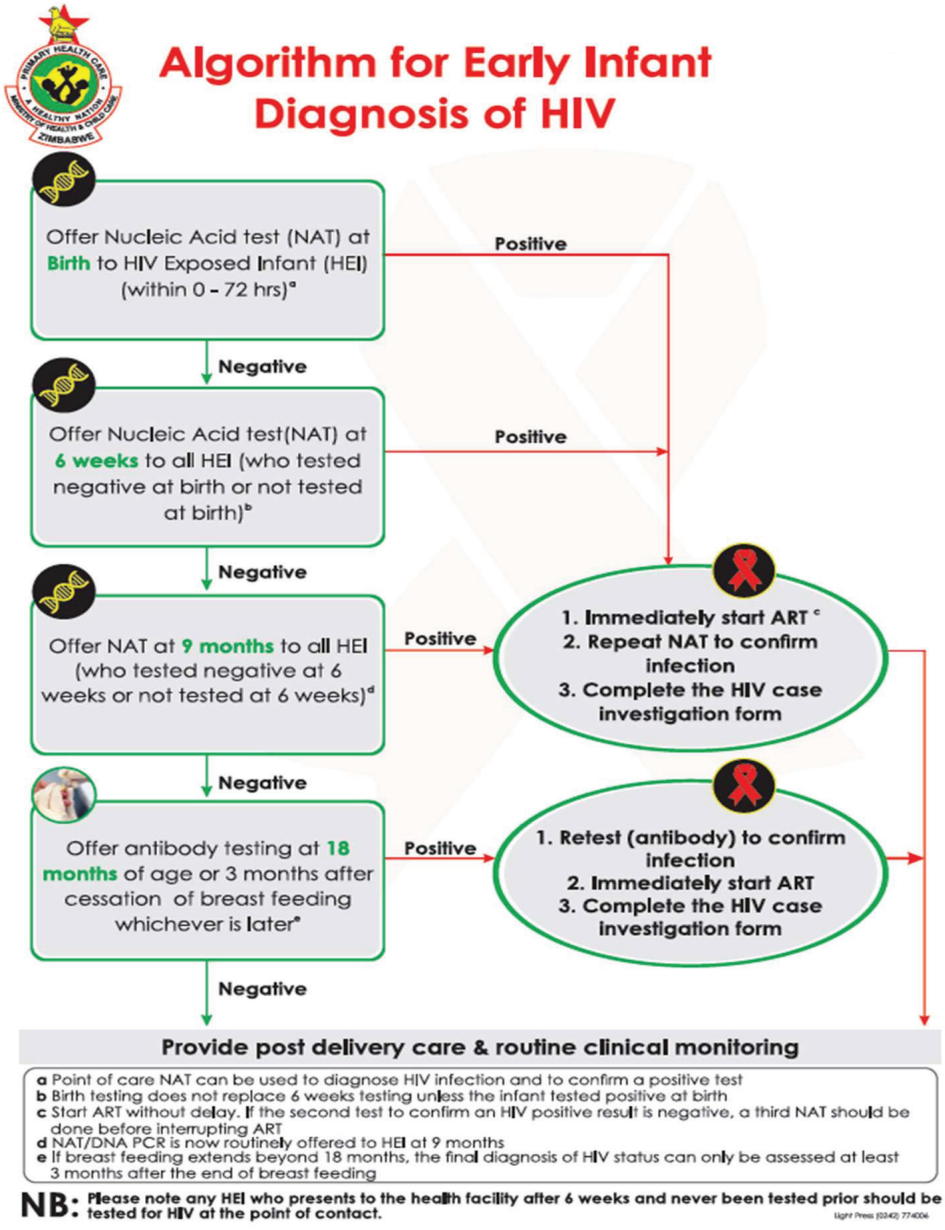


Figure 6. 5: Infant Diagnosis Algorithm

Source: Zimbabwe Early Infant Diagnosis Algorithm

a Point of care NAT can be used to diagnose HIV infection and confirm a positive result

b Birth testing does not replace 6 weeks testing unless the infant tested positive at birth

c Start ART without delay. If the second test to confirm an HIV positive result is negative, a third NAT should be done before interrupting ART

d NAT/ DNA PCR is now routinely offered to HEI at 9 months

e The risk of HIV transmission remains as long as breastfeeding continues. If the 9-month test is conducted earlier than 3 months after cessation of breastfeeding, infection acquired in the last days of breastfeeding may be missed. Retesting at 18 months or 3 months after cessation of breastfeeding (whichever is later) should be carried out for final assessment of HIV status.

f If breastfeeding extends beyond 18 months, the final diagnosis of HIV status can only be assessed at the end of breastfeeding.

If breastfeeding ends before 18 months, the final diagnosis of HIV status with antibody testing can only be assessed at 18 months.

Antibody testing should be undertaken at least 3 months after cessation of breast feeding (to allow for development of HIV

(antibodies). For infants younger than 18 months of age NAT should be performed to confirm infection. If the infant is older than

18 months, negative antibody testing confirms that the infant is uninfected; positive antibody testing confirms infant is infected.

Chapter 7 Paediatric Antiretroviral Treatment

HIV infection disproportionately impacts infants and young children. In the absence of any intervention, up to 52% of children die before the age of two. If HIV positive children are not started on ART by the age of five, up to 75% of them will die. As a result, identification of all children living with HIV should be prioritized. In addition, all children younger than five years are considered to have advanced HIV disease unless they have been on ART for at least 1 year and are clinically stable.

7.1 Case Finding Strategies outside of PMTCT

a. Facility based testing- Determine the exposure status of all infants and children attending malnutrition wards, TB wards, paediatric wards, outpatient, and EPI clinics
b. Index case and family testing- Test infants and children without final outcomes living in the households of known HIV-positive parents or siblings
c. Targeted testing- Test known HIV-exposed infants and children whenever they present sick
d. Community based Testing - Community engagement and community-based services play an important role in supporting HIV-exposed infant care
    i. Early Childhood Development screening,
    ii. EPI
    iii. Outreach testing
    iv. Orphans and Vulnerable Children
    v. Door to door screening, including hard to reach areas
e. Utilise the Paediatric HIV Screening tool when providing HTS to children

7.2 ART Initiation

The goal of ART for children is to improve quality of life and decrease HIV related morbidity and mortality.

- ART should be initiated in ALL children living with HIV.
- Children are a priority for HIV treatment and should be started on ART the same day whenever possible.
- Counselling to prepare caregivers and children for ART is very important but should not delay ART.
- Health workers to initiate ART immediately if the 1st test result for NAT is positive and then offer re-test to confirm the result. ART initiation in children should not be delayed by pending re-test results. For rapid HIV test at 18 months or above, re-test before ART can be offered immediately without delaying ART initiation

- Investigate and manage opportunistic infections including TB before ART initiation.

N.B. ART should be started in any child with active TB disease as soon as possible and within 2 weeks following the initiation of anti-tuberculosis treatment, regardless of the CD4 cell count and clinical stage.

- Co-trimoxazole prophylaxis should be initiated at 6 weeks post-natal or at first contact after 6 weeks for all exposed infants or infected children.
- A baseline CD4 test is recommended to identify children with Advanced HIV disease, however, CD4 count is no longer used to assess eligibility of ART initiation.
- Health workers should develop a plan for age and mental development-appropriate disclosure to children and disclosure assistance to care givers

7.2.1 When to Start ART in Children Younger than 10 Years of Age

ART should be initiated in ALL children living with HIV, regardless of WHO clinical stage and at any CD4 count.

7.2.2 What regimens to use in children

Raltegravir (RAL) based regimens can be used from birth and have a faster reduction of viral load. RAL is prescribed to neonates with confirmed HIV infection according to the national EID algorithm, who weigh at least 2kg at birth and have a gestational age of >37 weeks. Dosing is based on WHO weight-based recommendations.

DTG-based regimens are preferred for children older than 4 weeks and weighing at least 3kg. For children who may not tolerate DTG, LPV/r remains the preferred alternative regimen. All stable children on other regimens >4 weeks of age and weighing ≥3 kg should be transitioned to DTG based regimens.

While viral load monitoring remains a good practice to deliver appropriate care to CLHIV, viral load should not be considered a precondition to undertaking a programmatic or individual transition and children should not have their transition to DTG delayed due to lack of documented viral load.

Table 7. 1: First-line ART regimens for children and neonates

	NEONATES (0 to 4 weeks of age)	CHILDREN (>4 weeks of age)
Preferred	AZT+3TC+RAL	ABC+3TC+DTG
Alternatives	AZT+3TC+NVP	ABC+3TC+LPV/r
Special circumstances	AZT+3TC+LPV/r	ABC+3TC+EFV$^{\mu}$ AZT+3TC+LPV/r$^{\infty}$

µFrom 3 years of age
∞In cases where no other alternatives are available

Important considerations

- Efavirenz should not be used in children younger than 3 years
- Neonates starting ART with a RAL-based regimen should transition to DTG after 4 weeks.
- TAF can be used in children weighing more than 25kg
- Regimens and dosage should be adjusted appropriately based on age and weight at each visit

Considerations for DTG use in children

- DTG 10mg dispersible scored tablets are recommended for use in children living with HIV who are at least 4 weeks of age and weigh at least 3kg and can be used up to 20kg.
- For children who weigh 20 kg or more, the DTG 50 mg single film-coated tablet is recommended in combination with ABC + 3TC. A child should only be switched to DTG 50mg tablet when they can swallow the tablet whole.
- NB: As the paediatric DTG dispersible tablets are much better absorbed than the DTG 50mg film-coated tablet used for patients >20kgs, the dosing for the two products is not 1:1. If there is a need to transition between the two formulations,DTG dose of the 50mg film coated tablet is approximately equal to 3x10mg dispersible tablets.
- For children living with HIV who weigh 30 kg or more, the FDC of TLD is recommended.

Table 7. 2: WHO recommended dosing for Neonates (0 to 4 weeks)

			Weight-Based Dosing					
			2-3 kg		3-4 kg		4-5kg	
Drug	Strength (Oral liquid or tablet)		AM	PM	AM	PM	AM	PM
AZT	10mg/ml		1ml	1ml	1.5ml	1.5ml	2ml	2ml
3TC	10mg/ml		0.5ml	0.5ml	0.8ml	0.8ml	1ml	1ml
AZT/3TC	60/30mg dispersible tablet		-	-	1 tablet	1 tablet	1 tablet	1 tablet
RAL	10 mg/mL (Oral granules for suspension: 100 mg/sachet)	< 1week old	0.4 ml once daily		0.5ml once daily		0.7ml once daily	
		> 1week old	0.8ml	0.8ml	1 ml	1ml	1.5ml	1.5ml

Table 7. 3: WHO recommended dosing for children from 4 weeks for DTG-based regimens

Recommended Daily Dosing							
Formulation	3 – 5.9 kg	6 – 9.9 kg	10 – 13.9 kg	14 – 19.9 kg	20 – 24.9 kg	25 – 29.9 kg	≥ 30 kg
ABC/3TC 120/60mg scored dispersible tablet	1	1.5	2	2.5	3	–	–
DTG 10mg scored dispersible tablet	0.5	1.5	2	2.5	[transition to DTG 50mg]*	–	–
ABC/3TC 600/300 mg tablet	–	–	–	–	–	1	–
DTG 50 mg tablet	–	–	–	–	1	1	[transition to TLD]
TDF/3TC/DTG 300/300/50 mg tablet	–	–	–	–	–	–	1

Table 7. 4: WHO recommended dosing for LPV/r and ABC/3TC

		Recommended Daily Dosing												
		3 – 5.9kg		6-9.9kg		10-13.9kg		14-19.9kg		20.24.9kg		25-29.9kg		≥30kg
Drug	Strength	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM/ PM
ABC/ 3TC	120 mg/ 60mg tablet	0.5	0.5	0.5	1	1	1	1	1.5	3		Adult 600/300*		TLD
	60mg/ 30mg tablet	1	1	1.5	1.5	2	2	2.5	2.5	6				
LPV/r Granules	40mg/ 10mg sachet	2	2	3	3	4	4	5	5	DTG 50mg				
LPV/r tablets	100mg/ 25mg tablet	-	-	-	-	2	1	2	2					

7.3 Second- and Third-Line ART Regimen in Children

When preparing to start second or third-line ART in Children there is need for Intensive adherence counselling with a clear discussion that the regimen is likely to be the last option for the foreseeable future. The choice of the third-line regimen should be made in consultation with an HIV expert. Third-line regimen must be based on results of genotypic test results. Table 7.5 details the recommended 1st, 2nd and 3rd line ART regimens.

Table 7. 5: Summary of sequencing options for first-line, second-line and third-line preferred and alternative regimens

First-line ART regimen	Second-line ART regimen	Third-line ART regimen
Two NRTIs + DTG	Two NRTIs + LPV/r (or ATV/r)	DRV/r + 1–2 NRTIs + DTG Optimize the regimen using a genotype profile for children younger than three years
Two NRTIs + LPV/r	Two NRTIs + DTG	DRV/r + 1–2 NRTIs + DTG Optimize the regimen using a genotype profile for children younger than three years
Two NRTIs + NNRTI	Two NRTIs + DTG	Two NRTIs + (ATV/r, LPV/r or DRV/r + DTG

Important Considerations

- DRV/r cannot be used for children younger than three years
- DTG dose must be doubled when used in Integrase Inhibitor experienced patients

Consider the following before switching ART regimens:

- The child should have received the regimen for at least 24 weeks (six months).
- Adherence to therapy should be assessed and considered to be optimal.
- Any inter-current OIs should have been treated and resolved.
- Before considering changing treatment due to growth failure, ensure that the child is receiving adequate nutrition.

7.4 Medicines Interactions

Interactions of other medicines with ARVs is an important consideration for children on ART. Important interactions are the same as those in adults. See Chapter 8 section 8.5

7.5 Scheduled Visits

Post initiation visits are monthly then change to 3 monthly when patient is stable.

1. Services should be delivered across a continuum of care. This requires integrated and linked service provision at all levels of the health system, from primary to secondary to tertiary (specialist) care, embracing all elements of the health system.
2. During these visits the following actions should be taken:
   - Growth should be monitored, and development assessed
   - Infant-feeding practice should be reviewed regularly, and appropriate supportive counselling and appropriate referrals provided.
   - Breast feeding is recommended for all babies - Exclusive breastfeeding for 6 months with addition of complementary feeding thereafter.
   - The baby should continue breastfeeding for 24months and beyond.
   - Immunizations should be given according to the national guidelines. The BCG vaccination should still be given at birth, but BCG should not be given to children with symptomatic HIV infection.
   - Always look for and treat opportunistic infections at every visit to the clinic.
   - Be aware of and watch for potential medicine interactions. The management of TB in HIV-infected children and the treatment of severe HIV infection with ARVs is complicated by the potential for multiple medicine interactions. (See Chapter 5 section 5.5.1)

7.6 Psychosocial Factors

While using the family approach, 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.

The process of disclosure to the child should be initiated as early as possible, usually after seven years of age. Please note that adherence is optimal in children who know their status and are supported to adhere to medicines.

Health workers, in consultation with the care givers, should develop a plan for disclosure that is age and mental development appropriate for the child. Care givers may require assistance and health workers should provide the necessary guidance.

7.7 Administering Medicines

Recommendations for children need to take into consideration the age and weight of the child, the availability of paediatric formulations of the medications, the palatability of the medications, other medicines that the child is taking, PMTCT regimens used and the effect of food on the absorption of the medicines.

- Medicine doses must be adjusted as the child grows.
- Dosing is by weight; therefore, caregivers should be encouraged to bring the child for weighing at ALL clinical visits
- Medicines may be dispersed in water or, crushed and mixed with a small amount of food and administered immediately. (Take note of exclusive breastfeeding for babies below 6 months)
- Give information to the caregiver.
- Use pill boxes if available.
- Standardization is important to safely dispense correct doses.

7.8 Advanced HIV Disease in Children

All children younger than five years (who are not already receiving ART and clinically stable) are considered to have advanced HIV disease (AHD) because evidence shows that 80% of all children initiating ART have severe immunosuppression. AHD is defined as WHO stage 3 or 4 or a CD4 count <200 cells/mm3 for children five years or older (the same definition used for adults). All children younger than five years living with HIV are considered as having advanced HIV disease, although those who have been receiving ART for more than one year and are established on ART and older than two years should not be considered to have AHD and should be eligible for multi-month dispensing.

Children and adolescents who had previously initiated ART and are re-engaging with care after a period of ART interruption should be assessed for AHD and should be offered the AHD package as appropriate.

The main interventions known to reduce morbidity and mortality among children living with HIV can be summarized as Screen, Treat, Optimize and Prevent AIDS (STOP AIDS)..

Screen:

TB: Screen for TB using a clinical algorithm followed by X-ray when indicated and if available

Cryptococcal infection among adolescents: Serum or plasma or blood cryptococcal antigen screening followed by lumbar puncture if positive or symptomatic
Malnutrition:

Weight-for-height

Height-for-age
Mid-upper arm circumference among children 2–5 years old

Treat:

TB, severe pneumonia, severe bacterial infections, cryptococcal meningitis and severe acute malnutrition

Optimize:
Rapid antiretroviral therapy start – within seven days with optimal regimens
Antiretroviral therapy counselling

Prevent:

Bacterial infections and Pneumocystis pneumonia - Cotrimoxazole prophylaxis
TB - TB preventive treatment
Cryptococcal meningitis among adolescents - Fluconazole pre-emptive therapy
Vaccinations

Table 7.6 below summarises the package of care for children who have AHD.

Intervention	Component	<5 years	5-9 years	10-19 years
Screening and diagnosis	Systematic screening for TB at each clinic visit using any one of the symptoms of the current cough, fever, weight loss, night sweats or close contact with a person with TB for children younger than 10 years	Yes	Yes	Yes
	Use C-reactive protein for screening for TB disease additionally	No	No	No
	Use of the chesat X-ray for screening for TB disease additionally	Maybe considered	Maybe considered	Yes
	WHO-recommended rapid diagnostic test, (induced or expectorated) spitum,gastric aspirate, stool or nasopharyngeal aspirate or other Extrapulmonary specimens (induced or expectorated)	Yes	Yes	Yes
	Inpatients in HIV wards in which the TB prevalance is >10% use WHO recommended rapid diagnostic tests	No	No	No
	LF-LAM assay (73,74)	Yes	Yes	Yes
	Cryptococcal antigen screening (specimen serum, plasma or whole blood) If blood cryptococcal antigen posetive or symptomatic, lumbar puncture	No	No	No
Prevention, prophylaxis and pre-emptive treatment	Pneumococcal conjugate vaccine (catch-up)	Yes	No	No
	Co-trimoxazole	Yes	Yes	Yes
	TB preventive treatment	Yes	Yes	Yes
	Fluconazole pre-emptive therapy for crytococcal antigen-positive without evidence of meningitis	Not applicable	Not applicable	Yes

[a]Depending on the resources available, C- reactive protein, chest X-ray or molecular WHO-recommended rapid diagnostic test may be used in addition tothe four-symptom screen to enhance TB screening among adolescents.

[b]See text for when to discontinue

[c]Screening for cryptococcal antigen followed by pre- emptive antifungal therapy among cryptococcal antigen-positive adolescents to prevent the develop of invasive crytococcal disease is recommended before initiating or reinitiating ART for adolescents living with HIV who havea CD4 count <100 cells/mm^3(strong recommendation, moderate - certainty evidence) and may be considered at a higher CD4 count threshhold of <200cells/mm^3(conditional recommendation)

Table 7. 6: Screening, diagnosis, and prevention components of the package of care for children and adolescents with advanced HIV disease

The main differences in the package of care for children compared with adolescents and adults is that routine cryptococcal antigen screening and pre-emptive therapy are not recommended for children younger than 10 years because of the low prevalence of cryptococcal meningitis in this age group. However, if a child younger than 10 years presents with signs and symptoms of meningitis, cryptococcal meningitis should still be considered and the appropriate investigations and treatment for this should be implemented. (For detailed management of Advanced HIV Disease see Chapter 10 of these guidelines)

7.9.Use of Cotrimoxazole Prophylaxis in Children living with HIV

Cotrimoxazole prophylaxis is a feasible, well-tolerated and inexpensive intervention to reduce HIV-related morbidity and mortality among children living with HIV. Initiate cotrimoxazole prophylaxis in all children living with HIV. Cotrimoxazole prophylaxis must be continued until adulthood. The following table highlights cotrimoxazole dosing in children.

Table 7. 7: Cotrimoxazole dosing in infants and children

Age/ Weight	Recommended daily dosage	Suspension (5ml – 200mg/40mg)	Paediatric Formulation (100mg/20mg)	Single – strength adult tablet (400mg/80mg)	Double – strength adult tablet (800mg/160mg)
<6 months or <5 kg	100mg sulfamethoxazole/ 20 mg trimethoprim	2.5ml	1	¼	-
6 months – 5 years or 5 – 15 kg	200 mg sulfamethoxazole/ 40 mg trimethoprim	5ml	2	½	-
6 – 14 years or 15 – 30 kg	400 mg sulfamethoxazole/ 80 mg trimethoprim	10ml	4	1	½
Frequency – Once daily					

Source: Adapted from World Health Organization. Guidelines on co-trimoxazole prophylaxis for HIV-related infections among children, adolescents, and adults. Recommendations for a public health approach. Geneva, WHO, 2006:15 (Table 3).

7.10 General care and managing comorbidities among Children and Adolescents

Children living with HIV, including those on ART, are at risk of developing chronic multi-system comorbidities and concomitant disability.
Comorbidities that are common include:

- developmental delay and neurocognitive impairment,
- mental health disorders, and
- organ system morbidities (chronic lung disease, heart disease, and kidney disease).

As access to treatment improves, children and adolescents living with HIV receiving ART should have the chance to have an improved quality of life and reach their full potential. Service delivery platforms need to plan how to implement this, since screening for chronic comorbidities and disabilities, neural development, and growth delays, promoting nurturing care and supporting the mental development of children and adolescents as they age are of paramount importance.

- Children and adolescents should do at least an average of 60 minutes per day of moderate- to vigorous-intensity, mostly aerobic, physical activity, across the week.
- Vigorous-intensity aerobic activities, as well as those that strengthen muscle and bone, should be incorporated at least three days a week
- Children and adolescents should limit the amount of time spent being sedentary, particularly the amount of recreational screen time

7.11 Treatment monitoring of ART

Monitoring children on ART is important to ensure successful treatment, identify adherence challenges and determine whether ART regimens should be switched in case of treatment failure. Compared with clinical or immunological monitoring, viral load testing provides an early and more accurate indication of treatment failure and the need to switch from first line to second-line drugs, reducing the accumulation of drug resistance mutations and improving clinical outcomes. Measuring viral load also helps to discriminate between treatment failure and non-adherence, following enhanced adherence support. Furthermore, viral load testing gives clients a measure of understanding, control, and motivation to adhere to treatment and understand their HIV infection. **Annual VL testing is recommended in children receiving ART**

7.12 Strategies to support retention and adherence

There is historically poor retention among children, especially for infants tested using early infant diagnosis within programmes to prevent the mother-to-child transmission of HIV.

Children who have undergone disclosure and are stable on ART stand to benefit from differentiated models of ART delivery. These services can be facilitated by nurses at primary care level

Solutions include:

- peer-to-peer support through enrolment into support groups and club refills
- using point-of-care early infant diagnosis to improve linkage.
- using sms, phone calls or GPRS printers to speed up the return of results from central laboratories; and
- using family-centred care service delivery models, in which the mother, her baby and her partner receive care at the same point of care.
- Longitudinal monitoring of mother baby pairs
- Appointment spacing in line with availability of recipients of care (during school holidays) facilitate retention and uptake of services
- Multi month dispensing
- Implementing adolescent friendly services
- Enrolment into programs for orphans and vulnerable children

Children living with HIV, including those on ART, are at risk of developing chronic multisystem comorbidities and concomitant disability.

Chapter 8 Monitoring Patients on Antiretroviral Therapy

8.1 Introduction

Patients on ART need close monitoring to assess adherence to the treatment regimen, tolerance, the side effects of the medications, and the efficacy of the treatment. Health workers should document patient visit's records in the patient-held booklet (OPD card). Clinical assessments and laboratory tests are important in assessing individuals following a positive HIV diagnosis to assess for co-infections, NCDs and other co-morbidities that may impact on treatment response

8.2 Initial Evaluation

Before commencing ART, all patients should have a detailed history taken, a physical examination carried out, and basic laboratory tests performed. Prior to commencing ART, the patient should be re-tested to confirm HIV positive status, plus it is essential to screen and test for TB in all patients. Document the patient's WHO clinical stage in his or her facility-held booklet 'Greenbook 'and in the patient-held booklet.

The following baseline investigations and measurements are recommended:

- CD4 cell count (To assess for advanced HIV disease)
- Full blood count (Especially if AZT is going to be used)
- Serum creatinine clearance test (Especially if TDF is going to be used)
- Liver function tests (ALT)
- Blood pressure
- Syphilis test (If available)
- Hepatitis B and C virus screening (If available)

In patients with advanced HIV disease, additional screening tests for TB and cryptococcal infection must be done (See chapter 10)

8.3 Monitoring adherence to treatment

Strict adherence (which is at least 95% adherence) to recommended treatment regimens is important for treatment to be effective. Counseling and the provision of accurate information to all patients (treatment literacy) is an important determinant of treatment adherence. Information on side effects should be provided, and patients should be told what to expect from the treatment. Patients should be encouraged to seek help between visits as needed. Patients should be instructed to bring all medications and containers at each visit.

Providers should carry out an adherence assessment to determine whether the medications have been taken as per schedules agreed upon at every visit.

8.4.Frequency of clinic visits

Initially the patient should be seen at one month, 3 months and 6 months after ART initiation. After the first six months, the patient can be seen at reduced frequency depending on whether they are stable or not. When clients are clinically stable and on chronic medication, they do not necessarily need to be seen by the clinician at every visit. (Refer to the Operational and Service Delivery Manual/OSDM).

A client (adult, child over two years, adolescent, pregnant and breastfeeding woman, member of a key population) established on ART (any treatment line) is defined as someone who:

- Has no current OIs
- Has good understanding of lifelong adherence
- Is at least six months on their current regimen
- Has a VL < 50 copies/ml in the last six months

There are three main types of clinic visits:

- A clinical visit is a scheduled appointment where the clinician makes a thorough assessment and reviews monitoring blood tests. An established patient on ART should be seen for a clinical assessment every 12 months
- A refill visit is a scheduled appointment where a patient has a pre-filled prescription and attends pharmacy directly to collect their medicine. Clients coming for a re-fill do not need to see a nurse for a consultation.
- An unscheduled visit is when a patient attends in-between refills or clinical visits when they develop any problems and will require to be seen by a clinician

A virtual / telephone visit should be considered for patients on ART who require consultation or adherence support

8.5 Monitoring for ARV toxicities

The patient should be provided with written and verbal information on potential side effects and should be requested to report immediately for examination should side effects occur. There is a need to watch out for common side effects such as anemia, renal impairment, CNS symptoms and weight gain.

Weight Gain

ART regimens that include TAF and/or an INSTI (especially dolutegravir) are associated with greater increases in weight as compared with other classes or agents; this association with greater weight change may occur after initiation of ART or after regimen switch. The mechanism for this weight gain is not known. Patients must be advised to exercise regularly and consume a healthy diet. It is important to monitor the body mass index (BMI) of patients on ART and institute lifestyle changes for those with a BMI>30 kg/m2.

Central Nervous System Toxicities

Hallucinations, abnormal dreams, depression, mental confusion, and convulsions can occur especially with Efavirenz. These events tend to occur within the first month. In some cases, they can persist for months and not resolve at all. Insomnia has been reported with the use of Dolutegravir

Metabolic Abnormalities

Hyperglycemia i.e., development of diabetes and hyperlipidemia should be anticipated with the long-term use of ARVs. Check blood sugar and lipid levels when clinically indicated.

Anaemia

Anaemia is a recognized side effect of AZT. Check haemoglobin after the first month of Zidovudine use

Other Side Effects

Mild side effects such as headache, fatigue, gastrointestinal upsets, and diarrhoea occur fairly frequently, but serious side effects occur rarely. Mild side effects usually occur early in treatment and often wear off and should be treated symptomatically. Side effects of medicines are summarized in table 8.1 below:

Table 8. 1: Common types of toxicity associated with ARV medicines

ARV	Major types of toxicity	Risk Factors	Suggested Management
ABC	Hypersensitivity reaction	Presence of HLA-B*5701 gene	Substitute AZT or TDF.
AZT	Anaemia, neutropaenia	Baseline anaemia or neutropaenia CD4 cell count of ≤200 cells/ mm^3	Substitute TDF or ABC
	Lactic acidosis or severe hepatomegaly with steatosis Lipoatrophy, lipodystrophy Myopathy	BMI >25 (or body weight >75 kg) Prolonged exposure to NRTIs	Substitute TDF or ABC
TDF	Chronic kidney disease Acute kidney injury and Fanconi syndrome	Underlying renal disease Older than 50 years old BMI <18.5 or low body weight (<50 kg), notably among women Untreated diabetes Untreated hypertension Concomitant use of nephrotoxic drugs or a boosted PI	Substitute AZT or ABC or TAF
TAF	Body weight gain Dyslipidemia	Female sex Concomitant use of DTG	Monitor body weight and promote anti-obesity measures (Such as diet, physical exercise). If significant increase despite measures, consider substituting with ABC/ AZT or TDF
DTG	Hepatotoxicity Hypersensitivity reactions	Coinfection with hepatitis B or C Liver disease	Substitute another therapeutic class: EFV or boosted PIs
	Insomnia Body weight gain or obesity	Older than 60 years Low CD4 or high viral load Female African ethnicity	Consider morning dose or substitute EFV, boosted PI or RAL Monitor body weight and promote anti-obesity measures

EFV	Persistent central nervous system toxicity (Such as dizziness, insomnia and abnormal dreams) or mental symptoms (anxiety, depression and mental confusion)	Depression or other mental disorder (previous or at baseline) Daytime dosing	For central nervous system symptoms, dosing at bedtime. EFV 400 mg/day is recommended or an DTG if EFV 400 mg is not effective at reducing symptoms
	Hepatotoxicity	Underlying hepatic disease Coinfection with hepatitis B or C Concomitant use of hepatotoxic drugs	For severe hepatotoxicity or hypersensitivity reactions, substitute another therapeutic class (INSTIs or boosted PIs)
	Gynaecomastia	Risk factors unknown	Substitute another therapeutic class (INSTIs or boosted PIs)
ATV/r	Indirect hyperbilirubinaemia (Clinical jaundice)	Presence of UDPglucuronosyltransferase 1-1 enzyme (UGT1A1*28 gene)	This phenomenon is clinically benign but potentially stigmatizing. Substitute only if adherence is compromised.
DRV/r	Hepatotoxicity	Underlying hepatic disease Coinfection with hepatitis B or C Concomitant use of hepatotoxic drugs	Substitute with ATV/r or LPV/r. When it is used in third-line ART, limited options are available

8.6 Key ARV medicine interactions

Key Points

- Whenever patients start or switch antiretroviral drugs or start new concomitant medications, it is important to evaluate potential medicine interactions.
- Many medicines and medicine classes have clinically significant interactions with ARVs.
- There are also important interactions between several ARVs.
- It is important to consult a regularly updated database to assess whether medicines can be co-administered and whether dose adjustment is required.
- Herbal medications may also have interactions with ART medicines (e.g., St John's wort and garlic), but data on herb–medicine interactions are very limited

Table 8.2 below highlights the key medicine interactions with ARV medicines and suggested management.

ARV Medicine	Key Interaction	Suggested Management
DTG	Rifampicin	Double the daily dose of DTG by giving it twice daily (50mg 12 hourly in adults). Continue with twice daily dosing of DTG for 2 weeks after use of rifampicin has ended
	Metformin	Avoid high-dose metformin with DTG; Maximum daily dose of Metformin is 1gram
	Polyvalent cation products containing Mg, Al, Fe, Ca, and Zn. Multivitamins supplements	Use DTG at least two hours before or at least six hours after supplements
	Carbamazepine	Double the dose of DTG
	Phenobarbitone / Phenytoin	Use alternative anticonvulsant
	Amodiaquine	Use alternative anti-malarial
EFV	EFV may lower the efficacy of some long-acting hormonal contraceptives	Use alternative or additional contraceptive methods e.g., Condoms
	Hormonal contraceptives	Use alternative or additional contraceptive methods

8.7 Immune Reconstitution Inflammatory Syndrome

The term "immune reconstitution inflammatory syndrome" (IRIS) describes a collection of inflammatory disorders associated with paradoxical worsening of pre-existing infectious processes following the initiation (or switching) of antiretroviral therapy (ART) regiments in HIV-infected individuals. Pre-existing infections in individuals with IRIS may have been previously diagnosed and treated or they may be subclinical and unmasked by the host's regained capacity to mount an inflammatory response. Common immune reconstitution illnesses in Zimbabwe are TB, cryptococcal meningitis, Kaposi Sarcoma, and recurrent herpes simplex virus.

IRIS is NOT indicative of treatment failure or medicine side effects. It is not a reason to stop ART except in life threatening cases. ART regimen must not be changed. Continue ART and manage the opportunistic infection.

8.8 Monitoring effectiveness of ART

The effectiveness of ART may be monitored by assessing clinical improvement, immunologic function

(CD4 count / CD4%), **and HIV viral load (VL).** It is necessary to assess response to treatment through regular careful clinical examinations backed where possible by simple laboratory tests.

VL testing is the gold standard for monitoring response to ARV medicines as it is more sensitive and can detect adherence problems and treatment failure much earlier than CD4 count testing and clinical evaluation.

8.9 HIV viral load monitoring

Viral load should be monitored routinely at 6 months and at 12 months after ART initiation, and then annually thereafter. The following figure highlights the algorithm for viral load monitoring.

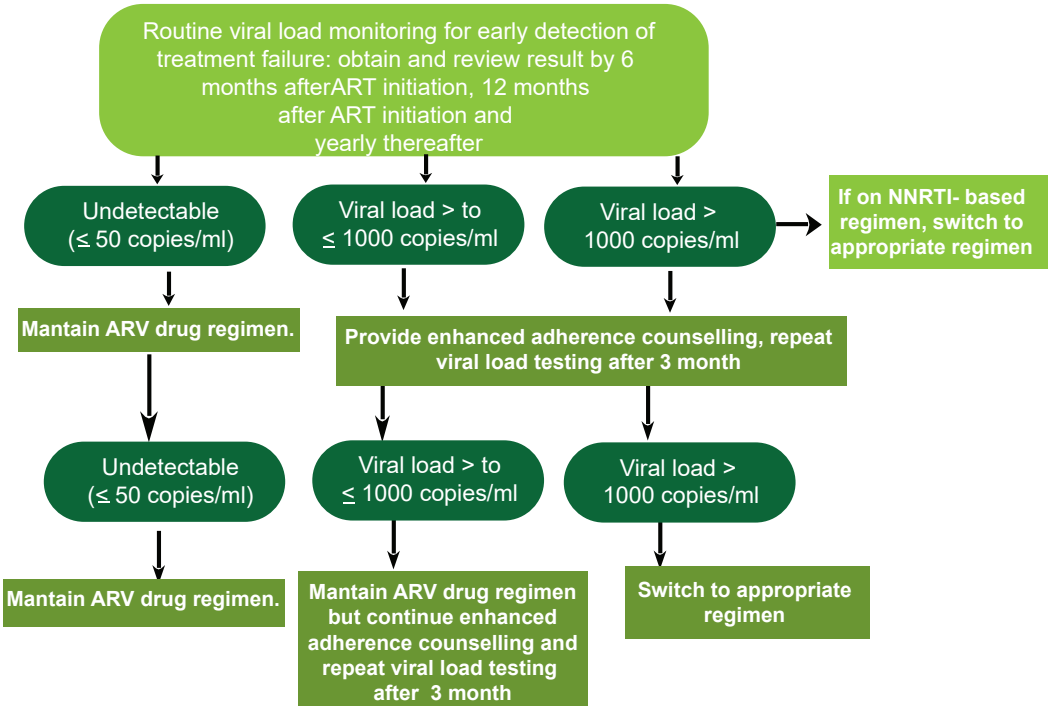


Figure 8. 1: Routine HIV viral load monitoring in patients receiving ART (Source: WHO 2021 Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring)

a Switch after a single elevated viral load should be considered
b A second viral load may be considered before regimen switch if DTG-based regimens are unavailable and the results of a viral load test can be returned and acted on rapidly

8.10 Diagnosis of ART treatment failure

The best way to diagnose ART treatment failure is through VL load monitoring as highlighted in figure above. Clinical and immunological failure as highlighted in table 8.3 below have low sensitivity and positive predictive value.

Table 8. 3: Virological, immunological, and clinical treatment failure (WHO 2021)

Virological failure	Viral load greater than 1,000 copies/ml based on two consecutive VL measurements after 3 months with enhanced adherence counselling. ART switch after first viral load >1,000 copies/mL for those receiving NNRTI-based regimens
Immunological failure	Children Younger than 5years – Persistent CD4 level below 200cells/mm^3 Older than 5 years – Persistent CD4 levels below 100 cells/mm^3 Adults and adolescents CD4 count below 200 cells/mm^3 following clinical Failure or persistent CD4 levels below 100cells/mm
Clinical failure	Children New or recurrent clinical event indicating advanced or severe immunodeficiency (WHO stage 3 and 4 clinical conditions with exception of TB after 6 months of effective treatment Adults and Adolescents New or recurrent clinical event indicating severe immunodeficiency (WHO stage 4 clinical condition) after 6 months of effective treatment

8.11 HIV and people older than 50 years

The following are important considerations when looking after elderly patients living with HIV:

- ART is especially important for older individuals because they have a greater risk of serious non-AIDS complications and potentially a blunted immunologic response to ART
- Adverse medicine events from ART and concomitant medicines may occur more frequently in older persons with HIV than in younger individuals with HIV
- Polypharmacy is common in older persons with HIV; therefore, there is a greater risk of interactions between antiretroviral medicines and concomitant medications. Potential for drug-drug interactions should be assessed regularly, especially when starting or switching ART and concomitant medications.

- Mental health disorders are a growing concern in aging people with HIV. A heightened risk of mood disorders including anxiety and depression has been observed in this population. Screening for depression and management of mental health issues are critical in caring for persons with HIV
- Regularly monitor for comorbid conditions like diabetes mellitus and cardiovascular conditions.

Chapter 9 Managing Opportunistic Infections and Comorbidities

9.1 Introduction

Antiretroviral therapy (ART) has reduced mortality and morbidity associated with HIV and transformed HIV into a chronic disease requiring lifetime care. Co-infections and comorbidities, including physical and mental health conditions and substance use disorders, are common among people living with HIV (PLHIV). Comprehensive HIV care includes combination HIV prevention, the promotion of general health and well-being, maintaining quality of life, screening, the prevention and management of coinfections and comorbidities. This chapter provides a brief overview of common and important concomitant conditions among people living with HIV. This includes information on cotrimoxazole prophylaxis, the diagnosis, prevention and treatment of TB, viral hepatitis, cervical cancer prevention, nutrition, vaccinations, and managing common mental health disorders.

9.2 Cotrimoxazole Prophylaxis

Cotrimoxazole is used to treat a variety of bacterial, fungal, and protozoan infections. Cotrimoxazole prophylaxis is a feasible, well-tolerated and inexpensive intervention to reduce HIV-related morbidity and mortality among people living with HIV. The adult and adolescent dose recommended for use in Zimbabwe is 960 mg daily. See chapter 7 of these guidelines for details on the use of cotrimoxazole in children. Table 9.1 below summarizes the recommended criteria for initiating and discontinuing cotrimoxazole prophylaxis

Table 9. 1: Criteria for initiating and discontinuing co-trimoxazole prophylaxis

Population	Criteria for initiating cotrimoxazole	Criteria for discontinuing cotrimoxazole
Adults (including pregnant women) living with HIV	WHO clinical stage 2, 3 and 4 CD4 cell count < 350 cells/mm^3	Stop for those who are clinically stable, with evidence of immune recovery (CD4>350 cells/mm^3) and/or suppression of viral loads on ART
Children and adolescents living with HIV	Initiate for everyone regardless of WHO clinical stage or CD4 cell count As a priority: – Initiate for everyone younger than five years regardless of WHO clinical stage or CD4 cell count – Initiate for everyone five years and older with severe or advanced HIV disease (WHO clinical stage 3 or 4) or CD4 cell count < 350 cells/mm^3	Continue until adulthood then use adult criteria for discontinuing
HIV-exposed infants	Initiate for everyone starting at 4–6 weeks after birth	Until the risk of HIV transmission ends, and HIV infection is excluded with age-appropriate test
People living with HIV and TB	Initiate for everyone with active TB regardless of CD4 cell count	Until the criteria for discontinuation for adults or children are met

ADDITIONAL CRITERIA FOR DISCONTINUATION OF COTRIMOXAZOLE PROPHYLAXIS

- Cotrimoxazole prophylaxis may need to be discontinued in the event of an adverse drug reaction (ADR). Although severe reactions to co-trimoxazole are uncommon, these may include extensive exfoliative rash, Stevens–Johnson syndrome, or severe anaemia or pancytopenia.
- Patients and caregivers should be counselled on the potential adverse effects and advised to stop the drug and report to the health facility if cotrimoxazole-related adverse events are suspected. Health care workers must report all suspected ADRs to the MCAZ.

9.3 TB/HIV Collaborative Activities

Management of TB and HIV requires close collaboration between the National TB Program and AIDS programmes. HIV care settings should implement the following TB control strategies:

- Intensified TB case finding
- Infection prevention and control at all clinical encounters
- TB preventive therapy (TPT)

Intensified TB case finding

- All HIV positive clients should be routinely screened for TB at every encounter with a health care worker, using a four-symptom checklist (current cough, night sweats, loss of weight and fever) and/or a CXR (where available) to timely assess their eligibility to be commenced on TB preventive therapy or treatment
- Among children younger than 10 years who are living with HIV, systematic screening for TB disease should be conducted using a symptom screen including any one of the symptoms of current cough, fever, night sweats and poor weight gain. Consider client history such as close contact with a person with TB disease.
- All HIV positive clients with a positive history to any one of the symptoms on the checklist and or having an abnormal CXR should be classified as presumptive TB cases and MUST have one sputum sample collected and submitted for TB investigation using the Xpert MTB/Rif assay as preferred diagnostic test
- All HIV positive patients who have advanced HIV disease should have the Urine Lateral flow

Lipoarabinomannan Assay (LF-LAM) to assist in TB diagnosis.

- Other non-sputum samples such as nasogastric lavage, nasopharyngeal aspirates, and stool for children under 5 years as well as organ specific samples can be collected for investigation depending on screening findings. New WHO-re commended rapid diagnostic instruments such as Truenat MTB-Rif can be used for initial diagnosis where currently available

TB Preventive Therapy (TPT)

Latent TB is defined as a state of persistent immune response to stimulation by Mycobacterium tuberculosis antigens with no evidence of clinically manifest active TB disease. Among people living with HIV, the combined use of TB preventive treatment and ART has been shown to benefit both TB prevention and mortality, including for people with a higher CD4 cell count. In the absence of contraindications, TPT must be initiated at the time of ART initiation.

Who is eligible for TPT?

- Adults and adolescents including pregnant women living with HIV (Pre- ART & on ART)
- Children living with HIV (Pre-ART & on ART)
- HIV infected adults, adolescents, and children contacts of active TB cases
- HIV negative adults, adolescents, and children who are contacts of active TB cases

Exclusion criteria for TPT

Adults and adolescents living with HIV should be screened with a clinical algorithm; those who do not report any one of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered TPT. The following patients should be excluded:

- Patients who have symptoms and signs suggestive of active TB
- Patients on treatment for TB
- Completion of TPT within the past 3 years

TB preventive treatment options

The following options are recommended for the treatment of latent TB infection regardless of HIV status:

- Six months of daily isoniazid
- Three months of weekly rifapentine plus isoniazid
- Three months of daily isoniazid plus rifampicin
- Six months of daily Levofloxacin

TPT should be repeated every 3 years in people living with HIV. Table 9.2 below details the recommended regimens for TPT in Zimbabwe

Table 9. 2: Recommended regimens for TPT in Zimbabwe

Population Group	Preferred Treatment	Alternative
Adults		
PLHIV on EFV and DTG based regimen	Three months of weekly Rifapentine and Isoniazid (3HP)	Six months of daily Isoniazid alone (6H)
PLHIV on TAF, PIs and NVP based regimen	Six months of daily Isoniazid alone (6H)	-
HIV negative contacts (adults and adolescents > 15 years)	Three months of weekly Rifapentine and Isoniazid (3HP)	Six months of daily Isoniazid alone (6H)
Children		
CLHIV on EFV-based regimen (Adolescents, children > 2 years)	Three months of weekly Rifapentine and Isoniazid (3HP)	Six months of daily Isoniazid alone (6H)
CLHIV on DTG, PIs and NVP based regimen	Six months of daily Isoniazid alone (6H)	-
HIV negative contacts (Children under 15 years)	Three months of daily Rifampicin and Isoniazid (3RH)	Six months of daily Isoniazid alone (6H)
Special Groups		
MDR-TB Contacts	Six months of daily Levofloxacin (6LFX)	-

Pyridoxine should be prescribed in ALL patients receiving INH based TPT especially 6H. Its unavailability should not be a barrier to initiate 3HP or 3RH.

Infection prevention and control at all clinical encounters

People who work or receive care in health care settings are at higher risk for becoming infected with TB; therefore, it is necessary to have a TB infection control plan as part of a general infection prevention and control program designed to ensure the following:

- prompt detection of infectious patients,
- airborne precautions, and
- treatment of people who have suspected or confirmed TB

The following measures should be in place.

- Administrative controls
- Environmental controls
- Use of respiratory protective equipment

Diagnosis of TB

The clinical picture of TB disease is often non-specific and in isolation does not enable its accurate diagnosis, requiring bacteriological testing for all people with signs and symptoms of TB disease. People living with HIV may have an atypical clinical picture, especially those with advanced disease, further complicating the clinical diagnosis of pulmonary and extrapulmonary forms of TB disease.

Use of Rapid Molecular Diagnostics (MTB/RIF Assays)

Approved rapid molecular diagnostics such as the Xpert MTB/RIF or Truenat MTB-Rif Assay should be used for the initial diagnosis of TB. Conventional microscopy, culture, and drug susceptibility testing (DST) should be used for treatment monitoring and further diagnostic testing as recommended in the national TB guidelines.

Xpert MTB/RIF should be used in preference to conventional microscopy and culture as the initial diagnostic test for cerebrospinal fluid specimens from patients suspected of having TB meningitis.

Use of LF-LAM

Urine lateral flow (LF-LAM) may be used to assist in the diagnosis of active TB in adult patients with advanced HIV disease, with or without signs and symptoms of TB (pulmonary and/or extra-pulmonary)

Use of CXR / Radiology

Chest x-ray is an important TB screening technique for all people including PLHIV among other TB high risk groups. Abnormal findings aid in the clinical evaluation and diagnosis of TB in the absence of microbiologic confirmation. Other radiological investigations apart from CXR can also aid the diagnostic work out for TB.

Management of TB

The recommended regimen for drug-sensitive TB is a standardised, weight based six-month TB regimen containing two months of isoniazid, rifampicin, pyrazinamide, and ethambutol followed by four months of rifampicin and isoniazid. Refer to national TB guidelines for the management of drug resistant TB (Clinical Management of Drug-Resistant Tuberculosis Guidelines).

Table 9. 3: Summary of First-line TB Treatment Regimens

	Regimen	Intensive Phase	Continuation Phase
ADULTS	2HRZE/4HR OR 6HR	2 months HRZE	4 months HR OR (6 months HR in TB of meninges, bone, joint, pericardium, disseminated spinal disease)
CHILDREN	2HRZE/4HR OR 10HR	2 months HRZE	4 months HR OR (or 10HR for patients with TB of the meninges, bone joint, pericardium, military TB or TB spine)

** H- Isoniazid; R- Rifampicin; Z- Pyrazinamide; E- Ethambutol*

Timing of ART

Among people living with HIV, not yet on ART, who have been diagnosed with TB, ART must be commenced after a minimum of 2 weeks of TB treatment to reduce risk of immune reconstitution inflammatory syndrome.

For the detailed management of TB refer to the national TB management guidelines

9.4 Management of Cryptococcal Disease

Cryptococcal disease is one of the most important opportunistic infections among people living with advanced HIV disease and is a major contributor to mortality. Early diagnosis and treatment of cryptococcal meningitis (CM) is key to reducing mortality from cryptococcal disease. Health-care professionals should have a low threshold for suspecting cryptococcal meningitis among people with advanced HIV disease. Immediate ART initiation is not recommended for adults, adolescents and children living with HIV who have cryptococcal meningitis because of the risk of increased mortality and ART initiation should be deferred 4–6 weeks from the initiation of antifungal treatment. Figure 1 below details the algorithm for the screening and management of CM in people living with HIV

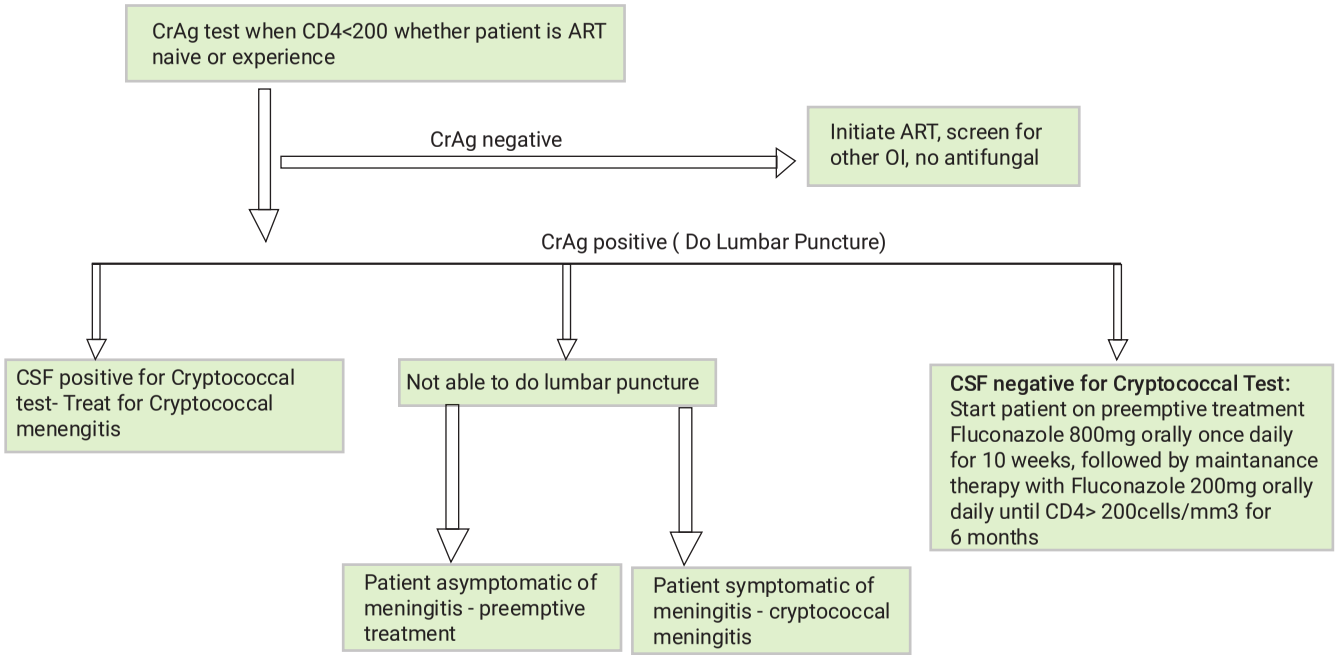


Figure 9. 1: Screening and Management of CM

Treatment of CM

CM is treatment has three phases i.e., Induction, consolidation, and maintenance. There are various regimens recommended for the treatment of CM as detailed in Table 9.4 below:

Induction
The following is recommended as the preferred induction regimen. • Liposomal Amphotericin B 10mg/kg as a single dose plus Flucytosine 100mg/kg/day and Fluconazole 1200mg/day for two weeks The following induction regimens are recommended as alternative options. • For adults, adolescents and children, a short-course (one-week) induction regimen with liposomal amphotericin B (3-5 mg/kg per day) and flucytosine (100 mg/kg per day, divided into four doses per day) is the preferred option for treating cryptococcal meningitis among people living with HIV • Two weeks of liposomal amphotericin B (3-5mg/kg per day) + fluconazole (1200 mg daily, 12 mg/kg per day for children and adolescents up to a maximum of 800 mg daily) • Two weeks of fluconazole (1200 mg daily, 12 mg/kg per day for children and adolescents) + flucytosine (100 mg/kg per day, divided into four doses per day)
Consolidation
Fluconazole (800 mg daily for adults or 6–12 mg/kg per day for children and adolescents up to a maximum of 800 mg daily) is recommended for the consolidation phase for eight weeks following the induction phase
Maintenance
Fluconazole (200 mg daily for adults or 6 mg/kg per day for adolescents and children) is recommended for the maintenance phase until CD4 count >200 for 6 months and VL<1000copies/ml for 6 months

Monitoring patients receiving Amphotericin B

Usage of Amphotericin B and flucytosine requires laboratory monitoring of the patient. Serum Creatinine, electrolytes including magnesium and FBC (Flucytosine can cause bone marrow toxicity) should be monitored weekly

Timing of ART

Immediate ART initiation is not recommended among adults, adolescents and children living with HIV who have cryptococcal meningitis because of the risk of increased mortality and should be deferred 4–6 weeks from the initiation of antifungal treatment.

Defer ART for 4-6 weeks from the initiation of CM treatment.

ART should be continued in patients already on ART at the time of CM diagnosis

9.5 Viral Hepatitis

Liver disease caused by coinfection with HBV or HCV is an increasing cause of morbidity and mortality among people living with HIV, including among people receiving ART. Concurrent infection with HIV usually results in more severe and progressive liver disease and a higher incidence of cirrhosis, hepatocellular carcinoma, and mortality. People living with HIV are a priority group for early diagnosis of viral hepatitis coinfection and provision of ART.

Use of ARVs in HIV and Hepatitis B Coinfected Patients

ART should be prioritized for people coinfected with HIV and HBV with evidence of severe chronic liver disease.

Treatment should be provided regardless of ALT levels if client has chronic HBV with clinical evidence of liver cirrhosis.

Treatment regimens of choice should always include a TDF/3TC backbone

Abrupt treatment discontinuation of TDF/3TC, may be associated with HBV reactivation, hepatic flares and, in rare cases, hepatic decompensation.

9.6 Mental Health

People living with HIV are at high risk of mental, nervous system and substance use disorders. Depression is one of the most prevalent mental health comorbidities in people living with HIV. People living with HIV who have depression are less likely to achieve optimal treatment adherence. Treatment or lack of treatment for mental health disorders can affect general health, adherence to ARV drugs and retention in care and may lead to potential side-effects and medicine interactions being overlooked.

Assessment and management of common mental health disorders should be included in the package of HIV care services for all individuals living with HIV.

Screening for symptoms of depression, generalised anxiety disorder, psychosis and substance abuse using standard tools is an important part of comprehensive HIV care. Available community-based resources for mental health and social support should be mapped and regularly updated at all health facilities for effective referrals.
Documented screening for anxiety and depression should be carried for the following clients

- All clients at a minimum during their annual clinical review
- Screen Adults annually at clinical visit
- 18–24-year-olds every six months at clinical visit.
- Adolescents at least twice a year at their clinical visit (suggest alternate 4 monthly visits)
- Any RoC with red flag issues (including substance misuse)

More frequent mental health screening should be conducted for:

- Any client with unsuppressed viral load
- Any client with substance abuse disorders?
- Any client re-engaging in care
- For adolescents and key populations more frequent screening may be clinically indicated.

A. Community: All clients can be screened community-based and/or mobile mental health services such as the Friendship Bench using community mental health screening tools [SSQ-14]

- Clients identified as “At Risk” of depression and/or anxiety should be offered problem solving therapy (PST) by Community-based peer counsellors and/or mobile mental health services such as the Friendship Bench [The Friendship Bench provides one-to-one treatment through trained peer counsellors].
- “At Risk” clients should be referred to Health Facility according to Stepped Care Algorithm and Client Referral Pathway (see Appendix 3)

B.Health Facility:
Routine Mental Health screening: All clients should be routinely screened for anxiety and depression

- according to subpopulation recommendations, starting with four initial screening questions below.

Ask:

1. During the past month, have you felt like you were losing interest or pleasure in doing things?
2. During the past month, have you felt down, depressed, or helpless?

If: client answer 'yes' to either question document 'PHQ+' – administer PHQ9
Ask:
1. Over the last 2 weeks, how often have you felt nervous anxious or on edge?
2. Over the last 2 weeks how often have you not been able to stop or control worrying?

If: client answer 'yes' to either question document 'GAD+' – administer GAD7
OR

Referred Clients: Referred Clients who have already undergone Shona Symptom Questionnaire (SSQ14) screening and/or clients with red-flag issues (virological failure, missed appointments, challenging psychosocial issues):

- Facility service provider should proceed to administer the Patient Health Questionnaire 9 (PHQ9) and Generalised Anxiety Disorder 7-item assessment (GAD7 and manage according to Stepped Care algorithm (See Appendix 2) and Client Referral Pathway accordingly (See Appendix 3).
- Occupational therapist & social services should be involved in the management
- Outcomes of mental health screening should be documented in client OI/ART Care Booklets.
- Clients with mental illness who are stable and on long-term medication should be able to receive their chronic repeat medication via a similar refill system as their ART while having specialist clinical review as appropriate.
- All nurses/clinicians may initiate antidepressants and antipsychotic medications that are recommended in the Zimbabwean EDLIZ.

Important! Any client presenting with red-flag issues; Acute Instability; Suicide Ideation; Self-harm; Psychoses; Alcohol or Other Sedative Withdrawal; Acute Alcohol Intoxication; Sedative Overdose or Intoxication; Any adolescent or Pregnant/Breastfeeding woman with moderate to severe depression/anxiety requiring pharmacotherapy; Victims of Intimate Partner Violence (IPV) or Gender Based Violence (GBV):

- Manage According to mhGAP Intervention guide Emergency Presentations of Priority MNS Conditions.

AND:

- Refer for mental health specialist care according to mental health patient referral pathway. (See Stepped-Care Algorithm- Appendix 2).

Special consideration for Adolescents Living with HIV

The prevalence of common mental health disorders (CMDs) among adolescents living with HIV is high – 54% according to a recent study on ALHIV in Zimbabwe. Therefore, screening should be done semi-annually. If a client screens as at risk of CMDs, rescreening should be repeated every 3 months until the client screens as not at risk anymore. Utilizing a task shifting approach with trained lay peer counsellors has been shown to be effective in both identifying and alleviating mental health conditions among ALHIV. Therefore, all ALHIV should be linked to trained lay peer counsellors where available.

Special consideration for Adolescents Living with HIV
The prevalence of common mental health disorders (CMDs) among adolescents living with HIV is high – 54% according to a recent study on ALHIV in Zimbabwe. Therefore, screening should be done semi-annually. If a client screens as at risk of CMDs, rescreening should be repeated every 3 months until the client screens as not at risk anymore. Utilizing a task shifting approach with trained lay peer counsellors has been shown to be effective in both identifying and alleviating mental health conditions among ALHIV. Therefore, all ALHIV should be linked to trained lay peer counsellors where available.

9.7 HIV and Non-Communicable Diseases (NCDs)

Compared with the general population, people living with HIV have increased risk of developing a range of chronic noncommunicable diseases, including cardiovascular disease, hypertension, diabetes, chronic obstructive pulmonary disease, kidney disease and cancer.

Assessment and management of cardiovascular risk should be provided for all individuals living with HIV according to standard protocols recommended for the general population.

Strategies for the prevention and risk reduction of cardiovascular diseases by addressing modifiable risk factors such as high blood pressure, smoking, obesity, unhealthy diet, and lack of physical activity should be applied to all people living with HIV.

Assessment and management of cardiovascular risk should be provided for all individuals living with HIV according to standard protocols recommended for general population.

9.8. Cervical Cancer

Women living with HIV (WLHIV) have a six-fold higher risk of cervical cancer than women without HIV, and cervical cancer is classified as an AIDS-defining condition.. This higher risk starts with an increased risk of acquiring HPV infection, lower chances of regression of pre-cancer lesions, more rapid progression to cancer and higher rates of recurrence following treatment.

The 2030 targets of the WHO global strategy are to achieve: 90% of girls fully vaccinated with HPV vaccine by age 15 years, 70% of women are screened with a high-performance test by 35 years of age and again by 45 years of age, and 90% of women identified with cervical disease receive treatment.

Recommendations on screening and treatment to prevent cervical cancer

- HPV DNA detection is the recommended primary screening test rather than visual inspection of the cervix with acetic acid (VIA) or cytology in screening and treatment approaches among WLHIV where resources permit.
- Existing programmes with quality-assured cytology as the primary screening test should be continued until HPV DNA testing is operational; existing programmes using VIA as the primary screening test should transition rapidly because of the inherent challenges with quality assurance
- HPV DNA primary screening test with triage rather than without triage is recommended to prevent cervical cancer among WLHIV, where HPV DNA Testing is not available, program should follow the VIA algorithm.

PRIMARY PREVENTION: Cervical cancer primary prevention promotes breaking transmission of HPV from an infected to an uninfected individual, which can be achieved through:

Abstinence from sexual exposure; **B**eing mutually faithful; **C**onsistent condom-use to reduce risk of HPV transmission (This does not guarantee 100% protection); **D**elaying sexual exposure until one is biologically and psychologically mature and able to negotiate safe sex.

2.Use of biological mechanism through HPV vaccination.

Three (3) doses of 0.5ml intramuscular HPV vaccine injections are administered within 6-months to 9–15-year girls as recommended in the Cervical Cancer Treatment guidelines.

NOTE: HPV Vaccines are not for treating women with past or current HPV infection

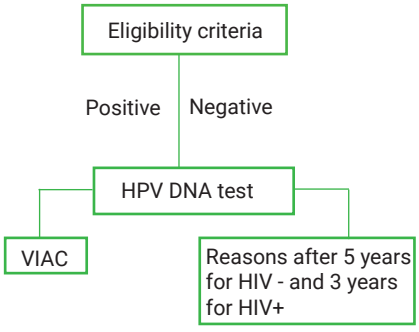
3. Male Circumcision: Male circumcision reduces the risk of HPV and HIV transmission.

SECONDARY PREVENTION: Secondary prevention aims at early detection and treatment of pre-cancer lesions.

Screening: Prioritize screening Women living with HIV (WLHIV) on ART using HPV DNA test then triage with VIA in single visit approach. Use VIA as single screening method where HPV test is not available.

Screening frequency & Target population: WLHIV with negative HPV result, re-screen every 3 years. WLHIV with positive HPV DNA, proceed to conduct VIAC. Annual rescreening is recommended for HPV-positive client with VIAC-negative result, while VIAC-positive client proceeds for treatment. [see algorithm below]. The national program targets screening women in 30 to 49-year age group. W.H.O. recommends earlier HPV DNA testing for WLHIV in a screen, triage and treat approach starting at 25 years.

HPV DNA screening algorithim



VIAC screening algorithim for HPV positive results

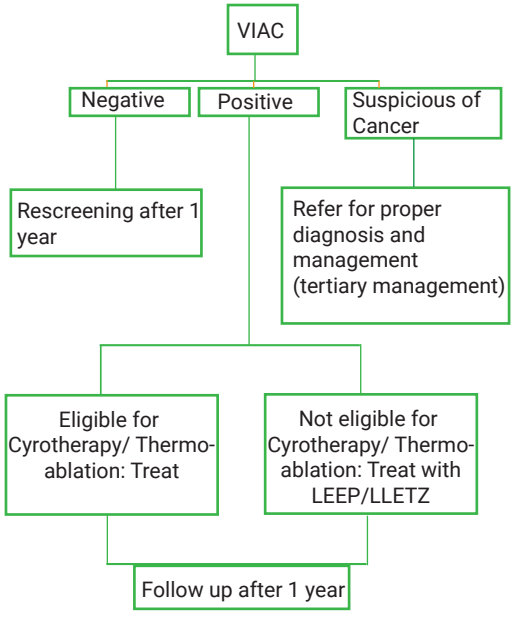


Figure 9. 2: Algorithm for cervical cancer screening using HPV DNA or VIA

Repeat VIAC is done 6 months after treatment (follow up after 6 months)

Treatment of Precancerous Lesions

Thermal Ablation/Cryotherapy: Treat eligible lesions in a single visit approach (SVA) where possible. Treat eligible pre-cancer lesions with thermal ablation or cryotherapy. (See eligibility criteria in text box below. Refer to the Job Aid for Conducting cold coagulation or thermal ablation for procedure).

Eligibility for Thermo-ablation and cryotherapy.
- lesions should not be suspicious of cancer
- Ensure full visibility of entire extent of lesion.
- Lesion should be occupying <75% of the cervix.
- Cryotip should cover the lesion.
- Exclude any anatomical deformities of cervix that prevent good application of cryotip/thermal probe.
- Client is not pregnant, or client is more than 12 weeks post-partum [Avoid using cryotherapy in pregnancy and reschedule until client is more than 12 weeks postpartum].
- If client has severe cervicitis, post-pone treatment of pre-cancer lesions and prescribe antibiotics as per National guidelines.

Loop Electrical Excision Procedure or Large Loop Excision of the Transformation Zone (LEEP/LLETZ) Reserve LEEP for pre-cancerous lesions not eligible for cryotherapy or thermal ablation, and as a diagnostic tool for suspicious lesions. Excised tissue should be sent for histologic examination.

NOTE: LEEP services are performed by trained medical doctors and specialised gynaecologists at district to tertiary hospitals, in settings which provide anaesthesia. (For procedure, refer to Job Aid)

Management of Complications:
Counsel recipients of care for the following warning signs

1. Early warning signs (usually in first 2-4 weeks): Fever for more than 2 days, severe lower abdominal pain associated with fever, foul smelling or pus-coloured discharge, bleeding heavier than seen in normal menses for more than 2 days and bleeding with clots.
2. Late warning signs (usually 1-3months): later onset abdominal pain with fever, severe menstrual cramping with minimal or no menstrual bleeding, and genital leaking of either urine or faeces.

9.9 Nutritional Support for people living with HIV

Introduction

The link between HIV and nutrition occurs at many different levels, including the physiological, individual, community and national adequate nutrition is required to delay disease progression, ensure, and improve immune response, optimize the benefit of ART, and prevent HIV transmission from mother to child. The impact of food and nutrition security plays a crucial role in the susceptibility, vulnerability and resistance of individuals and communities to the HIV epidemic. Children of mothers who are infected are especially vulnerable to malnutrition and mortality, either because of their own HIV infection or because of the deteriorating health of one or both parents. Infection with HIV is known to increase demand on nutrition even in the early stages of HIV infection when no symptoms are apparent. Malnutrition, HIV and AIDS are synergistic and together create a vicious cycle that additively weakens the immune system

Dietary Guidelines for people living with HIV

A healthy, balanced diet is one that provides the right foods, in the right amounts, combinations, and is safe and free from disease and harmful substances. The body cannot work properly if one or more nutrients are missing.

Balanced Diet

Children, adolescents, and adults are recommended to eat a four (4) star diet of staples/starch, fruits and vegetables, legumes and seeds and animal foods and products. Examples of recommended foods are as follows:

Staples, Roots, and tubers: Maize, wheat, rice, millet and sorghum, sweet potatoes, madhumbe/ amadhumbe and potatoes

Meat and meat products: Chicken, fish, liver, eggs, yoghurt, cheese, amasi/ hodzeko, sour milk, and milk

Legumes and seeds: Dried peas, beans, nuts,

Fruits and vegetables: Mango, passion fruit, oranges, dark- green leaves (spinach, rape, covo),
carrots, yellow sweet potato, pumpkin, banana, pineapple, watermelon, tomatoes, avocado, eggplant,
paw-paw, and cabbage

Water: Drink at least 2 liters or eight (8) 250 ml cups of water per day

When planning a healthy diet, it is important to include locally available or traditional foods as they are nutritious, wholesome, locally produced, and easy to grow

Nutritional Counselling

Effective nutrition counseling, care and support will improve the quality of life of people living with HIV, promotes well-being, self- esteem, and a positive attitude towards life.

HIV positive clients who have good nutrition are likely to.

- Have improved quality of life, being able to work and contribute to the family income
- Have prolonged good health, remaining active and able to care for themselves and help with the care of children and other dependents
- Have reduced illnesses and recover more quickly from infections, thereby reducing costs for healthcare
- Maintain a good appetite and stable weight
- Children tend to go to school regularly, resulting in better education and development
- Children have more energy to play and have fun.

Good nutrition should be one of the goals of counseling and care for PLHIV

Nutritional Requirements for PLHIV

Good nutrition for all individuals, especially those HIV and TB infected, requires the consumption of appropriate proportions of macronutrients (e.g., proteins, carbohydrates, and fats) and micronutrients (e.g., vitamins, minerals). The nutritional needs of PLHIV depend on the stage of disease progression. Required intake levels are suggested based on the absence or presence of symptoms such as fever, diarrhea, weight loss, and wasting. The following tables highlight the nutrient requirements of adults with HIV.

Table 9. 5: Nutrient requirements for adults living with HIV

Nutrient	HIV -Infected Asymptomatic (WHO Stage 1)	HIV-Infected Symptomatic (Stage 2 and above)
Energy / Carbohydrates	Increase intake by 10%	Increase intake by 20%
Protein	• Same as for the non-infected • Recommended uptake is 12-15% of the total energy needs or 0.8kg per kg body weight in females and 0.85kg per kg body weight in males	
Fat	Same as for a non-HIV infected person i.e., 30-35% of total energy needs	
Micronutrients	• Same as in the non-infected • Specific or multiple deficiencies must be managed using standard protocols • Micronutrient supplements can be used as an addition to a balanced healthy diet but must NOT replace a healthy diet	

Table 9. 6: Recommended intake for adolescents and adults on the stage of disease

Stage of disease	Recommended intake
HIV-Positive Asymptomatic (WHO stage 1)	Eat 3 meals and 2-3 snacks)
HIV Positive Symptomatic (WHO stage 2 and above	Eat 4 meals and 3 snacks

Pregnant and lactating women

The nutritional requirements for HIV positive pregnant and lactating women are summarized in the following tables.

Nutrient	HIV-infected asymptomatic (WHO stage 1)	HIV- Infected Symptomatic (WHO stage 2 and above)
Energy / Carbohydrates	Increase intake by 10%	Increase intake by 20-30%
Protein	30-50% of the non-pregnant woman	Same as the HIV negative woman which is 30-50% of the non-pregnant woman
Micronutrients	Daily iron-folate supplementation (400 µg of folate and 60 mg of iron) during six months of pregnancy to prevent anaemia, and twice daily supplements to treat severe anaemia Management of Iron/Folate deficiency Anemia and Iodine Deficiency remains the same as for the non-HIV-infected	Daily iron-folate supplementation (400 µg of folate and 60 mg of iron) during six months of pregnancy to prevent anaemia, and twice daily supplements to treat severe anaemia Management of Iron/Folate deficiency Anemia and Iodine Deficiency remains the same as for the HIV negative women
Energy	Increase intake by 10 percent + 500 kcal to support lactation	Increase intake by 20 to 30 percent + 500 kcal to support lactation
Protein	Same as for HIV negative women which is 30- 50% of the non-pregnant women	Same as for HIV negative women which is 30-50% of the non-pregnant women
Micronutrients	Management of Iron/Folate deficiency Anemia and Iodine Deficiency remains the same as for the HIV negative women	Management of Iron/Folate deficiency Anemia and Iodine Deficiency remains the same as for the HIV negative women

Nutritional assessment for PLHIV

For the detailed nutritional assessment for PLHIV refer to the national Nutrition, HIV & TB integrated guidelines 201

Chapter 10 Managing Advanced HIV Disease (AHD)

10.1 Introduction

Advanced HIV Disease (AHD) is defined as WHO clinical stage 3 or 4 or a CD4 cell count equal or less than 200 cells/mm3 for people living with HIV aged five years or older. All children younger than five years are considered to have advanced HIV disease. This is based on the rationale that most children younger than five years usually present for care with advanced immunosuppression, younger children have an increased risk of disease progression and mortality regardless of clinical and immune condition. Also varying age dependent CD4 count definitions for advanced immuno-suppression among children younger than five years make definitions based on CD4 count difficult to implement in programmatic settings.

Although children younger than five years are defined as having advanced disease at presentation, those who have been receiving antiretroviral therapy for more than one year and who are clinically stable should not be considered to have advanced disease and should be eligible for multi-month dispensing.

Children, adolescents, and adults who had previously initiated antiretroviral therapy and are re-engaging with care after a period of more than 90 days of ART interruption should be assessed for AHD and should be offered the AHD package as appropriate. PLHIV diagnosed with AHD based on CD4 count and or WHO clinical staging should reflexively be screened for TB and Cryptococcal Meningitis using TB LAM and Gene Xpert and CrAg respectively.

WHO definition of Advanced HIV Disease (AHD)

- For adults, adolescents, and children older than 5 years, AHD is defined as CD4 cell count <200 cells/mm3 or WHO stage 3 or 4 event.
- All children younger than 5 years old with HIV are considered as having AHD

10.2 Assessing for AHD

CD4 cell count is the best indicator of disease stage and immediate risk of death and thus should be used to identify people with advanced HIV disease. If access to CD4 count is limited or unavailable, WHO staging should be used. Table 10.1 summarizes the diagnostic recommendations for managing patients who have AHD.

Table 10. 1: Summary of diagnostic recommendations for Advanced HIV Disease

Intervention	Priority target population	Age
CD4 testing	• PLHIV newly presenting to care (ART naïve). • Patients returning to care who have interrupted ART for at least 90 days • Patients on ART who have suspected or confirmed treatment failure	All ages
LF-LAM testing	Outpatient and Inpatient settings: in HIV-positive adults, adolescents, and children • with signs and symptoms of TB • with advanced HIV disease • who are seriously ill or, • irrespective of signs and symptoms of TB and with a CD4cell count < 200. A negative LF-LAM test does not exclude TB; however, a positive LAM test confirms it	All ages
Cryptococcal antigen	Any PLHIV with CD4<200cells/mm^3 PLHIV with clinical stage 3 or 4 illness	>10 years

10.3 Providing a package of care

To address these leading causes of morbidity and mortality among people with AHD, it is recommended that health workers provide a package of interventions, including screening, treatment and/or prophylaxis for major opportunistic infections, rapid ART initiation and intensified adherence support interventions, be offered to everyone. Table 2 below summarizes the recommended components of package of care for patients with AHD

Table 10. 2: Components the package of care for people with Advanced HIV disease

	Intervention	CD4 cell count	Adults	Adolescents	Children
Diagnosis	LF-LAM for TB diagnosis among people with symptoms and signs of TB	Any CD4 count when patient seriously ill or stage 3 and 4	Yes	Yes	Yes
	Cryptococcal antigen screening	<200	Yes	Yes	No
Prophylaxis and preemptive treatment	Co-trimoxazole prophylaxis	≤350 Stage 2,3, and 4	Yes	Yes	All children born of HIV positive mothers from six weeks of age until they are tested and confirmed to be HIV negative
	TB preventive treatment	Any On ART or Post TB treatment (Immediately following the successful completion of TB treatment).	Yes	Yes	Yes
	Fluconazole pre-emptive therapy for cryptococcal antigen– positive people without evidence of meningitis	<200	Yes	Yes	Not applicable
	Rapid ART Initiation. Defer initiation if clinical symptoms suggest TB or cryptococcal meningitis	Any	Yes	Yes	Yes

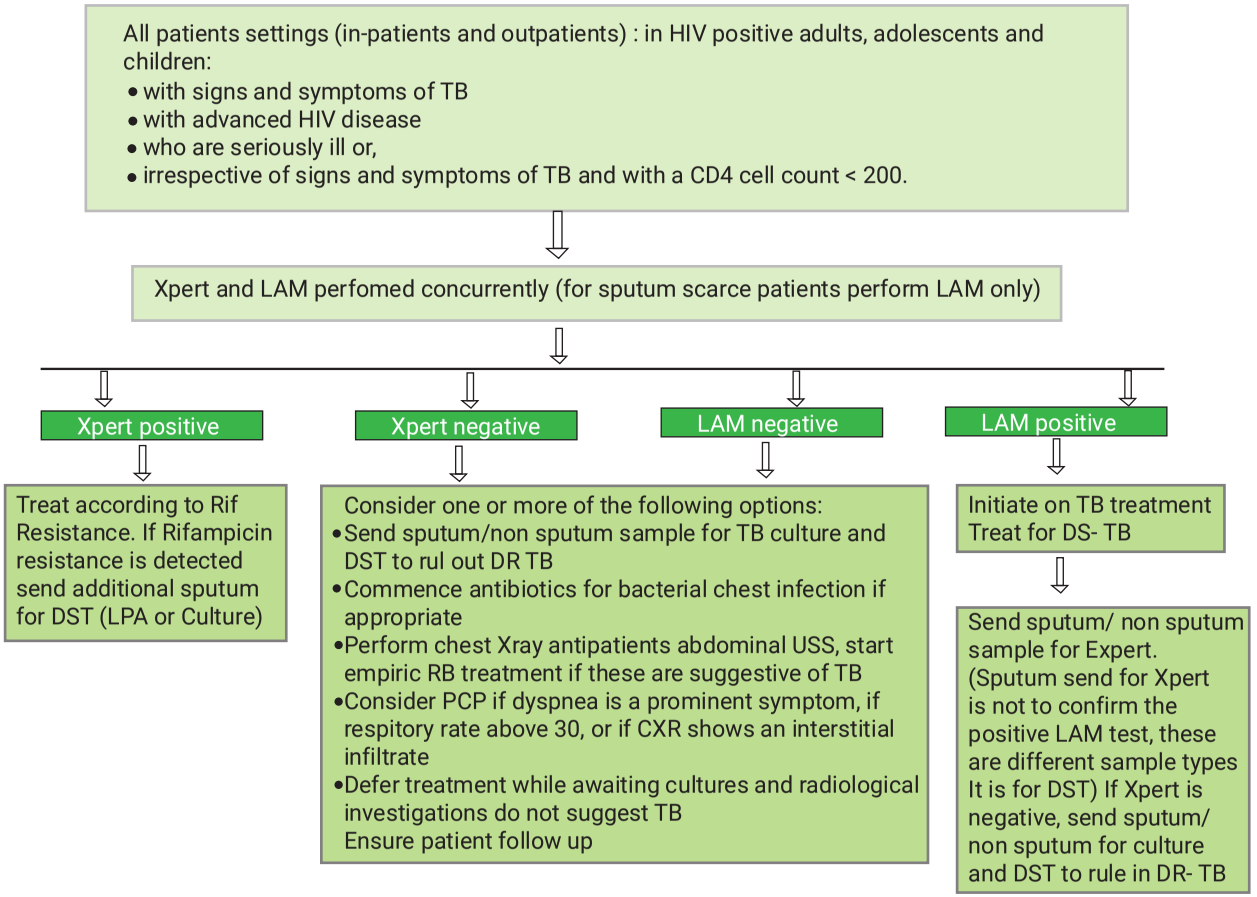
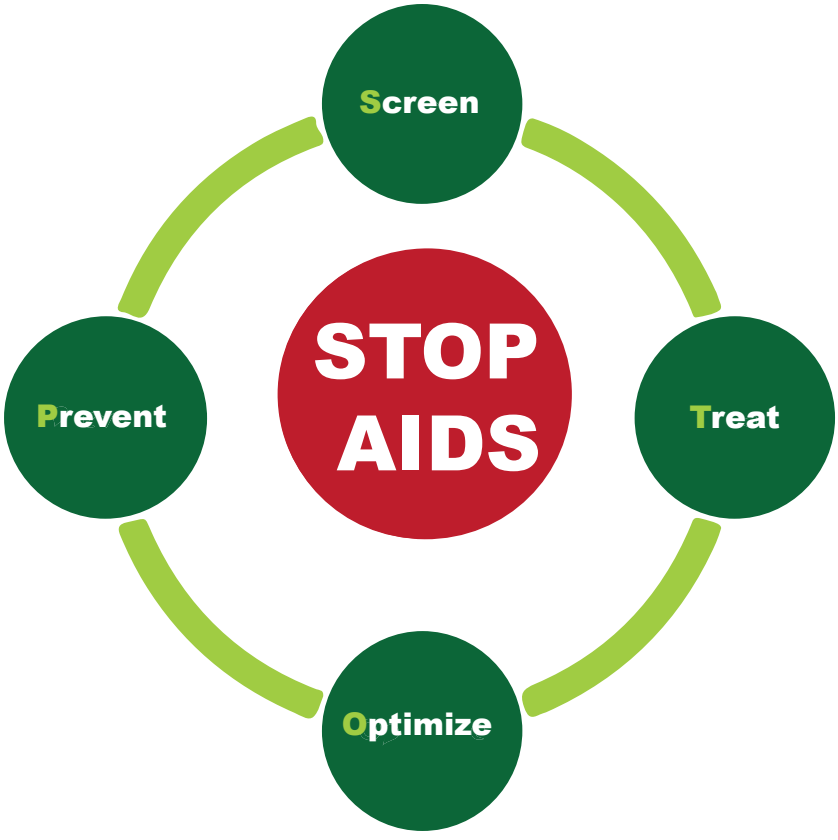


Figure 10. 1: Management of suspected TB in patients with AHD

The main interventions known to reduce morbidity and mortality among PLHIV can be summarized as **S**creen, **T**reat, **O**ptimize and **P**revent **AIDS (STOP AIDS)** as illustrated below.



Source: WHO 2021 Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring

The following box highlights the key interventions required to assist in the management of people with AHD

*The screening, prevention, and management of cryptococcal meningitis and Tuberculosis in patients with AHD is discussed in Chapter 9

Box 1: Screen, Treat, Optimize and Prevent AIDS.

Screen

Tuberculosis

Screen for TB using a clinical algorithm followed by X-ray when indicated and available**.**

Use the following diagnostic tests to confirm TB as applicable:

- Rapid molecular (Xpert® MTB/RIF OR ULTRA) on (induced) sputum, stool, gastric aspirate, or nasopharyngeal aspirate or other extrapulmonary samples if relevant.
- Lateral flow urine lipoarabinomannan (LF-LAM) assay

Cryptococcal infection among adolescents and adults

- Serum or plasma or blood cryptococcal antigen screening followed by lumbar puncture if positive or symptomatic

Malnutrition among children

- Weight for height
- Height for age
- Mid-upper arm circumference among children 2-5 years old

Treat

Treat TB, severe pneumonia, severe bacterial infections, cryptococcal meningitis and severe acute malnutrition according to national guidelines.

Optimize

- Rapid antiretroviral therapy starts - within 7 days with optimal regimens (except in patients with cryptococcal meningitis where treatment should be deferred for 4 – 6 weeks of antifungal treatment initiation).
- Antiretroviral therapy counselling.

Optimize

- Rapid antiretroviral therapy starts - within 7 days with optimal regimens (except in patients with cryptococcal meningitis where treatment should be deferred for 4 – 6 weeks of antifungal treatment initiation).
- Antiretroviral therapy counselling.

Prevent

- Bacterial infections and Pneumocystis pneumonia
- Co-trimoxazole prophylaxis

TB

- TB preventive treatment

Cryptococcal meningitis among adolescents and adults

- Fluconazole pre-emptive therapy

Vaccinations

- Pneumococcal vaccine
- Human papillomavirus
- Measles
- BCG
- COVID-19

Chapter 11 Combination HIV Prevention

11.1 Introduction

Combination prevention programmes use a mix of evidence-based biomedical, behavioural, and structural interventions designed to meet the current HIV prevention needs of individuals and communities to have the greatest possible impact on reducing the number of new HIV infections. Well-designed combination prevention programmes need to reflect the Zimbabwe HIV epidemiology and context. They should focus resources to reach populations at greatest HIV risk with effective, acceptable prevention interventions to address both immediate risks and underlying vulnerability. Biomedical interventions that reduce HIV risk practices and/or the probability of HIV transmission per contact event include condoms, voluntary medical male circumcision (VMMC), o pre-exposure prophylaxis (PrEP) post exposure prophylaxis (PEP), and treatment as prevention (TaSP)

11.2 Lubricated male and female condoms

Male condoms are estimated to reduce HIV transmission by at least 80% during vaginal sex and to offer 64% reduction in transmission during anal sex in men who have sex with men if used correctly and consistently. Evidence suggests that female condoms have similar protective effect for heterosexual transmission.

11.3 Voluntary Medical Male Circumcision (VMMC)

VMMC should continue to be promoted as an additional efficacious HIV prevention option within combination prevention for adolescent boys aged 15 years and older and adult men. VMMC reduces risk of HIV acquisition by up to 60%. Other benefits of VMMC include the reduced risk of some other sexually transmitted infections among women and men, including human papillomavirus, the cause of cervical and penile cancer. A minimum package of services, including safer sex education, condom promotion, the offer of HIV testing services and early management of sexually transmitted infections, must be delivered along with the male circumcision procedure.

Pre-exposure prophylaxis for preventing the acquisition of HIV (PrEP)

PrEP is the use of ARV drugs by HIV-negative individuals at substantial risk of getting HIV to reduce the risk of acquisition of HIV infection. Oral pre-exposure prophylaxis (PrEP) containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches.

Additional approaches like the Dapivirine vaginal ring, (DVR), may be offered as an additional prevention choice for women at substantial risk of acquiring HIV. Other PrEP innovations in the pipeline, include the injectable, Cabotegravir- CAB-LA and the dual prevention pill, that protects against both HIV and Pregnancy.The recommended regimen for daily oral PrEP is highlighted in Table 11.1 below:

Table 11. 1: Recommended regimens for daily oral PrEP

Regimen	Medicine	Dosage	Duration
Preferred	TDF (300mg) plus FTC (200mg)	Fixed dose combination one tablet once a day	Period of substantial risk
Alternative	TDF (300mg) plus 3TC β00mg)	Fixed dose combination one tablet once a day	Period of substantial risk

11.4.1 Indications for daily oral PrEP

Daily oral PrEP will be made available to all individuals who are HIV NEGATIVE and are at substantial risk of HIV acquisition as determined by an individual risk assessment. The following are indications for PrEP based on client's history over the past 6 months:

- HIV negative and has a sexual partner with HIV who has not been on effective therapy for the preceding 6 months OR
- HIV negative and sexually active AND has any of the following:
- Vaginal or anal intercourse without condoms OR
- A sexual partner of unknown HIV status OR
- A sexual partner with one or more HIV risk factors, OR
- A history of an STI by lab testing or self-report or syndromic treatment of STIs OR
- Any use of post-exposure prophylaxis (PEP), OR
- Anyone requesting PrEP

However, individuals belonging to certain population groups may be at higher risk of HIV infection than others and should be offered PrEP. These may include:

- Sex workers
- Sero-discordant couples (the HIV sero-negative partner)
- Adolescent girls and young women
- Pregnant and breast-feeding women
- High-risk men (MSM, prisoners, long distance truck drivers) and
- Transgender people

The above criteria of population groups should however not be the sole consideration. Individual risk assessment should be made based on various behavioural and other factors to assess vulnerability to expand access to a wider range of populations in different settings and circumstances

11.4.2 Contraindications for daily oral PrEP

- HIV positive status
- Unknown HIV status
- Suspected acute HIV infection
- Allergy to TDF and / or FTC in the PrEP regimen
- Unwilling/unable to adhere to daily PrEP
- Known renal impairment
- Estimated creatinine clearance <60 ml/min (if known)

11.4.3 Monitoring Clients on daily oral PrEP

PrEP is safe, with no side-effects for 90% of users. However, about 10% of people who start PrEP will have some short-term mild side-effects. These include gastrointestinal symptoms (nausea, decreased appetite, abdominal cramping, or flatulence). Dizziness or headaches have also been reported. Such side-effects are usually mild and resolve without stopping PrEP. Typically, these symptoms start in the first few days or weeks and last a few days and usually less than 1 month. The following table 11.2 details the recommended guidelines for assessing and monitoring renal function for individuals receiving oral PrEP.

Table 11. 2: Assessing and Monitoring Renal Function for Clients Receiving daily Oral PrEP

Population(s)	Initiation Screening	Follow-up Screening
Individuals 29 years and younger with no kidney-related comorbidities	Optional	If not conducted or if baseline test is normal, follow-up is optional until 30 years of age or if kidney-related comorbidities develop. If conducted, and baseline test result is <90 mL/min, conduct follow-up screening every six to 12 months, if available.
Individuals 30–49 years with no kidney-related comorbidities	Conduct once within one to three months of oral PrEP initiation, if available.	If baseline test is normal, further screening is optional until 50 years of age or if kidney-related comorbidities develop. If baseline test result is <90 mL/min, conduct follow-up screening every six to 12 months, if available.
Individuals 50 years and older Individuals of any age with kidney-related comorbidities Individuals with previous creatinine screening of <90 mL/min	Conduct once within one to three months of oral PrEP initiation, if available.	Conduct follow-up screening every six to 12 months, if available.

When screening is conducted, any individual with a result ≥60 mL/min can safely be prescribed oral PrEP. Since results can be reviewed at a follow-up visit, waiting for results should not delay oral PrEP initiation. If the results are <60 mL/min, the test should be repeated on a separate day before stopping oral

PrEP, and oral PrEP should be stopped if the result of the repeat test is abnormal. Creatinine clearance usually returns to normal levels after stopping PrEP. Oral PrEP can be restarted if results are confirmed to be ≥60 mL/min within one to three months after stopping medicines. Follow up procedures for clients receiving oral PrEP are detailed in table 11.3 below.

Table 11. 3: Daily oral PrEP follow-up procedures

Intervention	Schedule following PrEP initiation
Confirmation of HIV negative status	Every 3 months
Address side effects	Every visit
Provide STI screening, condoms, contraception, or safer conceptionservices	At every visit
Counselling regarding effective PrEP use (adherence), prevention of sexually transmitted infections, recognition of symptoms of sexually transmitted infections, and issuesrelated to mental health, intimate partner violence, and substance use and HIV risk assessment	Every visit
Where available	
Hepatitis C antibody	Consider testing MSM every 12 months. Incident HCV infections have been reported among PrEPusers who deny injection drug use

11.4.4 When to discontinue daily oral PrEP

The duration of PrEP use may vary, and individuals are likely to commence and stop PrEP depending on their risk status at different periods in their lives. PrEP can be stopped 28 days after the last possible exposure to HIV if the client is no longer at substantial risk for HIV infection. It should also be stopped if client:

- Develops renal disease (Creatinine Clearance <60ml/Min)
- Has a severe adverse medicine reaction which though rare may include kidney and liver problems, bone loss and potentially fatal lactic acidosis
- In sero-discordant couples when HIV infected partner on ART has a suppressed viral load

11.4.5 Event-Driven Pre-Exposure Prophylaxis (ED-PrEP)

ED-PrEP, also called on-demand PrEP, event-based PrEP, intermittent PrEP or 2+1+1, is effective in reducing the likelihood of acquiring HIV infection for men who have sex with men (MSM).

ED-PrEP is the taking of PrEP for a period that is as short as three days and timed to correspond with anticipated sex. ED-PrEP use is only approved for all individuals assigned male at birth not exposed to exogenous hormones such as gender-affirming hormone therapy.

Furthermore, ED-PrEP is contraindicated in individuals with HBV infection.

Approved Medicines for ED-PrEP

Tenofovir Disoproxil Fumarate/Emtricitabine (TDF/FTC) is the preferred regimen ED-PrEP.

Guidance for Offering ED-PrEP

ED regimen: Start ED-PrEP with a loading dose of two pills taken **2–24 hours** before having sex to ensure sufficient drug levels to provide protection. Continue taking one pill of PrEP at the same time as the loading dose daily until **two days** after the last potential exposure. This process should be repeated for each period of potential exposure to HIV.

ED-PrEP Effectiveness

Like daily oral PrEP, ED-PrEP can reduce HIV acquisition through sexual transmission among all individuals assigned male at birth not exposed to exogenous hormones by more than 90% when taken as prescribed. ED-PrEP combined with other HIV prevention strategies, such as condom and lubricant use, harm reduction and treatment for drug use, reduction in number of sexual partners, and effective antiretroviral treatment for partners living with HIV, as applicable, can further reduce the likelihood of HIV acquisition.

ED-PrEP is not recommended to anyone other than those assigned male at birth and not using estradiol-based exogenous hormones

11.4.6 PrEP using the Dapivirine Vaginal Ring (DVR)

Although Dapivirine Vaginal Ring may be offered to women who are unable to use daily oral PrEP, MOHCC recommends that this should be implemented under research settings to gather enough evidence for its wider use.

The dapivirine vaginal ring is a woman-initiated option to reduce the risk of HIV infection. It is a flexible silicone device containing the non-nucleoside reverse transcriptase inhibitor ARV medicine, dapivirine, which is slowly released over 28 days into the vagina, the site of potential infection.

The dapivirine ring acts locally, and systemic absorption is low. The ring should be continuously worn in the vagina for one month, including during menses, and then should be replaced by a new ring. The risk of HIV-1 infection is reduced 24 hours after ring insertion. Like oral PrEP, the dapivirine vaginal ring should be provided to women in combination with other prevention interventions and health services.

Monitoring clients using the dapivirine vaginal ring

- HIV testing is required before the dapivirine vaginal ring is offered and should be conducted every 3 months
- Adherence support should be a key part of service provision

11.4.7 PrEP using Long-acting Injectable Cabotegravir (CAB-LA)

The long-acting HIV-1 integrase strand transfer inhibitor, Cabotegravir, an analog of dolutegravir, has been approved for PrEP. The long-acting formulation of cabotegravir is administered as an eight-weekly intramuscular injection. Zimbabwe will be adapting CAB-LA once it has been prequalified by WHO

11.5 HIV Post-Exposure Prophylaxis (PEP)

HIV PEP should be offered and initiated as early as possible for all individuals with exposure that has the potential for HIV transmission, preferably within 72 hours. For individuals who may not be able to access services within this time, providers should consider the range of essential interventions and referrals that should be offered to clients presenting after 72 hours. Eligibility assessment should be based on the HIV status of the source whenever possible.

11.5.1 The following types of exposure may warrant HIV PEP.

Body fluids: blood, blood-stained saliva, breast milk, genital secretions (vaginal secretions and semen), cerebrospinal, amniotic, peritoneal, synovial, pericardial, or pleural fluids. Although these fluids carry a high risk of HIV infection, this list is not exhaustive. All cases should be assessed clinically, and the health care workers should decide whether the actual exposure constitutes a significant risk.

11.5.2 Exposure that does not require HIV PEP includes:

- When the exposed individual is already HIV positive
- When the source is established to be HIV negative
- Exposure to body fluids that do not pose a significant risk: non-blood-stained saliva, urine and sweat.

11.5.3 Post Exposure Prophylaxis after Sexual Assault (Rape or Sexual Abuse) or High-Risk Sexual Encounter

It is recommended that a victim of rape or sexual abuse or who has had an unprotected high risk sexual encounter, presenting within 72 hours of exposure be counselled and provided with the medicines recommended for post occupational exposure prophylaxis. It is important to try to determine the HIV status of the perpetrator. If that is not possible, it may be assumed that the perpetrator is HIV-positive, and the survivor is provided with the treatment as listed below. Refer the client to the nearest support center for sexual assault survivors.

11.5.4 ARVs to be used in Post Exposure Prophylaxis

Immediately after exposure, all exposed adult and adolescent individuals should take the following regimen for a month:

Tenofovir (TDF) 300 mg plus Lamivudine (3TC) 300 mg plus Dolutegravir (DTG) 50 mg once daily

The regimen for children younger than 10 years is as follows:

AZT + 3TC is recommended as the preferred backbone regimen

ABC + 3TC or TDF + 3TC (or FTC) can be considered as alternative regimens.

DTG is recommended as the preferred third medicine for HIV post-exposure prophylaxis for children younger than 10 years.

An age-appropriate alternative third medicine can be identified among ATV/r, RAL, DRV, EFV

11.5.4 ARVs to be used in Post Exposure Prophylaxis

Toxicity of PEP regimens is rare. Clinical monitoring is sufficient. See Chapter 8 section 8.4 for common toxicities for individual medicines

11.6 Treatment as Prevention (TAsP)

Treatment as prevention (TasP) refers to HIV prevention methods and programmes that use antiretroviral treatment (ART) to decrease the risk of HIV transmission.

When adhered to consistently, ART can reduce the HIV viral load in an individual's blood, semen, vaginal fluid, and rectal fluid to such a low level that blood tests cannot detect it. This is described as an 'undetectable' viral load or viral suppression. In these circumstances, if someone's viral load remains undetectable, they cannot transmit HIV to others. Viral suppression can only be confirmed if a person is accessing regular treatment support, monitoring and viral load testing from a healthcare professional.

11.7 Summary of HIV Prevention Strategies

The following are proven HIV prevention strategies available in Zimbabwe that may be used in combination:

1. Abstinence or delayed sexual debut among the youth
2. Mutual faithfulness to an uninfected partner
3. Correct and consistent use of male and female condoms
4. TAsP - Effective treatment of HIV positive people
5. Voluntary medical male circumcision
6. Pre-exposure prophylaxis
7. Post exposure prophylaxis
8. Economic empowerment of adolescents and young adults (males and females) to reduce risky sexual behaviours

Chapter 12 Reporting of Adverse Drug Reactions (ADRs) by Health Workers

12.1 Reporting of Suspected ADRs

Adverse Drug Reaction (ADR): A response to a medicine which is noxious and unintended, which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.

Adverse Event: Any untoward medical occurrence that may present during treatment with a pharmaceutical product, but which does not necessarily have a causal relationship with this treatment. Treatment failure is also considered as an adverse event.

All healthcare workers, including doctors, pharmacists, nurses, other health professionals and the patients are requested to report all suspected adverse reactions to drugs (including vaccines, X-ray contrast media, herbal medicines especially when the reaction is unusual, potentially serious, or clinically significant. It is vital to report an adverse drug reaction and adverse events to the Medicines Control Authority of Zimbabwe, which is the National Pharmacovigilance Centre, even when all the facts are not available or there is uncertainty that the medicine caused the reaction.

Pharmacovigilance activities are coordinated by the Medicines Control Authority of Zimbabwe (MCAZ) as the National Pharmacovigilance Centre in collaboration with the Ministry of Health and Child Care (MoHCC) public health programs and the Directorate Pharmacy Services (DPS-MoHCC) and all key stakeholders both in the public and private health sector. The Zimbabwe National Pharmacovigilance Policy Handbook provides more detailed information on the Zimbabwe National Pharmacovigilance system, and outlines the roles of the different stakeholders. It also provides information on the pharmacovigilance indicators for public health programs, and the minimum requirements for a pharmacovigilance system.

12.2 Who Should Report

- All health professionals (in the public or private sector). This includes physicians, pharmacists, and nurses, including public health professionals, staff in medical laboratories and pathology departments, and pharmaceutical companies.
- Patients or patient's family members
- General public

- Health and community workers (who are literate) should be encouraged to report, preferably to the clinician who prescribed the treatment, or directly to the MCAZ.

12.3 When to Report Suspected ADRs and ADR Reporting Tools

An ADR report should be submitted to the MCAZ, as soon as possible after the reaction. Adverse drug reaction reports can be submitted online using the MCAZ Electronic Pharmacovigilance (e-PV) system, which can be accessed from the Online Services tab of the MCAZ website, by using the URL https://e-pv.mcaz.co.zw or by using the mobile and desktop applications. After registering on the E-PV platform and logging on to the reporting platform using the right credentials, the landing page will display the different forms that a user has access to. The mobile and desktop applications have offline functionality i.e. reports can be completed offline, saved, and submitted later when internet is available. The mobile applications for Android and iOs users can be downloaded from the Google Play Store and the Apple App Store respectively, by searching for the app "MCAZ Pharmacovigilance". For detailed guidance on how to navigate the E-PV system, refer to the Pharmacovigilance Electronic Reporting System User Manual accessible on the MCAZ website (www.mcaz.co.zw) and https://e-pv.mcaz.co.zw/Once submission is made on-line, the e-ADR form is received by the MCAZ.

Alternatively, the standard Spontaneous ADR reporting form can also be completed and submitted to the MCAZ premises or sent via email to mcaz@mcaz.co.zw. Hard copies of the spontaneous Adverse Drug Reaction Report Forms are available on request from MCAZ.

Consumers, patients or patient representatives may report using the standard ADR reporting form or the e-ADR form, accessible from the Online Services tab MCAZ website using the following link: https://primaryreporting.who-umc.org/ZW.

It is better not to wait until final results and information such as hospital letters are received, because the report may be forgotten. These additional details can be sent to the MCAZ later. All ADR reports once submitted, are treated in an anonymous format.

12.4. ADRs to be Reported to the MCAZ

- All ADRs to marketed medicines or medicines added to the Essential Medicines List
- All serious reactions and interactions
- All known and unknown ADRs
- Unusual or interesting adverse medicine reactions
- All adverse reactions or poisonings to traditional or herbal remedies

- Suspected contamination
- Questionable stability
- Defective components
- Poor packaging or labeling
- Therapeutic failures

12.5 Reporting a Suspected ADR

The following steps should be followed when reporting ADRs:

Step 1: Obtain Patient History and Do a full Examination

- Take a comprehensive medicine and medical history
- Conduct physical examination as some medicines produce distinctive physical signs.
- Establish time relationships i.e., the time from the start of therapy to the time of onset of the suspected reaction.
- Determine if there are other possible causes for the new symptoms (e.g., patient's underlying disease, other medicine/s, over-the-counter medicines, or complementary medicines; toxins or foods) and conduct further investigations e.g., FBC, ALT, U & E. Laboratory tests are especially important if the medicine is considered essential in improving patient care or of the lab test results will improve management of the patient
- Describe the reaction as clearly as possible and, where possible provide, an accu rate diagnosis

Step 2: Check the Known Pharmacology of the Medicine.

- Is the reaction known to occur with the particular medicine as stated in the package insert or other reference?
- If the reaction is not documented in the package insert, it does not mean that the reaction cannot occur with that particular medicine.

Step 3: Management of the ADRs

Manage the patient based on the findings and the guidance in table 10 In addition, consider Dechallenge and Rechallenge.

- Re-challenge refers to starting the same medicine after having stopped usually for an adverse event.
- A positive rechallenge refers to the adverse events recurring after restating the medicine. Stop the medicine
- All products defects of concern that require addressing using MCAZ product defect form.

- A negative rechallenge is when the adverse event does not recur after restarting the medicine. Continue the medicine
- Rechallenge is only justifiable when the benefit of re-introducing the medicine to the patient outweighs the risk of recurrence of the reaction
- Dechallenge refers to the stopping of a drug usually after an adverse event
- Positive dechallenge refers to the adverse events disappearing after the stopping of the drug. In this event consider substituting with another drug OR rechallenging with the same drug
- Negative dechallenge refers to the adverse event not disappearing after the stopping of the drug. In this event, refer for further investigations and consider other potential drugs that can cause similar adverse events.

Example see Cotrimoxazole desensitization Appendix 4

12.6 Components of a Complete Case Report

Complete case reports include the following elements:

- Description of the adverse events or disease experience, including time to onset of signs or symptoms.
- Suspected and concomitant product therapy details (i.e., dose, lot number, schedule, dates, duration), including over-the-counter medications, dietary supplements, and recently discontinued medications.
- Patient characteristics, including demographic information (e.g., age, race, sex), baseline medical condition prior to product therapy, co-morbid conditions, use of concomitant medications, relevant family history of disease, and presence of other risk factors.
- Documentation of the diagnosis of the events, including methods used to make the diagnosis
- Clinical course of the event and patient outcomes (e.g., hospitalization or death)
- Relevant therapeutic measures and laboratory data at baseline, during therapy, and after therapy, including blood levels, as appropriate.
- Information about response to dechallenge and rechallenge; and
- Any other relevant information (e.g., other details relating to the event or information on benefits received by the patient, if important to the assessment of the event).

12.7 How to Minimize Occurrence of ADRs

Some ADRs are unavoidable and cannot be prevented. However, most ADRs can be prevented by following the basic principles of rational use of medicines that are described as follows:

- Use few medicines, whenever possible
- Use medicines that you know well
- Do not change therapy from known medicines to unfamiliar one without good reasons.
- Use textbooks and other reference material providing information on medicine reactions and interactions.
- Take extra care when you prescribe medicines known to exhibit a large variety of interactions and adverse reactions (anticoagulants, hypoglycemic, and drug affecting the CNS) with careful monitoring of patients with such reactions.
- Beware of the interaction of medicines with certain food stuffs, alcohol and even with household chemicals.
- Review all the medicines being used by your patients regularly, taking special notice with those bought without prescription (over the counter, complementary).
- Be particularly careful when prescribing to children, the elderly, pregnant and nursing women, the seriously ill and patients with hepatic and renal diseases.

Careful ongoing monitoring is also essential in these patients.

If the patient shows signs and/or symptoms not clearly explained by the course of their illness, think of adverse drug reaction. If you suspect an adverse reaction, consider stopping the medicine or reduce the dosage as soon possible and please report the adverse drug reaction to the Medicines Control Authority of Zimbabwe (MCAZ).

12.8 Follow-Up

All reports of serious events should be followed up if details are incomplete. This may require the involvement of health professionals in a clinical setting who have been trained and appointed for this type of work. Occasionally follow-up information is required to fully assess reports of non-serious events. Follow-up requests should be kept to a minimum as they can discourage further reporting. Examples of follow-up information might be essential missing details, information on the outcome, the result of re-challenge, the results of laboratory tests, and post-mortem results from health facilities where autopsy is undertaken.

12.9 Feedback to Reporters

The pharmacovigilance centre (MCAZ) will provide feedback to anyone who reports an ADR. Further feedback information will be provided to the reporter after causality assessment by the MCAZ PVCT Committee.

Benefits of reporting to the health worker and the patient.

- Improved patient confidence in professional practice
- Improved quality of care offered to patients• Reduced medicine related problems leading to better treatment outcomes
- Satisfaction in fulfilling moral and professional obligation on the part of the health worker
- Improvement in the knowledge of the health worker

Protection of Health worker who reports an ADR

Reporting adverse drug events promotes patient safety and improves quality of care. Adverse drug reaction reports do not constitute an admission that a health professional contributed to the event in any way. The outcome of the report, together with any important or relevant information relating to the reaction that has been reported, will be sent back to the reporter as appropriate. The details of the report will be stored on a confidential database. The name of the reporter or any other health professionals named on a report and the patient will be removed before any details about a specific adverse drug reaction are used or communicated to others. The information obtained from the report will not be used for commercial purposes. The information is meant to promote patient safety by improving ADR detection, ADR case management causality assessment, signal detection and benefit -risk minimization management and communication in a way that improves therapeutics and ultimately patient safety. The MCAZ online and mobile app medicines and vaccines safety (ePV system has local inbuilt -in site reporting tracking system, causality assessment, uploading of deidentified and anonymized ADR reports onto the WHO Drug International Monitoring Program VigiBase database for further disproportionate analysis signal detection and VigiRank, quality analysis known as VigiGrade completeness score.

Annex 1:
WHO clinical staging of HIV disease in adults, adolescents & children

Source: Adapted from WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children. Geneva, World Health Organization, 2007 (www.who.int/hiv/pub/guidelines/ HIVstaging150307.pdf).

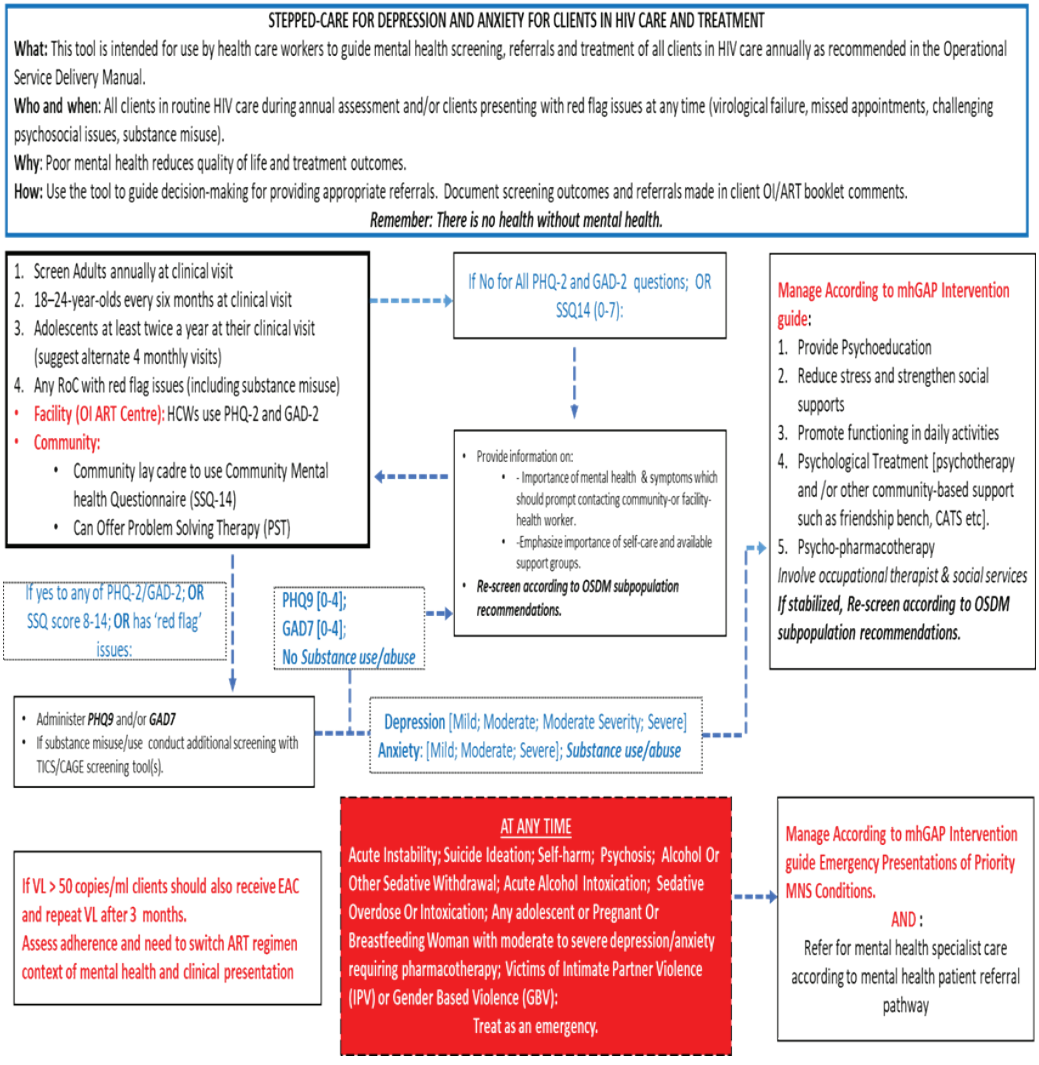
Adults and adolescents[a]	Children
Clinical stage 1	
Asymptomatic Persistent generalized lymphadenopathy	Asymptomatic Persistent generalized lymphadenopathy
Clinical stage 2	
Moderate unexplained weight loss (<10% of presumed or measured body weight) Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis) Herpes zoster Angular cheilitis Recurrent oral ulceration Papular pruritic eruption 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 Papular pruritic eruption Fungal nail infections Extensive wart virus infection Extensive molluscum contagiosum 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[b] 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)
Adults and adolescents[a]	**Children**
Clinical stage 3	
	Symptomatic lymphoid interstitial pneumonitis Chronic HIV-associated lung disease, including bronchiectasis
Clinical stage 4[c]	
HIV wasting syndrome Pneumocystis (jirovecii) pneumonia Recurrent severe bacterial pneumonia	Unexplained severe wasting, stunting or severe malnutrition[d] not responding to standard therapy Pneumocystis (jirovecii) pneumonia Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)

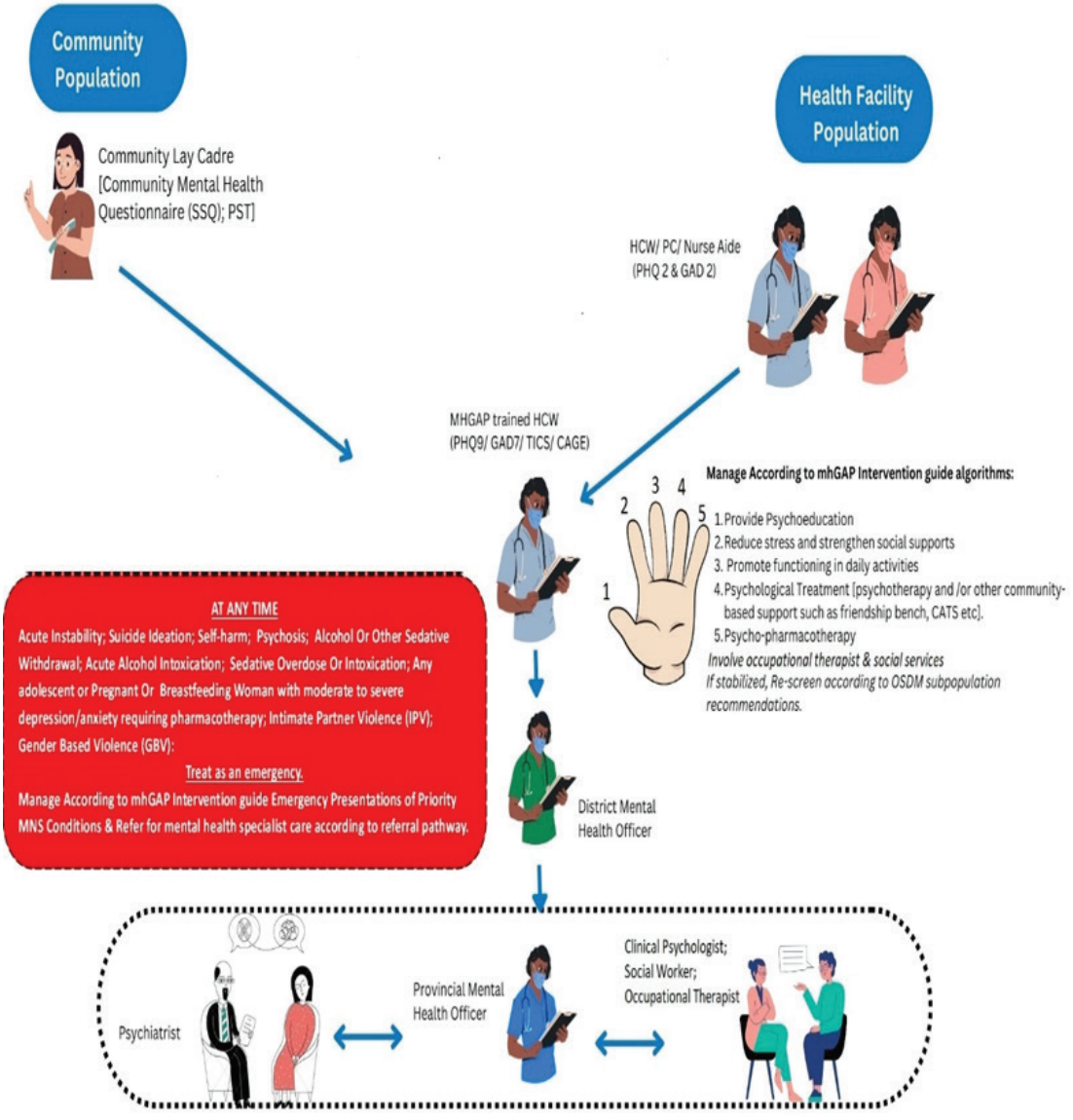
HIV wasting syndrome Pneumocystis (jirovecii) pneumonia Recurrent severe bacterial pneumonia Chronic herpes simplex infection (orolabial, genital or anorectal of more than 1 month's duration or visceral at any site) Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) Extrapulmonary 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[d] 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) Cerebral or B-cell non-Hodgkin lymphoma 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 either weight for height <–3 z-score or mid-upper arm circumference <115 mm or the presence of oedema.

Appendix 2:
Stepped Care Algorithm for Screening Depression and Anxiety Among Clients in HIV Care and Treatment



Appendix 3:
Mental Health Client Referral Pathway



Appendix 4:
Shona symptom questionnaire for the detection of depression and anxiety

Client name:_____Client ID:_____ Date: _____

	Musvondo rapfuura: During the course of the past week:	Ehe Yes	Aiwa No
1	Pane pamaimboona muchinyanya kufungisisa kana kufunga zvakawanda here? Did you sometimes think deeply or think about many things?		
2	Pane pamaimbotadza kuisa pfungwa dzenyu panwechete here? Did you find yourself sometimes failing to concentrate?		
3	Maimboshatirwa kanakuita hasha zvenhando here? Did you lose your temper or get annoyed over trivial matters?		
4	Maimborota hope dzinotyisa kana dzisina kunaka here? Did you have nightmares or bad dreams?		
5	Maimboona kana kunzwa zvinhu zvangazvisinga onekwe kana kunzwikwa nevamwe? Did you sometimes see or hear things others could not see or hear?		
6	Mudumbu menyu maimborwa dza here? Was your stomach aching?		
7	Maimbovhundutswa nezvinhu zvisina mature here? Were you frightened by trivial things?		
8	Maimbota dza kurara kana kushaya hope here? Did you sometimes fail to sleep or did you lose sleep?		
9	Pane pamaimbonzwa muchiomerwa neupenyu zvekuti makambochema kana kuti makambonzwa kuda kuchema here? Were there times when you felt life was so tough you cried or wanted to cry?		
10	Maimbonzwa kuneta here? Did you feel run down (tired)?		
11	Pane pamaimboita pfungwa dzekuda kuzviuraya here? Did you sometimes feel like committing suicide?		
12	Mainzwa kusafara here mune zvamaiita zuva nezuva? Were you generally unhappy with the things you were doing each day?		
13	Basa renyu raive rave kusarira muma shure here? Was your work lagging behind?		
14	Mainzwa zvichikuomerai here kuti muzive kuti moita zvipi? Did you feel you had problems deciding what to do?		
	Scoring : Add together the number of questions to which the client responded " yes"	Total Score: