KINGDOM of ESWATINI
Ministry of Health

Eswatini Integrated HIV Management Guidelines

2022

World Health Organization Eswatini

PEPFAR
U.S. President's Emergency Plan for AIDS Relief

Preface

Eswatini has made significant strides towards achieving the UNAIDS 95-95-95 targets set for 2025. This is evidenced by preliminary data from SHIMS3, which reported that 94% of adults 15 years and older living with HIV are aware of their status, 97% of those aware of their status are on antiretroviral therapy (ART), and 96% of those on ART have achieved viral suppression. However, further analysis of HIV data shows that there are sub-population differences. To close these gaps, the country needs to scale up provision of prevention services among those at risk, and ensure timely treatment for those lagging sub-populations. It is therefore important to prioritise key populations, males, especially young men as well as adolescents and young children to be retained in care, if the country is to maintain the gains attained so far. A significant proportion of deaths among PLHIV are from non-AIDS-related causes, hence the need to provide integrated services. These guidelines address innovations like HIV self-testing (HIVST), Pre-Exposure Prophylaxis (PrEP) for HIV prevention, package of care for clients with advanced immunodeficiency and the introduction of newer drugs formulations and new differentiated service delivery (DSD) models. With the introduction of new drugs, emphasis has also been made on strengthening pharmacovigilance.

The emergence of the COVID-19 pandemic has also emphasised the need for integrated services and ensuring patient-centred care. HIV service delivery has been decentralised in to the community and psychosocial interventions have been introduced as a means to retain patients in care particularly in adolescents and in those re-engaging into care. The country has been and continues to integrate other services into the HIV program. Of note, sexual and reproductive health services have been successfully integrated into most health facilities with contraception and cervical cancer screening being offered within ART clinics. To increase the uptake of HIV services among the male population, voluntary male circumcision is also offered in selected health facilities, some of which have opened male-centred clinics. Integration of non-communicable diseases (NCDs) management especially diabetes mellitus and hypertension screening and treatment are currently ongoing within the country. Due to the effect of HIV on the outcome of COVID-19 coinfection, vaccination is also being encouraged and promoted among all PLHIV.

As the global economic climate changes coupled with the country's steps towards achieving epidemic control, it is very important to ensure that the gains attained so far are maintained and sustained. This requires a clear understanding of donor-funded programs and intervention components that are critical for the country to achieve and sustain epidemic control and how these components can be transitioned to the government if not already within government structures. Additionally, healthcare workers across all cadres should maintain to date understanding of these innovative approaches, incorporating them into daily practice.

These guidelines provide the standards and recommendations for the Government of the Kingdom of Eswatini's vision of ending AIDS as a public health threat. To achieve this vision, we need a continued concerted effort from all stakeholders at all levels of service delivery to translate these guidelines into action. Meaningful engagement of recipients of care from the constituency of PLHIV at all levels of care is vital in achieving this goal.

I would like to take this opportunity to thank the Ministry of Health program leads, technical working group members, recipients of care, key stakeholders and implementing and development partners for their contribution and support in developing and implementing these guidelines.

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Acknowledgements

The 2022 Eswatini Integrated HIV Management Guidelines have been made possible by the commitment of the Eswatini National AIDS Program thematic leads and their implementing partners. This team worked tirelessly to ensure that the guidance given in this document is up to date, evidence-based and applicable in the Eswatini context. The guidelines content development was led by the thematic leads and focal people within the Ministry of Health. Appreciation goes to the following, **Dr Advocate Dlamini** (National ART coordinator), **Dr Clara Nyapokoto** (HIV care and treatment), **Dr Nicholas Kisyeri** (DSD), **Sindy Matse and Khanyisile Lukhele** (Prevention), **Vusi Maziya, Mndeni Sukati, Bongiwe Mhlanga, Melody Mdluli, Sabelo Mlambo** (VMMC), **Lenhle Dube** and **Musa Ginindza** (HTS), **Harriet Mamba** (LCM), **Nobuhle Mthethwa** (Paediatrics care and treatment), **Gugulethu Madonsela** and **Malvern Masango** (TB/HIV and AHD), **Setsabile Gulwako** (M&E), **Bonisile Nhlabatsi**, **Wiseman Mngometulu** and **Ntombikayise Dlamini** (SRHU-PMTCT), **Nompilo Gwebu** (APS), **Nhlanhla Magagula** (Risk communication), **Mpumelelo Mavimbela** (STIs), **Ntombi Ginidza** (NCDs), **Thembi Dlamini** (Quality Improvement); **Promise Dlamini, Salaphi Dlamini, Nokuphila Zondi, Mduduzi Mpingo, Sakhile Dlamini, Tivumile Dludlu** (Psychological care and support), **Fikile Ngwenya** (supply chain and Pharmacovigilance).
For their technical support, appreciation also goes to country directors and contributors from the WHO country office, PEPFAR, USAID, CDC, UNAIDS, GU, the ASPIRE Project, URC, ICAP, MSF, FHI 360, Jhpiego, Baylor, AHF, TLC, PSI and PACT. To the different civil society organisations and recipients of care who participated in this guideline development, your input is greatly appreciated.

The Ministry of Health would like to acknowledge the technical support and expertise provided by **Mpumelelo Ndlela** and **Qhubekani Mpala** from the Clinton Health Access Initiative (CHAI) for their secretariat role and impeccable work in consolidating and formatting these guidelines.

Special appreciation is given to the SNAP program manager **Mr Muhle Dlamini** who provided overall oversight of the guideline development process.

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Acronyms

3TC	Lamivudine
ABC	Abacavir
ACEI	Angiotensin-converting enzyme inhibitor
AHI	Acute HIV infection
ALT	Alanine aminotransferase
ANC	Antenatal care
ARB	Angiotensin receptor blocker
ART	Antiretroviral therapy
ARV	Antiretroviral (drug)
AST	Aspartate aminotransferase
ATT	Anti-tubercular therapy
AZT	Zidovudine
BCG	Bacillus Calmette-Guerin
BDQ	Bedaquiline
DMA	Delamanid
DRV/r	Darunavir/ritonavir
DSD	Differentiated services delivery
DTG	Dolutegravir
ECP	Emergency contraception
EID	Early infant diagnosis
EFV	Efavirenz
EIMC	Early infant male circumcision
eIP	Enhanced infant prophylaxis
eMTCT	Elimination of mother-to-child transmission
EPI	Expanded programme on immunization
FDC	Fixed-dose combination
FTC	Emtricitabine
GBV	Gender-based violence
HBeAg	Hepatitis B envelope antigen
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCTZ	Hydrochlorothiazide
HCV	Hepatitis C virus
HCW	Healthcare worker
HIVST	HIV self-testing
CCB	Calcium channel blocker
CIHTS	Client-initiated HIV testing services
CPT	Co-trimoxazole preventive therapy
CrAg	Cryptococcal antigen
INSTI	Integrase strand transfer inhibitor
IPV	Intimate partner violence
IRIS	Immune reconstitution inflammatory syndrome
IUD	Intrauterine device
LAM	Lipoarabinomannan
LDL	Low-density lipoprotein (cholesterol)
LEEP	Loop electrosurgical excision procedure
LFA	Lateral flow assay
LF-LAM	Lateral flow urine lipoarabinomannan assay
LPV	Lopinavir
LPV/r	Lopinavir/ritonavir
LTBI	Latent tuberculosis infection
MDR-TB	Multidrug-resistant tuberculosis
MNCH	Maternal, new born and child health
NAT	Nucleic acid test
NNRTI	Non-nucleoside reverse-transcriptase inhibitor
NRTI	Nucleoside reverse-transcriptase inhibitor
NSAID	Non-steroidal anti-inflammatory drug
NVP	Nevirapine
PCR	Polymerase chain reaction
PEP	Post-exposure prophylaxis
PI	Protease inhibitor
PIHTS	Provider-initiated HIV testing services
PJP	Pneumocystis jiroveci pneumonia
PLHIV	People living with HIV
PMTCT	Prevention of mother-to-child transmission
PrEP	Pre-exposure prophylaxis
STI	Sexually transmitted infection
SUAC	Stepped-up adherence counselling
TB	Tuberculosis
TPT	TB preventive therapy
TDF	Tenofovir disoproxil fumarate
VIA	Visual inspection with acetic acid
VL	Viral load
VMMC	Voluntary medical male circumcision
WHO	World Health Organization
HPV	Human papillomavirus
HTS	HIV testing services
DBS	Dried blood spot

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1 INTRODUCTION

1.1 Background

The 2022 Eswatini Integrated HIV Management Guidelines are aligned with the National Health Sector HIV/AIDS Response Plan and current global guidance including the WHO's Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery and Monitoring: Recommendations For a Public Health Approach (July 2021). These Guidelines replace the 2018 Integrated HIV Management Guidelines.

The Eswatini National AIDS Program (SNAP) thematic leads led the development of these guidelines, providing leadership, coordination, and critical reviews. Sub-Technical working groups, such as HTS, LCM, Prevention, Adult care and treatment, Adherence and psychological care and support, non-communicable diseases, STIs, TB/HIV and Advanced HIV, PMTCT and Paediatric Care and Treatment created specialized content for each chapter. Experts from the Ministry of Health, bilateral, multilateral, and implementing partner organizations drafted the respective sections of the guidelines. Additional input was received from WHO and other international experts.

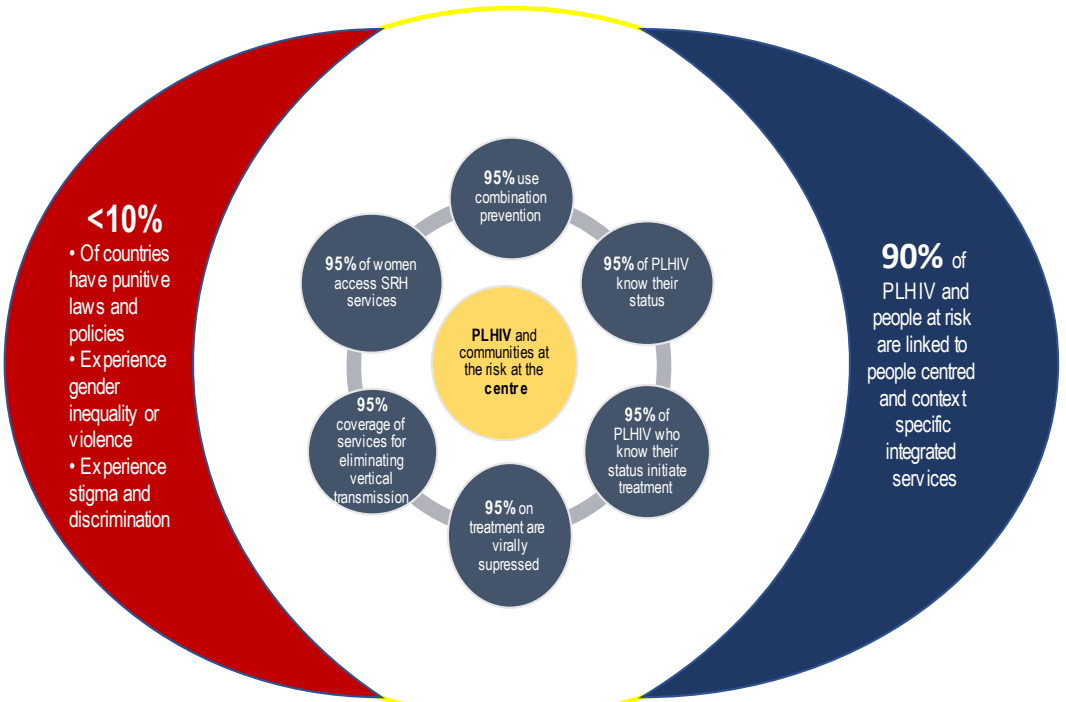
These guidelines aim to standardize and promote the continued provision of comprehensive, quality, and client-centred prevention, care and treatment services. The goal of these new guidelines is to promote service uptake and retention, resulting in improved client outcomes, improved quality of life, and a decline in new HIV infections, HIV-related illnesses and mortality. After surpassing the 2020 UNAIDS targets, the country's goal is to sustain the successes achieved so far while offering patient-centred care.

Throughout the continuum of HIV care, from prevention to treatment, clients should be evaluated and offered differentiated care that takes into consideration their preferences and clinical conditions. Differentiated service delivery (DSD) is defined as "a client-centred approach that simplifies and adapts HIV services across the cascade, in ways that both serve the needs of people living with HIV better and reduce unnecessary burdens on the health system" (Journal of the International AIDS Society). DSD allows for integrated health services, and high-quality care, and has been shown to improve uptake of services and retention. *See Figure 1.1* below.

All health facilities that provide HIV services in Eswatini should implement the HIV services packages as outlined in these guidelines. A multi-disciplinary approach to care by clinicians, counsellors, expert clients, pharmacists, laboratory staff and community workers is critical for the successful implementation of these guidelines. Primary health care facilities are ideally placed to strengthen community health systems and empower communities with the knowledge to facilitate uptake of HIV services as well as strengthen linkages and client follow-up systems.

END AIDS by 2030 by providing people-centred care. To ensure this, Eswatini will

- provide people-centred care that is focused and organized around the health needs, preferences and expectations of people and communities, upholding individual dignity and respect, especially for vulnerable populations, and engage and support people and families to play an active role in their care by informed decision-making;
- offer safe, acceptable and appropriate clinical and non-clinical services in a timely fashion, aiming to reduce morbidity and mortality associated with HIV infection and to improve health outcomes and quality of life in general; and
- promote the efficient and effective use of resources.



Adapted from: https://www.unaids.org/en/resources/presscentre/featurestories/2021/july/20210721_2025-aids-targets

Figure 1.1: Patient-centred Care as a tool to end AIDS by 2030

Table 1.1 How to Use These Guidelines

Updates and changes	
Outside reference	
Important messages	
Tools	
Dosing information	

1.2 Summary of Major Changes

Chapter 1 Introduction	• Background • Usage of guideline • Summary of major changes
Chapter 2 Prevention of HIV	• Change of terminology from serodiscordant to sero-different couples • Event-driven oral TDF-based ED-PrEP as a 2+1+1 regimen can be offered to HIV-negative clients assigned male at birth (and not on exogenous hormones), as an alternative dosing schedule from daily oral PrEP, to prevent HIV transmission from sexual exposure. • The Dapivirine ring may be offered as an additional prevention choice for cis-gender women at substantial risk of HIV as part of a combination prevention approach. • An HIV post-exposure prophylaxis (PEP) regimen with three drugs is preferred for all persons accidentally, occupationally, sexually or otherwise exposed to HIV. • DTG is recommended as the preferred third drug for HIV PEP. • When available, ATV/r, DRV/r, LPV/r and RAL may be considered as alternative third drug options for PEP in adults.
Chapter 3 HIV Testing Services	• HIV testing services should be offered to all clients with unknown HIV status at every point of contact in the health facility and community settings. • The HIV testing screening tool will be used to determine how often a client with a previous HIV-negative result will need to be re-tested for HIV. • Client-initiated HIV testing services and provider-initiated HIV testing services are two approaches to be used at the entry point to HIV prevention, care, and treatment services. • Targeted testing, including index testing (testing the family members and sexual partners of people diagnosed with HIV) and social network testing (testing the sexual partners and peers of HIV-positive key populations), are the preferred methods of testing. • To encourage contacts of index clients with unknown HIV status to be tested, every HIV-positive client will be given information on client notification options, either through passive referral or assisted HIV partner notification services. • HIV Self-test kits/Oraquick can be distributed at the health facility level and performed privately in the client's home or facilitated by a healthcare worker in a private setting at a health facility. The age of consent for HIVST is 16 years. • All HIV tests conducted must follow the National HIV Testing Algorithm for children and adults. Referral and linkages to prevention or care and treatment services should be provided to both negative and positive clients, respectively. • Rapid tests (Determine™ and UniGold™) are antibody tests that can be used to definitively diagnose adults and children aged 18 months or older. DNA PCR is used to diagnose children less than 18 months of age and for inconclusive results according to the National HIV Testing Algorithm. • Retesting for verification - all clients with positive HIV results presenting for ART initiation should be re-tested, with a second specimen, preferably with a different tester, before ART initiation.

Chapter 3 **HIV Testing Services**	• DNA PCR has replaced Clearview tests as the tie breaker for inconclusive results when testing for HIV. • Quality assurance for counselling for HTS providers, supervisors and laboratory/National HTS Program is outlined in Table 3.15.
Chapter 4 **Referral and linkages**	• All clients testing HIV positive must be proactively linked (escort client or set an appointment) for ART initiation • Health care worker who identifies the HIV-positive client should ensure linkage of the client • All clients with positive HIV results presenting for ART initiation should be re-tested before they are initiated on ART preferably by a different tester. • All people living with HIV are eligible to start ART regardless of CD4 count or WHO staging to promote early ART initiation • Newly diagnosed HIV clients should be checked in the CMIS if they are genuinely new positive before they are linked for treatment. • All clients newly initiated on ART must be enrolled on enhanced counselling to support their adherence and retention • All clients found to be returning to care must be linked back to care as indicated in the extended LCM SOP • All clients testing HIV-negative should be linked to combination HIV prevention services • Combination HIV prevention is an approach that seeks to achieve maximum impact on preventing new HIV infections. • Bidirectional communication between facilities and communities is important to improve HIV linkages either to prevention or care and treatment. • Active tracing of clients who have disengaged from care must be routinely done for all clients
Chapter 5 **Basic Care Package for HIV-Positive Individuals**	• ART initiation may be offered in the community for clients who have mild or moderate immunosuppression and no current or previous history of clinical, immunologic or virologic treatment failure • For clients who initiate ART with a baseline CD4 count >350cell/mm^3, and show good clinical response, there is no value added by doing a follow-up CD4 count at 6 months • For clients who initiate ART with a CD4 count <350cell/mm^3, CD4 monitoring should be done by 6 months and 12 months after ART initiation. Once the client has 2 consecutive undetectable viral loads, CD4 monitoring can be stopped. If treatment failure is suspected, resume CD4 monitoring until the client has an undetectable viral load. • After one year on ART, clinically well adult clients can receive ART refills every 3-6 months, and clinical assessments every 6 months. • Children who have been receiving ART for more than one year and are established on ART, and older than 2 years should not be considered to have AHD and are eligible for MMD • The basic HIV chronic care package includes routine screening and management of non-communicable diseases, mental health and palliative care services as well as assessment of and offering of COVID-19 vaccination.

Chapter 5 **Basic Care Package for HIV-Positive Individuals**	• Less intensive (up to 3MMD) differentiated service delivery may also be offered to children at least 2 years of age, pregnant and breastfeeding women, clients with controlled comorbidities and key population
Chapter 6 **TB/HIV Collaborative Activities & Advanced HIV Disease**	• TB screening should be done for all PLHIV at every health care visit of contact with a healthcare worker using the national recommended 4 symptom TB screening tool including children and adolescents. Presumptive TB is defined as a patient reporting any one of the TB for symptoms • For PLHIV with presumptive TB, offer rapid ART initiation while rapidly investigating for TB, with close follow-up within 7 days to initiate TB treatment if TB is confirmed • X-pert MTB/RIF is a recommended TB diagnostic test and TB LF LAM is recommended diagnostic TB test for selected groups among PLHIV. See section 6.1.3 • C-Reactive Protein should be used for ART naïve patients as an additional TB screening tool. • TB initiation may be considered at ART initiation in patients without advanced HIV disease (clinically well) • 3 months of Rifapentine/Isoniazid (3HP) is the recommended TPT option except in pregnant and lactating women and children • Delay ART initiation for PLHIV with TB meningitis, Cryptococcal meningitis or Histoplasmosis • For TB patients other than TB meningitis, who are diagnosed with HIV, ART initiation should be started as soon as possible, preferably within 14 days of initiating TB treatment. • AHD patients with CD4 cell counts < 100 cells/mm³ should be screened for Cryptococcal Antigenemia • All children younger than 5 years who are not already receiving ART and clinically stable) are considered to have advanced HIV disease. Children who have been receiving ART for more than one year and are established on ART, and older than 2 years should not be considered to have AHD and are eligible for MMD • CSF CrAg is recommended for diagnosis of Cryptococcal meningitis • Single dose Liposomal Amphotericin B is recommended for the induction phase of cryptococcal meningitis treatment • Histoplasmosis screening and treatment are recommended for patients with AHD and symptomatic histoplasmosis • Fluconazole prophylaxis may be discontinued after 12 months of antifungals once the CD4 count is >100 cells/mm³ and virally suppressed
Chapter 7 **Adult Antiretroviral Therapy**	• ART may be initiated in the community for clinically well clients who are willing to follow up at a health facility of their choice. • ART should be (re)initiated from the entry point where the patient tests positive followed by referral to the ART clinic for ongoing management follow-up • Baseline Random blood sugar, Height, Weight, BMI, and screening for NCD family history are required for all patients initiating ART • Delay ART initiation for PLHIV with TB meningitis, Cryptococcal meningitis

Chapter 7
 	
Adult Antiretroviral Therapy
	• Clients initiating ART and at high risk of metabolic complications should be routinely monitored for metabolic adverse drug reactions
	• For patients on haemodialysis, the ART prescribed should be taken after a dialysis session.
	• Due to high pre-treatment NNRTI resistance in Eswatini, ART initiation on NNRTI-based regimens should be used as a last resort, particularly in treatment-experienced patients
	• Clients on an NNRTI-based regimen should be transitioned to a DTG-based regimen**. Transition can occur regardless of VL**, however, take note of viremia for future reference and to ensure adherence issues are addressed while switching
	• Point of care(POC) viral load testing may be done for ART patients who need expedited decision-making. See section 7.10.2 for priority clients for POC Viral Load testing.
	• VL should be measured by 6 months after ART initiation to confirm virologic response to ART. After 2 consecutive suppressed VL results taken at least 6 months apart, VL monitoring can be done annually and patient-guided into a DSD model of their choice.
	• Receipt of a high VL test result in a patient on an NNRTI-based regimen should trigger an immediate regimen switch while undergoing SUAC. Clients should be called to come to the facility within the next 7 days to begin SUAC. See
	• Figure 7.4 for the management protocol.
	• Two consecutive viral load test results above ≥1000 copies/mL taken three months apart with adequate adherence support should be used to determine virological failure when using plasma or dried blood spot specimens.
	• Do not keep patients on a failing regimen for a long time without appropriate action
	• Regimen switch to the second or third line should be done through a multidisciplinary approach
	• Use of DBS VL for clients presenting outside of normal phlebotomy hours and in children
	• Remnant blood samples of all clients with high viral load may be stored to be used for surveillance purposes to guide program and policy changes.
	• Engagement of social workers, psychologists and psychiatry nurses for clients with identified poor adherence
	• HIV drug resistance testing (genotype) should be requested for all clients with two consecutive viral load results above 1000copies/ml:
	  ○ while on drug-sensitive TB treatment during second-line treatment
	  ○ while taking a 2nd line regimen
	  ○ while taking a DTG-based ART first- or second-line regimen
	• Contact email for HIVDR support changed to:*snapthirdline@mohcoag.org.*
	• Patients with renal insufficiency, active viral hepatitis and on a third-line regimen should be managed at a doctor managed ART clinic

Chapter 8 **Prevention of Mother to Child Transmission of HIV (PMTCT)**	• As part of efforts to achieve the elimination of MTCT (eMTCT), all HIV-negative pregnant and lactating women should be offered PrEP using the OPT OUT approach • Pregnant and lactating women on PrEP should be retested according to the PrEP retesting schedule.

Chapter 8
 	
Prevention of Mother to Child Transmission of HIV (PMTCT)
	• All HIV-negative pregnant women not on PrEP should be re-tested every 2 months (aligned with the ANC scheduled visits) with the most optimal time point for retesting during the third trimester visit (34 weeks Gestation).
	• All HIV-negative lactating women should be re-tested at 6 weeks, 14 weeks, 6 months, 9 months, 12 months, 15 months and 18 months aligned with the mother-baby pair (MBP) schedule.
	• For pregnant women with inconclusive results after HTS; conduct Nucleic Acid Amplification Tests (NAAT) and initiate ART immediately while waiting for NAAT results
	• Virally suppressed mothers enrolled in a DSD model may continue to do so provided that all VLs are done on time (First ANC and 34 weeks).
	• Viral load monitoring schedules specific for pregnant and lactating women are:
	  ○ All newly initiated ART clients should receive the first viral load test 3 months after starting ART and thereafter align with the ANC VL schedule. If the next VL test date falls after delivery, then align with PNC/MBP VL schedule.
	  ○ Women on ART enrolling for ANC should receive a viral load test on their first ANC contact. A subsequent viral load test should be conducted at 34 weeks of gestation.
	  ○ VL testing is compulsory for all women on ART at 6 weeks post-delivery regardless of the previous viral load date. Subsequent VL tests during lactation are done every 6 months until the cessation of breastfeeding.
	• Early infant diagnosis:
	  ○ All HIV-exposed infants must be tested using DNA PCR at birth (0-3 days post-delivery)
	  ○ For all HIV exposed infants whose mothers are on a 2nd and 3rd line regimen, Baylor should be consulted to guide appropriate infant prophylaxis. This should be planned during the antenatal period
	• Any HIV positive pregnant and breastfeeding women with a detectable viral load at contact requires URGENT intervention:
	  ○ 1st line with a high VL while on a non-DTG-based regimen should have an expedited switch to 2nd line DTG-based regimen on the same day
	  ○ 2nd line clients with a high VL should have a genotype sent on the same day and then be placed on a 3rd line holding regimen while awaiting further guidance from the HIVDR committee: snapthirdline@mohcoag.org
	• Adherence assessment, identification of barriers and necessary support should be provided within a case management framework

Chapter 9 **ART For Children And Adolescents**	• All HIV-infected children and adolescents are eligible for rapid ART initiation regardless of CD4 count or WHO clinical stage. • All children, adolescents and caregivers should be well-prepared for ART to ensure good adherence and treatment success. • TDF+3TC+DTG (TLD) is the preferred first-line regimen for all adolescents weighing at least 40 kg. Alternative first-line regimens are outlined in ***Error! Reference source not found.*** • Prioritize assessment and rapid ART initiation in children and adolescents with advanced immunodeficiency as soon as possible (within 7 days) from the day of HIV diagnosis.

Chapter 9 **ART For Children And Adolescents**	• Paediatric >10 years of age and adolescent clients with advanced immune deficiency should be screened for cryptococcal meningitis using a serum Cryptococcal antigen (CrAg) test and TB presumptive adolescents and children should receive an LF TB-LAM test. • To expedite the decision-making in CALHIV, the first viral load test should be done 3 months after initiating ART then 6monthly thereafter • Children and adolescents with a VL > 50 copies/mL should be referred for stepped–up adherence counselling. • A viral load threshold of ≥1000 copies/mL should be used to determine virological failure when using plasma or dried blood spot specimens. • For second-line ART regimens, Atazanavir (ATV/r) is preferred over LPV/r due to its reduced pill burden. Clients can be switched from LPV/r regimens if they meet the requirements outlined in *Chapter 9 Section 9.6* • Third-line ART: Each child or adolescent should receive individualized treatment regimens based on ART history, and previous episodes of viraemia/HIV resistance testing/ genotyping results if second-line ART failure is confirmed. • Adolescents aged 17 to 19 years of age should be successfully transitioned to adult care. A detailed care package and checklist for a successful transition are provided in *Table 9.17* To promote long-term adherence and viral suppression, all facilities must have Teen Clubs. Facilities should also have dedicated days for children, especially those that are failing treatment

Chapter 10
 	
Management of HIV and Non-communicable Diseases
	• All clients infected with HIV should be routinely screened for cardiovascular risk factors, non-communicable diseases and mental health at enrolment and in subsequent visits.
	• Blood pressure should be monitored at every clinical visit.
	• Management of Hypertension in a client with HIV follows similar treatment protocols as for HIV-negative clients. However:
	  ○ Calcium channel inhibitors should be used with caution as they may interact with PIs producing increased serum levels of the former. Therefore, dose titration and ECG monitoring are required.
	  ○ Caution should also be exercised when combining diuretics with TDF by monitoring renal function that could be impaired due to added risk for interstitial nephritis.
	• A low-dose, enteric-coated aspirin 100 mg/day may be prescribed to reduce the risk of cardiovascular morbidity and mortality. Aspirin initiation should only be initiated by a doctor led service, following careful assessment of risk.
	• Annual symptom screening for diabetes mellitus and random blood sugar testing is recommended for establishing diagnosis of diabetes among PLHIV. Care and management of clients with Diabetes and HIV is described in *Section 10.3*
	• A high prevalence of depression is reported among PLHIV compared to the general population. Clients should be screened for depression using the PHQ9 assessment tool at initiation and every 6 months thereafter. Clients should be managed appropriately as described in *Section 10.6*
	• All clients should be evaluated for pain at every visit using a validated pain scale.
	• For methods and reporting on pharmacovigilance, refer to *Chapter 5, Section 5.12*

Chapter 7
 	
Adult Antiretroviral Therapy
	• Point of care(POC) viral load testing may be done for ART patients who need expedited decision-making. See *section 7.10.2* for priority clients for POC Viral Load testing.
	• VL should be measured by 6 months after ART initiation to confirm virologic response to ART. After 2 consecutive suppressed VL results 6 months apart, VL monitoring can be done annually and patient-guided into a DSD model of their choice.
	• Receipt of a high VL test result in a patient on an NNRTI-based regimen should trigger an immediate regimen switch while undergoing SUAC. Clients should be called to come to the facility within the next 7 days to begin SUAC. See *Figure 7.4* for the management protocol.
	• Two consecutive viral load test results above ≥1000 copies/mL taken three months apart with adequate adherence support should be used to determine virological failure when using plasma or dried blood spot specimens.
	• Do not keep patients on a failing regimen for a long time without appropriate action
	• Regimen switch to the second or third line should be done through a multidisciplinary approach
	• Use of DBS VL for clients presenting outside of normal phlebotomy hours and in children
	• Remnant blood samples of all clients with high viral load may be stored to be used for surveillance purposes to guide program and policy changes.
	• Engagement of social workers, psychologists and psychiatry nurses for clients with identified poor adherence
	• HIV drug resistance testing (genotype) should be requested for all clients with two consecutive viral load results above 1000copies/ml:
	  ○ while on drug-sensitive TB treatment during second-line treatment
	  ○ while taking a 2nd line regimen
	  ○ while taking a DTG-based ART first- or second-line regimen
	• Contact email for HIVDR support changed to:*snapthirdline@mohcoag.org*.
	• Patients with renal insufficiency, active viral hepatitis and on a third-line regimen should be managed at a doctor managed ART clinic

Chapter 8 **Prevention of Mother to Child**	• As part of efforts to achieve the elimination of MTCT (eMTCT), all HIV-negative pregnant and lactating women should be offered PrEP using the OPT OUT approach • Pregnant and lactating women on PrEP should be retested according to the PrEP retesting schedule. • All HIV-negative pregnant women not on PrEP should be re-tested every 2 months (aligned with the ANC scheduled visits) with the most optimal time point for retesting during the third trimester visit (34 weeks Gestation). • All HIV-negative lactating women should be re-tested at 6 weeks, 14 weeks, 6 months, 9 months, 12 months, 15 months and 18 months aligned with the mother-baby pair (MBP) schedule.

Transmission of HIV (PMTCT)	• For pregnant women with inconclusive results after HTS; conduct Nucleic Acid Amplification Tests (NAAT) and initiate ART immediately while waiting for NAAT results • Virally suppressed mothers enrolled in a DSD model may continue to do so provided that all VLs are done on time (First ANC and 34 weeks).

Chapter 8
 	
Prevention of Mother to Child Transmission of HIV (PMTCT)
	• Viral load monitoring schedules specific for pregnant and lactating women are:
	  ○ All newly initiated ART clients should receive the first viral load test 3 months after starting ART and thereafter align with the ANC VL schedule. If the next VL test date falls after delivery, then align with PNC/MBP VL schedule.
	  ○ Women on ART enrolling for ANC should receive a viral load test on their first ANC contact. A subsequent viral load test should be conducted at 34 weeks of gestation.
	  ○ VL testing is compulsory for all women on ART at 6 weeks post-delivery regardless of the previous viral load date. Subsequent VL tests during lactation are done every 6 months until the cessation of breastfeeding.
	• Early infant diagnosis:
	  ○ All HIV-exposed infants must be tested using DNA PCR at birth (0-3 days post-delivery)
	  ○ For all HIV exposed infants whose mothers are on a 2nd and 3rd line regimen, Baylor should be consulted to guide appropriate infant prophylaxis. This should be planned during the antenatal period
	• Any HIV positive pregnant and breastfeeding women with a detectable viral load at contact requires URGENT intervention:
	  ○ 1st line with a high VL while on a non-DTG-based regimen should have an expedited switch to 2nd line DTG-based regimen on the same day
	  ○ 2nd line clients with a high VL should have a genotype sent on the same day and then be placed on a 3rd line holding regimen while awaiting further guidance from the HIVDR committee: snapthirdline@mohcoag.org
	• Adherence assessment, identification of barriers and necessary support should be provided within a case management framework

Chapter 9 **ART For Children And Adolescents**	• All HIV-infected children and adolescents are eligible for rapid ART initiation regardless of CD4 count or WHO clinical stage. • All children, adolescents and caregivers should be well-prepared for ART to ensure good adherence and treatment success. • TDF+3TC+DTG (TLD) is the preferred first-line regimen for all adolescents weighing at least 40 kg. Alternative first-line regimens are outlined in *Table 7.4.* • Prioritize assessment and rapid ART initiation in children and adolescents with advanced immunodeficiency as soon as possible (within 7 days) from the day of HIV diagnosis. • Paediatric >10 years of age and adolescent clients with advanced immune deficiency should be screened for cryptococcal meningitis using a serum Cryptococcal antigen (CrAg) test and TB presumptive adolescents and children should receive an LF TB-LAM test. • To expedite the decision-making in CALHIV, the first viral load test should be done 3 months after initiating ART then 6monthly thereafter

	• Children and adolescents with a VL > 50 copies/mL should be referred for stepped–up adherence counselling. • A viral load threshold of ≥1000 copies/mL should be used to determine virological failure when using plasma or dried blood spot specimens.
Chapter 9 **ART For Children And Adolescents**	• For second-line ART regimens, Atazanavir (ATV/r) is preferred over LPV/r due to its reduced pill burden. Clients can be switched from LPV/r regimens if they meet the requirements outlined in Chapter 9 Section 9.6 • Third-line ART: Each child or adolescent should receive individualized treatment regimens based on ART history, and previous episodes of viraemia/HIV resistance testing/ genotyping results if second-line ART failure is confirmed. • Adolescents aged 17 to 19 years of age should be successfully transitioned to adult care. A detailed care package and checklist for a successful transition are provided in Table 9.17 To promote long-term adherence and viral suppression, all facilities must have Teen Clubs. Facilities should also have dedicated days for children, especially those that are failing treatment

Chapter 10
 	
Management of HIV and Non-communicable Diseases
	• All clients infected with HIV should be routinely screened for cardiovascular risk factors, non-communicable diseases and mental health at enrolment and in subsequent visits.
	• Blood pressure should be monitored at every clinical visit.
	• Management of Hypertension in a client with HIV follows similar treatment protocols as for HIV-negative clients. However:
	  ○ Calcium channel inhibitors should be used with caution as they may interact with PIs producing increased serum levels of the former. Therefore, dose titration and ECG monitoring are required.
	  ○ Caution should also be exercised when combining diuretics with TDF by monitoring renal function that could be impaired due to added risk for interstitial nephritis.
	• A low-dose, enteric-coated aspirin 100 mg/day may be prescribed to reduce the risk of cardiovascular morbidity and mortality. Aspirin initiation should only be initiated by a doctor led service, following careful assessment of risk.
	• Annual symptom screening for diabetes mellitus and random blood sugar testing is recommended for establishing diagnosis of diabetes among PLHIV. Care and management of clients with Diabetes and HIV is described in *Section 10.3*
	• A high prevalence of depression is reported among PLHIV compared to the general population. Clients should be screened for depression using the PHQ9 assessment tool at initiation and every 6 months thereafter. Clients should be managed appropriately as described in *Section 10.6*
	• All clients should be evaluated for pain at every visit using a validated pain scale.
	• For methods and reporting on pharmacovigilance, refer to *Chapter 5, Section 5.12*

2 HIV PREVENTION

2.1 HIV Combination Prevention Strategies

This chapter reviews the major recommended biomedical HIV prevention approaches in Eswatini. Preventing new HIV infections is critical to controlling the HIV epidemic in Eswatini. Combination HIV prevention is an approach that seeks to achieve maximum impact on preventing new HIV infections by combining biomedical, socio-behavioural, and structural interventions that are human-rights based and evidence informed and should be offered to all sexually active individuals, including adolescents. All clients testing HIV-negative should be linked to combination HIV prevention services. Eswatini's Combination Prevention package will be offered in line with the National HIV Prevention Core Package.

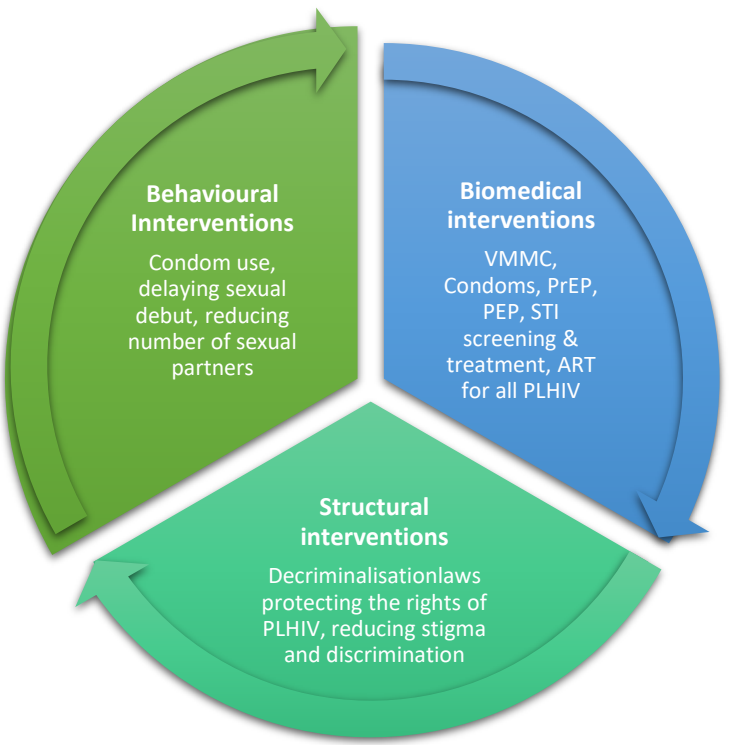


Figure 2.1 HIV Combination Prevention Strategies

Other biomedical interventions that reduce HIV risk practices and/or the probability of HIV transmission per contact include the following: VMMC, Condoms, PrEP, PEP, STI screening & treatment, ART for all PLHIV

2.2 Condoms

Consistent and correct use of condoms reduces sexual transmission of HIV, and other STIs by up to 94%, and prevents unwanted pregnancies. Male and female condoms should be available at all health facilities and in communities. To encourage correct and consistent condom use, at every visit, knowledge and skills in condom use should be assessed regardless of if the client is sexually active or not. Condom provision should be stigma-free and non-judgemental.

Table 2.1 Recommendations for Consistent and Correct Use of Condoms

Priority Groups	Key actions
Heterosexuals who engage in anal sex	▪ Counsel and demonstrate correct and consistent condom use ▪ Provide adequate condoms ▪ Provide condom-compatible lubricants to MSM and individuals practising anal sex. ▪ Provide information and counselling on HIV prevention for all, including adolescents
Men who have sex with men	
Transgender people	
Sex workers and clients of sex workers	
Sero-different couples (Specific counselling for couples who are trying to conceive, please refer to *Chapter 8, Section 8.2.1*)	
Adolescents (sexually active or not)	
Pregnant and breastfeeding women	

At every visit, assess knowledge and skill of condom use in all population (sexually active or not) to ensure correct and consistent condom use.

2.3 Sexually Transmitted Infections

There is substantial scientific evidence demonstrating that the presence of STIs increases the likelihood of both transmitting and acquiring HIV. Early detection and treatment of STIs is an effective tool in combination prevention strategy of HIV, particularly in priority populations at risk of risky sexual behaviour e.g., adolescents married people and key populations. Integration of STI screening, testing and treatment services into HIV programs is key to effective implementation. The treatment of STIs is the same for HIV-negative and HIV-positive individuals. For the treatment of common STIs in Eswatini, use Eswatini STI guidelines. All HIV-negative clients diagnosed with STIs should be offered HIV prevention interventions including PrEP, contraceptives, and VMMC as appropriate.

2.4 Voluntary Medical Male Circumcision

Medical male circumcision should be offered to all men/boys 10 years and older, especially those who are HIV-negative.

Early infant male circumcision

Early infant male circumcision (EIMC) is recommended for all male infants and can be done immediately after birth up to 60 days after birth

Early infant male circumcision (EIMC) is promoted during antenatal care (ANC) and is offered in labour and post-delivery. Preferably, EIMC should occur within the first 60 days of life (8 weeks). Refer to a trained healthcare worker (HCW) for the procedure. For those who are not circumcised within 60 days, continue to offer male circumcision for infants during the scheduled Expanded Programme on Immunization (EPI) visits.

Voluntary medical male circumcision

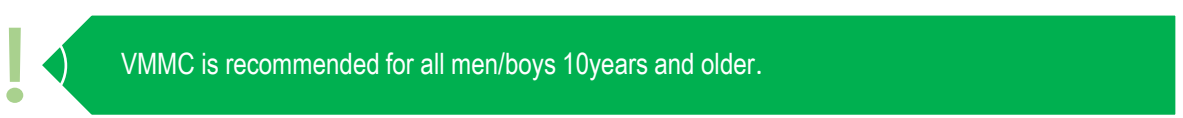
Voluntary medical male circumcision (VMMC) in Eswatini is provided by trained HCWs at health facilities or during outreach programs to adolescent and adult males. The surgical and device-based procedure can be performed by trained nurses or doctors following adequate IPC measures including proper disinfection and sterilisation procedures for reusable equipment. For male circumcision for HIV prevention, Eswatini only allows the use of the dorsal slit method for all surgical and Shang Ring for device-based procedures. Priority groups include men/boys aged 10–49 and all sexually active men. While the conduct of MCs to males aged 15 years and older is recommended in other settings, the national program desires to provide VMMC services to adolescents between the age of 10- and 14 years using a device-based method while maintaining the safety of the procedure and paying attention to the boys' capacity to provide informed consent.

To mitigate serious Adverse Events (AE) amongst adolescents with immature genitalia health care workers are encouraged to take note and evaluate the physical maturity of under 15 adolescent boys and defer the service until the penis is mature or offer a device-based circumcision.

Health care workers serving adolescent boys shall:

- Have the technical competence to provide adolescent-friendly health services and to protect and fulfil adolescents' rights to information, privacy, confidentiality, non-discrimination, non-judgmental attitudes and respect.
- Receive training on assessing adolescents' capacity to consent and how to engage parents in the informed consent process; age-specific developmental considerations and physical conditions, including those that require deferral or referral; and age-appropriate approaches to accurate and comprehensive HIV and sexuality education and counselling.
- Be able to assure a meaningful, age-appropriate, comprehensible informed consent process for every client capable of giving consent and how to advise and assist those who cannot yet give consent.

VMMC service provision should be seen as an opportunity to address the sexual health needs of men; such services should actively counsel and promote safer sexual behaviour. Messaging should be targeted to reach both men and women.



The VMMC package includes the following HIV prevention messages:

- Benefits of VMMC
- Emphasize correct and consistent use of condoms (dual protection).
- HIV testing services (HTS) and, if positive, linkages to care and treatment services. Males testing negative should be linked to other HIV prevention services.
- Promotion of safe sex practices and risk reduction counselling
- Prevention screening and treatment for STIs and, if positive, referrals to STI treatment and PrEP
- Post medical male circumcision care. HCWs and health facilities should routinely screen and refer men for VMMC

HCWs should educate women on the benefits of male circumcision so that they may encourage their partners to circumcise.

Demand generation should be implemented using a person-centred approach. It should be done to maximize uptake of VMMC and other prevention interventions, specifically among adult men and particularly those who may be at higher risk of HIV infection, such as those with multiple sexual partners, partners of sex workers, migrant populations, truck drivers, and men attending STI clinics. These and other priority populations identified by the national AIDS program shall be specifically targeted for services. Intra-facility demand generation must be implemented in all VMMC facilities for the service to be offered routinely.

2.5 Pre-exposure Prophylaxis

PrEP is the use of ARVs by HIV-negative people to reduce the probability of HIV acquisition during periods of potential exposure to HIV. PrEP should be offered as an additional prevention choice for people with substantial exposure to HIV infection, as part of a combination prevention approach that includes HTS services, exposure reduction counselling, diagnosis, and treatment of STIs, male and female condoms, lubricants, ART for all HIV-positive people, and VMMC.

Prescribing and refilling PrEP. Initiation: Any doctor or IMAI-trained registered nurse, who is also trained on PrEP (NARTIS training is not a pre-requisite.) Refill: Any doctor or IMAI-trained registered nurse or nursing assistant, who is also trained on PrEP

Priority and Key Populations for PrEP

HIV-negative individuals with substantial exposure to HIV that are requesting PrEP or are identified by a healthcare worker through an HIV-exposure assessment should be offered PrEP (please refer to *Annex 11.21* for the HIV testing screening tool).

Priority Populations that may benefit most from PrEP include:

- Sero-different couples
- Adolescent girls and young women (aged 16 - 24)
- Pregnant and lactating women
- Clients with STIs
- MSM
- Transgender (TG)
- Sex workers
- Men 20-34 years

Types of PrEP

There are different PrEP methods available in Eswatini. These guidelines will focus on oral TDF-based daily/ event-driven (ED) PrEP and the monthly Dapivirine ring, hereafter referred to as the "PrEP ring" as they are the only two methods currently recommended by the WHO for PrEP and available or expected to become available soon in Eswatini. Other methods are being developed, tested, and reviewed and guidance on other approved forms of PrEP, including long-acting 2-monthly Cabotegravir injections (CAB-LA), will be made available as appropriate.

Eligibility criteria for PrEP

Any PrEP method	• HIV-negative test on the day of PrEP initiation as per national Guidelines. • Absence of symptoms indicating acute HIV infection (AHI) in combination with exposure to HIV in the previous 14 days • No recent exposure within 72 hours to HIV indicates the need for PEP • Age ≥ 16 years, unless the client is a mature minor ≥ 12 years old • Client willingness to attend scheduled PrEP visits
Oral PrEP only	• No contra-indication for TDF + 3TC (oral PrEP users only) • Bodyweight ≥ 30 kg
Dapivirine ring only	• No contra-indication for Dapivirine

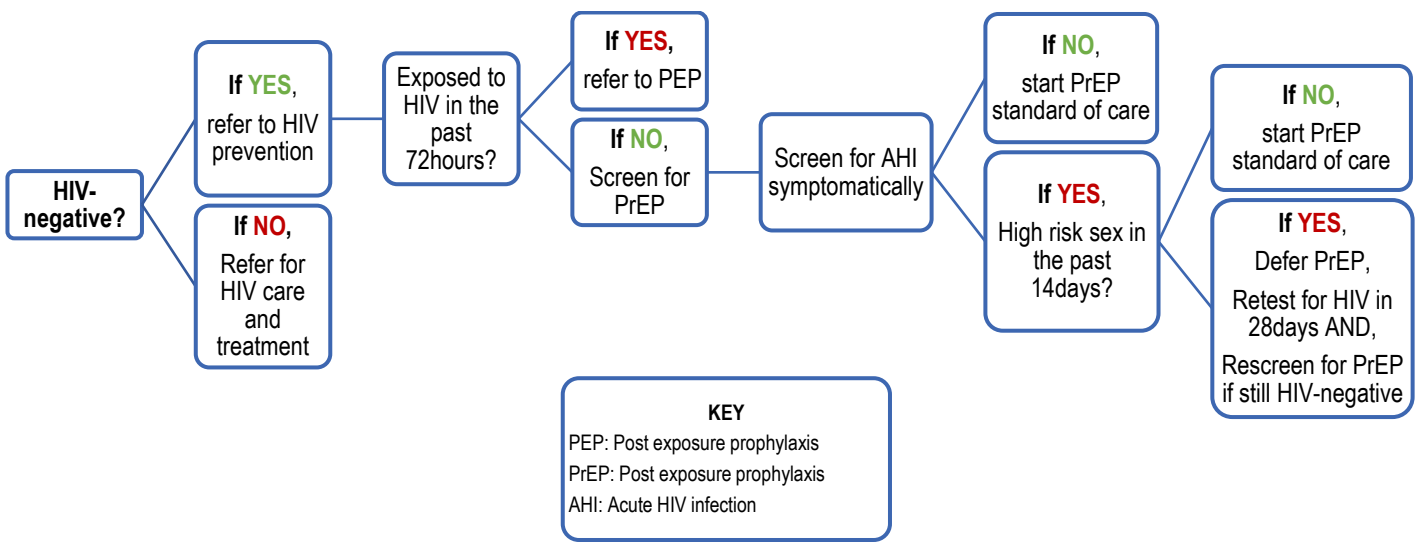


Figure 2.2 Flowchart for PrEP (oral PrEP or the ring) initiation- HIV Exposure and acute HIV infection (AHI) assessment

Table 2.2 Contradictions to oral pre-exposure prophylaxis

Any PrEP method	• Individuals with an HIV-positive test result using the national HIV testing algorithm. • Known exposure to HIV in the past 72 hours (offer PEP) • Signs of acute HIV Infection (e.g., flu-like symptoms, sore throat, lymphadenopathy, fever, skin rash) AND a recent exposure in the past 14 days; ○ if acute HIV infection is suspected, defer PrEP for 4 weeks and re-test the client. • Known creatinine clearance <60 mL/min. • Inability to commit to adhere to PrEP and to attend scheduled PrEP visits for repeat HIV testing and medication pick up.
Oral PrEP only	• Body weight <30 kg. • Age <16 years except for mature minors (adolescents 12-16) that are already sexually active.
Dapivirine ring only	• Allergy or hypersensitivity to the active substance or other substances listed in the product information sheet.

2.5.1 Oral PrEP

Recommended ARVs for Oral PrEP

In Eswatini, the recommended ARVs for oral PrEP are tenofovir (TDF) 300mg/ lamivudine (3TC) 300mg as a fixed-dose combination. Although not widely available, TDF 300 mg/ emtricitabine (FTC) 200 mg can be used instead.

Effectiveness of oral PrEP

The level of effectiveness provided by PrEP is strongly correlated with proper adherence, meaning it is important for clients to use PrEP methods as prescribed. When used as directed, daily PrEP can reduce the likelihood of HIV acquisition through sexual transmission by more than 90%. Like daily oral PrEP, ED-PrEP can reduce the likelihood of HIV acquisition through sexual transmission among people assigned male at birth (AMAB) who are not using oestradiol exogenous hormones by more than 90% when taken as prescribed.

Side effects of oral PrEP

TDF-based oral PrEP is safe regardless if taken daily or as event-driven PrEP (ED-PrEP). The major toxicities associated with TDF + (FTC or 3TC) are rare in PrEP exposure to date. Minor side effects (e.g., nausea, abdominal cramps, headaches) are relatively common (approximately 1 in 10 individuals in the first 1–2 months) but are mild and self-limiting if they do occur. Side effects should be anticipated and often do not require discontinuation of PrEP Elevated creatinine clearance happens but is a rare occurrence. Refer to the national PrEP Implementation Guidance on how to monitor and manage evaluated TDF-induced reduction in creatinine clearance. Refer to *Annex 0* for potential ARV interactions with other drugs.

Oral PrEP and other drug interactions

ARV drugs used for oral PrEP do not have any known interactions with contraceptive hormones and do not affect levels of gender-affirming hormones used by transgender individuals. There is some indication that the use of oestradiol-based exogenous hormones may reduce oral PrEP drug levels in people assigned male at birth (AMAB). Therefore, people AMAB who use exogenous hormones should not take ED-PrEP but can safely use oral daily PrEP.

There are no known interactions between oral PrEP medications and alcohol or recreational drugs. However, if a client or potential client thinks that their use of alcohol or other substances is interfering or may interfere with taking oral PrEP as directed, the PrEP provider should discuss and support behaviour change and offer additional prevention options, including condoms and condom-compatible lubricant.

Oral PrEP Use

Oral PrEP may be offered as a daily regimen or as an ED. ED-PrEP may be appropriate for people AMAB who are not using oestradiol-based exogenous hormones who find it more convenient, have infrequent sex (for example, fewer than two times per week on average), and can plan for sex at least two hours in advance, or who can delay sex for at least two hours. People AMAB eligible for ED-PrEP should have an option to decide which regimen works for them and be supported to switch between daily and ED-PrEP to effectively prevent HIV. For everyone else, including those using oral PrEP to prevent HIV from nonsexual exposures, only a daily regimen may be offered. Details on starting and stopping oral PrEP for different populations are in *Table 2.*3 below.

Recommended ARV Regimen for event-driven oral Pre-exposure Prophylaxis

TDF/3TC 300/300 mg or TDF/FTC 300/200mg by mouth.

Dose 1: 2 tablets 2 to 24 hours before sex.

Dose 2: 1 tablet 24 hours after the first dose

Dose 3: 1 tablet 24 hours after the 2nd dose.

ED-PrEP can be started 2 to 24 hours before having sex and need to be continued for 48 hours after sex. If more sex acts take place, PrEP can be continued daily as long as the sexual risk continues until 2 days after the last sexual act.

Table 2.3 Starting and stopping oral PrEP

Population (s)		Starting Oral PrEP	Stopping[1] Oral PrEP
People assigned males at birth using PrEP to prevent HIV acquisition during sex who are not using oestradiol-based exogenous hormones	Often includes: -cisgender men -transgender women who are not using oestradiol-based exogenous hormones -non-binary people assigned male at birth who are not using oestradiol-based exogenous hormones	Daily or ED: Take a double dose two to 24 hours before potential sexual exposure. Ideally, this loading dose should be taken closer to 24 hours before potential exposure.	Daily or ED: Take a single dose daily for two days after the last potential exposure.

Table 2.3 Starting and stopping oral PrEP (continue from the previous page)

Population (s)		Starting Oral PrEP	Stopping[1] Oral PrEP
People using oral PrEP to prevent HIV acquisition from nonsexual exposures People assigned females at birth People assigned males at birth who are using oestradiol-based exogenous hormones	Often includes: -anyone who shares injection-related materials -cisgender women -transgender men -non-binary people assigned female at birth -transgender women who are using oestradiol-based exogenous hormones -non-binary people assigned male at birth who are using oestradiol-based exogenous hormones	Take a single dose daily for seven days before potential exposure.	Take a single dose daily for seven days after the last potential exposure

[1]*Procedures for stopping oral PrEP are the same for clients who are discontinuing oral PrEP use indefinitely. Ideally, clients who are discontinuing PrEP use will alert their providers and receive support to use other HIV prevention practices if still needed.*
[2]*Injection drug use is mentioned in this guidance; however, first-line prevention strategies for people who inject drugs (PWID) are needle exchange and/or drug use harm reduction and treatment. There are some preventative effects of daily oral PrEP for this population, and it should be offered as part of a larger prevention package.*

PrEP does NOT eliminate the risk of HIV infection, and it does not prevent STIs or unintended pregnancies. It should, therefore, be offered as part of a combination HIV prevention package that includes condoms..

Additional guidance for event-driven PrEP

Clients AMAB who are not using oestradiol-based exogenous hormones may benefit from providers walking through some scenarios to support their effective use of ED-PrEP, *See Figure 2.3* below.

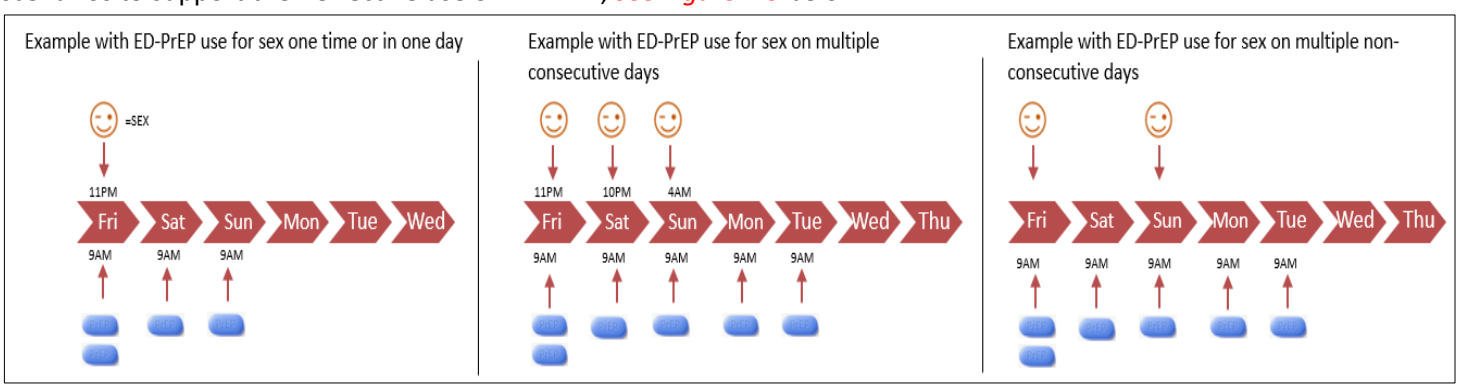


Figure 2.3 How to take Event-Driven PrEP

Switching Between ED-PrEP and Daily PrEP

Males may switch between ED-PrEP and daily PrEP due to changes in relationship status or sex partner(s) or moving to a new location, whereby the frequency and predictability of sex changes, or when a client's preferred dosing option changes.
For clients who are taking ED-PrEP, transitioning to daily dosing may be appropriate if sex becomes more frequent and less predictable. To transition, a client should continue daily dosing after the last exposure. Daily dosing would continue until sex becomes less frequent or more predictable again, or for as long as the client prefers the daily dosing option.

2.5.2 PrEP Dapivirine Vaginal ring

The Dapivirine ring also referred to as the PrEP ring, is an alternative option for women who wish to prevent HIV acquisition through receptive vaginal intercourse and are unable or do not want to take oral PrEP and is part of HIV combination prevention services. The ring has only been studied for the prevention of HIV among those assigned female sex at birth (AFAB) during receptive vaginal sex and the PrEP ring does not prevent HIV acquisition through any other mode of transmission.

2.5.3 Formulation of the PrEP ring

The ring is made of a flexible silicone material containing 25mg of a slow-released Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) called Dapivirine. The ring should be worn continuously in the vagina for 28 days and then replaced by a new ring. The Dapivirine ring acts locally and systemic absorption is low. The risk of HIV infection is reduced 24 hours after ring insertion

The DPV ring can be self-inserted into the vagina easily and discreetly by female users

2.5.4 PrEP ring effectiveness

The ring was clinically shown to reduce the likelihood of HIV-1 acquisition through vaginal sex in two randomized controlled trials: by 35% in IPM-027/The Ring Study and 27% in MTN-020/ASPIRE. Results from two subsequent open-label extension studies showed increases in ring use, with modelling data suggesting greater risk reduction – by over 50% across both studies – compared to the Phase 3 trials.

Possible side effects of the PrEP ring

Possible side effects related to the ring are typically mild and include urinary tract infections (UTI), vaginal discharge, vulvar itching, and pelvic and lower abdominal pain. These side effects usually occur during the first month of use and resolve without the need to remove the ring. Ring users should be counselled to contact their health care provider if they experience any urinary or reproductive tract changes, as these could be a sign of an STI or UTI needing treatment.

PrEP ring and other drug interactions

There are no known interactions between Dapivirine and contraceptive hormones, hormones used for gender-affirming hormone therapy, alcohol, or recreational drugs. However, if a client or potential client thinks that their use of alcohol or other substances is interfering or may interfere with the effective use of the ring, the provider should discuss and support behaviour change and offer additional prevention options, including condoms and condom-compatible lubricant.

PrEP Ring use

The ring may be offered as an option for people assigned female at birth (AFAB) who wish to prevent HIV acquisition through receptive vaginal sex and are unable or do not want to take oral PrEP, or when oral PrEP is not available. The ring must be self-inserted correctly into the vagina and worn for one month without removal for maximal protection. The ring must be in place for at least 24 hours before it is maximally effective. If a client wishes to discontinue the use of the ring, they can self-remove it. If the ring is temporarily removed (which is not recommended), it will be 24 hours again before reaching its maximal effect. Ideally, clients who are discontinuing PrEP use will alert their providers and receive support to use other HIV prevention practices if still needed.

Switching Between the PrEP Ring and Oral PrEP

- Clients may switch between the ring and oral PrEP
- Safety data on the simultaneous use of oral PrEP and the ring are limited. Although the use of both products is not likely to be less well-tolerated than when the drugs are used individually, more data are needed to confirm the safety and efficacy of simultaneous use of oral PrEP and the ring.
- Some clients may decide to use both the ring and oral daily PrEP at the same time. However, no evidence indicates that using them together will result in any additive advantage. Whatever the choice, adherence is important to optimize the effectiveness of either product. Further, inconsistent use of either or both would be ineffective for HIV prevention.

Stopping and Restarting PrEP Ring Use

- Clients may choose to stop and restart using the ring for several reasons which may include changes in relationship status or sexual practice(s) or moving to a new location where different privacy or access concerns are at play, when deciding to attempt pregnancy, or when a client's preferred HIV prevention option changes.
- Clients who have previously used the ring and decide to reinitiate ring use should go through the same procedures for an initiation visit as outlined below

PrEP Initiation visit

For most clients, PrEP can be initiated on the same days if the client is:

- HIV-negative
- Not indicated for PEP or suspected of having AHI
- Requesting PrEP or identified at substantial exposure to HIV
- Free from contraindications for use of their chosen PrEP method.

The following components are part of the initial PrEP initiation visit:

Table 2.4 components of the PrEP initiation visit

HIV testing and counselling	• If the clients test positive, the client should be initiated on/ referred for ART. • If the test result is inconclusive, defer PrEP and follow the national algorithm until a definite test result has been obtained.
PrEP eligibility screening	• Assess client for PrEP indication. This could be through an HIV exposure assessment or if the client requests PrEP • Assess for contraindications for use of the client's chosen PrEP method
Counselling	• PrEP counselling should be client-driven, based on their needs, resources, and preferences. • Counselling should include counselling on PrEP choice • For more details on counselling topics, refer to the PrEP implementation guidelines.
Screening for PEP eligibility and AHI	• Assess the client for any HIV exposure in the last 72 hours; if yes, consider PEP. • Assess the client for any signs and symptoms of Acute HIV infection.
Additional Laboratory testing*	• Creatinine monitoring at baseline is not required. • Hepatitis B testing is strongly encouraged for oral PrEP users. If negative, offer Hepatitis B vaccination. • Hepatitis C testing should be considered upon PrEP initiation and every 12 months thereafter, especially for MSM, people who inject drugs and people in prisons. Hepatitis C is not a contraindication for oral PrEP.
Screening for STIs*	• Management of STI as per standard treatment guidelines
Pregnancy testing and provision of contraceptives*	• Should be assessed and offered as indicated
Screening for mental health and substance abuse disorders*	• Provide supportive services or referrals as needed
Screening for GBV/IPV*	• Routine enquiry of GBV and first-line support, including referral to GBV services
Other services	• Provision of or referral to VMMC services • Screening for and treatment of non-communicable diseases.
PrEP initiation	• At Initiation, clients should be prescribed a single bottle/ ring and scheduled for a one-month follow-up visit. • The follow-up visit should be scheduled a few days before the pill supply will run out based on daily oral PrEP use or a week before the client should change the ring. • When possible, follow-up visits should be coordinated with visits for other services to reduce the number of times a client must return to receive services.

Follow-up appointments for PrEP users.

- The first follow-up appointment should be 1 month after PrEP initiation. This appointment is important to discuss experiences, possible side effects, effective use and to early identify any missed acute HIV infection upon initiation.
- HIV testing should be performed at every follow-up visit
- Creatinine testing should be done for some clients at the one-month follow-up appointment and as specified in *Table 2.5* below.
- Subsequent follow-up visits should be aligned with any other services provided to the client (e.g., family planning service, antenatal care, etc) or with a maximum duration of three months.

Table 2.5 Assessing and Monitoring Renal Function for Oral PrEP users

Kidney related comorbidities	Age	Initiation/ Baseline	Follow-up visit
No	<30 years	Optional	Optional (until age 30 or if kidney-related comorbidities develop If baseline KFTs are done and CrCL <90ml/min, conduct a follow-up every 6 months
No	30-49 years	Conduct creatinine test at 1 month	If CrCl ≥90ml/min, optional (until age 50 or kidney-related comorbidities develop) If CrCL <90ml/min, screening every 6 months.
Yes	Any age	Conduct creatinine test at 1 month	Screening every 6 months
No	50+		

2.6 Post-Exposure Prophylaxis

All HIV-negative individuals exposed to HIV are eligible for post-exposure prophylaxis (PEP) as prescribed by any registered nurse or doctor.

- Post-exposure prophylaxis (PEP) is the use of ARVs by HIV-negative people after the potential exposure to HIV to prevent infection with HIV.
- All persons potentially exposed to HIV accidentally, occupationally, sexually or otherwise should access PEP as early as 1 hour and within 72 hours to minimise the risk of transmission of HIV.
- All Registered doctors and nurses at any health facility level or community service delivery point can prescribe ARV drugs for PEP for any individual who presents with a history of exposure to HIV in the past 72 hours.
- A three-drug regimen is preferred for PEP.

Recommended ARV Regimen for Post-Exposure Prophylaxis

Adults/Adolescents ≥30kg :

- Tenofovir (TDF)* + Lamivudine (3TC) + Dolutegravir (DTG)
- If DTG is not available or contra-indicated, (ATV/r), DRV/r, LPV/r and RAL may be considered as an alternative 3rd drug option for PEP.

Children 10 years and younger or <30kg:

- Zidovudine (AZT) + 3TC is recommended as the preferred backbone regimen for PEP.
- ABC + 3TC or TDF + 3TC can be considered as alternative regimens.
- DTG is the preferred third drug for PEP in children as per approved dosing schedule.
- If DTG is not available or contraindicated, (ATV/r), DRV/r, LPV/r and RAL may be considered as an alternative 3rd drug option for PEP.

Considerations for Post-Exposure Prophylaxis

In the event of clients presenting after sexual assault, PEP to be initiated by HCW at first contact with client even without police form (RSP88) in all health care facilities or at a community service delivery point.

Table 2.6 Recommendations for Post-Exposure Prophylaxis

Consideration	Recommendation

Assessing Eligibility	• HIV PEP should be offered and initiated as early as possible for all individuals with the exposure that has the potential for HIV transmission, within 72 hours.
	• Eligibility assessment should be based on the HIV status of the source of potential exposure whenever possible and may include consideration of background prevalence and local epidemiological patterns.
	• The following types of exposure may warrant PEP:
	  ○ Body fluids: blood, blood-stained saliva, breast milk, genital secretions, cerebrospinal, amniotic, peritoneal, synovial, pericardial, or pleural fluids.
	  ○ Types of exposure: Mucous membrane from sexual exposure, splashes to the eye, nose or oral cavity and parenteral exposures.
	  ○ All clients should be assessed, and PEP should be offered to any client with any of the exposures as indicated above.
	• The exposure that does not require PEP includes:
	  ○ When the exposed individual is already HIV positive
	  ○ When the source of potential exposure is established to be HIV-negative unless the source has had an HIV exposure in the last 14 days and could be in the window period.
	  ○ Exposure to body fluids that do not pose a significant risk: tears, non-blood-stained saliva, urine and sweat.

Table 2.6 Recommendations for Post-Exposure Prophylaxis (continued from the previous page)

Consideration	Recommendation

Management at initial contact	• Counsel on risks and benefits of PEP and obtain verbal consent/assent for HIV testing.
	• HTS for both exposed and source individuals (where possible and applicable).
	• Offer PEP as soon as HIV risk exposure is established (as early as possible and within 72 hours) and if the exposed individual tests HIV-negative at baseline (if HIV testing is not available, HCWs can provide 1–2 days of PEP to cover the days until the HIV test can be performed).
	• If available, test women of childbearing age for pregnancy.
	  ○ Offer emergency contraception for all adolescent girls and women of childbearing potential.
	  ○ Copper IUCD fitted up to 5 days after unprotected sex
	  ○ Levonorgestrel 1.5mg po stat or 0.75mg taken 12hrs apart
	• Oral contraceptive pills 4 tablets taken 12hrs apart (Microgynon/ Ovral/ Lofeminal/)
	• Refer to a social worker or psychologist where applicable
	• No specific laboratory tests are needed except:
	  ○ Creatinine (if TDF-containing regimen and diabetic or hypertensive) and
	  ○ Haemoglobin (if AZT-containing regimen and suspect clinical anaemia)
	• Assessment of hepatitis B infection status is crucial but should not be a precondition for offering HIV PEP.
	• If the client is Hepatitis B positive, manage according to the Hepatitis B treatment algorithm (*see Annex 11.10*)
	• If negative and not fully vaccinated: Give Hepatitis B immunoglobulin within 7 days post-exposure then Hepatitis B vaccination on Day 0 (different injection site), 1 month and 2 months. For unvaccinated children <5 years, consult a paediatrician.

Time of initiation	• Initiate PEP preferably within the first hour or as soon as possible after exposure, but no later than after 72 hours. • If more than 72 hours: Conduct HTS and then repeat HTS after 8 weeks, but do not initiate ART for PEP. If confirmed HIV-positive, the client should be referred to care and treatment.
Duration of PEP	• The daily dose for 28 days (dispense all 28 days of treatment at the first visit).
Follow-up visits and counselling	• Follow-up with the client at 7 days and 28 days after starting PEP. As per the client's preference, a 7-day follow-up could be done telephonically. • At F/U visit, assess and manage side effects, provide adherence counselling and support, discuss HIV reduction, refer for trauma and mental health counselling if applicable, social support and safety and safe sex practices. • Provide results to any lab-related tests • For Hepatitis B positive clients, assess the need for ongoing Hepatitis B therapy. • Provide follow-up HIV testing 8 weeks after exposure. For HTS guidelines, see *chapter 3.*

Table 2.6 Recommendations for Post-Exposure Prophylaxis (continued from the previous page)

Consideration	Recommendation
Follow-up visits and counselling	• Offer PrEP to clients with a high likelihood of ongoing exposure to HIV. If the HIV test is negative upon completion of 28 days with PEP, the transition to PrEP can be made without a gap. • Adherence counselling, HIV risk reduction, trauma and mental health counselling, social support and safety, and safe sex practices
Other services for sexual assault and alleged sexual assault 	• Special consideration for survivors of sexual assault, particularly adolescents and children: offer supportive counselling as they are most likely to default on treatment • Offer STI prophylactic treatment for all (treat for vaginal/urethral discharge syndrome following the national STI algorithms); see National STI Algorithm for more information. • STI management and Hepatitis-B screening for penetrative cases is strongly recommended. • Alleged perpetrators are eligible for and should receive PEP services in situations of possible exposure. • Offer emergency contraception for non-pregnant women not on any contraceptive method or women not compliant/adherent to contraceptive dosing. • Document clinical evidence of assault and alleged assault and collect forensic evidence for medical-legal purposes. • Refer to the Health Sector Response to GBV - clinical management guidelines for additional details on post-rape care.
Repeat PEP users	• For clients who repeatedly use PEP or clients indicating the likelihood of future potential exposure to HIV, pre-exposure prophylaxis (PrEP) should be discussed as an option.

2.6.1 ART for People living with HIV

ARV drugs play a key role in HIV prevention. Treating PLHIV with ART is one of the effective strategies for preventing new HIV infections as PLHIV who achieve and maintain an undetectable viral load-the amount of HIV in the blood—by taking ART daily as prescribed cannot sexually transmit the virus to others. All people living with HIV are eligible to start ART regardless of CD4 count or WHO staging and HCWs should promote early ART initiation.

UNDETECTABLE = UNTRANSMITTABLE (U=U)

When the viral load falls below 200 copies/ml, the protective effect of ART for preventing new infections approaches 100%.
People taking ARVs who **achieve and maintain** undetectable viral load have close to zero chances of transmitting HIV to their sexual partners.

The U=U message has the potential to reduce stigma towards people living with HIV, increase demand for HIV testing and ART and improve adherence and this message should be well integrated in all prevention, care, and treatment programs.

3 HIV TESTING SERVICES

HIV testing services (HTS) is a critical entry point to HIV prevention, care and treatment services. All clients who receive HIV testing should be provided with their results. Based on the test result, the client should be linked to support, prevention and treatment services. It is ideal that clients receive a same-day diagnosis, as well as same-day linkages to prevention or treatment services.

Guiding Principles of HIV Testing Services

The overarching guiding principle for HIV Testing Services (HTS) in the setting of a changing HIV epidemic is to create and harness an enabling environment that promotes the implementation of a human rights-based, client-centred and micro-targeted HIV Testing services program. The national program, key stakeholders and service providers must ensure that the key principles are upheld at all times. The key principles include;

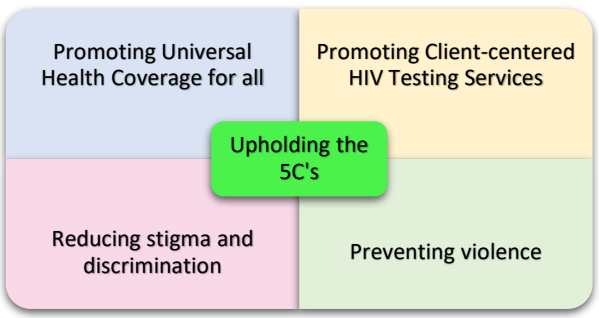


Figure 3.1 Summary Guiding Principles for HIV Testing services

Promoting universal health coverage, gender equality and health rights for all.

All HTS-related services (including index testing, HIV self-testing, HIV recency testing etc) are voluntary. No service provider, national HIV program staff (or their representatives) should coerce an individual to undertake these services.

The national HIV program, key stakeholders and service providers should strive to ensure equitable access to HTS to all eligible individuals regardless of sexual orientation, age, race, religious beliefs and nationality, at all times. Equitable access includes providing testing even if a client didn't screen as high risk and if the client requests an HIV test

Promoting client-centred HTS services

HTS services must be planned and designed with the client's needs and considerations in mind. Planners must consider the client's convenience, privacy, safety, socio-cultural environment and cost of HTS to ensure wide acceptability and uptake of services.

Reducing stigma and discrimination

All key players must strive to create an environment where the stigma associated with HIV testing and discrimination resulting from a positive HIV diagnosis is uprooted and stifled. All efforts must be made through multi-sectoral engagement, including the involvement of the key community structures to stamp out the stigma and discrimination associated with HTS.

Preventing violence

The safety of individuals seeking and undergoing HTS in various settings should be prioritized during the design, execution and monitoring of HTS. Stakeholders must ensure availability and implementation with fidelity, of culturally appropriate and sensitive tools to screen for risk of violence among individuals undergoing HTS. Systems to rapidly identify, respond and stabilise those that have suffered from violence as a result of undergoing HTS should be in place at all HIV testing service points. The 5 Cs are essential guiding principles to ensure a human rights-based approach in HTS. These principles are **C**onsent, **C**onfidentiality, **C**ounselling, **C**orrect test results and **C**onnection to HIV prevention, treatment and care.

Table 3.1 Upholding The 5Cs

Guiding Principles	Key Points
Informed Consent/Assent	∞ PIHTS: An opt-out approach is used where HTS is offered by a HCW and consent is assumed unless the client explicitly declines the HIV test. ∞ CIHTS: Clients requesting HTS and verbal consent/assent is obtained to conduct the HIV screening tool or test. ∞ Recency HIV Testing: A written consent is required for all clients eligible for HIV recency testing. ∞ HIVST: A verbal consent for HIVST is obtained for individuals 16years and older; a verbal assent by a legal guardian is obtained for a minor eligible for Paediatric Oral Fluid HIVST
Confidentiality	∞ Testing results and any discussions between the HTS provider and the client should not be disclosed to anyone without the expressed consent/assent of the person being tested. ∞ Shared confidentiality among HCWs to promote linkages and further client management should be explained to the client. ∞ Privacy during testing and counselling should be ensured
Counselling (pre and post-test)	∞ Accompany testing with appropriate, brief and high-quality pre-test information and post-test counselling. ∞ Messages should be tailored to the client's needs and focused on encouraging notification/disclosure of HIV status to sexual partners and family members or trusted others, where beneficial. ∞ Post-test counselling should also include messages designed to facilitate linkages to prevention and treatment services following HIV testing.
Correct test results	∞ Perform rapid HIV testing according to the relevant national testing algorithm including confirmation of all reactive self-test results. ∞ Adhere to national quality assurance standards to ensure correct and accurate results are given to the client. ∞ Re-test all people with an HIV-positive diagnosis using the full national rapid HIV testing algorithm before ART initiation.
Connections and linkages to prevention, care and treatment	∞ Refer and actively link all clients to appropriate HIV prevention, treatment, and other support services, according to their results.

3.1 HIV Testing Approaches

HIV testing services (HTS) are a critical entry point to HIV prevention, care and treatment services.

3.2 HIV testing service delivery approaches

HIV testing services should be offered to all clients with unknown HIV status at every point of contact in health facilities and community settings

3.2.1 Targeted testing

Targeted testing is intended to reach high-risk populations typically defined based on behaviour or clinical characteristics and includes priority groups such as:

- Men
- Children and adolescents (ages 0 - 19) and young women (15 – 29)
- Key populations

Targeted testing can be done in 2 primary approaches—PIHTS and CIHTS. These approaches can be done at the facility level and the community level.

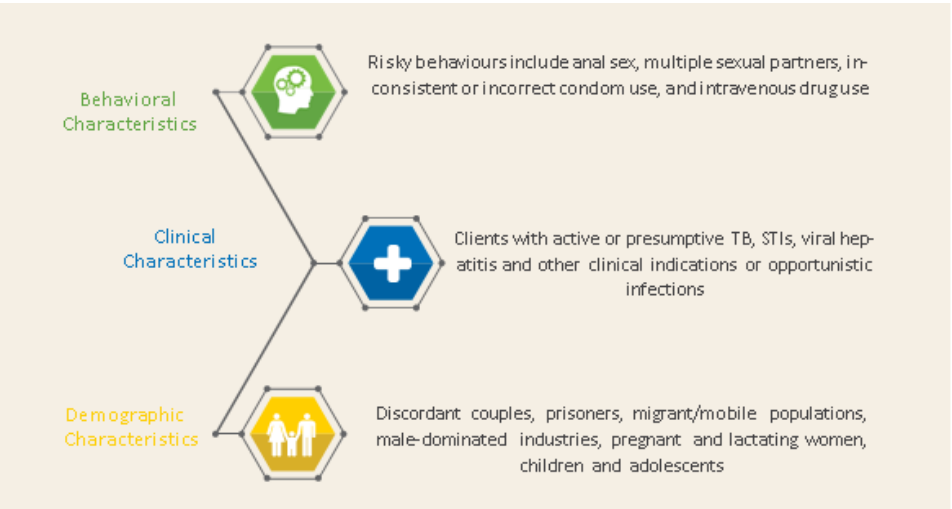


Figure 3.2 Targeted Testing

Facility-based HIV testing services

Facility-based HIV testing services encompass testing in a health facility or laboratory setting. Facility-based HIV testing services can be provided at stand-alone HIV testing services sites (often referred to as voluntary counselling and testing sites) or routinely offered at clinical sites (often referred to as provider-initiated testing and counselling).

Three strategies of selection may be implemented under facility testing

1. Diagnostic testing is the testing of individuals who present with signs or symptoms suggestive of HIV, including signs or symptoms of TB.
2. Targeted testing is the testing of subpopulations of increased risk as identified by behavioural, clinical, or demographic characteristics, or a combination of these such as MSM, FSW, individuals receiving STI care and treatment, or persons residing in high burden areas.
3. Universal/Routine testing is the testing of individuals presenting for medical attention regardless of presenting complaint. All people presenting for care in the following settings are considered at risk and should be tested for HIV: Antenatal and Postnatal Care Clinics, Family planning clinics, TB and STI clinics, malnutrition clinics (for children), and hospitalized patients, including children in inpatient wards and those requesting HIV testing.

Recommendation for universal/routine HTS

Sexual Partners / biological children of persons living with HIV including peers or social networks (index testing and social network testing)

- People with sexually transmitted infections confirmed or presumptive TB disease, or viral hepatitis.
- People with TB symptoms, even before the diagnosis of TB disease:
    - All individuals, including children, should be screened for TB symptoms, and people identified with confirmed or presumptive TB disease should be offered HIV counselling and testing services and linked to TB and HIV testing services if screened positive. This should be considered a dual infection control and case-finding strategy.
- Individuals who have never been tested or have not recently been tested for HIV.
- Persons who present to health facilities with signs and symptoms suggestive of underlying HIV infection, including presumptive and confirmed TB and malnutrition
- Pregnant and lactating women
- Children are known to have been exposed to HIV perinatally or during breastfeeding.
- Members of Key populations

Community-based HIV testing services

Community-based testing refers to HIV testing services offered in the community, outside a health facility. Community-based HIV testing services can be conducted by trained lay providers and peers using rapid diagnostic tests. WHO recommends community-based testing, especially to reach men, key populations and their partners, young people, and other vulnerable populations who may be less likely to be seen or tested in health facilities.

Community based HTS can be delivered in many ways and different settings and venues including:

- HIV testing services at fixed locations in the community, and workplace, including community-based voluntary counselling and testing sites.
- Mobile outreach in hotspots and communities (high recency geographic areas) such as hot spots, street-testing, offering HIV testing in shebeens (bars/taverns) and after-hours testing (moonlighting), churches, workplaces and educational establishments. peoples' homes, usually referred to as home-based HIV testing services offered to eligible members in all households in a certain area (that is, door-to-door) or more focused – for example, in the context of HIV partner services.
- Both index testing services and HIV self-testing (HIVST) are key strategies for targeted community-based testing

All testing sites should follow the master client flow to ensure all clients are screened for eligibility before being tested for HIV. Refer to HIV screening tools for eligibility for HIV testing.

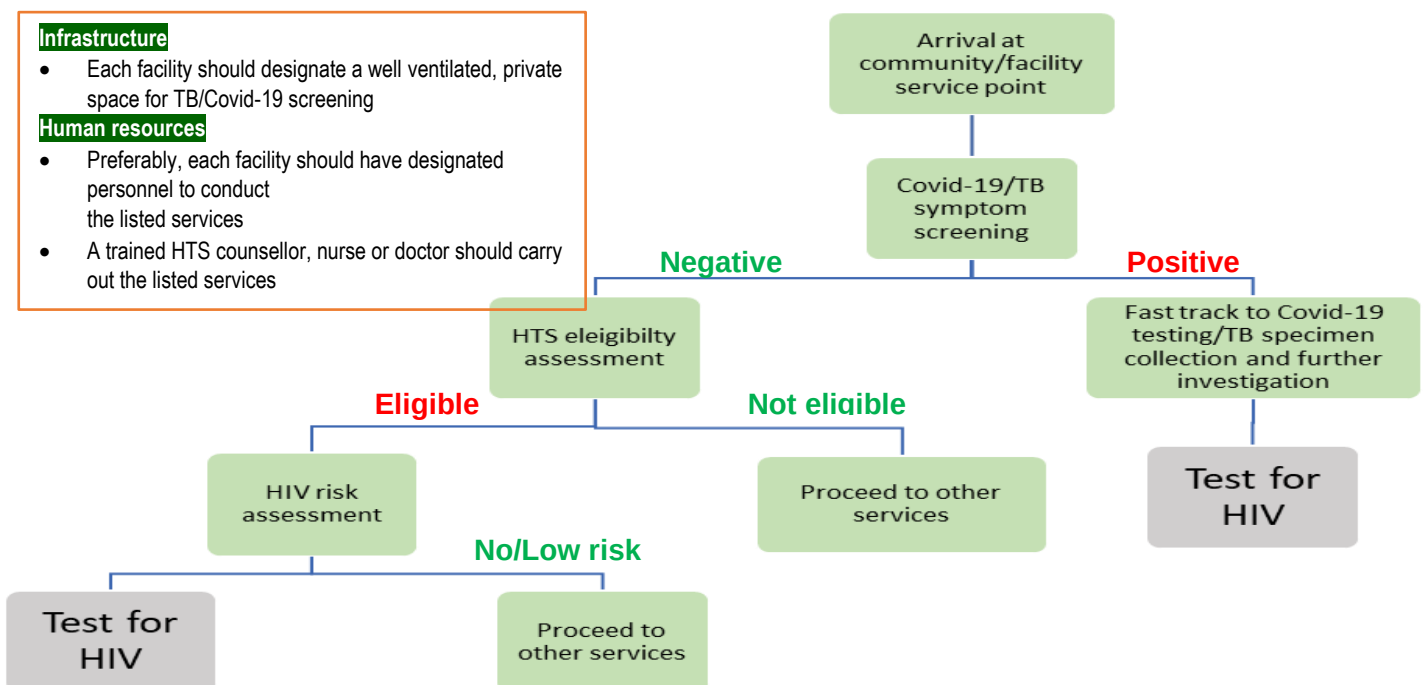


Figure 3.3 Provider Initiated HIV Testing Master Client Flow

3.2.2 HIV Self testing

HIV self-testing (HIVST) is a process in which the client collects his or her specimen and then performs an HIV test and interprets the result by him/herself, either alone or with someone he or she trusts. HIV self-testing does not provide a definitive HIV-positive diagnosis. Any positive HIV result must be confirmed by a HCW following national testing algorithms. HIVST can be initiated by an individual or delivered by a provider in a community or facility-based setting. HIVST can be client-initiated or provider-initiated. The age of consent for HIVST in Eswatini is 16 years. Offering choice in HIV self-testing service delivery options and types of test kits (such as between kits using oral fluid or blood) can help to reach more people.

Table 3.2 HIV self-testing approaches

Approach	Description
Assisted self-testing	Refers to a trained HTS provider giving an individual an in-person demonstration before or during HIVST on how to perform the test and interpret the test result. This approach can be used to support self-testers with disabilities, low literacy levels and individuals who may require or request direct assistance in the form of in-person demonstrations and explanations before, during and/or after testing. Assisted self-testing can be offered to an individual or a group.
Unassisted self-testing	This refers to when an individual self-tests for HIV and uses an HIVST kit without the help of a trained HTS provider and usually in the comfort of their own home.

Many people can perform HIV self-testing correctly with minimal or no support; however, some may need and want support, and it should be made available. This can include video instructions, virtual support or in-person demonstration or training. Providing a range of support options is important, if feasible. Support tools and packages should be adapted to address the local context, population needs and community preferences as well as considering available resources.

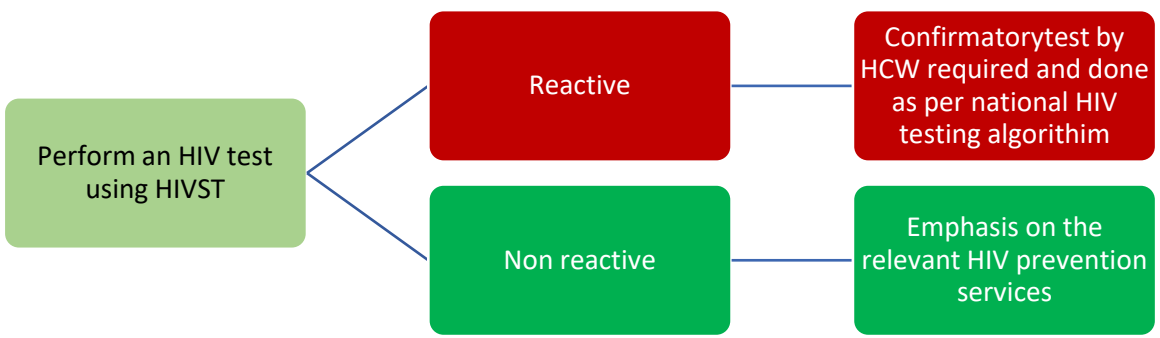


Figure 3.4 HIV self-testing flow chart

HIVST delivery models

Table 3.3 HIV self-testing service delivery models

Models	Description
Community-based	Distribution during campaigns, at events, mobile outreach or home-based (door-to-door) distribution. Integration with existing community-based testing programs can improve efficiency and optimize resources. Community-led models are likely to be successful.
Facility-based	Distribution from facilities or other fixed sites for use later or within the facilities. Kits can be given to HIV-positive or HIV-negative clients for secondary distribution.
Order online and receive via mail	A range of online platforms such as websites, social media, dating apps, and other digital media can be used. HIV self-testing kits can be provided for free, at a cost or with coupons/vouchers for a reduced cost.
Secondary distribution	Includes secondary distribution to partners or peers including distribution by HIV-negative and HIV-positive clients. Index clients can be given HIV self-testing kits by providers of facilities. Index clients can be given HIV self-testing kits by providers of facilities. Index clients can be given (oral-based) HIVST for testing of their biological child(ren) with unknown HIV status and non-biological children with exposure history and unknown status
Private pharmacies	Distribution from pharmacies for clients who may need testing through public-private partnerships and distribution
Retail outlets, and vending machines	Kits are typically provided at a cost to users but the price can be reduced through public-private partnerships and the distribution of coupons or vouchers.
Faith-best settings	Distribution from faith-based settings such as churches and mosques.
Workplace	Distribution to workers for testing themselves and/or for their partners. Consider sustainable models such as public-private partnerships and/or insurance packages to cover the cost.

Oral Based HIV Testing

Oral-based HIV testing may be administered to children aged 2 to 15 years who are:

- biological children of an HIV positive adult index case
- non-biological children living in the same household as the adult index parent/guardian where the child has a history of HIV exposure (i.e., the child's biological mother is HIV-positive, deceased, or whose HIV status is unknown) known to have an HIV positive sibling in the same household
- Parents or legal guardians eligible to receive HIVST kits for their children for oral-based testing are:
- All adults living with HIV (i.e., new positives or previously diagnosed on treatment) with eligible children
- HIV-positive men report that the child's biological mother is HIV-positive, deceased, or whose HIV status is unknown.
- The legal guardian of eligible children.

3.2.3 Partner Notification Services/ Index testing services

Partner notification and index testing services include:

- partner notification
- contact tracing
- index contact testing and family-based index case testing
- social network–based approaches.

All partner notification services should be voluntary. Whenever partner notification services and social network–based approaches are offered, the client should be informed of their benefits and potential risks and assured that their decisions about contacting partners and other people from their social networks are voluntary and not pressured. All index testing services must adhere to WHO's 5Cs minimum standards (consent, counselling, confidentiality, correct test results, and connection to appropriate HIV prevention and treatment services

Partner notification approaches (methods)

1. *Passive partner notification methods:*

Passive referral or client referral refers to when HIV-positive clients are encouraged by a trained provider to disclose their status to their sexual and drug injecting partners by themselves and to also suggest HIV testing to the partner(s), given their potential exposure to HIV infection.

2. *Assisted partner notification methods*:

I. **Provider:** Using the opt-out approach, a trained provider agrees with the HIV-positive client that they (the Health provider) will confidentially contact the HIV-positive client's partner(s) directly and offer the partner voluntary HTS**.**
Provider-assisted partner notification is the preferred method and should be prioritized.

II. **Contract:** When an HIV-positive client enters a contract with a trained provider to refer their partners to HTS within an agreed period (14 days) after which the provider contacts the partners (with the client's permission) directly and offers voluntary HTS.

III. **Dual:** When a trained provider accompanies an HIV-positive client when they disclose their HIV status to their partner(s). The provider also offers voluntary HTS to the partners.

IV. **Client referral:** when a trained provider requests the client to disclose their HIV status to their partner(s).

Care is needed to ensure the correct person is receiving the message, and that the anonymity/confidentiality of both the HIV-positive client and the notified partner is maintained. Couples and partners should be offered voluntary HTS with support for mutual disclosure to their possible contacts that may also have HIV.

Assisted notification is always voluntary and methods may include:

- face-to-face conversations by the index clients
- invitation slips from the facility
- phone calls, text messages from the facility

Ten Recommended steps for partner notification/index testing including children

(for more details refer to index testing SOPS)

1. Introduce the concept of index testing during the Pre-test session or PMTCT/ART visit
2. Offer index testing as a voluntary service to all clients testing HIV-Positive or with high viral load
3. If the client accepts participation, obtain consent to inquire about their partner(s) and biologic child(ren)
4. Obtain a list of sex and needle-sharing partners and biological children<19 years
5. Conduct intimate partner violence (IPV) risk assessment for each named partner.
6. Determine the preferred method of partner notification or child testing for each named partner/child
7. Contact all named partners and biological children<19 years with unknown status using the preferred notification approach
8. Record outcomes of partner notification and testing and family testing
9. Provide appropriate services for children and partner(s) based on HIV status
10. Follow-up with the client to assess for any adverse events associated with index testing.

Contact tracing

Contact tracing is the process of attempting to identify and reach partners, biological children and social networks of someone diagnosed with HIV to offer them HTS.

Index HIV testing

Index testing is a focused approach to HIV testing in which the household, family members (including children and adolescents) and sexual partners of people diagnosed with HIV (including those on ART) are offered and receive HIV testing services.

Social network-based HIV testing

A social network-based approach to HIV testing is an approach in which HIV testing services are offered to sexual partners or needle-sharing contacts as well as peers within the social network of key populations that have tested HIV-positive due to their increased probability of also being HIV positive.

Please refer to retesting guidance for contacts who are not first-time testers.

Please refer to the latest index testing Standard Operating Procedure (SOP) for detailed information on partner notification services.

Intimate Partner Violence (IPV) Screening *(See Section 3.3 below*) should be conducted on all patients offered partner notification services to assist in the choice of the most appropriate partner notification methods. People at risk of IPV should not be offered provider referral as a partner notification method.

For more information on safe ethical index testing, refer to:
https://www.pepfarsolutions.org/resourcesandtools-2/2020/7/10/pepfar-guidance-on-implementing-safe-and-ethical-index-testing-services

3.3 Intimate partner violence screening tool

IPV screening tool

SCREEN FOR PROBABLE INDEX TESTING INDUCED HEALTH RISK

NB: Ask the question below for each of the partners listed

"Do you anticipate any violence with partner (current or former) if/ when you disclose your HIV results??"

Yes ☐ No ☐

If patient answer "NO" to the above question:

1. Record the patient as "Not at risk" in the index testing register
2. DO NOT offer provider referral
3. You can offer Client referral, Contract referral and Dual referral depending on the patient preference.

If patient answer "YES" to the above question:

Record the patient as "at risk" in the index testing register

For all patients answering "YES" the counsellor is requested to ask the patients to share his/her limitations about possible violence from the partner or partners (current/ former) using the prompts below.

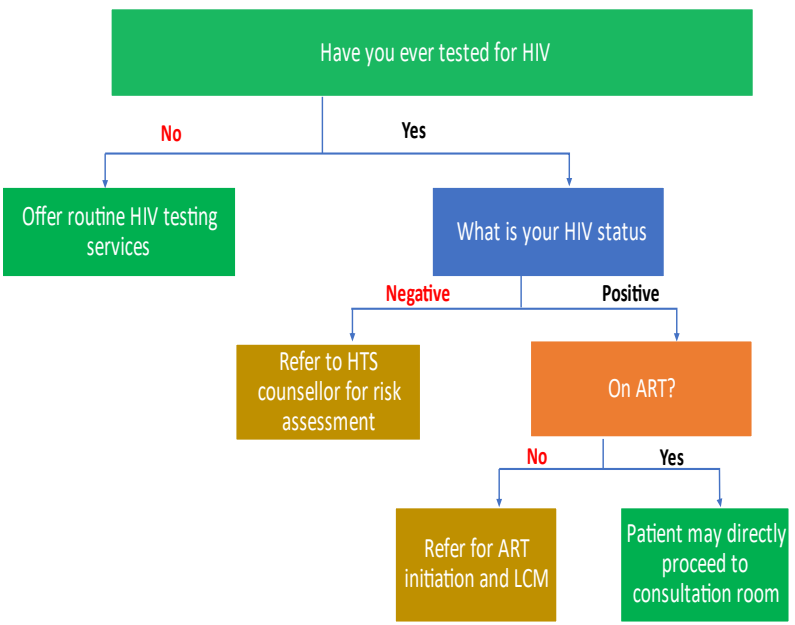
Then depending on the nature of the limitations advise on the most appropriate disclosure strategy such as the use of Provider Referral.

1. **Do you think your partner (current/ former) will physically hurt you or force you to do something sexually that makes you feel uncomfortable if you disclose to him/her or he/she finds out your HIV status?**
2. **Do you think your partner (current/ former) will emotionally hurt you if you disclose to him/her your HIV status or he/she finds out your HIV status?**
3. **Do you fear your partner (current/ former) will abandon you or chase you from the place you live or stop paying/ contributing towards rent/ bond?**
4. **Do you think your partner (current/ former) will stop financially supporting you or your children?**

NOTE: If client appears aggitated, sweaty, restless, crying or irritable during the discussion, stop all questions and refer to Health Provider for further counseling management (debriefing / Psychological First Aid/ Cognitive Behavior Therapy/ Clinical Therapy)

3.4 HIV Screening Tools

In Eswatini, approximately 95% of PLHIV are aware of their HIV status, therefore, targeted HIV testing is recommended to identify the 5% case-finding gap and to improve HIV positivity rates. With the efficient use of HIV screening tools, there should be a decrease in HIV testing volumes. Both community and facility HIV testing settings should apply accelerated efforts to expand the use of HIV eligibility screening tools. However, due to the increased risk of HIV acquisition among some clients and the benefits of preventative services for others, the HIV eligibility screening tools should not be administered among people identified with confirmed or presumptive TB disease, STI clients, index contacts, pregnant and lactating mothers or PrEP clients. Instead, HIV testing remains the standard of care for these clients. The HIV screening tools are in *Figure 3.5 and* ***Error! Reference source not found.*** below.



Aims of the HIV screening tools are as follows:

- **To ensure that testing reaches those most at risk for HIV infection**
- **To reduce unnecessary HIV testing among low-risk clients by testing only those identified as eligible for testing**
- **To identify individuals with the highest risk of HIV to receive HIV prevention interventions like PrEP or VMMC**
- **To streamline testing/resource in settings with shortage of staff/kits and inform prioritization of resources**

Figure 3.5 HIV testing eligibility screening tool for adults

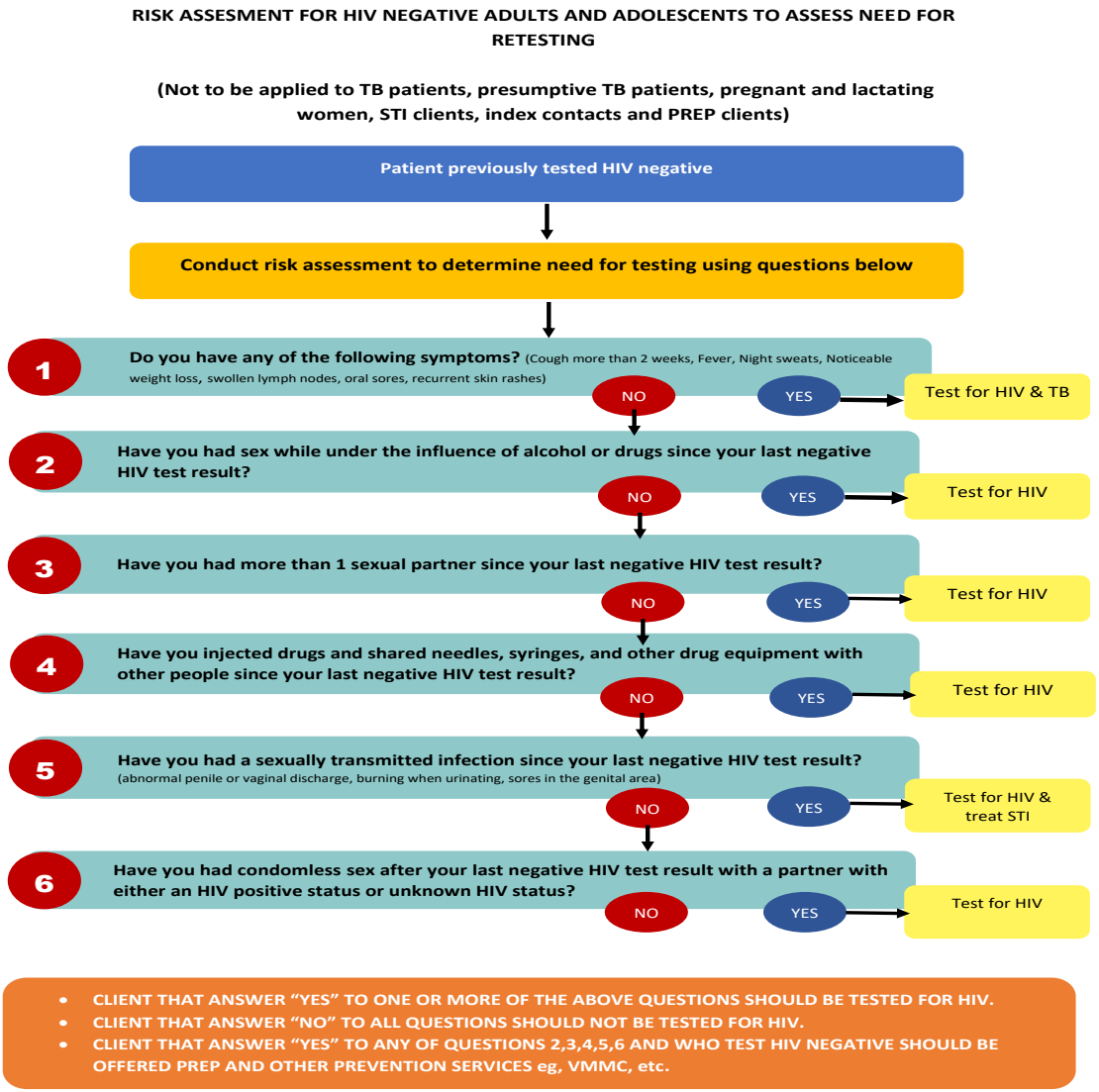


Figure 3.6 HIV risk assessment tool

3.5 HIV retesting

Table 3.4 Optimal retesting frequencies for various population groups

Population	When to Retest
General population	Based on HIV testing and screening tool
Couples and Partners	Sero-different couple: Based on the ongoing risk of exposure
	Sero-different couple: retest every 2 months until/unless partner has evidence of undetectable Viral Load Once partner maintains undetectable V/L, retest based on HIV exposure or annually
Pregnant and Lactating Women	All HIV-negative pregnant women should be re-tested every 2 months (aligned with the ANC scheduled visits) with the most optimal time for retesting being during the third trimester visit (34 weeks gestation). At delivery: Test every woman with unknown HIV status; test all women who have not tested in the third trimester All HIV-negative lactating women should be re-tested at 6 weeks, 14 weeks, 6 months, 9 months, 12 months, 15 months and 18 months aligned with the MBP follow-up schedule. *See Table 8.5*
Key Populations	Retest every 8 weeks
General population	Based on HIV testing and screening tool
Couples and Partners	Sero-different couple: Based on HIV testing and screening tool
	Sero-different couple: retest every 2 months until/unless partner has evidence of undetectable Viral Load Once partner maintains undetectable V/L, retest based on HIV exposure or annually

3.6 Verification of true new HIV tests and true new positive client's prior ART initiation procedure

The process includes the steps to be undertaken before HTS and ART initiation for all new clients. During pre-test counselling, an eligibility screening and risk assessment are undertaken as per the national guidelines to ensure the removal of clients who know their HIV status and may have been on ART before. History taking alone may not be objective hence the need to develop extra steps to verify one's HIV status.

The guidance on verification can be found in the recently developed verification SOP. The job aid below (Figure 3.7) shows a summary of the steps for the verification of positives. The process includes the steps to be undertaken before HTS and before ART initiation as a critical activity to address known positives and known unnecessary retests

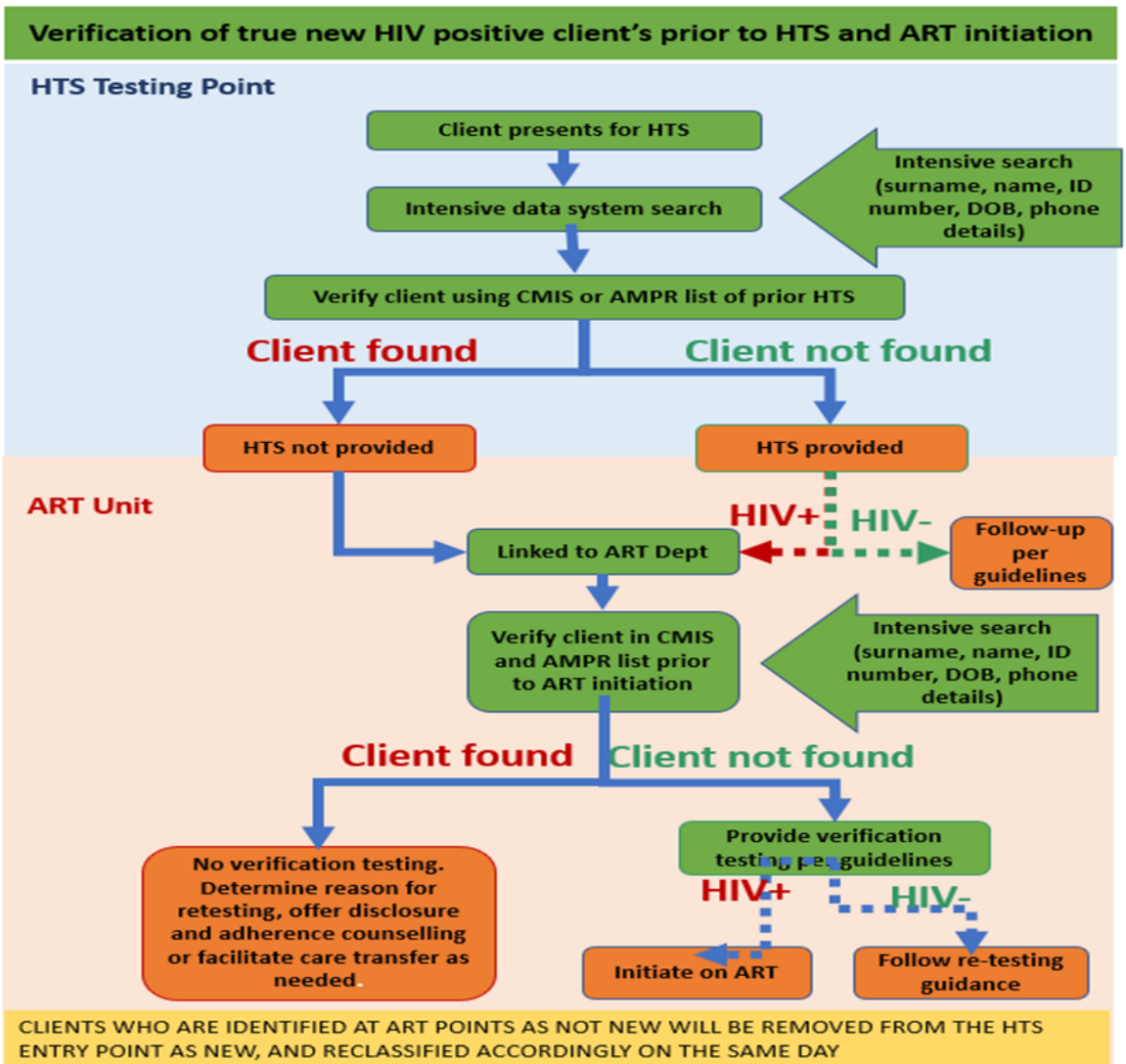


Figure 3.7 Verification of HIV status before registration

3.7 Pre-Test Information

Informed Consent

Obtain informed verbal consent in line with the 5 Cs of HTS.

Summary of Pre-Test Information

Table 3.5 Summary of pre-test information

Pre-test information included in both CIHTS and PIHTS
∞ The benefits of HIV testing (highlighting the positive benefits of knowledge of HIV status). ∞ The meaning of an HIV-positive and an HIV-negative diagnosis: » The services available in the case of an HIV-positive diagnosis, including where ART is provided. » The potential for incorrect results if a person already on ART is tested. » A brief description of HIV prevention options and encouragement of partner testing. » The fact that the test result and any information shared by the client is confidential.
Pre-test information included in both CIHTS and PIHTS
∞ The fact that the client has the right to opt out from testing and that declining testing will not affect the client's access to HIV-related services or general medical care. ∞ Potential risks of testing to the client in settings where there are legal implications for those who test positive and/or for those whose sexual or other behaviour is stigmatized. ∞ An opportunity to ask the HTS provider questions. ∞ Clinical and HIV prevention benefits of HIV testing. ∞ Benefits of ART and the Test and Start approach (starting treatment today or within 2 weeks of diagnosis). ∞ Encourage voluntary notification of partners and disclosure of status and option of assisted notification under index testing services. ∞ Confidentiality of testing and results. ∞ An offer to answer any question the client may have. ∞ Clarify misconceptions and myths about HIV transmission and risks ∞ Condom use demonstrations (male and female condoms). ∞ HIV testing screening tool (Annex HIV Testing Screening Tool) ∞ Gender-based violence assessments for adolescent girls and young women using health risk assessment tool ∞ Offer index testing services to the client should they test positive and elicitation of contacts can be done at this stage.

CIHTS should also include:	PIHTS should also include:	HIVST should also include:
∞ Preparation for testing and receiving results ∞ Suicide assessment and coping skills ∞ Development of a risk reduction plan	∞ Information on shared confidentiality ∞ Reassurance that refusal to test will not result in the client being denied care for their current health problem	∞ An HIVST positive result should be confirmed by a trained HTS provider following the recommended algorithm ∞ Directly assisted demonstrations on how to perform the HIVST
Inform the client about HTS Hotline in case the client wants to ask questions.		

3.8 HIV testing devices and procedure

Table 3.6 Types of laboratory tests for HIV screening and diagnosis

	Antibody Test				Virological Test
Test name	Rapid test			HIVST	NAT (RNA and/or DNA PCR)
	Determine HIV 1/2 	Uni-gold HIV 1/2 	Asante HIV-1 	Oraquick HIV self-test 	NAT (RNA and/or DNA PCR)  
Sample type	Capillary/venous whole blood, plasma			Saliva	Capillary/venous whole blood
Collection site	Finger			Mouth	Heel/Toe/finger
Window period	8 weeks			12 weeks	2-6 weeks
Indication	-Diagnosis for clients 18 months and older -*Surveillance			Self-Screening	-Diagnosis for clients under 18 months -Diagnosis of clients with inconclusive HIV rapid test results
Turnaround time (TAT)	20mins			20 mins	2-6 weeks

* The Eswatini HIV-1 recent infection surveillance (EHRIS) program tracks recent HIV infections by providing continuous epidemiological surveillance data on person, place, and time of HIV recent infections amongst adults 15 years and older to inform HIV prevention and epidemic control strategies

3.8.1 Antibody testing

HIV Rapid diagnostic tests detect antibodies to HIV and can be used to definitively diagnose adults and children 18 months of age or older. Eswatini has adopted the *two-test strategy* for the diagnosis of HIV. The two rapid tests approved for use are - **Determine** HIV1/2 and **UniGold** HIV1/2. However, a three-test strategy should be considered if HIV positivity in HIV testing services falls below 5%. *Also in ANC settings, the **dual HIV/Syphilis** rapid diagnostic tests may be considered the first test in the HIV testing strategy and algorithms.*

The **Asante** HIV-1 Rapid Recency assay is used to detect recent infection (an infection that was acquired within the past 12 months**)** among all newly diagnosed individuals 15 years and above.

The **Ora-Quick** HIV self-test is a triage test and does not provide a definitive HIV-positive diagnosis. A reactive (positive) HIV self-testing result needs to be followed by further testing from a trained provider to confirm HIV status, following the national testing algorithm.

3.8.2 Virological testing

- Nucleic acid testing (NAT) technologies for the qualitative detection of HIV DNA and/or RNA in whole-blood, plasma or dried blood spot can be used to definitively diagnose children less than 18 months of age. Serological antibody assays are not suitable for diagnosis since trans-placentally transmitted maternal HIV antibodies may persist in the child up until 18 months of age.
- The use of point-of-care technologies and the addition of NAT at birth (0-3 days) can improve rapid identification and treatment initiation among exposed infants.
- NAT (RNA and/or DNA PCR) may also be used to provide a definite diagnosis in case of a discordant result following HIV re-testing for verification before ART initiation.
- NAT (RNA and/or DNA PCR) may also be used as the last step to provide a definite diagnosis in case of an inconclusive test result in adults and children above 18 months.

Window period

The window period is the period from getting infected with HIV to the time of being able to detect HIV in serum/ blood. An individual is highly infectious during the window period. The length of the window period varies from individual to individual and depends on the HIV test used.

3.9 HIV Testing Algorithm

3.9.1 HIV testing in Infants and Children Less Than 18 Months

Virological testing should be used to diagnose HIV among all exposed infants less than 18 months. Diagnosis should be done at the earliest opportunity to offer optimal care and treatment of HIV-infected infants and the timing of the HIV test should be aligned with childhood immunization schedules (see PMTCT immunization schedule). A summary of the HIV testing algorithm for infants from birth is in *Figure 3.8* below

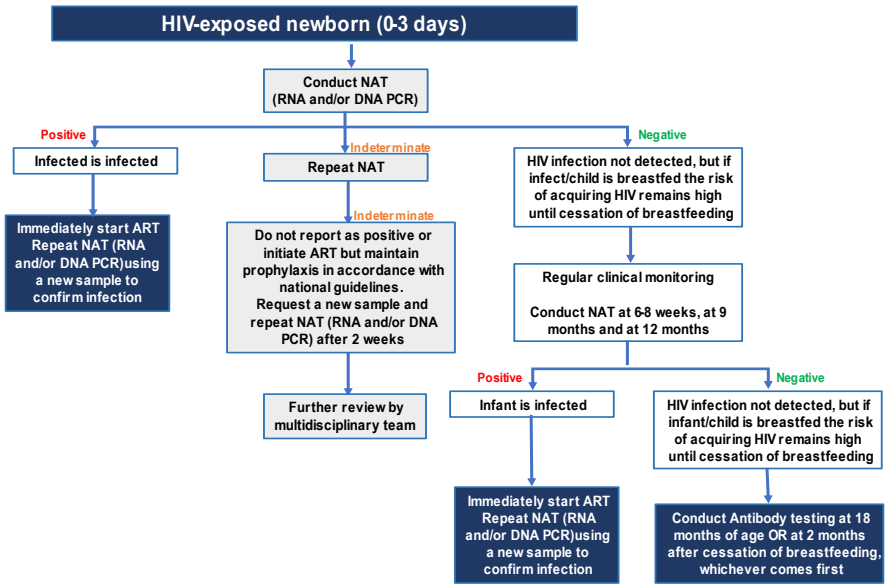


Figure 3.8 HIV testing algorithm for Infants and Children Less Than 18 Months

Indeterminate Test Results

Declining mother-to-child transmission rates globally and nationally have led to concerns about false-positive and indeterminate test results. However, an indeterminate range** of viral copy equivalents should be used to improve the accuracy of all nucleic acid-based early infant diagnosis assays as shown in *Table 3.7* below.

***Indeterminate range refers to a range of viral copy equivalents that would be too low to be accurately diagnosed as HIV-infected.*

Table 3.7 Indeterminate range cycle threshold equivalents of current nucleic acid infant diagnosis assays

Assay	Estimated indeterminate range cycle threshold
Abbott m-PIMA™ HIV-1/2 Detect	Not available
Roche COBAS® Ampliprep/COBAS® TaqMan® HIV-1 Qualitative Test v2.0	≥33
Roche COBAS® HIV-1 Quantitative nucleic acid test for use on the COBAS® 6800/8800 Systems	≥37

- Repeat samples following an indeterminate result should be given priority in the laboratory
- Infants/children with repeated indeterminate results need a multidisciplinary team of healthcare providers to support retention, tracking and status resolution.
- Clinical monitoring and further testing based on the national infant testing schedule need to be done until a definitive HIV status is established.

Confirmatory testing of positive test results and managing discordant results

- Infants with a positive result should receive a confirmatory test and be initiated on ART immediately while awaiting the result of the confirmatory test. NAT (RNA and/or DNA PCR) must be repeated using a new sample to confirm infection.
- If the second (confirmatory test) NAT is negative, a third NAT (RNA and/or DNA PCR) should be performed before considering interrupting ART. *Figure 3.9* below shows the confirmatory testing of HIV-positive infants.

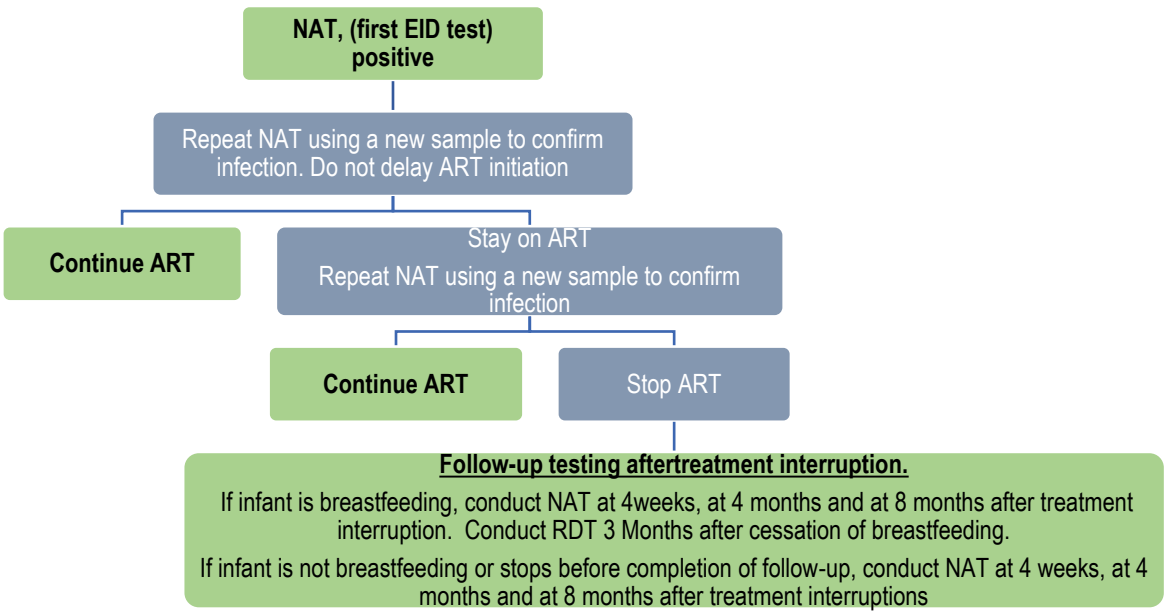


Figure 3.9 Confirmatory HIV testing algorithm for Infants and Children Less Than 18 Months

However, several factors should be considered when assessing infants for ART interruption after discordant test results (positive then a negative result) are followed by a third test with a negative result:

- The infant ought to have no clinical signs or symptoms suggesting HIV infection;
- A follow-up plan should be agreed on with the family, caregiver(s) and healthcare staff; and
- Tracking information (phone, address, etc.) of the family and caregiver(s) should be collected and confirmed.

The following factors should be considered when following up on any infant undergoing treatment interruption.

- Active follow-up is needed to ensure that a potentially infected infant is retained in care and reinitiates treatment if a viral rebound occurs.
- Viral rebound among infants living with HIV starting treatment early is expected to happen within eight months of interruption in >99% of cases).
- Infants who develop signs and symptoms indicating HIV infection should undergo immediate testing.
- Breastfeeding and continued risk of transmission require follow-up and appropriate testing throughout risk until final diagnosis.
- There is value in minimizing follow-up testing by leveraging existing opportunities for infant testing (based on the national infant testing schedule and immunization or well-child appointment schedules) until a final diagnosis is ascertained.

3.9.2 HIV testing in Adults, Adolescents and Children Older Than 18 Months

Eswatini follows a serial testing algorithm as depicted in *Table 3.8 and* Table 3.9 *below*

Table 3.8 Serial HIV Testing Steps for Rapid Testing in Adults and Children Above 18 Months

Perform HIV Testing Follows:
1. Perform testing with Test 1 (Determine) through a finger-prick. 2. If non-reactive, the result is interpreted and communicated as HIV-negative. 3. If reactive, a second test is done using Test 2 (UniGold). 4. If Test 2 (UniGold) is reactive, the result is interpreted and communicated as HIV-positive. 5. If Test 2 (UniGold) is non-reactive (i.e., Determine and UniGold are inconclusive), repeat testing using Test 1 (Determine) and Test 2 (UniGold) in parallel. Collecting blood by venepuncture is recommended to minimize client discomfort from subsequent multiple finger pricks. 6. If both repeat tests are non-reactive, the result is interpreted and communicated as HIV-negative. 7. If both repeat tests are reactive, the result is interpreted and communicated as HIV-positive. 8. If repeat tests remain Inconclusive (i.e., Determine test is reactive and UniGold test is non-reactive, or vice versa), appoint the client in two weeks and repeat parallel testing. 9. If both repeat tests are non-reactive, the result is interpreted and communicated as HIV-negative. 10. If both repeat tests are reactive, the result is interpreted and communicated as HIV-positive. 11. If repeat tests remain Inconclusive (i.e., Determine test is reactive and UniGold test is non-reactive, or vice versa) collect samples for NAT (RNA and/or DNA PCR) and send a sample to the National Reference Laboratory for testing. All specimens referred to the National Reference Laboratory should be accompanied by a Laboratory Request Form. Then appoint clients in two weeks to receive results. 12. If NAT (RNA and/or DNA PCR) results are Positive/ Detected, the result is interpreted and communicated as HIV-positive. 13. If NAT (RNA and/or DNA PCR) results are Negative/ Undetected, the result is interpreted and communicated as HIV-negative.

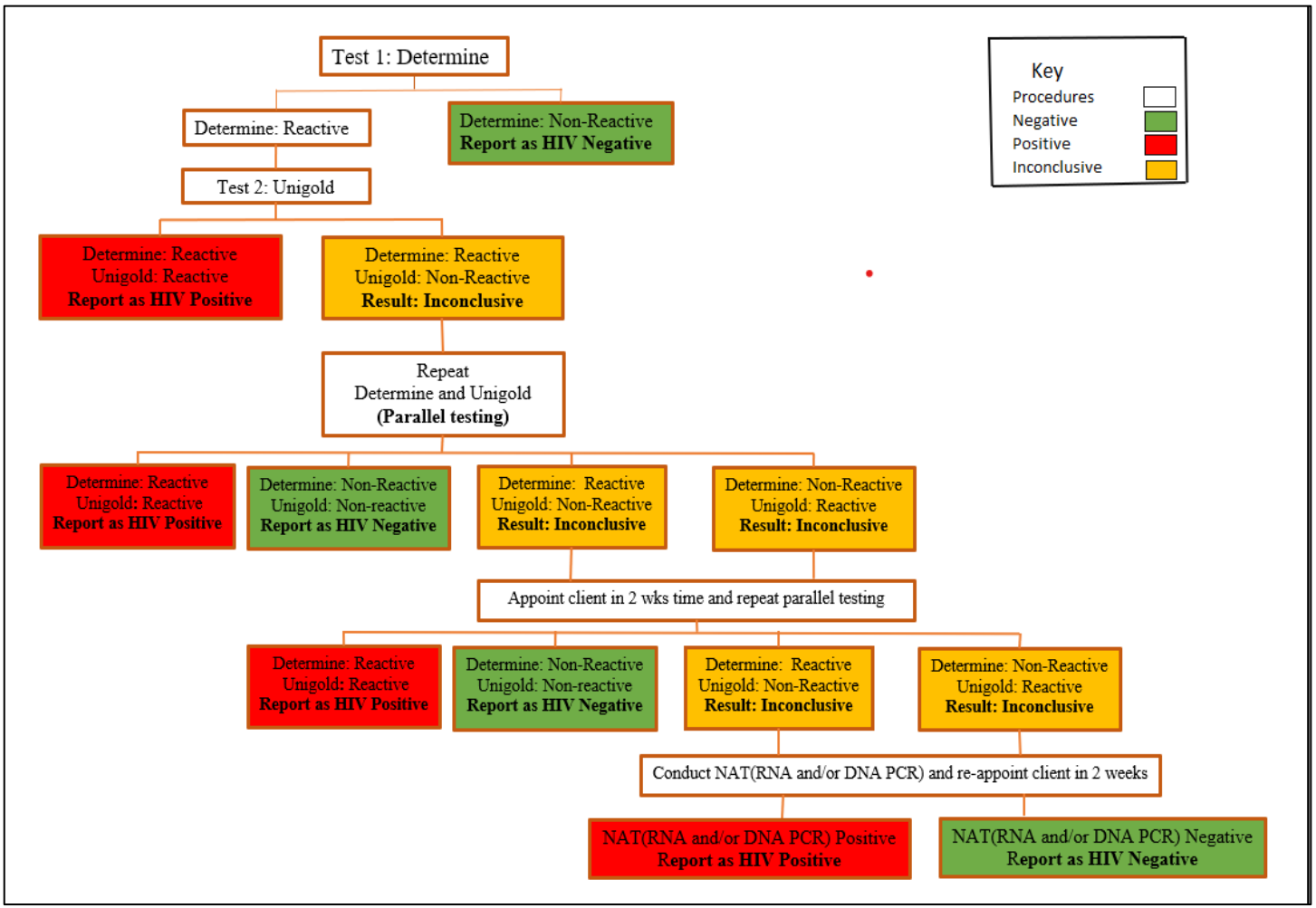


Figure 3.10 Eswatini Serial HIV testing algorithm for Adults and Children above 18 Months

3.10 Post-Test Counselling

General Post-Test Counselling Principles

All people living with HIV now qualify for ART irrespective of WHO clinical stage, CD4 count, age, gender, pregnancy status, coinfection status, etc. Post-test counselling should, at a minimum, include the following key messages that begin the ART treatment preparation process for all PLHIV:

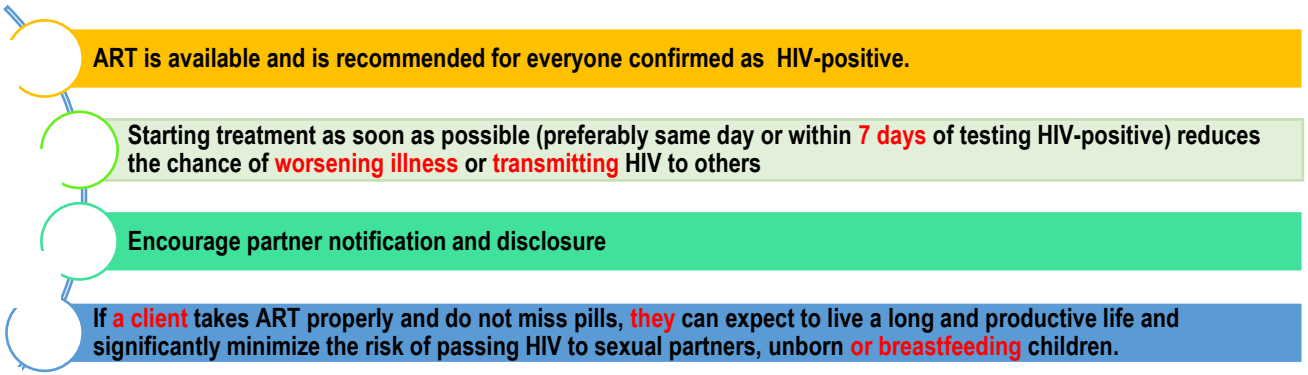


Figure 3.11 Summary of Post-Test Counselling

Table 3.9 Summary of post-test counselling

Post-test counselling for both positive and negative results should include:	
∞ Simple and clear communication of test results ∞ Check the client's understanding of the result ∞ Opportunities for the client to ask questions ∞ Development of a coping strategy for the client ∞ Assessment of referral needs for other services ∞ Discussion of disclosure of test results ∞ Discussion of partner and family referral for HIV testing ∞ Clarify misconceptions and myths about HIV transmission and risks ∞ Referrals for relevant services	
Counselling for HIV-negative clients should also include:	**Counselling for HIV-positive clients should also include:**
∞ Explanation of window period and recommendation of when to re-test based on their risk profile. ∞ Important to not encourage unnecessary re-testing. ∞ Discussion of partner testing, methods to prevent HIV such as VMMC, correct and consistent use of condoms, PrEP, PEP and reducing the number of sexual partners. ∞ Scheduling of ongoing supportive counselling sessions as per client need. Referral for prevention and other health services where indicated. ∞ Offer prevention services if eligible (VMMC, PrEP, Condoms, PEP)	∞ Supporting the emotions arising from the test result. ∞ Discussion of any immediate concerns. ∞ Informing the individual of available chronic HIV care and ART services. ∞ Informing client about benefits of Test and Start and active referral for treatment. ∞ Information on preventing HIV transmission. ∞ Discussion of "positive living." ∞ Scheduling a follow-up counselling session if indicated. ∞ Referral to HIV care services and support groups. ∞ Assisted partner notification, disclosure and follow-up as needed ∞ Conduct elicitation of contacts (sexual partner, biological children (if female), family members and associates) and identify index referral options for each contact ∞ Assessment of other SRH needs, including FP

Table 3.10 Additional Key Counselling Messages for Special Populations

Special Population	Specific counselling messages to be included:
Couples and partners	**Counsel on the following points:** ∞ Mutual support and disclosure. ∞ Male and female condom use. ∞ Contraception/ safer conception for future pregnancies. ∞ Partner and family testing and index testing services. ∞ Serodifference and how to stay negative, including offering PrEP for the negative partner in a serodifferent couple
Pregnant and lactating women	**Counsel on the following points:** ∞ Childbirth plans. ∞ Contraception/ safer conception for future pregnancies. ∞ Partner testing, notification and disclosure. ∞ Adequate nutrition for the mother, including iron and folic acid supplements. ∞ Infant feeding options. ∞ For HIV-positive pregnant and lactating women, Test and Start for the mother's health and PMTCT should be promoted as well as the importance of HIV testing for the infant reviewed.
Children	∞ Younger children should be told their status incrementally to accommodate their cognitive skills and emotional maturity in preparation for full disclosure.
Adolescents girls, Young women /men	∞ Listen and address adolescents' concerns. ∞ Focus on risky behaviour and develop risk reduction plans. ∞ If the test is positive, reassure them that they can live a long healthy life. ∞ Clarify misconceptions and myths. ∞ Provide condoms and refer to appropriate prevention, care and treatment services.
Key populations	∞ Remind clients of the modes of transmission of HIV. ∞ Provide and offer condoms, contraceptives and lubricants, and referrals for prevention, treatment and care, including the availability of PrEP, STI testing and treatment, and needle and syringe programmes. ∞ Offer options for Event led PrEP as per guidelines for MSM ∞ Discourage reuse of needles, razors and syringes. ∞ Encourage and support partner testing, notification and disclosure. ∞ Early treatment of STIs ∞ Encourage and emphasize VMMC

3.11 Testing for Recent Infection

HIV Recency Testing

The Eswatini HIV-1 recent infection surveillance (EHRIS) program was designed to monitor recent infections to guide targeted HIV preventive interventions. Recency testing can be used to describe the HIV epidemic, detect clusters of continuing or recent infections and intervene to prevent transmission.

A recent infection is an infection occuring approximately within the past 12 months

What is the goal of Recency testing?

The goal is to provide continuous epidemiological surveillance data on the person, place and time of HIV recent infections amongst adults 15 years and older to inform HIV prevention and epidemic control strategies.

Primary Objectives

Monitor trends in the proportion of testing recently infected on the Recent Infection Testing Algorithm (RITA) [Rapid test for HIV-1 recent infection (RTRI and VL)] among newly diagnosed PLHIV by select demographic and HIV risk variables to inform targeted HIV prevention and testing interventions.

- Identify geographic clusters associated with testing recently infected on the RITA to inform geographic prioritization of HIV prevention and testing interventions.

Recency testing implementation

Recency testing will be introduced during the routine HTS 'opt-out' approach and integrated into the current national HIV testing algorithm. Persons with a recent infection result on a rapid test for recent infection (RTRI) will undergo an additional test; Viral Load testing to confirm recency status. HIV recency testing results are for programmatic use only and are not disclosed to clients.

Recency testing eligibility criteria

Testing will be conducted at HTS entry points among consenting clients who meet the following criteria:

- Adults 15 years and older
- Newly diagnosed HIV cases at HTS visit (newly testing HIV positive) See *Section 3.6* on Verification of true new HIV positive clients before ART initiation procedure
- Clients willing to undergo all EHRIS procedures (RTRI and VL testing)

Laboratory Testing Methods

Rapid Test for Recent Infection

A blood sample will be collected *via finger prick* to preliminarily assess HIV recent infection using a POC Asante HIV-1 Rapid Recency Assay, a rapid test for recent infection (RTRI) that helps to distinguish recent infection (occurring within the past 12 months) from long-term infection (occurring over 12 months ago). The Asante rapid recency assay is designed as a lateral flow device with three lines, representing a control line (C), a positive verification line (V) and a long-term line (LT) to distinguish recent from long-term infection in 20 minutes,

Figure 3.12. The test is interpreted qualitatively by visual assessment of the presence or absence of the three lines.

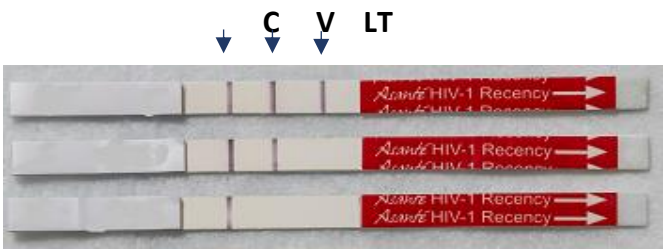


Figure 3.12 Point of care recent infection test strip illustration

Interpretation of RTRI Results

The HIV status of the client will be determined as outlined in the national HIV testing algorithm using a two-test process. The result of the RTRI will not impact the client's HIV diagnosis or clinical management and will only be used to determine recency status for surveillance purposes. RTRI results should be interpreted as follows:

- The presence of a control line (C), a verification line (V) and a long-term line (LT) on the RTRI will indicate an RTRI long-term infection.
- The presence of a control line and a verification line will indicate an RTRI recent infection.
- The presence of only a control line on the RTRI will indicate inconclusive RTRI results and will be recorded as HIV positive (if Determine and UniGold were both positive) with inconclusive recency status.
- The absence of a control line on the RTRI will indicate an invalid recency result.
- The presence of a long-term line without a verification line also represents an invalid recency test result.

If Determine is reactive and UniGold is nonreactive, the result of the RTRI will not be reported as the client has not been confirmed to be HIV positive at that point. If the client is later confirmed to be HIV positive, recency testing will be performed according to the recent infection testing algorithm (RITA).

Recent Infection Testing Algorithm

Clients with a recent infection status on the RTRI will be tested for HIV-1 viral load levels to classify recent infection status according to the RITA. Clients with RTRI recent infection status and a viral load result ≥ 1,000 copies/mL will be categorized as a RITA recent infection (Figure 2). A viral load of fewer than 1,000 copies/mL will be interpreted as a RITA long-term infection.

Clients that test long-term on the RTRI do not require additional testing and are classified as an RTRI long-term infection according to the RITA.

The Verification of all clients presenting at HTS and ART for initiation is critical to ensure true new positive clients. This will avoid the retesting of previously positive and on ART clients. Those who disengaged from care are linked to preferred facilities.

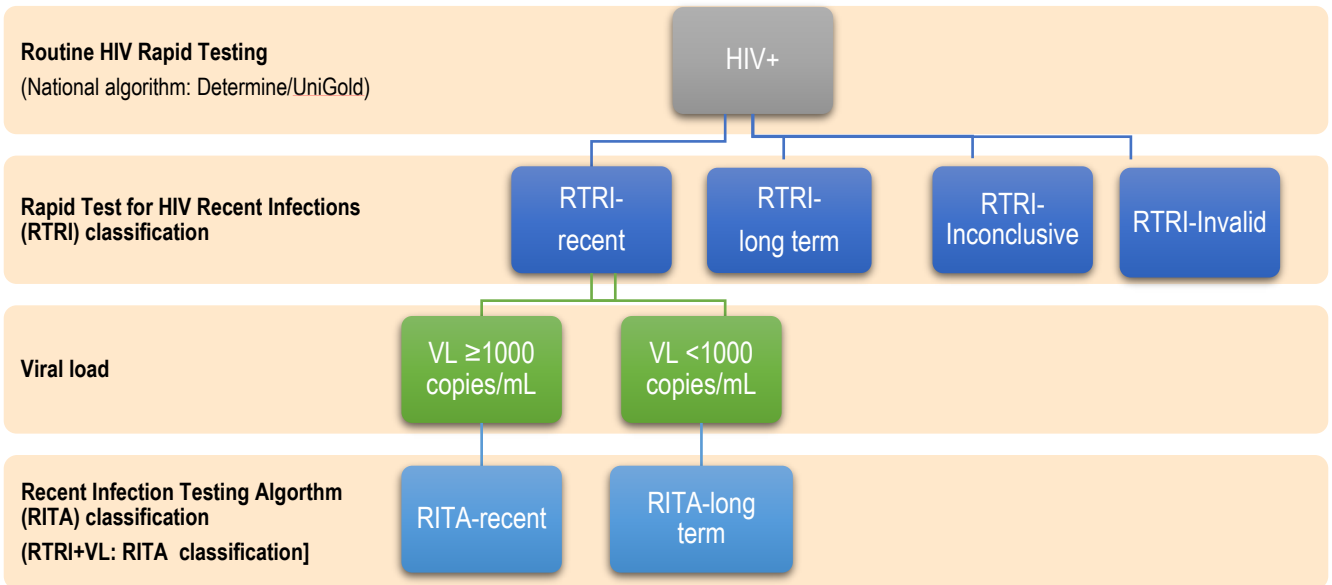


Figure 3.13 Interpretation of a Recent Infection Testing Algorithm Using a Rapid Test for Recent Infection and Viral Load Testing

Quality assurance in recency testing

To ensure the validity of the ASANTE test kits, monthly quality controls (QCs) are conducted using HIV-positive and negative plasma samples. Proficiency testing using dried tube specimens (DTS) to evaluate the competency of HTS providers is conducted bi-annually.

Data collection and documentation

HIV recency testing data will be captured electronically with the use of tablets installed with an Open Data Kit (ODK). Paper-based data collection forms will be used as a backup in the event of tablet failure or unavailability.

The recency test results will be only for program use and will not be returned to the clients because they will not change the final HIV diagnosis and the care or treatment to be prescribed. To prevent accidental disclosure of results to participants, will not be documented at the facility. To review recency testing coverage in HTS sites documentation if recency was done well accommodated in the HTS registers.

Table 3.11 Responsibilities to ensure quality assurance

HTS provider
∞ Run internal quality controls once weekly, for each new lot of test kits, for any new operator or when environmental conditions fall outside the range recommended by the manufacturer. ∞ Participate in HIV proficiency panel testing, provide timely feedback and document corrective actions for unsatisfactory performance. ∞ Store test kits in a temperature-controlled environment following the manufacturer's recommendation (2-30 degrees Celsius). Document temperature and maintain a cold chain ∞ Ensure samples are stored and transported appropriately ∞ Ensure that standard operating procedures exist and are adhered to for all procedures, including specimen collection and processing, testing algorithms and all test procedures, with QC and final reporting (following a verified testing algorithm). ∞ Administer counsellor reflection forms, client exit interviews ∞ Document and dissemination of quality assurance report ∞ Ensure information and testing aids are given to clients using the HIVST kits. ∞ Ensure active linkages and a strong aftercare mechanism for clients ∞ To identify non-conformance, routinely monitor indicators such as turnaround times for each assay, turnaround time for an overall testing report, rate of discrepant results, rate of invalid results, rate of specimen rejection, rate of test kit stock-outs, rate of supplies stock-outs and frequency of expiration of test kits.
HIVST distributor
∞ Undergo training to distribute HIVST kits, including directly assisted HIVST ∞ Store test kits in a temperature-controlled environment (temperature: 2-30 degrees Celsius), maintain a cold chain and ensure proper packaging, especially when going to the community or outreach ∞ Ensure active linkage information for reactive and non-reactive results, and a strong after-care mechanism for clients ∞ Manage HIVST inventory by adhering to stock monitoring, documentation and reporting procedures
Supervisor
∞ Ensure HTS providers and HIVST distributors are trained and provided with refresher training every year ∞ Ensure the facility (both fixed and mobile) has the capacity for cold chain management ∞ Ensure samples are stored and transported appropriately ∞ Ensure compliance with HIV testing/HIVST SOPs and national HIV testing algorithms. ∞ Provide supportive supervision for HTS providers based on quality assurance tools (sit-ins, compliance to SOPs and guidelines, etc) ∞ Monitor stock management of HIV testing commodities ∞ Appoint HTS focal to monitor quality aspects of testing ∞ Ensure active linkage of clients and after-care ∞ Proactively identify opportunities for improvement and relay recommendations to a higher level of management for broader implementation. ∞ Conduct competency assessments of testers at least once a year

Table 3.11 Responsibilities to ensure quality assurance (continued from previous page)

HTS Program
∞ Liaise with the lab on regular conduction of onsite supportive supervision for lab, point of testing sites, and individuals distributing HIVST ∞ Conduct HTS training and refresher training sessions regularly ∞ Ensure documentation and dissemination of quality assessment reports ∞ Timely review of HIV testing registers, HIVST registers, SOPs and QA tools ∞ Ensure samples are stored and transported appropriately ∞ Regular update and disseminate information on HIV testing and monitoring compliance with recommended testing algorithm(s) ∞ Engage all HIV testing points in an external quality assurance program of the Eswatini Health Laboratory services through participation in quarterly proficiency testing ∞ Ensure all HTS points are conducting competency assessments of testers at least once a year ∞ Conduct quarterly supportive supervisions at least once a year ∞ Conduct site readiness assessments on all new testing sites

4 REFERRAL AND LINKAGES

4.1 Introduction

- In Eswatini HIV testing and treatment programs have increased access to ART remarkably, however many PLHIV still initiate ART late, particularly males and people diagnosed in the communities.
- Linkages case management (LCM) is a Ministry of Health initiative, mainly aimed at the implementation of more efficient and effective ways that ensures clients testing HIV-negative are linked to prevention services and those testing HIV positive are linked to chronic HIV care. The client may either be referred from other health facilities or the community (Community ART)
- LCM is a peer-delivered model which includes individualized service, navigation, and index testing. LCM has been extended to 6 months to help improve the retention of clients on ART-enhanced LCM (eLCM)
- Patient-centred care for the different subpopulations must be implemented to improve linkages.
- The following strategies are aimed at improving HIV linkages:
  - flexi hours
  - integration of ART in all health facility departments
  - escorting clients to ART units and HIV prevention services
  - provision of comprehensive male and adolescent-friendly services in high-volume facilities
  - provision of community ART initiation or HIV prevention services depending on the client's HIV status
  - provision of escalation counselling for clients not ready to be initiated.
- Caregivers of children, and adolescents are to be provided with support for re-engaging to care.
- Rapid ART initiation should be emphasized for all PLHIV following a confirmed HIV diagnosis preferably on the same day of diagnosis (in line with the Test and Start policy).

All clients should be linked to care; however, the following populations should be prioritised for eLCM; infants, children, adolescents, men, key populations, pregnant and breastfeeding women and clients who have missed appointments or had disengaged from care.

For linkage to prevention services, the following populations should be prioritised: HIV-negative partners in sero-different sexual relationships, sexual partners of clients with detectable viral loads, key populations, adolescent girls and young women.

HIV referral and linkages is a critical component of prevention and treatment programs aimed at intensifying the country's effort towards achieving the global treatment and prevention targets for all population groups.

Delays in starting ART can have adverse effects, especially for infants, people with TB or advanced immunosuppression who are at high risk of death.

Community-based ART initiation and linkages to prevention and treatment services must be provided within seven days of diagnosis for clients with WHO stage 1 or 2 AND has no signs of opportunistic infections or any comorbidities that may require further assessment or investigation. All eligible clients should be offered an HIV test and start in the community based on the eligibility criteria outlined in *section 5.6.1*. However, the following populations should be prioritised: key populations, men, adolescents, and young people since their linkage is low compared to the other subpopulations.

4.2 Definition of Key Terms

Referral
This is the process of forwarding a client/patient to another service delivery point and it can be within the same health facility but different departments or to another health facility or from the community to the health facility.

Linkages
This is a process in which the client (HIV-negative/ positive) has reached the service point and has been provided with the services he/she needs.

∞ Clients referred from community to facility must be referred using a comprehensively filled referral form and the health care worker referring the client has the responsibility to make a follow-up to determine if the client was linked for the services.
∞ A package of support interventions should be offered to ensure timely linkage to care for all PLHIV and linkage to prevention services for those testing HIV-negative yet at risk of getting infected.

The process of referral and linkages begins with demand creation for HIV testing, and HIV diagnosis and ends with enrolment in prevention, care or treatment and other health services:

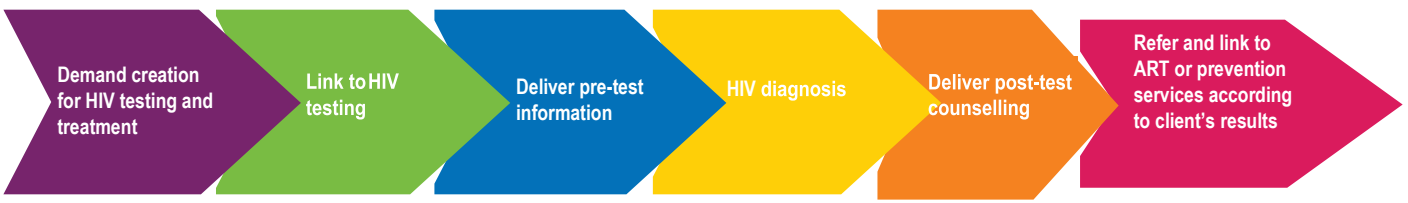


Figure 4.1 The process of referral and linkage

4.3 Responsibilities of HCW at the different stages of the referral and linkage process

Table 4.1 Responsibilities of HCWs in referral and linkages

Demand creation for HTS, prevention and treatment	-Provide information on the importance of HTS and testing options including HIV self-testing. -Provide information on risk assessment and available HIV prevention services -Provide information on the benefits of early ART initiation and the need to attain viral suppression. -Encourage clients who may have disengaged in care to come back and also sensitise them about the welcome back clinics and the services they offer
Linkage to testing	-Explore other service needs for the client that they must be linked to, such as family planning, STI or gender-based violence -Provide information on HTS service points and HIV self-testing
Delivery of pre-test counselling	-Provide pre-test giving information highlighting benefits of HIV testing,
HIV diagnosis	-Conduct HIV testing using the Eswatini HIV testing algorithm as indicated in the HTS chapter
Delivery of post-test counselling	-Provide post-test counselling according to the results of the client, meaning of HIV results and indicate post-test services available according to the results of the client.
Referral and linkage to HIV prevention and treatment	**HIV-negative client:** -Provide information on HIV prevention services, refer to and link for prevention services -Assess for prevention services eligibility -Ensure linkage to prevention services for priority populations at risk **HIV positive client** -Ensure the client is linked to treatment services including early ART initiation or refer the client to get services in another service point, - Check in the CMIS/APMR/registers if the client is a genuinely new HIV-positive client -Conduct ART readiness assessment to understand the service needs of their clients. -Make an effort to be aware of available referral services (both clinical services and community resources). -HCWs must comprehensively document the referral form, make receiving site aware that the client is expected and must complete the outcome of the referrals -Conduct eliciting of contacts (Index testing) -Offer assisted partner notification services for listed contacts -Enrol client on enhanced LCM -if it's a referred client, once the client is linked to the facility, LCM will now be implemented by the receiving facility

Before a client is referred for ART services, the HTS service provider must ascertain if the client is a genuinely new positive or is returning to care.

4.4 Principles of Linkage

- ART initiation should adhere to the overarching ethics of providing a client-centred approach, that is providing care that focuses on the needs, preferences, and expectations of the individuals.
- Linkages should uphold individual dignity and respect, especially for the vulnerable subpopulations
- Linkages should promote the engagement and support of people and families to play an active role in their care through informed decision-making.
- All people newly diagnosed with HIV should be retested to verify their HIV status before starting ART (*see HTS chapter* 3)
- Test and start should be provided to all clients living with HIV regardless of CD4 cell count,
- Clients with no contraindication to rapid ART initiation should be fully informed of the benefits of ART and offered rapid ART initiation, including the option of same-day initiation.

4.5 HIV linkages goals

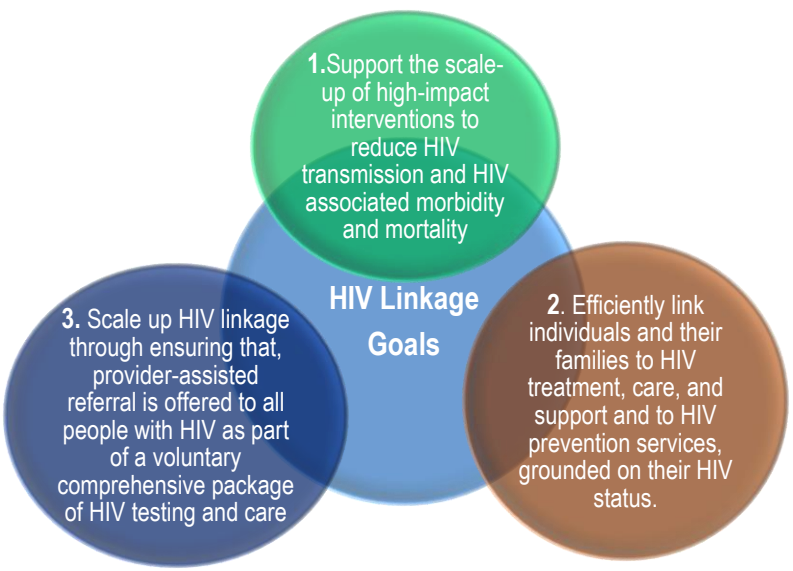


Figure 4.2 LCM goals

4.6 Interventions to improve HIV linkages for PLHIV

A client with an HIV positive result should be timeously provided with a package of supportive interventions. The following interventions should be provided to improve linkages and engagement in care:

This interventions should be provided to improve linkages and engagement in care

- i. Enhanced linkage case-management.
- ii. Support for HIV disclosure.
- iii. Continuity of index testing
- iv. Training of staff to provide ART integration in high volume departments
- v. Provision of peer support & treatment navigation
- vi. Use of data to track and improve quality linkage in facility and community level
- vii. Treatment literacy

4.7 Linkage to prevention services

Clients testing HIV-negative yet at risk of getting infected with HIV must be linked to prevention services while those testing HIV positive must be linked to treatment services or positive should be

Referral and linkages for combination prevention should focus on the needs of individuals and communities.

- ∞ Aim: To reduce HIV incidence among clients at risk of acquiring HIV.
- ∞ Clients that are testing HIV-negative yet are at risk of getting infected with HIV must be provided with an HIV prevention package according to the client's preferred, and acceptable method to address both immediate risk and underlying vulnerability. These may include at least the following:
  - VMMC, PrEP, PEP, condoms, STI screening and treatment, HIVST, and family planning.
- ∞ The following groups must be prioritized for the HIV prevention package:
  - AGYW, men, children, key populations, and pregnant and breastfeeding women since EHRIS data has shown that new infections are high amongst these subpopulations.
- ∞ Clients must be educated on the benefits of each prevention method and assured of support if they change their minds.
- ∞ To reduce stigma and discrimination against clients, prevention services should be integrated into existing services

4.8 Linkages to treatment services

HIV linkages can be done within the facility, between facilities, from community to facility or from facility to community
Bidirectional communication between facilities and communities is important to improve HIV linkages.

∞ For collaboration to be smooth, HIV Community testing partners should participate in facility multi-disciplinary meetings.

4.9 Types of linkage services

HIV linkages can be done within the facility, between facilities, community to facility or facility to the community
- Bidirectional communication between facilities and communities is important to improve HIV linkages.

∞ For collaboration to be smooth, HIV Community testing partners should participate in facility multi-disciplinary meetings.

Table 4.2 Types of linkage services

Linkage point	Health care worker responsibilities
Linkages within the same facility	HCWs should escort clients to the next point of service. Individuals diagnosed HIV positive or negative in a facility must be entered into an appropriate register after treatment/prevention services have been offered. Clients not ready for ART initiation should be enrolled into LCM and followed up as indicated in the LCM SOP and referred according to the facility escalation plan. Clients not ready for prevention services must be continuously given the right information and followed up.
Linkages from community to facility	Individuals testing HIV-positive and initiated on ART in the community or testing HIV-negative in the community must be given an appointment at the receiving facility for follow-up. They must have a date set for them in the appointment register of the receiving facility so that follow-up can take place if they miss their appointment. The HCW in the receiving facility should enrol the HIV-positive clients into LCM and provide HIV prevention services to willing HIV-negative clients. The receiving health facility should give feedback to community health care workers. Once the client is linked to a health facility, LCM will now be implemented by the facility. Community partners should submit chronic care files of clients initiated on ART in the community to the respective health facilities. The receiving health facility should assign ART numbers to these clients and submit the list back to community partners indicating if the client fulfilled the 2week visit. Feedback should also be given to community partners on clients who successfully accessed a prevention service.
Linkages between 2 facilities	Clients tested in a facility and referred to another facility for care/prevention must have an appointment set for them in the receiving facility so that follow-up can take place if they miss their appointment. The client's name and contact details are to be shared with the facility to where the client is being referred to.
Linkage from health facility to the community	Clients who need community services must be referred to community partners for linkage to community service points including projects such as OVC/DREAMS, social workers and psychologists for further support.

4.10 Summary of enhanced Linkages Case Management

Patient literacy and ART readiness assessment are integral interventions to retain clients in care and should be done at each clinical visit.

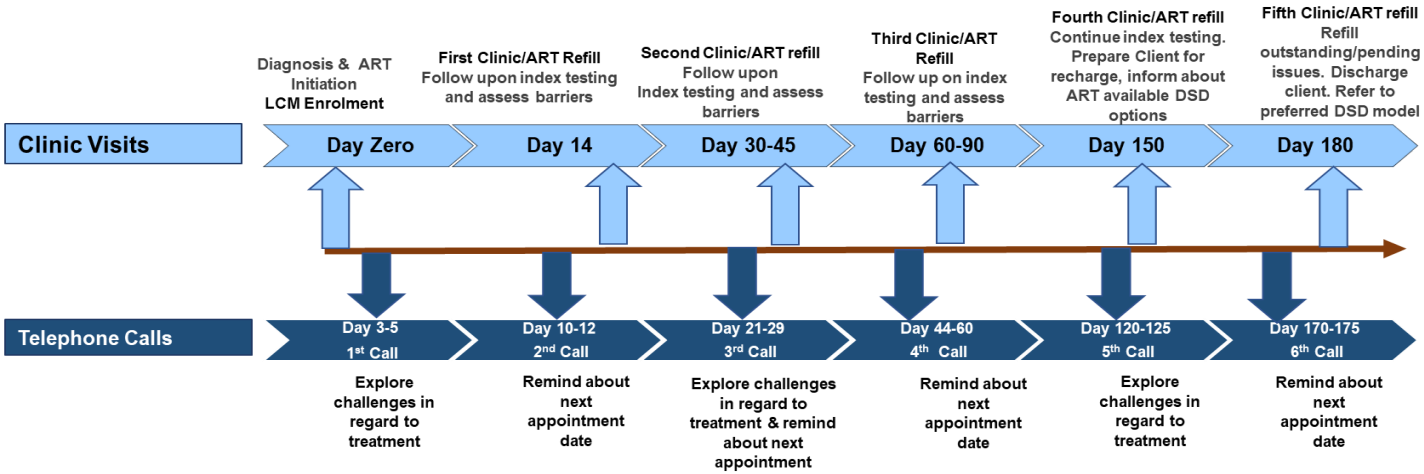


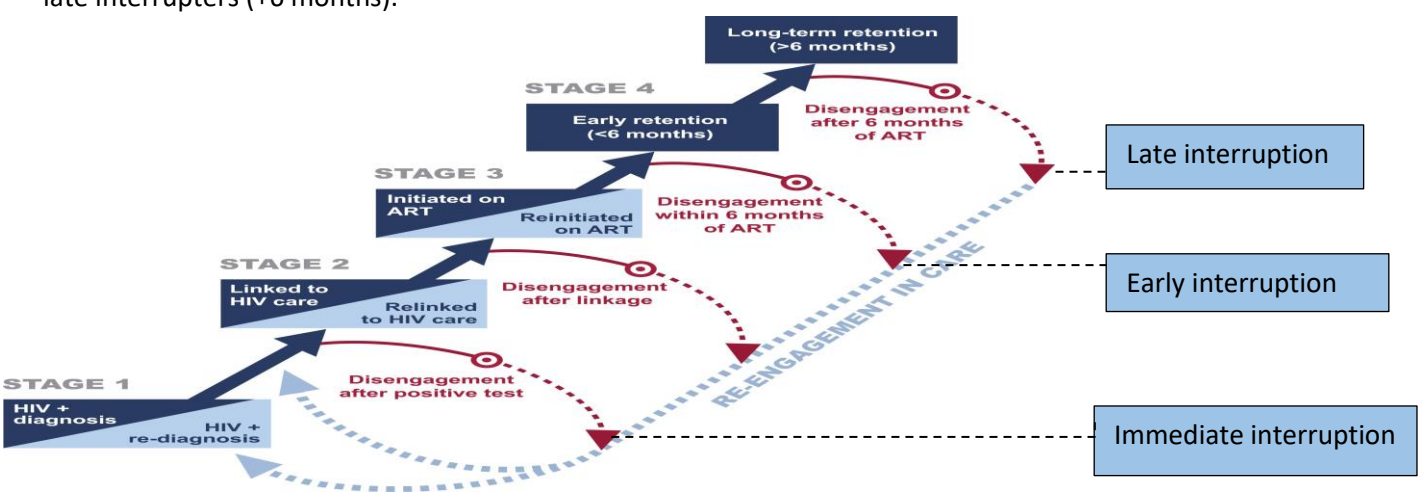
Figure 4.3 Enhanced LCM outline

4.11 Clients returning to care

Any clients who return to the facility either of their own accord or after tracing, more than 28 days after missing an appointment are said to be returning to care. Clients should be provided with the returning to care package as indicated in the enhanced LCM SOP *enhanced SOP (pages 62-67)*. Clients must be actively followed up in all stages to bring them back to care.

There are different stages of treatment interrupters, which are:

- immediate (<28-day post-initiation)
- early interrupters (>28 days <6 months) and,
- late interrupters (+6 months).



Source: Ehrenkranz et al, 2021, PLoS Medicine

Figure 4.4 Stages of HIV care and treatment

5 BASIC CARE PACKAGE FOR HIV-POSITIVE INDIVIDUALS

Important Contacts:

National Pharmacovigilance Centre
WhatsApp number +268 7655 7303
CMS 25184111

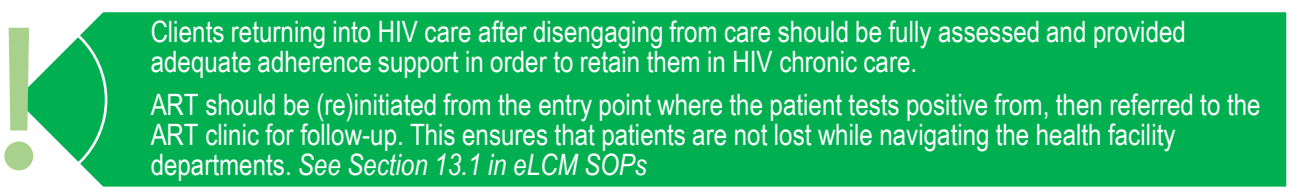
All clients who test HIV-positive should be linked to and enrolled on HIV chronic care on the same day of diagnosis. All health facilities should provide the basic HIV chronic care package as defined in this chapter.

The basic HIV chronic care package for people living with HIV (PLHIV) includes:

- Initial clinical evaluation and categorization of clients.
- Opportunistic infection screening and management, including the provision of prophylactic
- Adherence and psychosocial support services.
- Patient Education
- HIV index testing.
- Linkage to care and treatment
- Laboratory tests.
- Routine and structured clinical follow-up visits.
- Integration of HIV services with other health services such as
  - TB
  - Sexual and reproductive health i.e., family planning and cervical cancer screening and management
  - HIV prevention services including the provision of condoms and STI screening and management
  - Hepatitis B screening and management
  - Non-communicable disease screening and management
  - Mental health screening and management
  - Palliative care
  - Nutritional assessment
  - Immunisation

The basic HIV chronic care package should be differentiated based on the client's laboratory and clinical evaluation findings. *See Table 5.2* for definitions of relevant categories.

Pharmacovigilance is also an integral part of HIV service delivery. All adverse events should be reported to the National pharmacovigilance Centre. These include adverse events from all the medical products a patient on ART patient is taking. *See Section 5.12*



5.1 Assessment of PLHIV at Initial Contact

PLHIV present at different stages of disease progression. Upon presentation, clients should be assessed using baseline CD4 count, and clinical evaluation, including WHO clinical stage to determine whether the client has mild, moderate, or advanced immunodeficiency. See Table 5.7 for definitions of mild, moderate and severe immunodeficiency.

Clients must be offered differentiated service delivery according to their clinical presentation. For differentiated service delivery for clients on ART, *Section 5.7*

Table 5.1 Elements of Clinical Evaluation for PLHIV

HISTORY
Current and past medical history
History • Document current presenting complaints and symptoms. • Screen for opportunistic infections such as Covid-19, TB, cryptococcal meningitis, toxoplasmosis, Pneumocystis jiroveci pneumonia (PJP) and other bacterial infections. • Screen for STIs. • Document history of TB. • Document history of hepatitis B and hepatitis C. • Ask about any other past medical history (e.g., hypertension, diabetes, epilepsy, anaemia, Gastritis and Peptic ulcer disease). • Document previous or current ARV use (including for PMTCT), post-exposure prophylaxis (PEP), pre-exposure prophylaxis (PrEP), and ART. • Establish which current medications (prescription, non-prescription and herbal) are likely to adversely interact with ARVs. • Ask about drug allergies (especially sulphonamide drugs). • Family history of HIV testing
Psychosocial history
• Establish and document social support structures. • Establish the possible presence of mental health concerns, depression, substance use, etc. • Encourage disclosure to trusted significant others and sexual partners. • Elicit and begin to address possible barriers to adherence to treatment. • Link to an additional facility and community support resources. • Employment status and place of employment • Family history of NCDs *See Annex 11.22*

Table 5.1 Elements of Clinical Evaluation for PLHIV (continued from the previous page)

Sexual and reproductive history
• Discuss secondary prevention and avoidance of reinfection with STIs, including combined prevention approaches. • Ask about the HIV and ART status of the sexual partner(s). • Encourage HIV testing for all sexual partners of HIV-infected adults, all children of HIV-infected women, and all children whose mother's HIV status is unknown 9index testing). • Assess family planning intentions and contraceptive needs. • Screen females for cervical cancer annually and provide appropriate management. • Ask about current and past contraceptive use. • Assess condom use skills
Physical examination
General Appearance of the clients • The appearance of the client depends on the stage of the disease. The clients may look very healthy or be ill-looking and cachectic. Check for Jaundice, clubbing, oedema, nutritional status, lipodystrophy • Check vital signs (respiratory rate, temperature, heart rate, blood pressure, weight/Z score for children/growth chart) • Look for cyanosis, clubbing, jaundice, dehydration, pallor and oedema. • Calculate body mass index; use mid-upper arm circumference for pregnant women and children. • Temperature: Fever can be present. • Pulse: Tachycardia can be present. • Blood pressure: Hypotension, and hypertension can be present. • Respiratory rate: Tachypnoea can be seen during fever and respiratory tract infections • MUAC • Mental status examination and depression screening where indicated. • Look for signs of cryptococcal meningitis and TB as these illnesses will affect the timing of ART initiation; *see Section 6.2.* **Skin** • Look out for folliculitis, Kaposi sarcoma, flat warts, secondary syphilis, psoriasis/eczema, seborrheic dermatitis, fungal infections of skin and nails, viral infections like flat warts, molluscum contagiosum and herpes zoster, thin sparse hair etc. **Eyes** • Retinal haemorrhage, pallor, Kaposi sarcoma, squamous cell carcinoma of the eye, retinal infiltrates, herpes zoster, molluscum contagiosum.

Table 5.1 Elements of Clinical Evaluation for PLHIV (continued from the previous page)

Ear, Nose and throat

- Inflammation of the nasal turbinates may be present, tenderness over sinuses, suppurative otitis media, unilateral/bilateral hearing loss, Kaposi sarcoma, periodontal disease, dental caries in children, oral herpes simplex, oral hairy leucoplakia, oral thrush ± odynophagia, Non-Hodgkin's lymphoma, orolabial warts.

Lungs

- Oxygen saturation, cyanosis, dyspnoea, wheezes or stridor, Crackles and rhonchi, dullness to percussion, Increased tactile fremitus
- Cardiovascular system
- Look for signs of heart failure, A heart murmur, and muffled heart sounds can be found.

Abdomen

- Central obesity, Abdominal distension or tenderness can be found, Hepatomegaly, Splenomegaly, pregnancy and rule out intrauterine growth retardation

Genitourinary

- Vaginal or urethral discharge, genital ulcers/warts

Extremities

- Muscle weakness, Joint swelling, Muscle wasting and fat redistribution

Central Nervous System

Focal neurological deficits, confusion or altered mental status, peripheral neuropathy, and Gait disturbances may be present.

Diagnosis and treatment

- Assign a **provisional diagnosis** and order confirmatory tests.
- Document the initial WHO clinical stage and review laboratory tests to make a definitive diagnosis
- Manage the presenting illnesses: prompt treatment of inter-current illness contributes to the success of ART and reduces early mortality.
- Provide STI screening and management.
- Refer client for further management if malnourished (e.g., Food by Prescription or Integrated Management of Children Illnesses Guidelines).
- Provide or refer for COVID-19 vaccination and other pending immunisations
- Identify and prioritize care for clients with advanced immunodeficiency to improve client outcomes.
- Initiate ART and give review date.

5.2 Baseline Laboratory Evaluation of PLHIV

Baseline laboratory investigations are essential components of assessing clients for the start or restart of HIV chronic care.

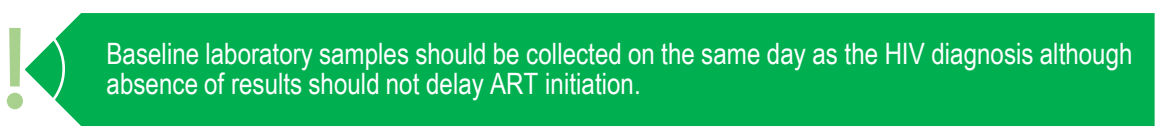


Table 5.2 Baseline Laboratory Evaluation Differentiated by Client Category

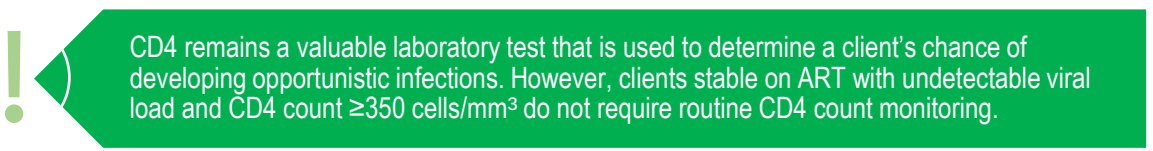
Population	Baseline Test	Comments
All PLHIV: Mild/ Moderate immunodeficiency	Re-testing for verification CD4 count FBC	Required; refer to *Chapter 3* on HIV testing services (HTS).
Advanced Immunodeficiency	TBLAM, CrAg, X-pert MTB/RIF, Serum CrAg ,CSF CrAg	Refer to *Section 6.2* for guidance If CD4 ≤100 cells/mm³, *see Figure 6.3* for the CrAg screening algorithm • If positive and symptomatic for meningitis, refer the client to the hospital for further investigation • If positive and asymptomatic, refer to Table 6.19 for fluconazole pre-emptive treatment. • Reflexive test following CD4 result of ≤100 cells/mm³
All TB presumptive clients	Lateral flow urine lipoarabinomannan assay (LF TB-LAM)	• LF TB-LAM is an additional diagnostic tool. • LF TB-LAM is now offered to all symptomatic PLHIV • If LF TB-LAM is positive, start DS-TB treatment and follow-up sputum results. *See Figure 6.1* for the TB screening algorithm.
All PLHIV	Alanine aminotransferase or aspartate aminotransferase (AST/ALT)	• Required to make management decisions for PLHIV with a positive HBsAg test • If not available, look for signs of liver disease before ART initiation.
All PLHIV	Creatinine	• Recommended for clients being initiated on TDF. • If not available, rule out renal dysfunction clinically before ART initiation, especially in clients with hypertension and diabetes, and run creatinine when later available. *See Section 7.5* and *Section 7.7.4*
	Haemoglobin/full blood count	• Full blood count with platelets and prothrombin time test can also be used in the absence of liver function tests. • Recommended for clients being initiated on zidovudine (AZT). If not available, perform point-of-care haemoglobin using HemoCue® or clinically assess clients for the presence of anaemia.
	Hepatitis B surface antigen	• Can be done as a rapid point of care test. • If positive, initiate the client on tenofovir (TDF)-based regimen.
	Pregnancy test	• Recommended for women of childbearing age including adolescent girls.
	Random blood sugar	• Recommended for patients at risk of developing diabetes mellitus and those initiating a DTG and PI-based ART regimen

5.3 Changing Role of CD4

Prioritise CD4 testing for new ART patients, suspected treatment failures and those re-engaging to care after treatment interruption >1 year

For clients who initiate ART with a baseline CD4 count >350cell/mm³, and show good clinical response, there is no value added by doing a follow-up CD4 count at 6 and 12 months

For clients who initiate ART with a CD4 count <350cell/mm³, CD4 monitoring should be done 6 and 12 months after ART initiation. Once the client has two consecutive undetectable viral loads CD4 monitoring can be stopped. If treatment failure is suspected, resume CD4 monitoring until the client has an undetectable viral load.



An individual's CD4 count determines the following:

- Immune status at enrolment (e.g., mild, moderate or advanced immunodeficiency)
- Immune status for clients on ART with viral load (VL) ≥1000 copies/mL and failing treatment or clients returning to care after a long interruption in treatment e.g., a year
- Evaluating the need for routine screening of opportunistic infection
    - If CD4 ≤100 cells/mm³, then do LF CrAg screening should be completed
- If CTX prophylaxis should be started, stopped or restarted
- Disease progression, for clients with HIV who have not initiated antiretroviral therapy (ART) *See Annex 11.26* for the use of CD4 and VL tests.

5.4 Co-trimoxazole Preventive Therapy (CPT)

CPT is used to prevent the following common opportunistic infections among PLHIV:

- Pneumocystis jirovecii pneumonia (PCP)
- Toxoplasmosis
- Diarrhoea caused by Isospora belli and Cyclospora species
- Certain bacterial infections, including bacterial pneumonia and urinary tract infections
- Also useful in Malaria endemic areas

CPT Indications

- Adults and adolescents (including pregnant women) with severe or advanced HIV clinical disease (WHO stage 3 or 4)
- Adults (including pregnant women) with CD4 cell count ≤350 cells/mm³
- All people living with HIV with active TB disease regardless of CD4 cell count
- All children < 5 years old diagnosed with HIV

When to start CPT

CPT should be started at enrolment into HIV chronic care.

Clients with active TB—adults, adolescents and children—should continue to receive CPT regardless of CD4 count, until completion of TB treatment. After TB treatment is completed, they can be assessed to determine if CPT can be stopped.

Cotrimoxazole Dosing

> ! Clients with a history of severe allergy to sulphur should not be given CPT. In such cases, dapsone is a safer alternative.

Table 5.3 Co-trimoxazole Prophylaxis Dosing for Adults, Adolescents and Children

Age	Weight	Suspension 200mg sulfamethoxazole (SMZ) + 40 mg trimethoprim (TMP)/ 5 mL	Paediatric Tablet 100mg SMZ + 20mg TMP Once daily	Single Strength Adult Tablet 400mg SMZ + 80mg TMP Once Daily	Double Strength 800mg SMZ + 100mg TMP Once Daily
6 weeks	<5 kg	2.5 mL	1	1/4	--
6 months to 5 years	5–15 kg	5.0 mL	2	1/2	--
≥ 6 years to 14 years	15–30 kg	10 mL	4	1	--
>14 years	>30 kg	--	--	2	1

Cotrimoxazole adverse events

Table 5.4 Co-trimoxazole Prophylaxis Toxicity Grading Scale for Adults and Adolescents

Toxicity Level	Clinical Description	Recommendation
Grade 1	Erythema	Continue prophylaxis with careful and repeated observation and follow-up. Provide symptomatic treatment, such as antihistamines.
Grade 2	Diffuse maculopapular rash, dry desquamation	
Grade 3	Vesiculation, mucosal ulceration	Discontinue Co-trimoxazole preventive therapy (CPT). Desensitization can be considered where a medical doctor is available (*see Table 5.5* on CPT desensitization).
Grade 4	Exfoliative dermatitis, Stevens-Johnson syndrome or erythema multiforme, moist desquamation	Permanently discontinue CPT. Refer client for hospital care.

> ! Document any allergic reactions clearly in the client's file and appointment card, and report through available pharmacovigilance tools (*see Annex 11.29*).

When to stop CPT

Continue CD4 monitoring as per viral load schedule while a client remains on CPT. Clients should continue CPT until the following occurs:

- The client has full immune recovery evidenced by an undetectable viral load, or if VL is unavailable, at least one CD4 counts >200 cells/mm³ for clients above 5 years of age and >350 cells/mm³ for children 3-5 years
- no history of PJP or toxoplasmosis or other opportunistic infections.
- Severe (Grade 3 or 4) adverse reaction to CPT or any other sulphur-containing medication.
- Severe kidney disease (creatinine clearance <50 mL/min)
- Severe liver disease (aspartate aminotransferase/ alanine aminotransferase [AST/ALT] >5 times the upper limit of normal)
- There is no history of PJP or toxoplasmosis.

The reason for stopping CPT should be documented in the client's file and appointment card.
If CPT must be permanently discontinued due to an allergic reaction, dapsone is an acceptable alternative

Recommended Dapsone done:Adults and adolescents: 100mg po od with foodChildren: 2mg/kg od

5.5 Co-trimoxazole desensitization in adults and adolescents

In instances of Grade 3 reactions to CPT, consider desensitization as described below.
In clients with a Grade 4 reaction to CPT, do not attempt desensitization: immediately refer the client to a hospital for further management. Clients undergoing desensitization should be closely monitored.

Table 5.5 Co-trimoxazole Prophylaxis Desensitization for Adults and Adolescents

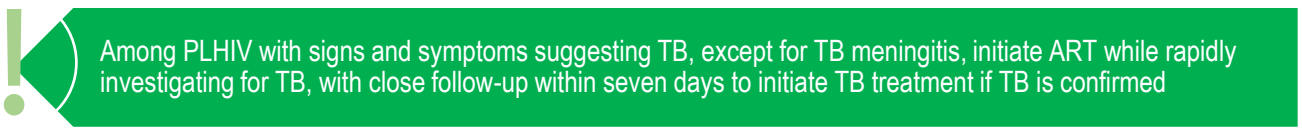
Step	Dose	Suspension*	Tablet
Day 1	80 mg SMZ + 16 mg TMP	2 mL of oral suspension	N/A
Day 2	160 mg SMZ + 32 mg TMP	4 mL of oral suspension	N/A
Day 3	240 mg SMZ + 48 mg TMP	6 mL of oral suspension	N/A
Day 4	320 mg SMZ + 64 mg TMP	8 mL of oral suspension	N/A
Day 5	400 mg SMZ + 80 mg TMP	N/A	1 single-strength SMZ–TMP tablet
Day 6 and onward	800 mg SMZ + 160 mg TMP	N/A	2 single-strength SMZ–TMP tablets or 1 double-strength tablet

The Co-trimoxazole oral suspension is (200 mg SMZ + 40 mg TMZ) / 5 ml

5.6 ART initiation

All PLHIV are eligible for rapid ART initiation (within 7 days of HIV diagnosis) regardless of CD4 count or WHO clinical stage (except for clients with cryptococcal or TB meningitis). The following priority populations should be evaluated urgently and offered rapid ART initiation as they are at risk of poor outcomes:

- Clients with advanced immunodeficiency (CD4 ≤200 cells/mm³ or WHO clinical stage 3 or 4). ART should be delayed only when meningitis or another central nervous system infection is suspected Infants and young children ≤5 years old
- Pregnant and breastfeeding women
- Clients with Tuberculosis (TB)
- HIV-positive individuals in sero-different relationships
- Clients with hepatitis B virus (HBV) coinfection
- Clients with HIV-associated nephropathy



Clients returning to care

All clients returning to care should be evaluated for AHD and offered rapid ART initiation; delay ART initiation only if the client has TB meningitis and/or cryptococcal meningitis.

5.6.1 Community ART initiation

Rapid ART initiation should be prioritised for all eligible clients.

To provide patient-centred care while improving linkage to ART services, ART initiation may be offered in the community. Community ART initiation will be implemented following these guiding principles:

- Only where the team has a trained clinician to offer the ART readiness assessment, pre-ART counselling and ART initiation
- The client should be willing to be linked to a health facility of their choice and should be able to attend a clinical visit at the health facility within 2 weeks of community ART initiation. There is a need to integrate the implementation of the basic package of care either in the community or at the 2-week visit at the facility to identify AHD, especially to acquire a baseline CD4. Refer to *Table 5.7 and Table 5.7* for the package of care for stable clients
- The client is clinically well, with WHO clinical stage 1 or 2, AND has no signs and symptoms of OIs or any comorbidities that may require further assessment or investigations. It is recommended that these patients get the required information and get benefits from same-day or rapid initiation within 7 days.
- For clients returning to care presenting with the old medical record, there must be no history of treatment failure, or current immunological or clinical failure. As clients who disengaged from care are at risk of interrupting treatment again, there must be an emphasis on a plan for psychosocial support to foster retention for all treatment interrupters with the involvement of treatment supporters, community support structure etc.

If these principles are not met the client should be referred to the nearest health facility for assessment and ART initiation and not be initiated within the community.

5.7 Differentiated service delivery (DSD)

Differentiated service delivery, previously referred to as differentiated care, is a person-centred approach that simplifies and adapts HIV services across the cascade in ways that both serve the needs of people living with and vulnerable to HIV and optimize available resources in health systems. The principles of differentiated service delivery can be applied to prevention, testing, linkage to care, ART initiation and follow-up and integration of HIV care and coinfections and comorbidities. Differentiated service delivery for HIV treatment has become a critical component of recognizing the diversity of needs of people living with HIV (WHO, 2021).

5.7.1 Differentiated service delivery in HIV prevention, testing and linkages

To reach the remaining people living with HIV who do not yet know their status the principles of differentiated service delivery will help identify service gaps and adapt HTS services to client needs. The aim is to provide a systematic approach that will consider the core components of the first 95: mobilizing, testing and linking to prevention and/or treatment.

DSD simplifies and adapts HIV services across the HTS cascade, to reflect the preferences and expectations of various groups of PLHIV, while reducing unnecessary burdens on the health system. It supports shifting resources to clients; who are most in need and hence, in the context of HIV testing, is aimed at developing HIV testing strategies, targeted at identifying those PLHIV who do not yet know their status, to link them to HIV care and identifying people who need and want HIV prevention services, including PrEP, to link them to these services.

When described as a service delivery model for HTS, these three components (mobilizing, testing and linking) are necessary and should be included in the design of the model. Alongside the core components, the DSD model shall use building blocks as a foundation of HTS DSD.

These are:

- ***What*** services are provided (the package of services)?
- ***Where*** are HIV testing services delivered (location of mobilizing, testing and linking)?
- ***When*** are HIV testing services delivered (time of day and frequency of mobilizing, testing and linking)?
- ***Who*** is providing HIV testing services (the cadres performing the mobilizing, testing and linking)?

HIV programs require strong linkages between testing, prevention, clinical care, and social support services, which are often delivered by different providers working in diverse locations that range from communities to Health facilities.

Following an HIV-negative result, the client should receive information about HIV prevention strategies, including PrEP, and if the client desires, linked to PrEP services, preferably at the same location and/or on the same day.

PrEP should be offered as an additional prevention choice for people at substantial risk of HIV infection, as part of a combination of prevention approaches that include HTS services, risk reduction counselling, diagnosis and treatment of STIs, male and female condoms, lubricants, ART for all HIV-positive people, and VMMC. PrEP, including all current and introduced methods, can be offered in and outside of healthcare facilities to meet the needs of HIV-negative clients who need and want HIV biomedical prevention.

5.7.2 Differentiated service delivery in HIV care and treatment

- Long-term care and adherence should be promoted by allowing clients with undetectable VL to choose models of care that best suit their needs when accessing ART services. Differentiated ART Service Delivery (DSD) models seek to*:*
- Empower clients to actively participate in their care
- Reduce client-related costs of accessing care
- Allow equitable service allocation as determined by individual client category needs
- Supporting clients to achieve and maintain viral load suppression (VLS) by facilitating retention in care" (providing models adapted to clients' needs supports retention in care and subsequently VLS.
- Keep clients motivated to remain in care by ensuring clients have an undetectable viral load
- Improve adherence through population-specific care in the treatment delivery

Further guidance is provided through the updated DSD guidelines

HIV care should be differentiated according to clinical evaluation, laboratory evaluation and client needs. This approach will ensure that services are client-centred address the client's needs and expectations and improve efficiencies as well as client outcomes. Care packages for stable clients should also be defined whether at the facility or community. Priority patients can be provided with 3-6 multi-month dispensing (MMD) of treatment where appropriate, recognizing their specific needs – paediatric patients require growth monitoring; KPs need STI screening per guidelines; HEI need immunization visits to be synchronised with mother's, most of who have been stable on ART etc

5.7.3 Multimonth Dispensing (MMD)

PLHIV on ART for at least 6 months with an undetectable viral load and who are clinically well on ART are eligible for up to three months of refills (3MMD).

The definition of being established on ART (stability) should be applied to all populations, after resolving any acute issues, including the following:

- receiving antiretroviral therapy (ART) for at least 12 months;
- have no current illness, which does not include well-controlled chronic health conditions;
- a good understanding of lifelong adherence and
- demonstrate evidence of treatment success with at least one suppressed viral load result within the past six months.

Table 5.6 MMD for different population groups

Population	MMD
2nd line ART patients	Up to 3MMD
3rd line ART patients	Up to 3MMD
Patients with controlled comorbidities	Up to 3MMD
Children between 2-5years	Up to 3MMD
Children and Adolescents 5-19years old	**Up to 6MMD**
Pregnant and breastfeeding women	Up to 3MMD
Key populations	**Up to 6MMD**
Adults	**Up to 6MMD**

The populations mentioned above for MMD, often represent specific cohorts in which retention and suppression of viral loads have been challenging and may benefit more from differentiated service delivery for HIV treatment models adapted to their needs.

Multi-month refills and dispensing may be used alone or within any of the categories of differentiated service delivery for HIV treatment, each of which provides additional benefits to both the health system and clients. Multi-month refills may also be used for children older than two years since the dosage is adjusted less frequently beyond that age.
Only children 2 – 5 years with consistent, knowledgeable and committed caregivers are eligible for multi-month refills up to 3MMD
See Chapter 9 Section 9.16 for more information on DSD in children.

Table 5.7 Definition of Client Categories for Differentiated HIV Service Delivery

<table>
<tr><th colspan="3">All People Living with HIV (PLHIV)</th></tr>
<tr><th colspan="3">Clients initiating or reinitiating ART or on ART for <1 year</th></tr>
<tr><th>Advanced Immunodeficiency (Advanced HIV Disease)</th><th colspan="2">Mild or Moderate Immunodeficiency (Clinically Well)</th></tr>
<tr><td>Children 5 years and older:
• Same as adults plus those with CD4 count less than 25%
See also Section 6.2</td><td rowspan="2">Mild immunodeficiency:
• Presenting or returning to care when clinically well (WHO clinical stage 1 disease and/or CD4 cell count ≥350 cells/mm³)
• Such individuals may be ART naïve, may have interrupted treatment, or failing treatment</td><td rowspan="2">Moderate immunodeficiency:
• Presenting or returning to care with WHO clinical stage 2 disease and/or CD4 cell count between 200-350cells/mm³
• Such individuals may be ART naïve, may have interrupted treatment, or failing treatment</td></tr>
<tr><td>Children under 5 years:
• All children less than 5 years old are managed as clients with advanced immunodeficiency (advanced disease)</td></tr>
<tr><th colspan="3">Clients on ART for ≥1 year</th></tr>
<tr><th colspan="2">Clients classified as not established on ART</th><th>Clients established on ART</th></tr>
<tr><td colspan="2">If a client has 1 or more of the following characteristics:
• Detectable viral load or failing ART regimen
• CD4 <200 cells/mm³
• Adverse drug reactions
• Active opportunistic infections
• Non-adherent to treatment
• Substance use disorder
• Comorbid conditions requiring frequent monitoring
• Children under 5 years of age</td><td>If a client has the following characteristics:
• Lower than detectable limit viral load
• No severe opportunistic infections
• CD4 ≥200 cells/mm³
• Treatment adherent
• No adverse drug reactions
• ≥5 years and has a consistent and reliable caregiver
These clients are eligible for 6month refills and DSD
See chapter 9 for eligibility criteria for children.</td></tr>
</table>

5.7.4 Differentiated package of care for clients who have been on ART for less than 12 months

In Eswatini, clients who have been on ART for less than 12 months are considered not to be established on ART and therefore eligible for up to 3 months of refills.

Table 5.8 Differentiated HIV services: Package for entering to care / less than one year on ART

HIV Chronic Care Package				
Client category	**What is included in the basic care package?**	**Where is care provided?**	**When is care provided?**	**Who will provide care?**
Presenting or returning with **mild or moderate immune deficiency** (clinically well)	The basic chronic care package includes (refer to *Section* ***Error! Reference source not found.*** for the basic care package): • Client readiness assessment before initiating ART • Rapid ART initiation • Treatment • Literacy/Adherence support • TB preventive therapy [TPT] and Co-trimoxazole (CTX) preventive therapy [CPT]) if CD4 count ≤350cells/mm³ • Management of possible side effects • Index HIV testing • Provision of condoms • Assessment of family planning needs • Screening and management of NCDs • Enrolment into LCM	Health facility and Community See *section 5.6.1* for eligibility criteria for community ART initiation	**Soon after HIV diagnosis,** • ART initiation within 7 days • CTX from enrolment if eligible; see Section 5.4 on when to stop • TPT within 1-month post-ART initiation see *Section 6.1.5* • ART refill • 1st clinical visit 2 weeks after ART initiation • Monthly refills through the first 6 months • Every 3 months after the first 6 months on ART if an undetectable VL is achieved • For more information on the ART refill schedule, *see Chapter 7* Table 7.6,	Nurses Doctors Expert clients Laboratory teams Pharmacy teams

Table 5.8 Differentiated HIV services: Package for entering to care / less than one year on ART (continued from the previous page)

HIV Chronic Care Package				
Client category	**What is included in the basic care package?**	**Where is care provided?**	**When is care provided?**	**Who will provide care?**
Presenting or returning with **advanced immuno-deficiency** (advanced HIV disease)	Basic chronic care package as listed above. • Emphasis is on the advanced immuno- deficiency package: • CrAg screening • LF TB-LAM testing • Management of OIs • *See Section 6.2* for the full Advanced Disease package	Health facility only	**Soon after HIV diagnosis,** • ART initiation within 7 days after ruling out CNS infections e.g., TB and Cryptococcal infection. • CTX from enrolment; see Section 4.6 on when to stop • TPT from one-month post-ART initiation see • ART refill: • After initiating ART: 2 weeks • First 6 months on ART: every 1 month until clinically stable. More frequent visits may be warranted • After 6 months provide up to 3MMD if virally suppressed and does not need frequent follow-up. *See Table 5.6*	Nurses Doctors Expert clients Laboratory teams Pharmacy teams

5.7.5 Differentiated package of care for clients who have been on ART for at least 12 months

PLHIV on ART for at least 12 months are eligible for up to six-month refills (6MMD) provided they fit the definition of being established on ART.

Table 5.9: Differentiated package of care for clients who have been on ART for at least 12 months

Client Category	HIV Chronic Care Package			
	What is included in the basic care package?	**Where is care provided?**	**When is care provided?**	**Who will provide care?**
Established on ART	The basic care package includes: • Differentiated service delivery models • HIV Index testing • Provision of condoms • Refill of NCD medications • Assessment of family planning needs	Health facility and community	Clinical assessment: • Every 6 months • ART refill: Every 3–6 months	Doctors Nurses Expert Clients Laboratory teams Pharmacy teams Community health care teams
Not established on ART	Basic care package emphasis is on: • Adherence Counselling and psychosocial support • If there is evidence of treatment failure timely switching to 2nd or 3rd line regimen is necessary • Advanced HIV disease package (if CD4 <200cells/mm³); CD4 testing for high-risk clients (returning to treatment and failing on ART – HVL) then apply the AHD package of care to those fitting the criteria. *see Section 6.2* • Management of other comorbidities and adverse drug reactions to common first-line ARVs (*see Annex 11.3, 11.4, 11.5*) • Special clinic days for clinically unstable clients e.g., targeting clients suspected to be failing treatment • HIV Index testing • Assessment of FP needs/contraception	Health Facility *See section 5.6.1 for eligibility criteria for community ART initiation*	Clinical assessment: • Every 1 month, or frequently as needed • • ART refill: • At least every 1 month • Special clinic days e.g., Paediatric Days, specific days for clients completing SUAC sessions	Using the Multidisciplinary team approach

5.7.6 Available DSD Care Models for Clients on ART

After 1 year on ART, clinically well clients who are considered established in care should be offered an opportunity to choose one of the less intensive different ART service delivery models to enhance their adherence. Clients not established in care should be offered more intensive DSD models at facilities. Established in care clients are free to switch from model to model for as long as they are eligible for the model of delivery chosen.

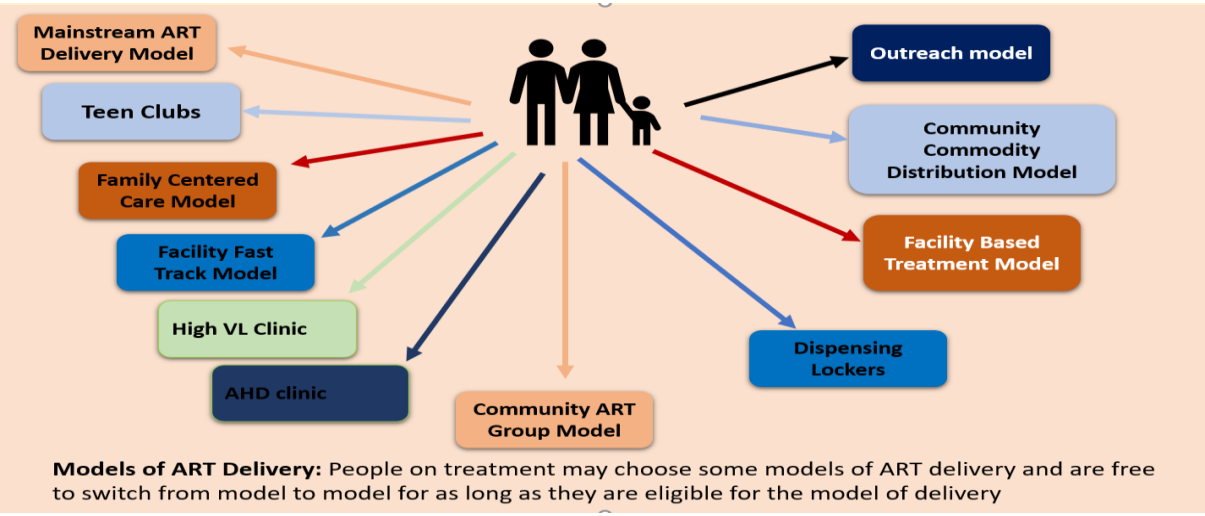


Figure 5.1 DSD models of care available in Eswatini

Stable adult clients who are considered established on ART and eligible for less intensive DSD models may choose any of the less intensive models listed below.

Table 5.10 Intensive and less intensive DSD models

Facility based	Community-based
More intensive	
Mainstream care (Standard of care / conventional model)	
Viremia clinics (high VL clinic / Challenge clinic)	
AHD Clinics	
Less intensive	
Fast track + appointment spacing	Outreach
Appointment spacing without fast track	
Facility-based treatment clubs (MNCH, NCDs, KPs, etc.)	Community-based ART groups (CAGs)
Teen clubs	Community commodity distribution (CCD)
Family-based treatment clubs	
Dispensing lockers	

Refer to DSD guidelines for more details on the different DSD models available in the country.

Assessment for DSD eligibility and client preference for ART dispensation (quantity of drugs and preferred DSD model) has to be done at each clinical visit. HCWs should assess whether the client still fits in the DSD model or should be enrolled in a different DSD model or needs to go back to the mainstream care

5.8 Prevention, Screening and Management of COVID-19 and other Common Opportunistic Infections

All PLHIV should be screened for opportunistic infections and treated appropriately. Common opportunistic infections among HIV clients, especially clients in Eswatini with advanced immunodeficiency (advanced disease), include TB, cryptococcal meningitis, PJP, Kaposi sarcoma, cervical cancer, recurrent bacterial pneumonia, recurrent oral candidiasis, oesophageal candidiasis, herpes zoster and toxoplasmosis.

For detailed management of opportunistic infections not covered in these guidelines, please refer to the Eswatini Standard Treatment Guidelines.

5.8.1 COVID-19

In a publication by the WHO, HIV appeared to be a significant independent risk factor for severe or critical illness at hospital admission and in-hospital mortality.

The increased risk associated with HIV infection means that PLHIV should be prioritised for vaccination campaigns

The risk of poor outcomes is higher in PLHIV with COVI-19, particularly if they also have other comorbid conditions like hypertension, diabetes mellitus, obesity, TB, and chronic kidney and liver disease.

- Health care workers should counsel patients on the importance of maintaining an undetectable VL as well as managing comorbid conditions.
- Unvaccinated patients should be continuously encouraged to register for and receive full vaccination at their nearest vaccination centre.
- Patients should be educated not to go for vaccination when they suspect having COVID-19 symptoms but rather after the resolution of symptoms. Clients who previously tested positive for SARS-Cov-2 are encouraged to seek medical review. Refer to COVID-19 case management guidelines for more information
- Infection prevention measures of wearing face masks, hand washing, social distancing and cough etiquette among others should be emphasised in all PLHIV.

Some diseases present with similar symptoms to COVID-19. For patients presenting with COVID-19 like symptoms, HCWs should look out for other differentials e.g., TB, Malaria and manage them accordingly as they may be a contributing factor to morbidity and mortality.

Vaccinated PLHIV should be encouraged to report vaccine adverse events through the toll-free number "977".

Steroids are known immunosuppressants which have drug interactions with some ARVs. However, dexamethasone used in COVID-19 patients with severe respiratory distress syndrome is given over a short duration and does not warrant dose adjustment of EFV, PIs and DTG. Conversely, EFV may decrease dexamethasone concentrations, and doubling the dexamethasone dose is therefore recommended. No drug-drug interactions are expected between ARV drugs and the COVID-19 vaccines.

5.9 Basic package of care for children and adolescents living with HIV

The overall goals of care for the HIV-infected child are the same as those for all other children; maintaining good health and preventing disease as well as support for the child/adolescent and the family. This can be achieved by providing comprehensive history, physical examination, lab investigation, general medical care and treatment of intercurrent illnesses should be conducted as summarised in the table below.

Table 5.11 Clinical assessment in children and adolescents

Presenting complaints	• Current symptoms, duration, recurrency • Systems review • TB screening	
Past medical history	• Recurrent symptoms • Serious illnesses • Hospitalizations • Chronic medications, allergies • Previous medicines including traditional herbs, ART regimens and over the counter prescriptions • Previous VL and adherence • Allergies and ADRs (pharmacovigilance)	
	Infant's medical history • Gestational age (especially for low-birth-weight birth-tested infants) • Labour and delivery • Birth weight and developmental history • Breastfeeding and nutritional history • Immunization history and PMTCT	**Adolescent History** • Age at puberty, menstruation • Sexual history including GBV/IPV screening
Family history	• Primary and secondary caregivers • Index testing (family testing) and PHDP	• Mother's medical history including PMTCT

	• Family history of illnesses including TB • Family members on ART	• HIV disease stage (CD4, Viral load, WHO stage)

Table 5.11 Clinical assessment in children and adolescents (continued from the previous page)

Social history	• School history • Religious and cultural beliefs • Source of financial support • Community/ OVC support
Physical examination	• General examination, Growth assessment (Weight for age, weight for height, BMI for age) • Comprehensive physical/ systemic examination • Head circumference in children <2 years, (may be indicative of cognitive or developmental delay) • Developmental evaluation. • Cognitive and physical/sexual development assessments are important in adolescents *(Tanner stages, Annex 0)* +/- referral to Speech/OT
Adherence counselling	• Review plan for adherence support and refer for additional psychosocial support as required • Disclosure and adherence barriers evaluation, child health literacy
Psychosocial support and palliative care	• Assess for stigma and discrimination • Link caregiver/client to a psychosocial support group • Assess for any social challenges the client might have including alcohol/drug abuse and depression screening. • Refer for palliative care when required
Orphans and vulnerable children (OVC)	• Conduct basic assessment for vulnerability (refer to social workers) • Provide HIV testing for family members either at the facility or community level as appropriate • Refer and link to an OVC/DREAMS Program, Babby clubs or caregiver support groups

Laboratory examination/ evaluation	• Repeat confirmatory DNA PCR for infants (<24 months) and re-testing for verification in children (> 24 months) and adolescents (aged 10 – 19yrs)
	• Creatinine (if initiating on TDF or for very sick children)
	• LF TB-LAM testing for children and adolescents with presumptive TB or with advanced disease (*refer to Chapter 6, Figure 6.1)*
	• Serum CrAg screening for children and adolescents with advanced disease (refer to *Chapter 6, Figure 6.2*)
	• Syphilis serology for sexually active or pregnant adolescents (VDRL, TPHA, RPR) *See STI guidelines* for interpretation of results
	• CD4 cell count (AHD package of care as per *Table 6.17*)
	• Hb (preferably full blood count if available)
	• Random blood glucose
	• Lipid profile annually
	• ADOLESCENTS
	  ○ Pregnancy status
	  ○ HBsAg screen
	  ○ STI screening and management

	• Do NOT delay treatment initiation for baseline laboratory assessments or while confirmatory DNA PCR is pending

Rapid ART initiation: All CALHIV should be offered same-day initiation and when not possible, rapid ART initiation (as soon as the patient is ready, preferably within 7 days)- except for clients with AHD, See *section 6.2* on AHD

General medical care, prophylaxis and treatment of opportunistic infections and intercurrent illnesses

- CALHIV should be provided general/ emergency care prophylaxis and treatment of opportunistic infections and intercurrent illnesses
- Children should initiate LTBI treatment
  - within 1 month on ART (after TB is ruled out),
  - on the day of TB treatment completion,
  - if <12 months and with a history of TB contact
- For fluconazole prophylaxis *see section 6.2*

Note:

After a baseline clinical evaluation has been completed utilizing a thorough history and clinical examination, the client's WHO clinical stage can be determined to further understand the severity of the client's clinical condition and the associated risk of mortality and determine the urgency of ART initiation and the follow-up requirements. Children with advanced HIV disease (AHD) require more frequent clinical reviews.

Treatment of HIV infection

- All CALHIV should be offered same-day initiation and when not possible, rapid ART initiation (as soon as the patient is ready, preferably within 2 weeks)
- Opportunistic infection screening, treatment and Prophylaxis
- Children with HIV present commonly for evaluation and treatment of illness. The integrated approach to the management of childhood illness remains the most effective method for managing sick children.
- The risk of opportunistic infections correlates with the degree of immunosuppression. CD4 is higher in infants than in older children and adults, with normal values declining over the first few years of life. The CD4% is relatively independent of age. It is recommended that both the CD4 and CD4% are monitored in children and the lower of the 2 values used to determine the degree of immunosuppression and decision making.

CDC immunologic classification of HIV infection in children < 13 years of age

Table 5.12 Immunologic classification of HIV in children

	CD4+ lymphocyte count (cells/UL) and CD4%		
Immunologic categories	**<12 months**	**1-5years**	**6-12 years**
No evidence of immunosuppression	25%	≥25%	≥500 or >25%
Moderate immunosuppression	15-24%	15-24%	200-400 or 15-24%
Severe immunosuppression	15%	< 15%	<200 or < 15%

All infants and CALHIV should be evaluated using WHO clinical staging *(See Annex 11.29*)

Common clinical conditions in CALHIV:
Common clinical conditions associated with HIV include candidiasis, dermatitis and other skin conditions, diarrhoea, lower respiratory tract infections, septicaemia, otitis media, sinusitis and failure to thrive (growth failure).

Oral and dental conditions: Candidiasis and angular cheilitis, Gingivitis and stomatitis due to CMV, HSV, Dental carries, Lymphoma
Dermatitis: Atopic and Seborrheic dermatitis, Eczema, Psoriasis, Drug eruptions, Viral warts, molluscum contagiosum
Gastroenteritis: cryptosporidiosis, Isosporiasis, CMV, atypical mycobacteria and, HIV enteropathy
Respiratory infections: Bacterial pneumonia, PCP, TB, LIP, Bronchiectasis, Viral pneumonitis
Viral pneumonitis: Respiratory Syncytial Virus (RSV), parainfluenza virus, influenza virus, adenovirus, varicella, measles and CMV

Cycle of events leading to clinical deterioration and growth retardation in persistent diarrhoea
Assess for dehydration and ensure good hydration in all cases. Children with persistent or chronic diarrhoea should be managed as inpatients and treatment depends on the specific cause of diarrhoea (*see Standard treatment guidelines*)

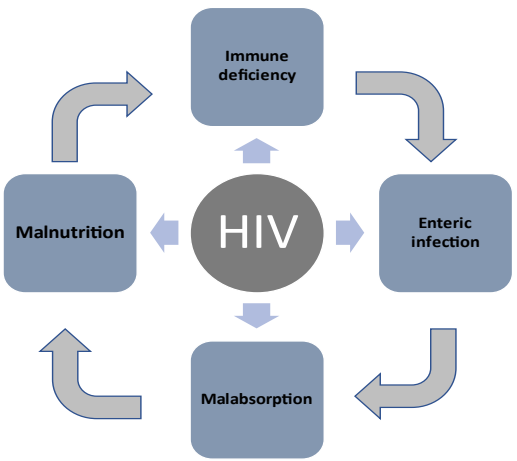


Figure 5.2 Cycle of events following chronic diarrhoea

HV encephalopathy
HIV infection of the brain interferes with the achievement of childhood milestones and may present as stasis, slowing or retardation of developmental milestones or localized damage. Management involves early ART initiation, referral to a neurologist and additional support with physical therapy and social workers.

5.9.1 Growth monitoring

Growth is a predictor of improved health outcomes, potential metabolic complications of HIV infection and /or ART and survival. The growth, nutrition and metabolism of HIV-infected children is an important aspect of providing basic care as it is well recognized that HIV-infected children do not grow as well as HIV-negative children even with adequate virological control.

As HCWs conduct nutritional assessments, it is important to:

- Take a history from the caregiver. Ask the type of feeding, appetite, age at which child was weaned and symptoms of underlying illness e.g., TB.
- Conduct physical examination including the child's mid-arm circumference, weight and height (and from birth through to 2 years of age, head circumference).
- Review the growth chart at each clinical assessment
- The increased risk of malnutrition is due to several reasons including:
- Decreased food intake due to anorexia associated with illness, oral ulcers, and oral thrush
- Increased nutrient loss due to malabsorption, diarrhoea, HIV enteropathy
- Increased metabolic rate because of infections, OIs and the HIV infection itself.

Physical and neurological Development

Development is the progressive acquisition of new skills over time and reflects the integrity of the CNS. It involves the assessment of gross motor, fine motor, language and communication as well as adaptive and social functioning. Developmental delay is the failure to attain the appropriate milestones for a child's age. Please note the developmental milestones (*appendix 11.30*).

Table 5.13 Developmental red flags in children

AGE	DEVELOPMENTAL PROBLEM
Birth- 3 months	Failure to alert to environmental stimuli Rolling over before 2 months Persistent fisting at 3 months
4-6 months	Poor head control Failure to smile Failure to reach for objects by 5 months
6-12 months	No baby sounds or babbling
12 -24 months	Lack of consonant production Hand dominance before 18 months No imitation of speech and activities by 16 months
Any age	Loss or regression of previously attained milestones

Adolescent development

Neurological delays can present as developmental delay, cognitive deficits, behavioural problems, psychiatric manifestations, and school failure in young children.

Table 5.14 Stages of adolescent social and psychological development

Adolescent stage Age (years)	Early adolescence 12-14yrs	Mid- adolescence 15- 17yrs	Late- adolescence 18-19yrs
Social Orientation	Family oriented	Increasing independence	Adult relationships
Peer relations	Striving for autonomy	Alliance to a peer group	Intimacy in friendships
Thought processes	Concrete	Abstract thinking begins Concrete thinking under stress	Abstract thinking Future orientation
Psychosexual development	Concerned about physical development	Sexual experimentation	Romantic relationships

Delays in physical development can present as delayed puberty in adolescents. *(See Tanner's maturation scale- appendix 0)*

5.9.2 Mental Health

- Children and adolescents are susceptible to psychological disturbances due to HIV itself and perceptions regarding HIV in their environment. Some of the most common psychological disturbances include depression and anxiety, internalized stigma, post-traumatic stress disorder, cognitive difficulties, perceived lack of social support, alcohol/drug addiction and suicide. Any of these can significantly interfere with a patient's sense of well-being and adherence. It is important to assess all areas of the life of a child/ adolescent using SHADSS approaches (School, Home, Activities, Depression/Self-esteem, sexuality and safety).
- All CALHIV should receive basic screening for depression and general mental health before initiating ART, annually and when adherence challenges are identified. This is particularly so for all CALHIV who previously interrupted treatment or have suspected/confirmed treatment failure.
- CALHIV with mild depression should receive supportive counselling. Those with moderate-severe depression should be managed as per guidelines (*see chapter 10 section 10.6*).

Prevention of Other Infections through Immunizations and prophylaxis

Prevention of Other Infections through Immunizations and prophylaxis significantly reduces the frequency of invasive infections. This should be started and completed according to the recommended schedule (*see national immunisation schedule*). *See Annex 11.33*

5.10 Sexual and Reproductive Health

5.10.1 STIs in PLHIV

All PLHIV should be assessed for symptoms of STIs. Syphilis screening using Rapid diagnostic test (RDT) Treponema pallidum haemagglutination assay (TPHA) should be performed as a baseline investigation for all sexually active adults and adolescents living with HIV. Sexual partners of clients with STIs should be contacted and treated as well. Early diagnosis and effective

treatment of STIs can contribute significantly toward reduced HIV transmission. For more information, *see the National STI Guidelines.*

Adolescents who have STIs are at a higher risk of acquiring HIV. The same biological and social factors that increase vulnerability to STIs also increase vulnerability to HIV infection.

Management of STIs in PLHIV

Management of STIs in PLHIV is the same as for HIV-negative persons except for Genital herpes. Refer to STI guidelines.

Table 5.15 STIs Commonly Found in PLHIV

STI	HIV Co-infection Considerations	Treatment
Genital ulcer syndrome	• Treatment for genital ulcer syndrome • in HIV-positive clients is the same as for HIV-negative clients. • Clients with HIV are more likely to experience extensive and more severe forms of ulceration and treatment failure; additionally, ulcers heal more slowly. • Increased doses and a more prolonged duration of therapy may be necessary. • Weekly follow-up should occur until there are no lesions.	• For chancroid ulcers in HIV-infected persons: Cipro floxacillin is the drug of choice. • For HIV clients with donovanosis: gentamicin 1 mg/kg IV 3 times a day should be added if the improvement is not evident within the first few days of therapy.
Disseminated Genital herpes	• Persistent and/or severe mucocutaneous ulcerations involving large areas of perianal, scrotal or penile skin are indicative of HIV coinfection. • Doses and duration of treatment with • acyclovir should be increased.	• Acyclovir 400 - 800 mg orally 3 times daily until complete clinical healing of lesions. • see the rest of the Treatment in the STI guidelines
Vaginal discharge Syndrome (VDS)	• VDS is characterized by abnormal vaginal discharge in terms of increased quantity, and/or unusual colour or malodour. N. gonorrhoea and C. trachomatis can cause cervicitis Trichomonas. vaginalis, Candida. albicans and bacterial vaginosis can all cause abnormal discharge.	• Ceftriaxone 500mg IM stat replaces 250mg dosage of the same across all syndromes that are gonorrhoea related • The rest of the management see STIs Guidelines
Urethral discharge syndrome	• Gonococcal, chlamydial and other • Non-gonococcal urethritis may facilitate HIV transmission, and clients should be made aware of this fact during counselling.	• Treatment is the same for HIV-negative and HIV-positive • *See STI Guidelines.*

Table 5.15 STIs Commonly Found in PLHIV (continued from the previous page)

Candidiasis	• Candidiasis affecting multiple sites, including the vulva and vagina, glans, and prepuce, often occurs in HIV disease. • Relapses of candidiasis are frequent.	• Miconazole vaginal pessaries, 200 mg inserted at night for 3 nights • Clotrimazole vaginal tablet, 100 mg, inserted at night for 7 nights • Nystatin pessaries 200 000 units, inserted at night for 7 nights
Genital warts	• There is a high prevalence of genital warts in persons with HIV. • Warts may be multifocal, extensive and poorly responsive to treatment and are more likely to recur. • Malignant transformation of genital warts may occur more commonly in PLHIV.	• ART and restored immunity improve outcomes of treatment for genital warts • Screen for cervical cancer • *See Standard Treatment Guidelines*

For other STIs like Inguinal Buboes, scrotal swelling and lower abdominal pain in women, *refer to STI guidelines*

HIV testing services should be offered routinely for all clients with STIs. In some cases of STI/HIV coinfection, larger doses and/or longer treatment duration of the drugs may be required. Clients with STI/HIV coinfection should be followed regularly and for a longer duration. Excessive use of antimicrobials should be avoided. All clients with STIs should receive individual counselling on risk reduction and prevention of transmission to partners, together with the provision of commodities.

STIs in Children and Adolescents

Apart from neonatal infections and congenital syphilis, the occurrence of STIs in children and adolescents below 18 years of age invariably indicates sexual abuse. If identified, both emotional and legal support is recommended for the child as part of the comprehensive management of STIs in children and adolescents. Adolescents are not always empowered to negotiate for safe sex so should be screened and treated following the STI screening tool.

In rare instances, the following STIs may not indicate sexual abuse:

- Chlamydial vaginitis, can be acquired perinatally and manifest up to the age of 3 years
- Genital warts, unless supported by other evidence
- Bacterial vaginitis alone
- Candidiasis

5.10.2 Contraception

Contraceptive needs, Pregnancy history, including the first day of the last normal menstrual period, should be documented at every visit.

The following contraceptive methods are offered in Eswatini:

- Condoms (both male and female)
- Oral contraceptives
- Injectable contraceptives
- Subdermal implants
- Intrauterine contraceptive devices (IUCDs)
  - Copper-bearing IUCDs, widely available in public health facilities
  - Levonorgestrel-releasing IUCDs (Hormonal IUD), available in some private facilities
- Tubal ligation - bilateral tubal ligation
- Vasectomy
- Natural methods
  - Rhythm method/ Withdrawal method/Breastfeeding/Lactational amenorrhoea method
  - Abstinence/ Outercourse
  - Symptoms-based methods: Monitoring basal body temperature and cervical secretions

If blood pressure is ≥160/100 mm Hg, do not provide COCs. Help her choose a method without oestrogen, but not a progestin-only injectable. Blood pressure measurement is desirable before starting a hormonal method. However, where the risks of pregnancy are high and few methods are available, a woman should not be denied a hormonal method simply because her blood pressure cannot be measured. If possible, she can have her blood pressure measured later at a time and place convenient for her.

Hormonal contraception can be taken by women who:

- have varicose veins
- have never conceived
- have anaemia/have a history of anaemia
- are over 40years of age
- have just had an abortion, miscarriage, or ectopic pregnancy

Some family planning methods are contraindicated with antiretroviral drugs (ARVs). *See Annex 11.5* for interactions between ARVs and hormonal contraceptives.

Due to drug-to-drug interactions, Jadelle should never be used with EFV
PrEP can be taken safely with all family planning methods and can be used safely when breastfeeding

For additional information regarding family planning counselling, refer to National Family Planning Guidelines.

5.11 Monitoring Clients Initiated on ART

All clients diagnosed with HIV should be assessed and managed according to the appropriately differentiated care package (*see Table 5.7*). Clients are eligible to initiate ART regardless of CD4 count or WHO clinical stage and preferably within 7 days of HIV diagnosis. Same-day initiation is encouraged for clients who are ready to start ART; treatment literacy and empowerment of lifelong treatment should continue during the first few weeks/months of ART.

Table 5.16 Summary of Basic Care Package for PLHIV

	Reason for not being on ART						**Every client, every visit**
	Personal Choice			**Opportunistic Infection**			
	Follow-Up Schedule	ART Initiation	At Each Review	Follow-Up Schedule	ART Initiation	At Each Review	
Presenting with advanced immunodef-iciency (advanced HIV disease) (CD4 <200 cells/ mm3 or WHO clinical stage 3 or 4)	Weekly clinical review until client initiated on ART.	Prioritis-ed for ART initiatio n within 7 days. Rule out Cryptoc occal meningi tis first	Screen for opportunistic infections (including TB). For clients with CD4 <200 cells/ mm3, *see section 6.2*, AHD. Schedule additional counselling sessions if necessary. Provide CPT.	Clinical review dates are to be schedule d following the opportun istic infection treatmen t plan.	Aim to initiate ART as soon as clinically stable.	Provide enhanced support for adherence to opportunistic infection treatment. Screen for additional opportunistic infections. Schedule additional counselling sessions, if necessary, and Provide CPT.	At each visit, prepare the client to be ready to start ART and manage opportunistic infections. Conduct readiness assessment for beginning ART. Review clinical symptoms and signs, medication use, and side effects. Assess adherence and psychosocial barriers and provide ongoing counselling. Provide acute care, if necessary. Manage current illnesses and complaints. Resupply prophylaxis. If ART initiation is delayed for more than 6 months, repeat pre-treatment CD4 count at 6 months Rule out any adverse drug reactions and manage appropriately
Presenting with mild or moderate immunodeficie ncy (clinically well) (CD4 >200 cells/ mm3 or WHO clinical stage 1 or 2)	Clinical review every 2 weeks until client initiated on ART.	Aim for rapid ART initiation.	Screen for opportunistic infections (including TB). Provide CPT. and TPT.	Clinical review dates are to be scheduled following the opportuni-stic infection treatment plan.	Aim to initiate ART as soon as clinically stable.	Provide enhanced support for adherence to opportunistic infection treatment. Screen for additional opportunistic infections. Schedule additional counselling sessions. If necessary, provide CPT.	

Table 5.17 Basic care for PLHIV at ART initiation

	Clients Presenting with Mild or Moderate Immunodeficiency (clinically well) (CD4 >200 cells/mm3 or WHO clinical stage 1 or 2)			Clients Presenting with Advanced Immuno- deficiency (advanced disease) (CD4 <200 cells/mm3 or WHO clinical stage 3 or 4)	
		Adults	**Children/ Adolescents**	**Adults**	**Children/ Adolescents**
Clinical review	Current and past medical history	x	x	x	x
	Psychosocial history	x	x	x	x
	Adverse drug reaction	x	x	x	x
	Sexual and reproductive history	x	x	x	x
	General impression, vital signs and nutritional assessment	x	x	x	x
	General examination	x	x	x	x
Vaccination status	Covid-19, HPV, HBV, childhood immunisation	x	x	x	x
Counselling focus	Preparation for early ART initiation	x	x	x	x
	Promotion of benefits of early ART initiation	x	x	x	x
Baseline Laboratory tests	<u>All clients:</u>				
	Re-testing for verification	x	x	x	x
	CD4 count	x	x	x	x
	LF TB-LAM (If TB screening is positive)			x All symptomatic PLHIV Inpatients with CD4 <200 Outpatients with CD4 <100 regardless of symptoms (*Refer to TB diagnosis 6.1.3*	
	CrAg			x If CD4 ≤100 cells/mm3	x **For children > 10 years old** If CD4 ≤100 cells/mm3 or less than 25%

Table 5.17 Basic care for PLHIV at ART initiation (continued from the previous page)

	Clients Presenting with Mild or Moderate Immunodeficiency (clinically well) (CD4 >200 cells/mm3 or WHO clinical stage 1 or 2)			**Clients Presenting with Advanced Immuno-deficiency (advanced disease) (CD4 <200 cells/mm3 or WHO clinical stage 3 or 4)**	
Baseline laboratory tests	**Clients initiating ART:**				
	AST/ALT	x	x	x	x
	Hepatitis B surface antigen	x	x	x	x
	Hb/FBC	x	x	x	x
	Creatinine	x	x	x	x
	RBS				
Sexual and reproductive health	Family planning counselling and services	x	x	x	
	STIs	x	x	x	x
	Cervical cancer screening	x	x	x	x
Prophylaxis	CPT	*Refer to section 5.4*		X	x
	TPT	x	x If >12 months of age or ≤12 months with TB contact	x If active TB is ruled out	x If >12 months of age and active TB is ruled out
	Fluconazole	N/A		x If CrAg+ and asymptomatic.	
Opportunist-ic infection screening	TB	x	x	x	x
	Cryptococcal meningitis	x	x	x	x
	Kaposi sarcoma	x	x	x	x
	Cervical cancer	x	x Sexually active adolescents only	x	x Sexually active adolescents only
	Respiratory infections	x	x	x	x
	Covid-19	x	x	x	x
Follow-up visits	**Clients initiating ART:**				
	In 2 weeks	x	x	x	x
	Clients not initiating ART:				
	Every 2 weeks	x	x		
	Every 1 week			x	x

5.12 Pharmacovigilance in ART

What is Pharmacovigilance?

Pharmacovigilance is defined as the science and activities concerned with the detection, assessment, understanding, and prevention of adverse reactions (ADR) to medicines (i.e., adverse drug reactions). The ultimate goal of this activity is to improve the safe and rational use of medicines, thereby improving the client's care and public health.

What is an Adverse Event (AE)?

Any unfavourable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, whether considered related to the medicinal product. Adverse events can be mild moderate or severe: they can also be serious. Adverse events can be mild, moderate or severe.

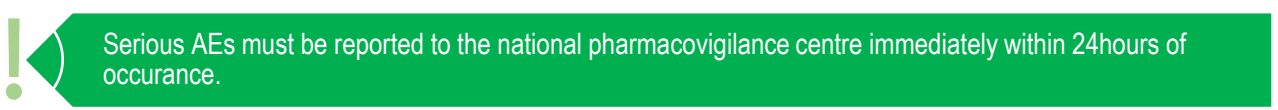
Mild AEs: Awareness of signs or symptoms, but easily tolerated and are of minor irritant type causing no loss of time from normal activities. Symptoms do not require therapy or a medical evaluation; signs and symptoms are transient.

Moderate AEs: Events introduce a low level of inconvenience or concern to the participant and may interfere with daily activities, but are usually improved by simple therapeutic measures; moderate experiences may cause some interference with functioning

Severe AEs: Events interrupt the patient's normal daily activities and generally require systemic drug therapy or other treatment; they are usually incapacitating.

Serious Adverse Events (SAE) are defined as any untoward medical occurrence(s) that at any dose results in death, hospitalisation or prolongation of existing hospitalisation, persistent or significant disability/incapacity or a congenital anomaly or birth defect. Refer to the National Pharmacovigilance guideline for more information on adverse events. Severe AEs may not SAE

Severe AE ≠ Serious AE (SAE)



What is an Adverse Drug Reaction (ADR)?

ADRs are commonly defined as a response to a medicine that is noxious and unintended, including lack of efficacy, which occurs at any dosage and can also result from an overdose, misuse, or abuse of medicine.

What are the different methods of reporting adverse events/reactions?

Spontaneous reporting

This is the primary method used in Eswatini. It is the main mechanism for passive surveillance used to generate signals/alerts of adverse events, which can then be investigated further. This method of reporting covers all medicinal products at all levels of health facilities in the country.

Active PV reporting

An ongoing systematic collection, analysis, interpretation and dissemination of the client's medicine safety data. It involves the systematic screening, recording and reporting of adverse events especially severe adverse events, serious adverse events (SAEs) and adverse effects of special interest (AESIs). All deaths are to be reported and as much relevant information on ascertainment of the cause of death should be consistently collected. Reporting of AEs and other events (e.g., pregnancy, lactation exposure) may be required, primarily based on what is known about the safety profile of the new agent and also for other possible harms which have not yet been described.

All SAEs and Severe (Grade 3 or 4) AEs detected should be reported to the NPC within 24-48 hours using active PV reporting form or the **WhatsApp number +268 7655 7303** .

Who should report AEs/ADRs?

All healthcare workers, including doctors, dentists, pharmacists, nurses, and other health professionals are required to report all suspected adverse reactions/events to medicines (including vaccines, X-ray contrast media, and traditional and herbal remedies), potentially serious or clinically significant. *See Annex 11.27*

Monitoring and reporting drug therapy problems—including adverse drug reactions and medication errors—should be an integral part of clinical practice for ensuring client safety and optimal treatment outcomes. Health care workers should alert clients to the potential of experiencing toxicities in their medication and advise clients on when to report to their healthcare providers.

Importance of PV report

A well-completed AE/ product quality form submitted could result in any of the following:
Additional investigations into the use of the medicine in Eswatini
Educational initiatives to improve the safe use of the medicine
Appropriate package insert changes
Changes to treatment guidelines
Removal of the medicine from the market

What types of reactions should be reported?

The following adverse events should be reported (even if you are not certain the medicine caused the event):
All suspected AE/ADRs to medicine, whether serious/minor, unexpected or unusually severe reactions which also include:

- Product Quality
- Lack of efficacy
- Treatment failure
- All suspected ADRs associated with medicine errors
- All serious reactions and interactions
- All adverse reactions to traditional or herbal remedies

What product quality problems should be reported?

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

How can AE/ADRs be prevented from occurring?

Some AE/ADRs are unavoidable and cannot be prevented. However, most AE/ADRs can be prevented by following the basic principles of rational use of medicines: **patients receive medications appropriate to their clinical needs, in doses that meet their requirements, for an adequate time, and at the lowest cost to them and their community**

How do you recognize ADRs and AEs in clients?

Healthcare workers prescribing medicines including ART should collect information that includes client details (e.g., age, sex, weight), details on the drug (e.g., dose, duration of treatment), details on the suspected reaction or reactions (e.g., description of the event, seriousness, outcome), medical history of the client, and other concomitant medication that the client was taking. The following approach helps assess possible ADRs and AEs:

- Take a proper history and do a proper examination of clients.
- Establish time relationships between the adverse event and suspected medicine.
- Carry out a thorough physical examination with appropriate laboratory investigations if necessary.
- Effects of De-challenge and rechallenge should be determined.
- Check the known pharmacology of the medicine.
- Ensure that all identified are appropriately managed before reporting. Further guidance on PV shall be provided on the National Pharmacovigilance guideline.

How are adverse drug events/reactions reported?

An adverse drug event/reaction/product quality report form is provided on paper and should be completed in as much detail as possible before submitting it to the Pharmacy department through their monthly orders to the national pharmacovigilance centre (NPC) at the Central Medical Stores. Alternatively reporting forms can be sent to the **NPC WhatsApp number +268 7655 7303**

6 TB/HIV COLLABORATIVE ACTIVITIES & ADVANCED HIV DISEASE

The chapter gives guidance on the prevention, screening and management of tuberculosis (TB), advanced HIV disease (AHD) and Histoplasmosis among PLHIV

6.1 TUBERCULOSIS

6.1.1 Introduction

Tuberculosis is an infectious disease caused by Mycobacterium tuberculosis (MTB) bacilli. It is the leading cause of death among people living with HIV (PLHIV), accounting for about a third (512 000) of all global HIV-associated deaths in 2019.
PLHIV are 20 times more likely to progress from latent TB infection to active TB compared to HIV-negative individuals, with a 10% annual risk for PLHIV and 5-10% lifetime risk for HIV-negative individuals. TB preventive treatment (TPT) is recommended for the treatment of latent TB infection (LTBI) in people at risk of progressing to active TB. TPT is known to reduce the risk of developing active TB by 60-90%, and to reduce mortality among PLHIV by 37% independent of ART.

TB/HIV collaborative activities

Counselling on risk reduction behaviour to reduce the risk of TB transmission at home, in public and health facilities should be included in HIV care. Infection prevention in health facilities is the responsibility of the facility, including cough triage and management track for patients with cough and diagnosed TB. The following TB/HIV collaborative activities should be implemented at all entry points that provide HIV and TB care:

Table 6.1 Prevention of TB among PLHIV

Prevention and treatment of TB among PLHIV
Intensified TB case-finding
I. Screen all clients for TB using the integrated TB/Covid-19 screening tool and refer them for either TB prophylaxis or TB treatment services.
II. TB preventive treatment (TPT)/treatment of latent TB infection (LTBI)
III. To prevent the development of active TB, offer TPT to all clients who are eligible unless there are contraindications to TPT.
Infection prevention and control of TB (IPC)
I. Refer clients with active TB to a TB clinic if available; separate patients with presumed and demonstrated infectious TB patients from the rest in facility waiting areas and ensure adequate airflow.
II. Triage and fast-track patients with positive symptom screen and early initiation of TB treatment rapid triage and provide a surgical mask for clients with cough in waiting areas.
III. Ensure that facilities have an up-to-date infection control plan with IPC focal points who implement and monitor IPC indicators
Prevention and treatment of HIV infection in clients with active TB
I. Provide HTS to all clients with presumptive or diagnosed TB.
II. Ensure HIV prevention interventions for HIV-negative TB clients and early ART initiation for TB clients living with HIV.
III. Provide TPT for TB/HIV coinfected clients who have completed their TB treatment.

6.1.2 TB Screening

Systematic TB Screening among PLHIV

PLHIV should be systematically screened for TB disease using the WHO 4 symptoms screen (W4SS) tool at each clinical visit to a health facility. PLHIV are 15-22 times more likely to develop active TB disease compared to people without HIV, as such all efforts must be made to intensify systematic TB screening among this group. The national TB screening tool is recommended for screening PLHIV for TB.

TB screening tests

The following screening tests are recommended when available to improve sensitivity

Table 6.2 TB screening tests

Name of screening test
C- Reactive Protein (CRP) with a cut-off point of>5mg/l • A general marker for inflammation can be performed as a point of care test • C-reactive protein should be used in patients, not on ART or presenting for ART initiation. A confirmatory diagnostic test for TB should be considered after a positive screen using CRP among PLHIV.
Chest X-ray (CXR) • CXR and W4SS combined to provide improved sensitivity and similar specificity to W4SS alone for all PLHIV subgroups • Most sensitive screening tool for PLHIV on ART

Chest X-ray and C – reactive protein may be useful in improving the sensitivity of the four-symptom screen where feasible. The different TB screening algorithms are highlighted below.

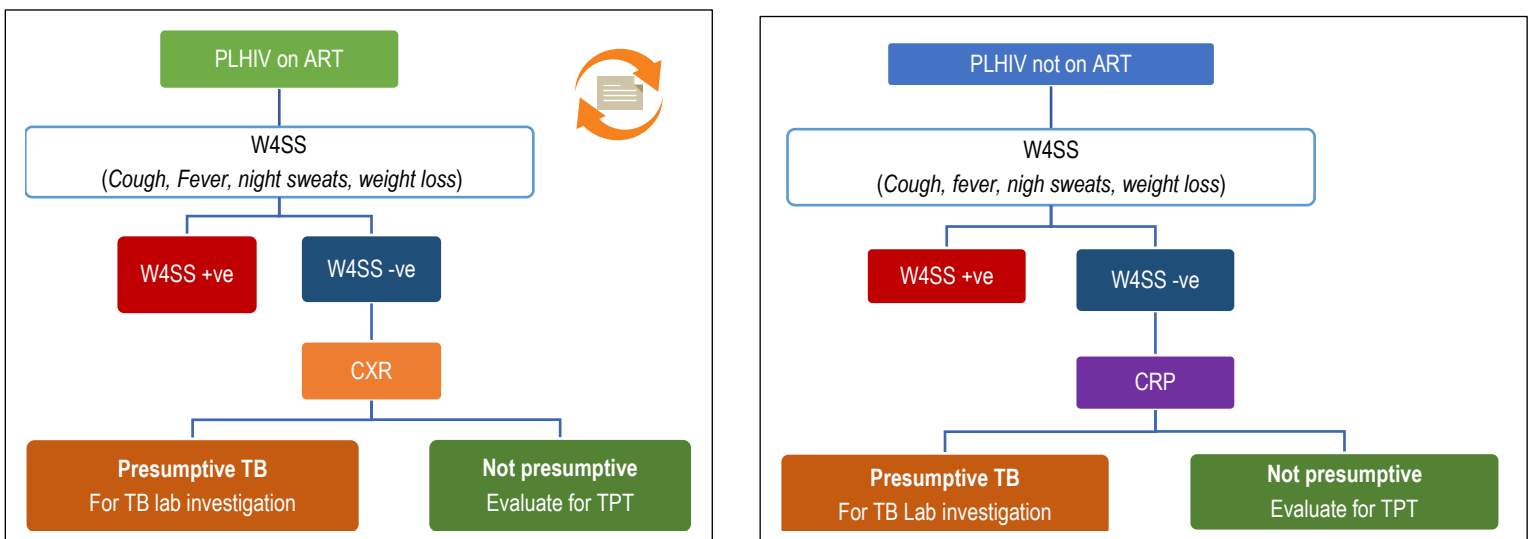


Figure 6.1 TB screening algorithm for PLHIV

Due to limited capacity and access to radiograph services currently, the chest x-ray recommendation for screening may not be implemented until further notice!!

6.1.3 TB Diagnosis

All PLHIV who are TB presumptive should be evaluated for TB using TB LAM and Xpert MTB Rif (ultra).

The standard diagnostic tests for TB among PLHIV are Xpert MTB/RIF (Ultra)and LF urine LAM. Specimens from specific sites such as lymph nodes, and pleural fluid, may be obtained when extrapulmonary TB is suspected. Investigation to exclude drug-resistant TB should be done according to national TB treatment guidelines.

- The use of LF urine LAM in TB diagnosis has been expanded to all PLHIV presumptive of TB as well as certain groups of patients with AHD as shown in *Figure 6.1* below.
- Clients with a positive TB LAM but no signs and symptoms of TB may require sputum induction for Xpert MTB/RIF (ultra). Note airborne transmission precautions should be observed in the setting of TB as well as COVID-19.

The use and interpretation of the two tests in PLHIV, including advanced HIV disease in the diagnosis of TB, is shown in *Figure 6.1* below;

Children living with HIV

In children with signs and symptoms of TB, Xpert Ultra and LF LAM should be used as the initial diagnostic tests for TB rather than smear microscopy/culture and phenotypic drug susceptibility testing (DST). Investigations should be done to rule out TB drug resistance on sputum, nasopharyngeal aspirate, gastric aspirate or stool.

Due to the difficulty in obtaining sputum specimens in children, sputum induction may be considered (see TB guidelines). Stool nasopharyngeal or gastric aspirates and urine specimens may be used as a complementary specimens for the diagnosis of TB in children.

6.1.4 TB Treatment

For more information on the diagnosis and management of TB, refer to the current National Tuberculosis Control Program Manual.

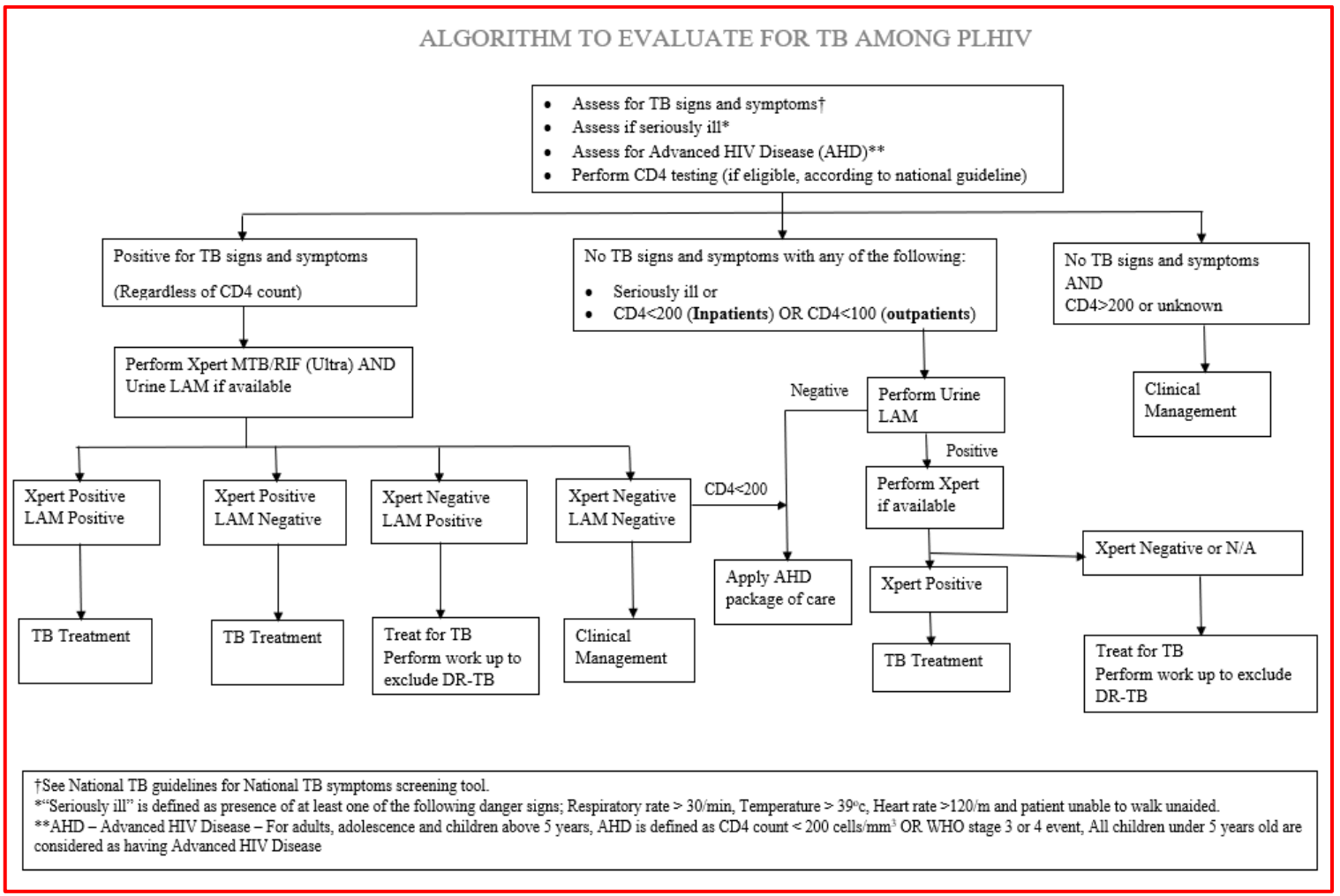


Figure 6.2 Algorithm to evaluate TB among PLHIV

6.1.5 TB Prevention

TB Preventive Treatment (TPT)/Treatment of Latent TB infection (LTBI)

- Latent TB is defined as a state of persistent immune response to stimulation by Mycobacterium tuberculosis with no evidence of clinically active TB disease. About a quarter of the world's population is infected with TB. TPT for PLHIV is part of the TB preventive treatment for people living with HIV. TPT used in combination with ART has been shown to benefit both TB prevention and mortality, even at higher CD4 cell counts.
- The following are the recommended LTBI treatment (TPT) options in Eswatini;

Table 6.3 Recommended TPT Options

Population Group	Preferred regimen	Alternative regimen
ART patients eligible for Cotrimoxazole (CTX)[a]	• 3 months of Rifapentine/Isoniazid/Vitamin B6 (**3HP/Vit. B6**) • 1 month of INH/Rifapentine (**1HP**), once available [b] • 6 months of FDC (**INH/Vit. B6/CTX**) [c]	6 months of INH monotherapy (6H)
ART patients not eligible for Cotrimoxazole [d]	3HP/Vit. B6 [e]	• 6 months of FDC (**H/Vit. B6/CTX**) • 6 months of INH (**6H**)
HIV-negative (household contact of people with bacteriologically confirmed pulmonary TB , other at-risk groups)	• 3months of Rifampicin/Isoniazid (**3RH**) • 4months of Rifampicin (**4R**)	6 months of INH (6H)
DR-TB contacts	**MDR-TB/RR-TB/Rif mono-resistance** • Levofloxacin + Ethambutol **INH Mono and PDR** • Levofloxacin + Ethambutol • For Pre-XDR and XDR prophylaxis, refer to expert consultations	

[a] Patients eligible for CTX include - New patients on ART, patients with detectable V/L, and patients returning to care.

[b] 1 HP is recommended only for adolescents > 13 years

[c] Preferred regimen for pregnant and lactating women

[d] Note: 6 months of FDC (H/Vit. B6/CTX) can still be given in the absence of 3HP if CTX is not absolutely contraindicated

[e] 3 HP regimen is only recommended for children > 2 years

Timing for TPT initiation

TPT should be initiated 4 weeks after ART initiation. However, TPT initiation on the day of ART initiation may be considered, especially among stable clients without Advanced HIV Disease.

Table.6.4 When to Start TPT in PLHIV, by Client Category

Patient category	When to Start TPT
Adults, adolescents and children ≥12 months	Initiate LTBI treatment after 1 month on ART*
Infants <12 months and with a history of TB contact	Initiate LTBI treatment after clinically ruling out TB
Clients on TB treatment	Initiate LTBI treatment on the day of TB treatment completion
Clients with presumptive TB	Initiate LTBI treatment after TB is ruled out through a diagnostic evaluation
Pregnant and lactating women**	Initiate LTBI treatment within 1 month on ART* Initiate LTBI treatment after clinically ruling out TB

**Stable patients may initiate TPT together with ART, but AHD patients may be initiated on TPT one month after initiating ART.*
*** TPT can be initiated at any gestational age.*

! Rifapentine is contraindicated in pregancy

Refer to Section 9.8 for more information on TPT in children. TPT regimens and dosing by the population at risk are tabulated as follows:

Table 6.5 TPT Dosing

At risk population	Drug regimen	Dose per kg body weight	Maximum dose
PLHIV	6 months daily INH (**6H**) (Isoniazid onotherapy)	Age ≥10 years: 5mg/kg/day Age <10 years: 10mg/kg/day	INH 300 mg daily for 6 months
	FDC of (**INH/Vit B6/CTX**)	10 years and older	1 tablet daily x 6 months
	3HP* Weekly Rifapentine plus isoniazid for 3 months (Rifapentine 300mg/ Isoniazid 300mg per tablet) 12 doses	Weight Isoniazid Rifapentine **Individuals ≥ 12 years and ≥ 25kg** • 3 tablets weekly plus 25 or 50 mg plus Vitamin B6 **Children <12 years or Weight < 25kg** • Isoniazid 10mg/kg x 6 months (range, 10-20mg) plus Vitamin B6 25mg	Isoniazid, 900 mg/ Rifapentine, 900 mg *Although 3HP can be given to children ≥ 2 years old, child-friendly formulations are currently unavailable

Table 6.6 Table TPT Dosing (continued from the previous page)

At risk population	Drug regimen	Dose per kg body weight	Maximum dose
PLHIV	**1HP** daily	**Age ≥13 years (regardless of weight band)** Isoniazid 300 mg/day + Rifapentine 600 mg/day plus Vitamin B6	Isoniazid 300 mg/Rifapentine 600 mg daily for 1 month
Household contacts	Three months of daily Rifampicin plus isoniazid **(3RH)**	**Weight** **Tablets** 4-7 kg 1 8-11kg 2 12-15kg 3 16-24kg 4 >25 kg Adult dose	
	Four months of daily rifampicin **(4R)**	**Age ≥10 years**:10 mg/kg/day **Age <10 years**:15 mg/kg/day	
	6 months daily **(6H)** (Isoniazid monotherapy)	**Age ≥10 years**: 5mg/kg/day **Age <10 years**: 10mg/kg/day	

There is no need to repeat TPT in patients who have previously completed a TPT cycle. People who may be considered for a repeat cycle include people with a new household contact to a bacteriologically confirmed pulmonary TB case and patients completing TB treatment after having completed a TPT course.

Preventive treatment for Drug-Resistant TB

Preventive treatment should only be considered for high-risk DR TB household contacts following a risk assessment
Preventive treatment for multidrug-resistant TB requires a different regimen using a fluoroquinolone or other second-line agents as tabulated in the following table.

Table 6.7 Risk Assessment for DR TB household contacts

Assessment of exposure	Response	
Relationship to source patient:		
Approximate hours spent with source patient in two weeks before diagnosis		
Ask the following ten questions: **for each "yes" response, give one point**	Yes	No
1. Is the index case, the child's mother?	Yes	No
2. Is the index case the child's primary caregiver	Yes	No
3. Does the index case sleep in the same bed as the child?	Yes	No
4. Does the index case sleep in the same room as the child?	Yes	No
5. Is the index case coughing?	Yes	No
6. Does the index case have pulmonary TB	Yes	No
7. Does the index case have GXP-positive sputum?	Yes	No
8. Does the index case live in the same household as the child?	Yes	No
9. Does in the index case see the child every day	Yes	No
10. Is there more than one adult TB case in the child's household		
Score of ≥6 with clinician judgement means intense exposure		

Table 6.8 Preventive Treatment for Drug-Resistant Contacts

DR-TB contacts		
DRTB	Drug regimen	Maximum dose
MDR-TB/RR-TB/Rif mono-resistance	Levofloxacin + Ethambutol (6 months)	15-20mg/kg + 15-25mg/kg
INH Mono and PDR	Levofloxacin + Ethambutol (6 months)	15-20mg/kg + 15-25mg/kg
Fluoroquinolone resistance (Pre-XDR and XDR)	Send to expert panel review	

Monitoring of TPT clients

Clients on TPT should be routinely monitored for adherence, adverse events and TB screening at all visits.

- Stable patients should be reviewed at their standard HIV care visits and ART patients on DSD models should have their TPT refills and other appointments synchronized.
- Additional follow-up strategies should be put in place to follow up patients on TPT with multi-month dispensing/scripting (MMD)
- At each review, assess for:
  - Adherence to therapy
  - Toxicity (hepatitis, neuropathy, rash, etc.)
  - TB symptoms.
- Hold TPT and refer to the medical officer (MO) if there are major side effects e.g.,
  - Symptoms of acute hepatitis and elevation of ALT three times ULN or
  - When ALT increases 5 times or more the ULN

! TPT refill dates must be synchronized with ART refill or clinic visits

Management of TPT Adverse events

The following table presents the management of LTBI treatment adverse event

Table 6.9 Management of TPT ADRs

Drug	Adverse events	Management
Isoniazid	Asymptomatic elevation of serum liver enzyme concentration, hypersensitivity reactions, gastrointestinal intolerance and hepatotoxicity.	In the event of itching or localized rash, provide antihistamines and monitor closely. If a systemic rash develops, continue antihistamines and perform clinical and laboratory evaluation. If there are systemic symptoms, fever, urticarial, mucous membrane involvement, blistering, oedema or wheezing, discontinue INH immediately and do not re-challenge.
Rifampicin and Rifapentine	Cutaneous reactions, hypersensitivity reactions, gastrointestinal intolerance, and hepatotoxicity	If hypersensitivity reactions (flu-like symptoms: fever, chills, headache, dizziness, rash but in severe cases can present with hypotension and shock) are severe discontinue and do not re-challenge.

Table 6.10 Management of TPT ADRs (continued from the previous page)

Drug	Adverse events	Management
Rifampicin and Isoniazid	Rash	• Withhold and do not re-challenge if LTBI treatment is found to be the cause of grade 3 or 4 hypersensitivity. • Otherwise, re-challenge once rash resolves starting with isoniazid alone at 1/6 normal dose on day 1 then full dose on day 2 and subsequently and monitor closely, especially on the completion of antihistamines (at least weekly to 2-weekly for the first month then monthly). • If close monitoring is not possible, do not re-challenge. • If a rash does not recur, continue isoniazid monotherapy ensuring that the client gets a total of 180 doses. • If rash recurs, do not rechallenge with Rifampicin and/or isoniazid.

TPT completion timelines

Table 6.11 TPT completion timelines

Regimen	Total duration (months)	Expected number of doses	80% of recommended doses	Extended time for treatment completion (days): original treatment duration +33% additional time
6 months of daily isoniazid (**6H daily**)	6	182	46	239
3 months of daily Isoniazid and rifampicin) (**3RH daily**)	3	84	68	120
3 months of weekly Isoniazid and rifapentine **(3HP weekly**)	3	12	11	120
1 month of daily Isoniazid and rifapentine (**1HP daily**)	1	28	23	38
4 months daily Rifampicin (**4R daily**)	4	1201	96	160

Management of TPT interruptions

The management of TPT interruptions is important to ensure patients receive the required therapeutic doses.
TPT should be completed within 6-9 months. 180 doses are required for effective preventive therapy.
The following table shows the management of TPT interruptions according to the TPT regimen.

Table 6.12 Management of TPT Interrupters by regimen

TPT regimen	Duration of treatment interruption	Next step	
3HR, 4R, 6H	Less than 2weeks	Resume preventive treatment immediately upon return and add the number of days of missed doses to the total treatment duration. Do not change the scheduled date of the next follow-up visit but the last follow-up visit will be postponed by the number of extra days to compensate for missed doses (e.g., If a child on 3HR missed 3 days of treatment, continue preventive treatment for a total duration of 3 months + 3 days from the date of start).	Address the reason for interruption. Counsel the person on TPT and the caregiver on the importance of adherence to preventive treatment. Review and agree with the person on TPT and the caregiver about the best ways to improve adherence. *See Table 6.11* for the thresholds of regimen prolongations due to consecutive or erratic interruptions.
	More than 2 weeks	If treatment interruption occurred after more than 80% of doses expected in the regimen were taken, no action is required. Continue and complete the remaining treatment as per the original plan. If less than 80% of doses expected in the regimen were taken, and the treatment course can still be completed within the expected time for completion, i.e., treatment duration + 33% additional time, no action is required. Continue and complete the remaining treatment as per the original plan. If less than 80% of doses expected in the regimen were taken, and the treatment course cannot be completed within the expected time for completion, consider restarting the full TPT course	
3 HP	Weekly schedule of one dose missed	If the missed dose is remembered within the next 2 days, the person can take the dose immediately. Continue the schedule as originally planned (i.e., continue to take the remaining doses following the same schedule). If the missed dose is remembered more than 2 days later, the person can take the missed dose immediately and change the schedule for weekly intake to the day the missed dose was taken until treatment completion. This will avoid 2 weekly doses being taken less than 4 days apart	
	More than 1 weekly doses of 3HP missed	If between 1–3 weekly doses are missed, treatment is continued until all 12 doses are taken, thus prolonging the treatment duration to a maximum of 16 weeks. If, however, 4 or more weekly doses are missed, consider restarting the full TPT course. If adherence to a weekly routine is not possible, consider discontinuing 3HP and offering an alternative (daily) regimen	

Table 6.13 Management of TPT Interrupters by regimen (continued from the previous page)

TPT regimen	Duration of treatment interruption	Next step	
1 HP	Less than one week	If more than 80% (23) of doses expected in the regimen were taken no action is required, just complete the remaining doses. If less than 80% (23) of doses expected in the regimen were taken, resume treatment immediately upon return and add the missed doses to the total treatment duration to complete the course within a maximum of 6 weeks.	
	More than 1 week	If more than 7 consecutive doses were missed, consider restarting the complete course of 1HP regimen. If more than 7 doses were missed intermittently, resume preventive treatment immediately upon return and add the missed doses to the total treatment duration to complete the course within a maximum of 8 weeks. If adherence to 1HP is not possible, consider discontinuing it and offering an alternative daily regimen or 3HP	

TPT patient education

Patient education and counselling are important in ensuring adherence to TPT

Client health education and counselling

The patient is educated on the following:

- Basic facts and benefits of LTBI treatment and duration of therapy, dose, time etc.
- Side effects of the treatment and reporting promptly to the health facility (e.g., yellowing of eyes, itchy skin rash, abdominal pain with vomiting) emphasize the effects of using traditional medicines, alcohol and drugs in combination with TB medication.
- Importance of appointment keeping, adhering and completing treatment, assist the patient to choose one adherence aide such as cell phone, TV, calendar or radio reminders.
- Importance of availability of support systems, getting to the clinic, taking medication, reminder strategies, storing medication)
- The patient is assessed for any intentions to get pregnant and encouraged to report promptly should she have a plan to get pregnant

Symptom awareness

- All PLHIV should be educated on the importance of seeking medical care promptly if they or any person they live with develop signs and symptoms suggestive of active TB (e.g., any cough with blood-stained at times, chest pains, weakness, weight loss, fever, night sweats)

Management of Household TB contacts

- All household contacts of the TB patients regardless of bacteriological confirmation of the index case should be evaluated for TB and offered HIV testing and counselling. TPT should be offered to all eligible contacts who are HIV-positive or are children under 5 (regardless of HIV status) who do not have symptoms and signs suggestive of TB and children > 12 months living with HIV without active TB.

TPT Outcomes

TPT outcomes should be documented in the patient records: electronic or paper-based.

Transferred out is no longer considered an outcome as it does not show the definitive outcome of a TPT initiation. It is the responsibility of the initiating facility to follow-up on all patients transferred out to document the outcome at the end of the TPT course.

Table. 6.14 TPT patient outcomes:

TPT treatment outcomes	Definition
Completed treatment	Received the full course of; • Daily INH/Lfx + Eth within 6 to 9 months (180 doses) • Weekly Rifapentine-INH within 3-4 months (12 doses) • Daily RPT-INH within 8 weeks (30 doses for 1HP). • Daily Rifampicin within 4 months (90 doses)
Lost to follow-up	Took Isoniazid monotherapy then interrupted for ≥ 60 days or Took Rifampicin and Isoniazid then interrupted for >30 days or Took Rifapentine and Isoniazid then interrupted for >30 days. Took 1HP and was interrupted by >7 consecutive days
Died	Death from any cause while on TPT.
Failed treatment	Developed active TB while on TPT.
Treatment discontinued	TPT was stopped by a healthcare worker due to toxicity/adverse effects or any other reason.
Not evaluated	No documented outcome. Efforts should be made to document appropriate outcomes by the initiating facility.

ART for TB patients

For clients who develop TB while taking ART, review ART treatment for any necessary changes to the regimen or dosage and move the client to the TB clinic for the duration of the TB treatment. For more information on the treatment of DR-TB/ HIV Co-infection refer to the current National Tuberculosis Control Programme Manual. Refer to *Annex 11.16* for ART dose adjustments in paediatrics on TB treatment

Table 6.15 Recommended Adult ART Regimens for TB/HIV Coinfected patients

Client Category	Recommended ART regimen	Comments
Clients already on TB treatment presenting for ART initiation	TDF/3TC/DTG Qam + DTG 50mg Qpm	• Start ART as soon as possible with increased DTG dosing of 50mg twice daily • Return to standard DTG dosing 50mg once daily two weeks after the completion of TB treatment
Clients developing TB while on a DTG-based ART regimen		Clients must return to DTG 50mg once daily 2 weeks after completing TB treatment.
Developing DS-TB while on an EFV-based ART regimen	Continue with EFV based regimen	Check VL at the end of treatment. If VL is undetectable, the client can be transitioned to a once-daily FDC of TDF+3TC+DTG two weeks after completion of TB treatment If VL is detectable immediately switch to the second line and continue adherence support refer to the ART section
Developing DS-TB while on a Protease inhibitor (PI) based ART regimen	Consult an experienced HIV clinician or snapthirdline@mohcoag.org before choosing these options: **TB patient on LPV/r** • Super boost LPV/r to 400 mg/400 mg by adding 300 mg Ritonavir and continue until 2 weeks after completion of TB treatment • Double dose of LPV/r to 800 mg/200 mg twice daily. Double dosing is only for clients >10yrs of age and continues until 2 weeks after completion of TB treatment • If evidence of VL suppression in the past 3-6months, switch to a DTG-based second-line regimen and continue twice daily DTG until 2weeks after completion of TB treatment **TB patient on ATV/r or DRV/r:** • Do not combine with RIF • Change to DTG twice daily if DTG naïve or LPV/r with adjustments as stated above if DTG experienced **Patients who may be failing ART** • Follow the guidance on managing treatment failure	
For Clients with Multidrug-Resistant TB		
EFV and Bedaquiline (BDQ)	EFV should not be used with BDQ. EFV induces CYP3A activity and co-administration with BDQ may result in reduced BDQ exposure and loss of BDQ activity. DTG is the preferred INSTI for clients receiving BDQ.	
Delamanid (DLM) and ARVs	DLM is generally considered safe to administer with ART. Evidence shows safety with EFV, TDF and LPV/r. No LPV/r dose adjustment is needed for TB patients on DLM No long-term studies have been done on potential drug-to-drug interactions with DLM and ARVs DTG is the preferred INSTI for clients receiving DLM	

For all clients, maintain the same NRTI backbone provided there is no dose adjustment necessary, and the client is virally suppressed

ART should be started as soon as TB treatment is tolerated, preferably **within** 2 weeks of initiating tuberculosis treatment, except for clients with TB meningitis

Table 6.16 TB Treatment Drug Interactions

Drug Combination	Considerations
Rifampicin and (LPV/r)	• LPV/r can be used with RIF. • Super boost the LPV/r (1:1 lopinavir and ritonavir) by adding ritonavir. • Closely monitor the client for toxicity (especially gastrointestinal intolerance) and virological failure.
Rifampicin and oral contraceptive pills	• Oral contraceptive pills may not be effective when administered with RIF. • Women of childbearing age should either receive a contraceptive pill containing a higher dose of oestrogen (50µg) or use another form of contraception (e.g., medroxyprogesterone). • Emphasize concomitant condom use during this period.
DTG and all TB treatments	• Preference is for clients to be maintained on a fixed-dose combination of TDF+3TC+EFV for the duration of TB treatment. • Check VL at the end of TB treatment. If the viral load is undetectable: the client can be transitioned to a once-daily FDC of TDF+3TC+DTG two weeks after completion of TB treatment. If the viral load is detectable, start SUAC. • If the client is on a DTG regimen, the DTG dose needs to be given as 50 mg twice daily until at least 2 weeks after the client has completed TB treatment. This may increase the occurrence of DTG side effects.

6.2 Advanced HIV Disease (AHD)

Definition of Advanced Immunodeficiency

- Adults, adolescents, and children over 5 years who have a CD4 count ≤200 cells/mm3 (or a CD4 count of less than 25% for children) or a WHO clinical stage 3 or 4
- All children with HIV who are younger than 5 years **and have not been on treatment for at least 12months** are considered to be a high-risk group and are therefore managed as having advanced immunodeficiency (advanced disease). Children above 2 years who have been on ART, and are stable, for at least one year may not be considered as having AHD.

- CD4 count is the gateway to AHD screening. In the absence of CD4 count, clients with WHO stage 3 or 4 should be managed as having AHD.
- Semi-quantitative CD4 count test (e.g., VISITECT) can be used in the assessment of AHD

6.2.1 Management of Clients with Advanced Immunodeficiency

Clients with advanced immunodeficiency are at high risk of opportunistic infections including TB, cryptococcal meningitis (CCM), toxoplasmosis, Pneumocystis Jirovecii Pneumonia (PJP), and other bacterial infections. Clients may also progress to advanced immunodeficiency (advanced HIV disease) while on treatment, if they are not on an effective regimen, adherence is not adequate or they develop resistance.

Advanced HIV package of care

A defined package of care interventions includes screening, treatment and prophylaxis for major opportunistic infections, rapid initiation of antiretroviral therapy (ART) and intensified treatment adherence support, for people presenting to care with advanced HIV disease to reduce HIV-associated morbidity and mortality.

Table 6.17 Package of Care for Clients with Advanced Immunodeficiency

Area of package	Intervention	CD4 Count	Adults and Adolescents	Children < 10 years
Screening and diagnosis 	Sputum for Xpert/Xpert ultra MBT/RIF as the first test for TB diagnosis in symptomatic patients	Any	Yes	Yes
	Urine LF-LAM for TB diagnosis in symptomatic patients or those with low CD4 count	**Symptomatic patients**: All patients regardless of CD4 count with TB signs and symptoms **Seriously ill patients***: All patients regardless of CD4 count or TB signs and symptoms **Inpatient setting**: CD4<200 cells/ml regardless of TB signs and symptoms **Outpatients setting**: CD4<100 cells/ml regardless of TB signs and symptoms	Yes	Yes
	Cryptococcal antigen CrAg screening	CD4 ≤ 100 cells/ml	Yes	No
		CD4 ≤ 200 cells/ml	May be considered**	No
	Histoplasma antigen test	All PLHIV	Yes	Yes
Prophylaxis and pre-emptive treatment	Cotrimoxazole prophylaxis (CPT)	CD4 ≤350cells/mm³ or WHO stage 3 or 4	Yes	Yes
	TB preventive treatment (TPT)	Any	Yes	Yes
	Fluconazole pre-emptive treatment for CrAg-positive patients without evidence of meningitis	CD4 ≤100 cells/ml	Yes	No
		≤200cells/ml	May be considered as above	No

Table 6.18 Package of Care for Clients with Advanced Immunodeficiency

Area of package	Intervention	CD4 Count	Adults and Adolescents	Children < 10 years
	Itraconazole prophylaxis for Histoplasma antigen-positive patients	Any CD4 count until 12 months or stable on ART and virally suppressed	Yes	Yes
ART initiation	Rapid ART initiation	Any	Yes	Yes
	Defer ART initiation if signs and symptoms of TB, CCM or CNS histoplasmosis	Any	Yes	Yes
Adapted adherence support	Tailored counselling to support adherence to the AHD package, including home visits where feasible	≤200 cells/ml	Yes	Yes

**Seriously ill patients (adults): any one of the following: respiratory rate >30 per minute, temperature > 39°C, heart rate >120 beats per minute, or unable to walk unaided. This excludes danger signs that can be explained or are a result of other diagnosed conditions e.g., cardiac failure, other bacterial infections, malaria etc.*

***May be considered in high cryptococcal antigenemia settings with adequate testing capacity*

- Rapid ART initiation (within 7 days) is recommended to restore immune functioning and prevent further decline of CD4 cell count.
- Immediate ART in clients newly diagnosed with cryptococcal meningitis is not recommended due to the risk of life-threatening immune reconstitution inflammatory syndrome (IRIS). ART may be deferred for 6 weeks in patients diagnosed with cryptococcal meningitis and starting antifungal treatment.
- In TB-diagnosed clients, ART should be started within 2 weeks of starting TB treatment when the client can tolerate treatment.
- After ART initiation, clients need to be monitored closely for the following:
  - Adverse events
  - Clinical response
  - Development of IRIS
  - Non-adherence to ART

6.2.2 Cryptococcal infection and meningitis

Clients with cryptococcal infection may present with symptoms (symptomatic) or without symptoms (asymptomatic) of meningitis. Cryptococcal meningitis (CCM) has a high mortality rate. It is important to treat the cryptococcal infection before CNS involvement to reduce morbidity and mortality (pre-emptive treatment).

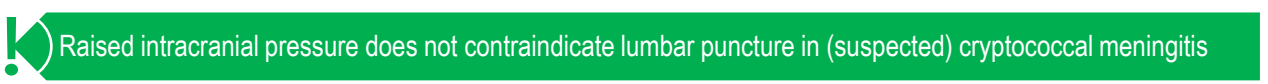
Clients with symptoms of meningitis should be referred to a medical doctor for further management as soon as the condition is suspected.

Symptomatic clients who have a positive blood CrAg result should receive lumber puncture (LP) if feasible and if there are no contraindications to LP. If CSF CrAg is positive, start treatment for cryptococcal meningitis. If CSF CrAg is negative or LP is not feasible, start pre-emptive treatment for cryptococcosis under close supervision while admitted.

With the availability of a safer, single-dose liposomal amphotericin B regimen, symptomatic serum CrAg positive patients where LP is not feasible may be considered for CCM treatment.

Contraindications to LP

- significant coagulopathy
- suspected space-occupying lesion based on focal nervous system signs (excluding cranial nerve VI palsy) or recurrent seizures and, where possible, confirmed by computed tomography (CT scan).
- major spinal deformity
- patient refusal after fully informed consent was sought.
- Infection around the site of LP



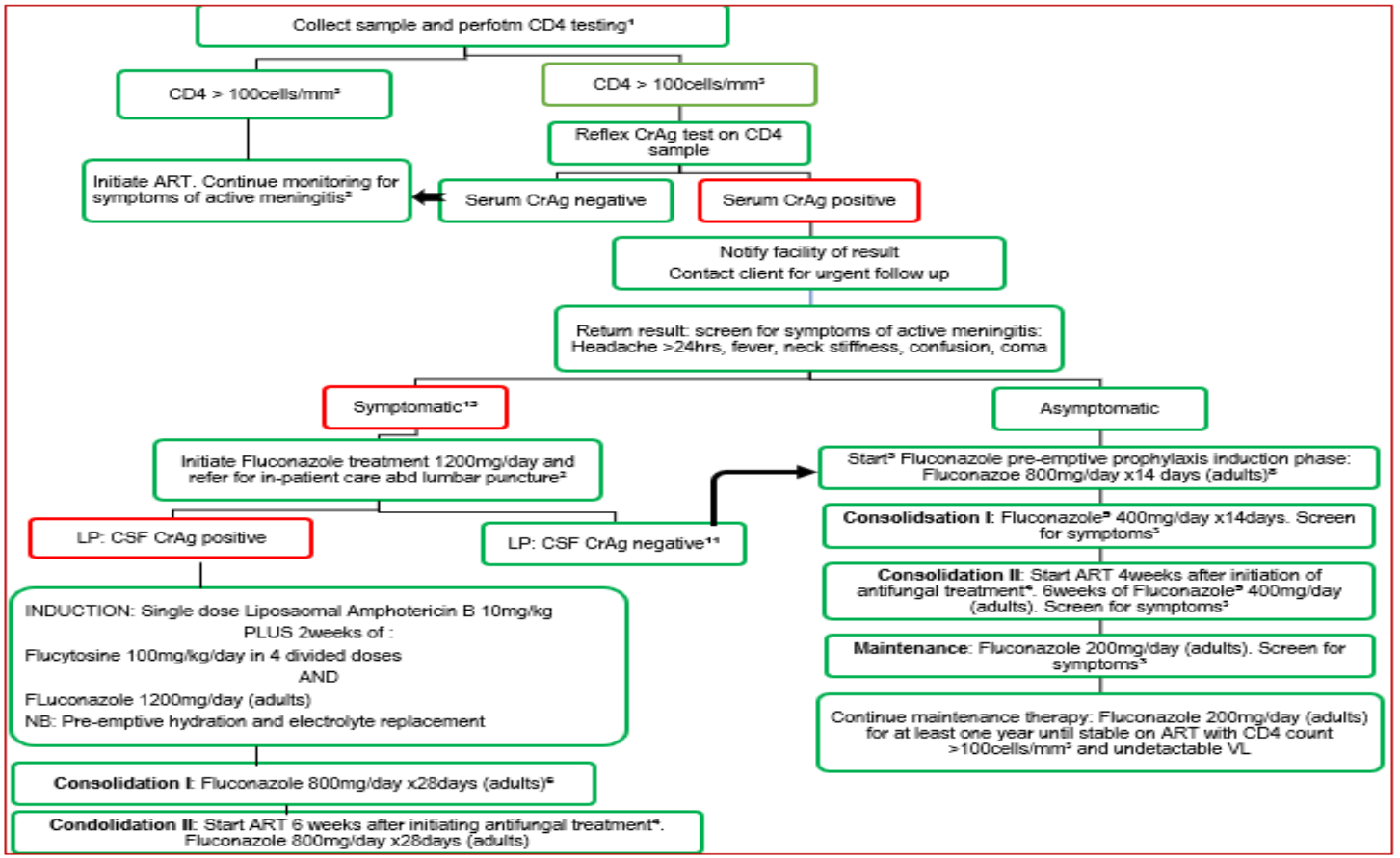


Figure 6.2 CrAg screening for PLHIV with AHD

[1] If CD4 count is done at POC, send another sample to Hub Lab for CD4 testing and reflexive CrAg+ testing

[2] All CrAg+ (positive) patients with signs and symptoms of meningitis should be admitted to appropriate health facilities

[3] If symptoms arise refer to Symptomatic protocol.

[4] Client should have a 2-week review after starting ART in Consolidation II. Align Fluconazole distribution with ART.

[5] Fluconazole dosage: 12mg/kg/day for children & adolescents up to maximum of 800mg/day

[6] Fluconazole dosage: 6-12mg/kg/day for children & adolescents up to maximum of 800mg/day

[7] Fluconazole dosage: 6mg/kg/day for children & adolescent up to a maximum of 200mg/day

[8] Fluconazole dosage: 12mg/kg/day for adolescents up to a maximum of 800mg/day

[9] Fluconazole dosage: 6-12mg/kg/day for adolescents up to maximum of 400mg/day.

[10] Do not discontinue maintenance therapy for children less than 2 years.

**India Ink may be used as an alternative in the absence of CrAg.*

[11] Evaluate and treat other causes of meningitis

[12] For the induction phase alternative regimen, please Table 6.19 below.

[13] Give stat dose of Fluconazole 1200mg if there is no access to LP. Refer the patient immediately for LP.

Table 6.19 Diagnostic Tests and management of Cryptococcal Meningitis

Diagnosis	Cryptococcal Meningitis	Cryptococcal Antigenemia
How to diagnose	Positive CSF CrAg with or without signs or symptoms of meningitis. An LP should be performed in all patients with positive serum CrAg regardless of signs and symptoms of meningitis, if feasible, to rule out cryptococcal meningitis.	Clients with positive blood CrAg LFA and not presenting symptoms of meningitis. See figure 6.5 for the screening algorithm.
Where to treat	If cryptococcal meningitis is suspected in the primary health care setting, the client should be urgently referred to a hospital or health centre for admission and further management.	Clients with positive blood CrAg LFA who do not have symptoms or signs of cryptococcal meningitis can receive fluconazole pre-emptive therapy at the health facility under close supervision. Consider LP if feasible and if there are no contraindications. See section 6.2.2 above
How to treat	**INDUCTION PHASE: Pre-emptive hydration and electrolyte replacement**	
	Cryptococcal Meningitis	**Cryptococcal Antigenemia**
	Pre-emptive hydration and electrolyte replacement • Insert two IV lines (one for Amphotericin B and the other for other IV medication) • Administer 1L Normal Saline with 20mmol Potassium Chloride (KCl) over 2 hours minimum before each Amphotericin B infusion. • Administer oral KCL 600mg twice a day for the duration of Amphotericin B infusion. • If available, magnesium supplementation should also be provided 500mg tablets of magnesium trisilicate twice daily (b.i.d)] • Do not supplement K+ if the patient has pre-existing renal impairment or hyperkalaemia. • If significant hypokalaemia (K+ <3.3mmol/L), increase potassium supplementation to 600mg-1200mg KCl tablets three times daily. • Monitor potassium and magnesium (Mg+) minimum twice weekly. NB: For patients on a single liposomal amphotericin B regimen, pre-emptive hydration and electrolyte replacement is done until **day 3** from the day of Liposomal Amphotericin B infusion.	N/a

Table 6.15 Diagnostic Tests and management of Cryptococcal Meningitis (continued from the previous page)

	Cryptococcal Meningitis	Cryptococcal Antigenemia
	INDUCTION PHASE: Antifungal therapy	
How to treat	Single dose Liposomal amphotericin B 10mg/kg stat dose plus Flucytosine 100 mg/kg/day divided into 4 doses/day x 14 days AND Adults : Fluconazole 1200 mg x 14days Children: 12 mg/kg/day for children to a maximum of 800mg/day X 14days Therapeutic CSF tapping: Recommended if opening pressure >20 cm H_2O, persistent headache, recurrent vomiting, or altered mental state.	Adults: Fluconazole 800mg once daily for 14 days. Adolescents: Fluconazole 12mg/kg/day x 14days for up to a maximum of 800mg/day. Routine screening and pre-emptive treatment are NOT RECOMMENDED for children < 10 years since the risk of CCM in this age group is low
Alternative induction regimens	**OPTION 1**: No Liposomal Amphotericin B Amphotericin B deoxycholate 1.0mg/kg/day x 1 week ***PLUS*** Flucytosine 100mg/kg/day x 7days followed by Fluconazole 1200mg x 7 days (adults) **OPTION 2**: Flucytosine unavailable Liposomal Amphotericin B 3mg/kg/day x 14 days ***OR*** Amphotericin B deoxycholate 1mg/kg/day x 14 days ***PLUS*** **Adults**: Fluconazole 1200mg daily x14 days, **Children and adolescents**: Fluconazole 12mg/kg/per day x 14days (up 800mg/day)	N/A
.	**CONSOLIDATION PHASE**	
	Adults: Fluconazole 800mg once daily for 8 weeks **Adolescents**: Fluconazole 6–12 mg/kg/day up to a maximum of 800 mg daily	**Adults**: Fluconazole 400mg once daily for 8 weeks. **Adolescents**: Fluconazole 6-12mg/kg/day for up to maximum of 400mg/day)

Table 6.15 Diagnostic Tests and management of Cryptococcal Meningitis (continued from the previous page)

	MAINTENANCE THERAPY
	Adults: Fluconazole 200mg once daily for at least 1 year until the client is clinically stable with CD4 >100 cells/mm³ **AND** a suppressed viral load is achieved. **Children & adolescents**: Fluconazole 6mg/kg/day up to a maximum of 200mg/day once daily for at least 1 year until the client is stable with CD4 > 100 cells/mm3 (or 25% for children 2-5 years) and suppressed viral load is achieved.
Contraindications	• History of hypersensitivity to fluconazole or other azole medicines. • Pregnancy.* • For potential interactions between ARVs and other drugs, *see Annex 0*
When to stop	• Secondary fluconazole prophylaxis can safely be stopped after one year in clients on ART who have suppressed viral load and have two consecutive CD4 counts >100 cells/mm3 taken 6 months apart. • Do not stop Fluconazole in children under 2 years

**Safety of fluconazole and Flucytosine in pregnancy is not yet established. However, the benefit of treatment of CCM outweighs the potential risk*

- CSF CrAg is preferred for diagnosis due to its higher sensitivity and ease of test
- CSF India ink may be used if CSF CrAg is not available

The gold standard test is a culture of cerebrospinal fluid for Cryptococcus neoformans, but its role in diagnosis is limited due to the long turnaround time.

For clients with advanced immunodeficiency, a positive blood CrAg with signs and symptoms of meningitis is an indication of an urgent LP. An LP may be performed among all clients with positive blood CrAg regardless of signs and symptoms of meningitis, if feasible, to rule out cryptococcal meningitis.

Routine use of adjunctive corticosteroid therapy during the induction phase is not recommended in treating HIV-associated cryptococcal meningitis among adults, adolescents and children.

Monitoring of CCM patients on treatment

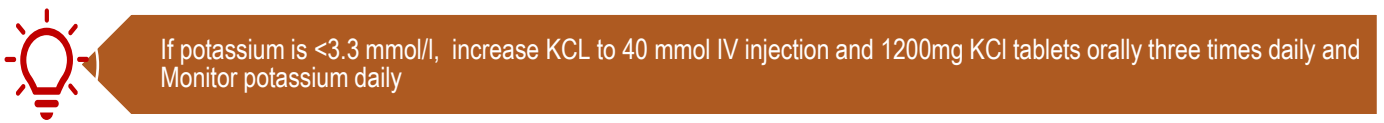
Patients on cryptococcal meningitis treatment need close monitoring for identification of raised intracranial pressure, drug toxicity and adverse events.

Toxicity monitoring

The following presents monitoring and the management of Amphotericin B toxicity

- Monitor daily for signs and symptoms of thrombophlebitis.
- Monitor full blood count (baseline & weekly) & renal function (baseline& twice weekly). Blood tests are recommended at baseline and on **day 4** after amphotericin B for patients on a single Liposomal Amphotericin B regimen.
- If amphotericin B-induced rigors occur, the infusion length can be increased.
- If significant hypokalaemia (Potassium <3.3mmol/L),
  - Increase potassium (K) supplementation to 1200mg oral KCl three times daily, monitor potassium daily
  - Consider increasing intravenous potassium chloride (KCl) supplementation to 40 mmol KCl under careful monitoring
- If hypokalaemia remains uncorrected, consider doubling magnesium (Mg) oral supplementation
- If monitoring facilities allow, monitor serum potassium daily

The following box presents the management of Hypokalaemia during CCM treatment:



Management of renal toxicity in patients receiving Amphotericin B:

If creatinine rises to 220 µMol (2.5mg/dl) or increases by >2 fold from baseline value:

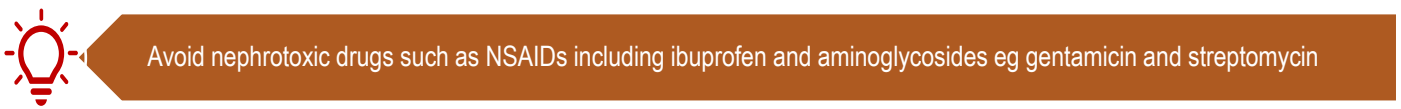
- Skip one Amphotericin B dose.
- Increase IV fluids to 1L 8 hourly, unless contraindicated.
- Check Creatinine the next morning.

If creatinine is improving

- Continue Amphotericin B deoxycholate at 0.7mg/kg/day or full dose of Liposomal Amphotericin B

'If creatinine is not improving:

- stop Amphotericin B and
- switch to fluconazole (1200mg) + 5-FC adjusting both doses for renal impairment.



Flucytosine (5-FC) may accumulate in patients with renal impairment owing to poor excretion. Hence there's a need for dose adjustment.

Table 6.20 The 5 –FC dose adjustment:

Creatinine Clearance (CrCl) ml/min	Individual dose (mg/kg)	Dose Interval
>40	25	6
40-20	25	12
20-10	25	24
<10	25	>24

Use the Cockcroft Gault formula to calculate CrCl. Est. creatinine clearance = (140 – age) * (weight in kg) / (72 * Cr in mg/dL) [Multiply result by 0.85 for women]

- The half-life of 5-FC is prolonged in patients with renal insufficiency; the average half-life is 85 hours (versus 2.4-4.8 hours in patients with normal renal function)
- 5-FC blood concentrations should be observed closely in these patients to monitor excretion – NOTE: Therapeutic Drug Monitoring is not offered in Eswatini
- If creatinine clearance reduces to <50 ml/min, give the same initial dose but reduce subsequent doses by 50%

Laboratory monitoring

The following table summarises the laboratory monitoring required during CCM.

Table 6.21 Laboratory monitoring during CCM treatment.

Laboratory test	Amphotericin B + Fluconazole	Amphotericin B & 5FC	Amphotericin B & Fluconazole
Haemoglobin	Baseline & weekly Hb	Baseline & weekly Hb	Baseline & weekly Hb
Creatinine & Potassium	Baseline and twice weekly	Baseline and twice weekly	Baseline and twice weekly
Full blood count		Baseline FBC and differential count. Weekly FBC	
ALT	Check levels if symptoms of hepatitis or jaundice develop		

Monitor fluid balance throughout CCM treatment

Clinical monitoring of CCM patients

Clinical response is the best way to monitor response to treatment. There is no role for follow-up CSF CrAg for treatment monitoring. CSF culture may be considered in case of symptoms relapse.

Raised intracranial pressure (ICP)

Cerebrospinal fluid opening pressure ≥20 cm H2O

ICP is the commonest cause of morbidity and mortality among CM patients.

Therapeutic lumbar puncture

- Drain 20 - 30ml volume per LP sufficient to reduce the CSF pressure to less than 20 cm H20 (or to 50% of the opening pressure)
- Repeat frequently if persistence or recurrence of symptoms or signs, until the second day of being symptom-free
- Measure CSF opening pressure where manometer available
- Regularly and carefully monitor clinical symptoms and signs

Routine use of adjunctive corticosteroid therapy during the induction phase is not recommended in treating HIV-associated Cryptococcal meningitis among adults, adolescents and children

6.2.3 Histoplasmosis

Definition: Infection caused by a fungus, Histoplasma capsulatum. The fungus lives in the environment, especially in the soil and originates from bird or bat droppings.

Infection occurs after inhaling the spores which settle in the lungs. In immunocompetent individuals, infection is often self-limiting, while among high-risk groups (immunosuppressed, elderly >55years, infants), severe infection may result from the dissemination of fungus from the lungs.

Signs and symptoms of histoplasmosis:

Fever

- Cough
- Fatigue (extreme tiredness)
- Chills
- Headache
- Chest pain
- Body aches

Diagnosis

- Disseminated histoplasmosis among PLHIV is diagnosed by molecular tests which detect circulating Histoplasma antigens in urine or blood. Antigen tests are highly sensitive (95%) and specific (99%). Culture and histological tests can also be used but their usefulness is limited by their complexities, variable performance, and long turnaround time.
- The following populations should receive routine Histoplasma testing.
  - All PLHIV (children> 5 years, adolescents and adults) with advanced HIV disease (CD4<200)
  - All PLHIV with the above signs and symptoms suggestive of histoplasmosis

Histoplasmosis Treatment

The table below highlights available treatment options for patients with Histoplasmosis

Table 6.22 Classification and treatment of histoplasmosis

Disease severity	Signs/Symptoms	Treatment
Severe to moderately severe	Presence of at least one sign or symptom of any one vital organ. Respiratory or circulatory failure, neurological signs, renal failure, coagulation anomalies and alteration of the WHO performance status greater than 2 (confined to a bed or chair for more than half of the waking hours and only capable of limited self-care).	**Induction phase** • Liposomal amphotericin B, 3.0 mg/kg, for two weeks OR • Deoxycholate amphotericin B (0.7–1.0 mg/kg) for two weeks Pre-emptive hydration and electrolyte replacement are critical to minimize the risk of toxicity due to amphotericin B **Maintenance phase** Itraconazole 200 mg twice daily for 12 months Antifungal may be discontinued before 12 months in clinically stable patients on ART and virally suppressed
Mild to moderate	Presence of signs and symptoms not involving the above vital organs	**Induction phase** Itraconazole 200 mg three times daily for three days **Maintenance phase** • Itraconazole 200 mg twice daily for 12 months. • Antifungals may be discontinued before 12 months in clinically stable patients on ART and virally suppressed. • Routine use of adjunctive corticosteroid therapy during the induction phase is not recommended in treating HIV-associated Cryptococcal meningitis Short-course steroid therapy may be considered in life-threatening IRIS-associated histoplasmosis

7 ADULT ANTIRETROVIRAL THERAPY

Important contacts

- **Baylor HIV/TB Hotline: 7848-5571**
- **National HIVDR clinical expert committee: snapthirdline@mohcoag.org**
- **VL and genotype results: 24045332**

7.1 Preparing Clients for ART

One of the main reasons for treatment failure and poor co-operation from clients is inadequate preparation. Before people start antiretroviral therapy (ART), healthcare providers should initiate a detailed discussion about the willingness and readiness of clients to initiate ART, the preferred antiretroviral (ARV) drug regimen, dosage, scheduling, likely benefits, possible adverse effects and the required follow-up and monitoring visits. The success or failure of ART often depends on whether the clients have been well prepared or not. The choice to accept or decline ART ultimately lies with the person and if they choose to defer initiation, ART can be offered again at subsequent visits. Client preparation promotes good adherence to treatment and reduces the risk of the development of drug resistance and treatment failure. There is a need to continue case management during the first few months of treatment to support early retention, adherence, disclosure and adjustment

Refer to *Annex 11.22* for ART readiness assessment

Adherence Counselling Before ART Initiation

It is recommended that all adult clients and children's caregivers participate in at least one individual counselling session before initiating ART. This counselling session should happen on the same day as the HIV diagnosis to encourage same-day initiation. When initiating ART, the clinician has to determine the client's understanding and readiness for initiating and adhering to lifelong treatment. Treatment supporters should be encouraged to attend the client's counselling sessions. It is important to identify and address barriers to treatment adherence including misconceptions. Adherence and psychosocial counselling are ongoing processes aiming to motivate clients to achieve and sustain treatment goals including maintaining undetectable VL, which reduces the risk of HIV transmission, drug resistance and treatment failure.

Adherence and psychosocial counselling should be individualised, and every client should have completed ART readiness assessment before ART initiation.

General Guidance on Adherence Counselling

- Welcome and praise the client for seeking care
- Introduce yourself and explain the process to the client
- Adopt a "no blame" approach to facilitate open and honest discussion.
- Actively involve the client in the decision-making for their care and treatment.
- Emphasize the benefits of ART and long-term optimal adherence even when feeling healthy. The main benefit is sustained viral suppression which leads to the following:
    - Improved quality of life
    - Decreased risk of development of opportunistic infections
    - Decreased risk of HIV developing resistance to ARVs
    - Close to zero risk of HIV transmission e.g., in pregnant and lactating women and, Sero different couples (U=U)
    - Better overall health outcomes and wellness

- Individualize the counselling interventions to identify and address specific barriers to initiating and adhering to treatment, such as the following:
    - Concerns about the personal need for ART when most clients starting treatment are feeling well
    - Specific concerns about taking ARVs and prophylactic treatment e.g., fear of side effects
    - Practical barriers to adherence including disclosure challenges
    - Foreseen challenges that may interrupt adherence on taking treatment for life including stigma and discrimination
- Use interventions to overcome any specific practical problems. Interventions might include the following:
    - Empower clients to monitor their compliance to treatment and to remain motivated to their treatment and life goals.
    - Simplify the dosing regimen (once daily regimen and fixed-dose combinations are preferred in current treatment. Use adherence aids such as pill boxes and phone alarms preferred
- If side effects are a problem:
    - Discuss benefits, long-term effects and options for dealing with side effects. Many of the ART-associated side effects are temporary and can be managed.
    - Discuss specifics of current treatment
    - Consider adjusting the dosage, substitution, or try other strategies such as changing the dose timing or formulation
- Facilitate disclosure of HIV status to trusted others such as a partner, family members or friends.
    - Engage treatment supporters in the care plan. Talk about medications being taken including herbal/traditional remedies and nutritional supplements as some may have drug-drug interactions with ARVs
- Acknowledge that clients' experience taking ART and their needs for adherence support may change over time.
    - Regularly review clients' knowledge, understanding and concerns about medicines and their perceived benefits.
    - Encourage disclosure, partner testing and index testing
- Assess client preference for ART dispensation and provide an overview of the available client-centred ART delivery models (DSD models) that meet their needs and support clients to attend.
    - Emphasize the importance of correct and consistent condom use to prevent STIs.
    - Put strategies in place for client-centric care models at least 1 year after starting ART, when the virus is fully under control.
- Basic education and regular screening for NCDs (Hypertension, Diabetes, Cervical Cancer, Prostate pathology, etc.)
- Assess the patient's mental health and psychological wellbeing, and manage or refer for appropriate services.
- Importance of comprehensive health education e.g., prevention of TB, family planning (dual protection), NCD screening, management and risk reduction, mental health and STI screening and management.

7.2 When to start ART

All PLHIV—children, adolescents, and adults—are eligible to immediately start ART regardless of CD4 count or WHO clinical stage. Health-care workers (HCWs) should promote early initiation of ART by all PLHIV, even when feeling healthy. ART should be started on the same day of HIV diagnosis except for clients with TB or cryptococcal meningitis or cryptococcal infection.

Test and start means all people living with(PLHIV) are eligible to initiate antiretroviral therapy(ART)-preferably within 7 days of HIV diagnosis to improve clinical outcomes and reduce the risk of HIV transmission.Same day initiation is encouraged for clients who are assessed as ready to start ART

Individuals who test positive for HIV and belong to any of the special populations listed below should be urgently assessed for rapid ART initiation:

- Clients with advanced immunodeficiency (advanced disease) (CD4 ≤ 200 cells/mm3 or WHO clinical stage 3 or 4)
- Children under 5 years of age
- Pregnant and lactating women
- Clients coinfected with TB
- The HIV-positive partner in a sero-different relationship i.e., individuals who identify themselves as sexual partners.
- Clients with Hepatitis B coinfection (If laboratory tests for hepatitis B surface antigen are positive.)
- Clients with HIV-associated nephropathy

Table 7.1 Timing of ART initiation

	Timing of ART Initiation			
Days After HIV Diagnosis	0	7 days	14 days	> 14 days
Definitions	Same day ART initiation			
	Rapid ART initiation			
	Early ART initiation			
				Delayed ART initiation

Delay ART initiation for clients with the following conditions:

- TB meningitis: 4 weeks after starting TB treatment
- Cryptococcal meningitis: 2-6weeks after starting antifungal treatment

7.3 Basic Principles of Antiretroviral Therapy

- ART regimens for treatment-naïve clients should contain at least three ARV drugs.
- Preferably, two Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs) and one Integrase Strand Transfer Inhibitor (2 NRTIs + 1 INSTI)
- Due to high levels of pre-treatment NNRTI resistance in Eswatini, the use of NNRTIs in ART clients is discouraged particularly in treatment-experienced clients. Where this cannot be avoided, avoid AZT as the backbone due to the risk of anaemia
- Regimen selection and dose should take into consideration factors such as age, weight, drug to drug interactions, comorbid conditions and diseases (e.g., hepatic dysfunction, renal dysfunction, infectious diseases like TB, viral hepatitis and chronic non-communicable diseases like cancer, epilepsy, mental disorders and diabetes mellitus) and potential interactions with other medications
- Fixed-dose combinations are preferred for use in first-line ART.

7.4 Recommended first-line regimen for adults and adolescents weighing >20 kgs

An optimal ART regimen is a combination that is the most effective, durable, safe, well-tolerated, and affordable treatment. To accomplish this, Eswatini has prioritized fixed-dose combinations and once-daily regimens for ART. These facilitate better adherence, acceptability and viral suppression. The recommended first-line regimen in Eswatini is:

A once-daily, fixed-dose combination of:
TDF (Tenofovir 300 mg) **+ 3TC** (Lamivudine 300 mg) **+ DTG** (Dolutegravir 50 mg) **- TLD**

Clients on ART especially new drugs like DTG based regimen require active pharmacovigilance monitoring and reporting

7.5 Alternative First-Line ART for Adults

Where an NNRTI backbone is to be used, EFV at a low dose (400 mg) in combination with TDF is recommended as the alternative first-line regimen for adults and adolescents living with HIV and initiating ART.

Only TDF/3TC/EFV FDC has EFV 400mg. EFV 600mg formulations may continue to be used until EVF 400mg single formulations are available on the market.

Avoid using a combination of AZT with EFV to prevent rapid resistance to AZT from developing because of the known high prevalence of pre-treatment NNRTI resistance in Eswatini. Additionally, AZT has tolerability problems and needs to be taken twice daily. With the administration of AZT, there is a risk of accumulating thymidine analogue mutations (TAMs) which compromise the use of other NRTIs.

Table 7.2 Alternative First Line regimens

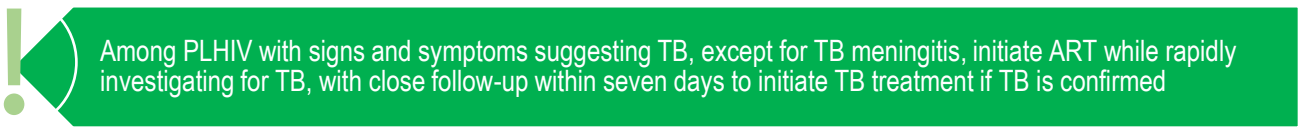
Alternative 1st line – Tier 1	ABC+3TC+DTG
Alternative 1st line – Tier 2*	TDF+3TC+EFV ABC+3TC+EFV
Use AZT only in special circumstances where TDF and ABC cannot be used	AZT+3TC+DTG AZT+3TC+EFV

7.6 Managing Clients delaying ART initiation

Clients who choose not to initiate ART on the day of HIV diagnosis should be enrolled into enhanced linkages case management (eLCM) and scheduled for further counselling to address barriers to ART initiation or for treatment of opportunistic infections. The goal is to initiate ART within seven days of diagnosis for better health outcomes. Refer to eLCM SOPs for a package of care for clients delaying ART initiation.

7.7 Special considerations when initiating ART

7.7.1 TB/HIV coinfection



Active TB/HIV coinfection in client initiating ART

- Tier 1: TDF/3TC (once daily) + DTG 50 mg twice daily

Continue twice daily DTG 50mg for 2 weeks after completion of TB treatment. After this period, continue TDF+3TC +DTG 50 mg once daily

- Tier 2: TDF/3TC+EFV 400 mg (once daily)

See Chapter 6, Table 6.15 for Recommended ART Regimens for TB/HIV Coinfected clients

7.7.2 Clients with Metabolic conditions

Diabetes Mellitus

Adjust metformin dose when starting or stopping DTG to maintain glycaemic control. Monitor closely for metformin adverse effects, glucose levels, and HbA1c. *See chapter 10, section 10.3*- Guidance on ART and diabetes.

Dyslipidaemia

When initiating ART to PLHIV with dyslipidaemia, prescribe statins for people with a 10-year cardiovascular risk exceeding 30%. See NCD guidelines for a non-laboratory-based cardiovascular risk assessment tool.

Obesity

WHO recommends statins for people with a 10-year cardiovascular risk exceeding 30%. See NCD guidelines for calculation of 10yr cardiovascular risk

Boosted PIs are contraindicated with simvastatin because of the risk of rhabdomyolysis.

For DTG induced Insomnia
- Advise clients to take DTG in the morning
- Substitute EFV for DTG if not tolerable provided there is no prior history on NNRTI resistance

See section *Error! Reference source not found.* on management of hyperglycaemia in ART clients on

7.7.3 Abacavir hypersensitivity reaction

Abacavir (ABC) is associated with hypersensitivity symptoms, especially in clients with the HLA B*5701 allele. The prevalence is however rare in our setting and there is no need to screen for HLA. Stop treatment immediately if a client has 2 or more of the following symptoms or signs of hypersensitivity on ABC:

- Fever
- Skin rash
- Gastrointestinal issues (e.g., vomiting, diarrhoea, nausea, abdominal pain)
- Constitutional symptoms (e.g., muscle aches, malaise, fatigue)
- Respiratory issues (e.g., cough, pharyngitis, dyspnoea)
- Central nervous system issues (e.g., headache, blurred vision, paraesthesia)

Health care workers must advise clients to stop ABC and come to the health facility immediately if 2 or more of the above symptoms occur while the client is at home, especially fever and rash.

In clients with ABC-induced hypersensitivity, substitute ABC with another ARV drug and do not reinitiate an ABC-based regimen at any time in the future. Be sure to document the client's hypersensitivity to ABC in the medical record in a visible manner and inform/educate the client.

7.7.4 Clients with Renal Dysfunction

For clients at risk of renal disease—including clients with any of the risk factors listed below—creatinine clearance should be calculated every time a serum creatinine result is reviewed.

Creatinine Clearance Calculation (Cockcroft-Gault Formula)

Men:

$$\frac{(140 - \text{age}) \times \text{weight in kg} \times 1.23}{\text{serum creatinine (in µmol/L)}}$$

Women:

$$\frac{(140 - \text{age}) \times \text{weight in kg} \times 1.04}{\text{serum creatinine (in µmol/L)}}$$

- Risk factors for renal disease:
- Known underlying renal disease
- Age >50 years
- Body mass index <18.5
- Diabetes mellitus
- Hypertension
- Receiving nephrotoxic drugs
- If a renal failure (creatinine clearance <50 mL/min) has been confirmed: do not use TDF: an ABC-based regimen is preferred.
- Adjust client ARV doses to the creatinine clearance, with special attention paid to 3TC.
- If ABC cannot be used, the TDF and 3TC dose can be adjusted according to the creatinine clearance, as described below

Table 7.3 Special consideration in initiating ART in renal clients

Medical condition	Recommended regimen
Hypersensitivity to ABC with renal dysfunction[b]	AZT + 3TC[b] + DTG[a]
Confirmed and/or suspected renal dysfunction (creatinine clearance <50 mL/min) [b] Presence of nephrotoxic drugs or other disease-associated nephropathy	ABC+3TC+DTG[b]
TB/HIV coinfection[a] with renal dysfunction[b]	ABC + 3TC[b] + DTG[a] AZT + 3TC[b] +DTG[a]

[a]Clients with Rif-sensitive TB/HIV coinfection can use DTG, but the daily dose needs to be increased to 50 mg twice daily until 2 weeks after completion of TB treatment.

[b]See Table 7.4 below for a revised dosing schedule for clients with renal dysfunction

Table 7.4 Dose Reduction Guidelines for TDF AND 3TC in clients with Renal Dysfunction (CrCl<50 mL/min

Creatinine Clearance (mL/min)	Preferred Abacavir (ABC) Dose	Tenofovir (TDF) Dose	Lamivudine (3TC) Dose
30 - 50	300 mg twice daily	300 mg every 48 hrs	150 mg once daily
15–29	300 mg twice daily	Avoid, unless receiving haemodialysis, then give 300 mg every 7 days after dialysis	100 mg (10 mL) once daily
5–14			50 mg (5 mL) once daily
<5			25 mg (2.5 mL) once daily after dialysis

For all clients diagnosed with renal failure, at each visit reassess the client and determine if they have acute kidney injury or chronic kidney disease and if they need dialysis.

Clients on DIALYSIS (chronic kidney disease):

- Substitute the offending drug (usually TDF) and adjust 3TC dose
- Adjust doses as indicated in Table 7.4 above
- Give Haematinics as indicated,

Clients not on DIALYSIS:

- Review cause of renal failure and repeat Serum Creatinine:
  - If evidence of acute kidney injury (AKI), treat the cause of AKI and repeat serum Creatinine
  - If kidney injury has resolved, and CrCl > 50 give normal ARV dose and monitor renal function closely
  - If CrCl is still <50, adjust doses as indicated above and monitor renal function closely

7.7.5 Clients with Viral Hepatitis Coinfection

Hepatitis is a syndrome characterized by a group of signs and symptoms that could have several causes: jaundice, raised liver enzymes, and hepatomegaly, among other symptoms, regardless of the virus that has caused it. Ascites, hepatic encephalopathy, variceal bleeding, and jaundice indicate decompensated cirrhosis. Acute hepatitis B virus (HBV) infection needs symptomatic treatment only.

This chapter focuses on chronic HBV (CHB) infection: HBV virus infection persisting beyond 6 weeks

In all cases of Hepatitis B/C, rule out other causes of liver disease e.g., **hepatotropic virus infection** (Hepatitis A, D and E viruses), **malaria**, **toxins** (e.galcohol) or **drugs** (antitubercular drugs – INH, rifampicin, pyrazinamide; antiepileptic drugs – phenytoin; paracetamol overdosing; etc.) and **biliary obstruction**.

HBV testing

HBsAg is the screening test. Follow the algorithm outlined in *Annex 11.10* ***Error! Reference source not found.*** for clients with a positive HBsAg result.

Where available, HBV DNA Nucleic Acid Tests (HBV DNA) following a reactive HBsAg serological test result are recommended to help further guide whom to treat or not treat if no evidence indicates cirrhosis and to monitor for treatment response. HBeAg testing can be used as an alternative to HBV DNA testing to determine eligibility for tenofovir prophylaxis. To determine the stage of infection or immune status, the following laboratory tests should be done at baseline: ALT, HBV DNA, and HBeAg. *See Annex 11.11* for interpretation of Hepatitis B results

HIV testing should be offered to the following populations:

- Key populations especially injection drug users, Men sleeping with men, and Commercial sex workers regardless of HIV status
- PLHIV for whom chronic viral hepatitis is clinically suspected (through symptoms, signs or laboratory markers)
- Sexual partners of PLHIV testing HBsAg positive
- Children, other family members and close household contacts of those with HBV infection
- Health-care workers: in all settings, it is recommended that HBsAg serological testing be offered, and HBV vaccination is given to all healthcare workers who have not been vaccinated
- For diabetic clients; the risk comes from non-adherence to infection prevention and control practices in at-home measurement of blood sugar and administering insulin
- Clients undergoing dialysis

Hepatitis B infection in pregnancy

Perinatal transmission of HBV tends to be high in pregnant women who have a high HBV viral load. Perinatal transmission can be reduced by identifying HBV-infected pregnant women and treating eligible women timeously as highlighted below. To protect neonates, give hepatitis B monovalent birth dose vaccine and immune globulin (where available) to neonates within 24 hours of birth and thereafter, according to the national infant immunisation schedule.

All pregnant women should receive HBsAg testing at least once (preferrably at first ANC) during pregnancy

Pregnant women should be tested for HBV DNA to guide the use of maternal antiviral therapy during pregnancy

HIV positive pregnant and breastfeeding women testing positive for HBV infection (HBsAg positive) should be started on a TDF-based ART regimen as antiretroviral therapy and for the prevention of mother-to-child transmission of HBV from mother to child

HBV Vaccination

Pregnant women, Haemodialysis clients, Key populations and diabetic clients should be prioritised for vaccination. HBV vaccination should be provided to all HBV-exposed neonates preferably within 24 hours of birth, after which the vaccine efficacy is markedly reduced. Refer to the national immunisation schedule for guidance.

Contraindications to vaccination

- Clients with an allergy to baker's yeast (Saccharomyces cerevisiae)
- Persons with a history of serious adverse events after receiving the HB vaccine

Vaccination of persons with moderate or severe acute illness, with or without fever, should be deferred until the illness resolves

Breastfeeding is encouraged for all HBV-positive women as the benefit outweighs the risk of transmission.
Testing of infants should only be done where there is an indication in which case it should be done after 9-12 months of age to avoid false positives from maternal antibodies.

HBV Treatment

Treatment should be offered to all adults, adolescents and children with chronic hepatitis B (CHB) and clinical evidence of compensated or decompensated cirrhosis based on aspartate aminotransferase to platelet ratio index [APRI] score >2 in adults, regardless of ALT levels, HBeAg status or HBV DNA levels.

Before starting treatment, the client should be evaluated for host liver injury, viral status and presence or absence of cirrhosis;
Host liver injury: depicted by persistently elevated ALT. Check ALT every 3 months. The serum ALT pattern is described as persistently normal, persistently abnormal, or intermittently abnormal.

Persistently normal ALT*: three ALT determinations that are below the upper limit of normal (ULN) measured at unspecified intervals during a 6–12-month period or at predefined intervals during a 12-months period.*
Persistently elevated ALT*: three ALT determinations that are above the ULN measured at unspecified intervals during a 6–12-month period or at predefined intervals during a 12-months period.*
Intermittently abnormal ALT*: fluctuating ALT levels during a 6-12-month period or at predefined intervals during a 12-month period*

Viral status: Offer treatment to adults with no evidence of host liver injury but are >30 years old and have persistently abnormal ALT with HBV DNA >20 000 IU/L regardless of HBeAg status. Where HBV DNA testing is not available, treatment may be considered based on persistently abnormal ALT levels alone, regardless of HBeAg status. If HBV DNA is reported in copies, divide it by 5 to get the international units (IU).
Presence or absence of cirrhosis: AST to platelet ratio (APRI) score is the preferred Non-Invasive Test (NIT) to assess the presence of liver fibrosis/cirrhosis at baseline and during follow-up. Fibrosis-4 (FIB-4) index is another NIT test that can be used to assess the presence of cirrhosis. Liver biopsy is the gold standard however non-invasive methods may be used. NITs include

APRI score >2 in adults, FIB-4 index > 3.25, transient elastography (fibro scan), and clinical assessment for the presence of symptoms such as ascites, and hepatic encephalopathy, variceal bleeding, and jaundice.

APRI SCORE CALCULATION* $APRI = \frac{\frac{\text{AST Level}}{\text{AST (Upper Limit of Normal)}}}{\text{Platelet Count } (10^9/L)} \times 100$	APRI ≤ 0.5 means the liver is completely free of fibrosis or has a tiny bit of scarring APRI ≥1.5 means the liver has scarring and likely has some cirrhosis ***AST and ALT measured in IU/L**
FIB-4 INDEX CALCULATION $FIB\text{-}4 = \frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet Count } (10^9/L) \times \sqrt{\text{ALT (U/L)}}}$	FIB-4 >1.45: a low predictor of fibrosis FIB-4 > 3.25: high predictor of fibrosis

Recommended First-Line ART for Clients Coinfected with Hepatitis B Virus

- TDF and 3TC are preferred in hepatitis B coinfected clients for long-term treatment of HBV as they lead to sustained HBV viral suppression, reversal of cirrhosis and fibrosis as well as a reduction in HBV-related mortality.
- If a client's ART regimen needs to be changed due to HIV drug resistance, both TDF and 3TC should be continued as part of the new second or third-line regimen to prevent hepatitis B viral load increase, ALT flares and hepatic decompensation.

Table 7.5 Recommended TDF and 3TC doses in HBV clients with renal failure

Creatinine clearance (ml/min)	TDF dose	Creatinine clearance ml/min)	3TC dose
30-49	300 mg every 48h	>30	Full dose
10-29	300 mg twice weekly (every 72-96 hours	15–29	150 mg stat, then 100 mg every 24 hours
<10 and not on Haemodialysis	Give other antivirals	5–14	150 mg stat, then 50 mg every 24 hours
On Haemodialysis	300 mg every 7 days or give other antivirals	<5 or on haemodialysis	50 mg stat, then 25 mg every 24 hours

Adapted from- https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/ AdultandAdolescentGL.pdf. Accessed 28/03/2022.

On Dialysis days, the client should take the ARV dose after the haemodialysis session

Use of ARVs in Clients with HIV/Hepatitis C Virus Coinfection

All HIV-positive individuals should be screened for hepatitis C virus (HCV) infection through an HCV antibody test.

- All clients with HIV/HCV coinfection should be evaluated for the treatment of HCV
- For HIV/HCV coinfected clients use a TDF + 3TC backbone in the ART regimen

ARVs slow the progression to cirrhosis due to HCV,

Treatment of HIV and HCV can be challenging due to overlapping toxicities or pill burden.

Treatment with direct-acting antiviral agents, rather than regimens with pegylated interferon and ribavirin is recommended for clients with HCV infection. (Contact physician when managing HIV/HCV coinfected clients)

Treatment monitoring

All chronic HBV clients, whether on treatment or not, need lifelong monitoring at regular intervals to assess disease progression, development of hepatocellular carcinoma, treatment response and toxicities. *See Annex 11.12*

7.8 Guidance on Regimen Optimization for adults and adolescents

This guidance applies to all adults and adolescents ≥30 kg, including pregnant and breastfeeding women, on an NNRTI-based regimen.

Transition to DTG in these clients is a priority due to high pre-treatment NNRTI resistance mutations in Eswatini.

> **!** Clients can be transitioned from an NNRTI based ART regimen to a DTG based regimen without a recent viral load, however, take note of clients with viraemia for future reference and to ensure adherence addressed while switching

Where clients have a recent viral load *Figure 7.1* below guides how to use viral load results (VL done in the past 3-6 months) to inform the transition to optimal ART regimens for adult clients. Transition all clients with undetectable or VL less than 200 copies/mL within the last 3-6 months to a DTG-containing 1st line regimen.

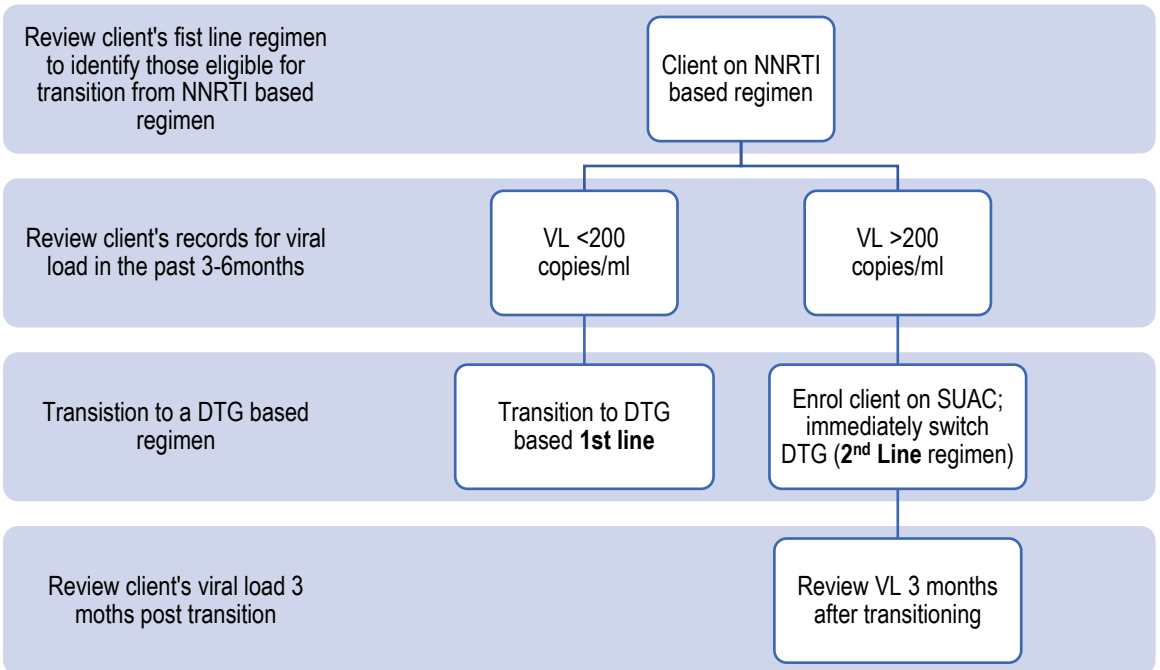


Figure 7.1 Adult Viral load consideration for Treatment Optimization

7.9 Clinical Monitoring of Clients on ART

When clients are initiated on ART they are monitored through clinical and laboratory assessments. Clients on ART should be monitored for adherence, toxicity and treatment failure. The aim is to achieve the following:

- Good adherence habits
- An undetectable viral load
- Adequate coping mechanisms and support systems

Monitoring people on ART is important to ensure successful treatment, identify adherence problems and determine whether ART regimens should be switched in case of treatment failure.

To achieve the above, routine monitoring, timely response to client's needs and appropriate clinical management is necessary. Differentiated care is offered based on the findings of clinical and laboratory monitoring.

During the first 3 months of treatment, clients should be reviewed monthly. The first review should be scheduled not more than 14 days after ART initiation.

Table 7.6 Clinical Review Schedule for the First Year of ART

	2 Weeks After Initiation	4 Weeks After Initiation	6week after ART initiation	Every 3 Months
Mild/moderate immunodeficiency (clinically well) CD4 count ≥200 cells/mm³	x		x	After 3 months on ART and VL is undetectable
Advanced immunodeficiency (advanced disease) CD4 count <200 cells/mm³	x	x	x More frequent follow-up if indicated	After 3 months on ART and VL is undetectable

Pharmacy personnel should dispense a two-week supply of ARVs during the ART initiation visit to allow clients to come for a two-week follow-up visit. If the client has mild or moderate immunodeficiency (clinically well) at the first clinical review and is adherent to treatment with no side effects at the 2-week review, then the client can start monthly reviews.

If the client has advanced immunodeficiency (advanced disease), opportunistic infections, toxicities or comorbidities, the second review should be 14 days later (i.e., 4 weeks after ART initiation). All clients with advanced immunodeficiency should be monitored closely (monthly or more frequently if indicated) until they are clinically stable. At each visit, monitor treatment adherence, adverse events, new or worsening opportunistic infections, and treatment adherence. Refer to *Chapter 5, Table 5.8.*

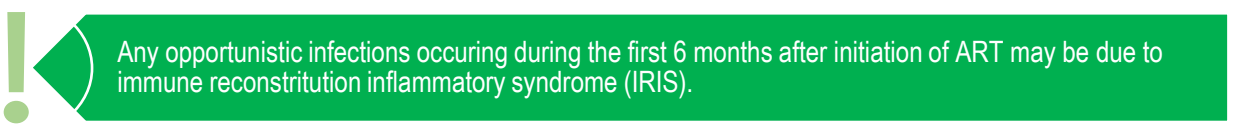
During the first 3 months of treatment, clients should be reviewed monthly. ART refills should follow the clinical review schedule of treatment. After 3months on ART and VL is undetectable, clients may be given up to 3MMD

Clients with an undetectable viral load 3months after ART initiation are eligible for 3 months refill.

For health facilities that have integrated other services into HIV care, ART refills should coincide with NCD refill days. For health facilities that have not yet integrated other services into HIV care, delink ART visits from NCD refills. In such instances, eligible clients can get up to 6MMD for ART and regular visits for other conditions.

The clinical review should include:

- Adherence counselling and support:
  - Include an assessment of adherence (e.g., pill count, self-reported adherence, assessment of barriers).
- Clinical monitoring
  - Conduct a clinical review of symptoms, signs, medication use and side effects.
  - Check for immune reconstitution inflammatory syndrome (IRIS).
  - Complete a physical examination, including determination of HIV WHO clinical stage and functional status. refer to *Chapter 5, Table 5.1*
  - Conduct screening for TB and opportunistic infections.
  - Provide acute care, if necessary.
  - Conduct pharmacovigilance assessment
  - Manage symptoms.
  - Manage comorbid conditions (e.g., diabetes, hypertension).
  - Verify doses and resupply ART.
  - Resupply Co-trimoxazole preventive therapy (CPT) and TB preventive therapy (TPT)] if indicated.
- And other services as required (*refer to Chapter 5*, Basic Care package)



- IRIS is seen when a client's impaired immune function is restored. IRIS is characterized by the clinical worsening (paradoxical) of a known condition or the appearance of a new condition (unmasking).
- Infectious pathogens most frequently implicated in the syndrome include mycobacteria tuberculosis, varicella zoster, herpes viruses, cryptococcus and cytomegalovirus.
- At the clinic level, healthcare workers should refer clients with suspected IRIS to the doctor or the hospital for further management.
- Clients with advanced immunodeficiency (advanced HIV disease) are at greater risk for IRIS after initiating ART and should be closely monitored.
- Dolutegravir (DTG) has been associated with a higher risk of IRIS due to rapid viral suppression. Clients initiating DTG should be closely monitored for IRIS.

7.10 Laboratory Monitoring of Clients on ART

Once a client has initiated ART, laboratory monitoring will be routinely done at pre-determined intervals to determine immunological and virological responses to ART as well as metabolic, liver and renal function

Table 7.7 Laboratory Monitoring

Laboratory Tests	All Clients at Baseline	If CD4 <100 cells/ mm³	3 months	12 months	After 12 months
Viral load*			x	x Return VL result	• If the second VL is undetectable, repeat, VL every year. • If VL is detectable and < 1000 copies/ml, see *Table 7.8*. If second VL ≥ 1000 copies/ml, *see, Figure 7.3* Repeat every 6 months for 3rd line clients

Laboratory Tests	All Clients at Baseline	6 months	12 months	After 12 months
CD4 count or CD4 %	x	x For paeds and AHD clients		If the viral load is detectable, monitor CD4 to assess the immune status and need for prophylaxis or an advanced immunodeficiency package
Haemoglobin (Hb) or Full Blood Count (FBC)	x	• Repeat according to clinical requirements • Repeat annually at the time of VL testing if on the AZT regimen		
Urea and Creatinine	x	x (TDF regimen)	x (TDF regimen)	Every 6 months (if on TDF) • At all visits (if known renal dysfunction)
Aspartate aminotransferase (AST)/ alanine aminotransferase (ALT)*	x			If stable, repeat every 12 months or if clinically indicated See *Annex 11.10 to 11.12 for* chronic HBV
Hepatitis B surface antigen (HbsAg)	x			Perform HBsAg any time before TDF is discontinued. (before switching ART regimen if this testing was not done or if the result was negative at baseline and the person was not vaccinated thereafter)
Hepatitis B DNA (Viral load)				If HBsAg is positive and ALT persistently abnormal

Table 7.7 Laboratory Monitoring (Continued from the previous page)

Laboratory Tests	All Clients at Baseline	6 months	12 months	After 12 months
Lateral flow TB-lipoarabinomannan assay (LF TB-LAM)	x (If TB-presumptive)	Repeat test at any point when CD4 drops to <100 cells/mm³ and TB-presumptive		
Cryptococcal antigen lateral flow assay (CrAg LFA)	x If CD4 count < 100 cells/ mm³	Repeat test at any point when CD4 drops to <100 cells/mm³		
Pregnancy Test	x (women/sexually active adolescent girls)	As required		
Non-communicable diseases screening • Blood glucose • Lipid Profile ○ Total cholesterol ○ Triglyceride	x Clients initiating DTG/PI **AT risk clients:** (Clients >50 years old, Obese, Family history of diabetes, or with a cardiovascular event)		x **For at-risk clients** (Clients >50 years old, Obese, Family history of diabetes, or with a cardiovascular event)	• Every 6 months for at-risk clients on DTG/PI • Every 6 months for 3rd line clients • Annually for all other clients on DTG, LPV/r or DRV/r
Cervical cancer screening VIA or Pap smear every 12 months	x		x	Every year
CRP	As required. Refer to TB guidelines and *Figure 6.1*			
Chest X-ray	As required. *Refer to Figure 6.1*			

7.10.1 CD4 monitoring

CD4 count testing is done for clinical staging of AHD. CD4 count testing should be done at baseline for all clients and 6 and 12 months after ART initiation for clients with moderate to severe immunodeficiency. *See section 0*. In settings in which routine viral load monitoring is available, CD4 cell count monitoring should be stopped for individuals who are stable on ART. See DSD *Section 5.7* for the definition of stable on ART

CD4 monitoring should be resumed for clients with

- High VL,
- WHO stage 3 or 4 illness,
- Returning to care after treatment interruption (returning to care after ≥ 1 year after missing an appointment)

If treatment failure is suspected, resume CD4 monitoring until client has an undetectable viral load.

For more details on the role of CD4 count, *refer to chapter 5, Section 0* Changing the role of CD4.

7.10.2 Viral load monitoring

To ensure timely intervention for clients with possible adherence issues, **viral load testing should be done by 6 months and at 12 months after ART initiation**. *See Figure 7.2* below. Refer to *Chapter 8, Figure 8.1* for VL testing in pregnant and breastfeeding women and *Chapter 9, Figure 9.5* for VL testing in children and adolescents.

After two consecutive undetectable VL results, VL monitoring can be done annually. A detectable viral load may indicate non-adherence, malabsorption, drug-drug interaction and/or possible treatment failure. See *Figure 7.3* and ***Error! Reference source not found.*** below for management of high viral load. Clients should be informed of the benefits of an undetectable viral load including U=U and DSD enrolment with MMD.

Point of care viral load

Point-of-care (POC) viral load testing may be used to monitor treatment among PL HIV receiving ART. POC VL testing allows for more rapid clinical decision-making in populations at risk who need prompt decision making e.g.

- Pregnant and breastfeeding women
- Infants, children, and adolescents
- People requiring a repeat viral load after a first elevated viral load to enable a rapid switch to a second- or third-line ART regimen
- People for whom treatment failure is suspected
- People presenting sick, living with advanced HIV disease, or having a known opportunistic infection (TB, cryptococcal infection, etc.)
- First scheduled viral load test for people re-engaging into care to assess the level of immune injury and a risk of disease progression
- PLHIV suspected to be failing ART while on DTG for less than two years
- For female clients, cervical cancer screening should also be done at the time of VL testing; at least once every year

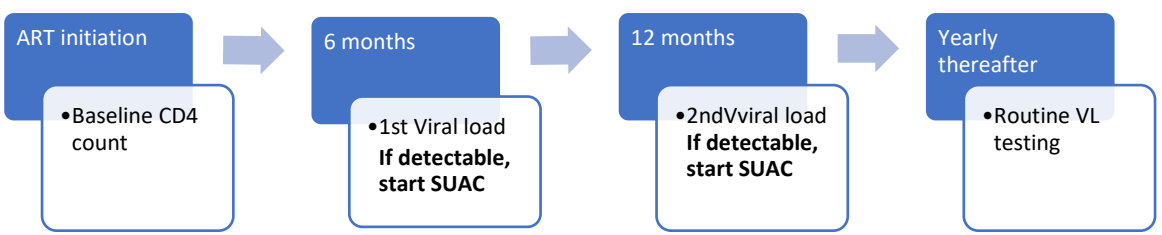


Figure 7.2 VL and CD4 monitoring schedule

If VL ≥50 - 1000 copies/mL, start Stepped Up Adherence Counselling (SUAC) and follow protocol for the management of high viral load. *See viral load testing algorithm Figure 7.3* below. Resume CD4 count monitoring if treatment failure is suspected. For clients with VL≥ 1000 copies/mL provide index HIV testing to their partners if they have a negative or unknown HIV status

Move to annual viral load monitoring only if the client has had 2 consecutive undetectable viral load test results 6 months apart.

If VL>1000copies/mL while on NNRTI based regimen and treatment failure is suspected, immediate switch to appropriate regimen is recommended.

An immediate ART switch after a single eleveted viral load result should not be considered for those receiving DTG-or PI-based regimens, since the likehood of drug resistance is minimal according to current evidence.

Targeted viral load monitoring can be done in clients presenting with new WHO treatment stage 3 or 4 opportunistic infections or whose treatment is suspected to be failing. Dried blood spot specimens (DBS) using venous or capillary whole blood can be used to determine HIV viral load. The same threshold of 1000 copies/mL is used to determine virological failure when using dried blood spot samples, as defined for testing in plasma.

Priority for DBS VL

- DSD
- Community commodity distribution (CCD)
- Hard to reach health facilities
- Infants
- Workplace ART and wellness clinics
- Teen clubs
- Clients with work or school commitments to improve their access to VL testing
- Facilities offering extended hours of service (early morning or late evening)
- All clients presenting as visitors and due for VL

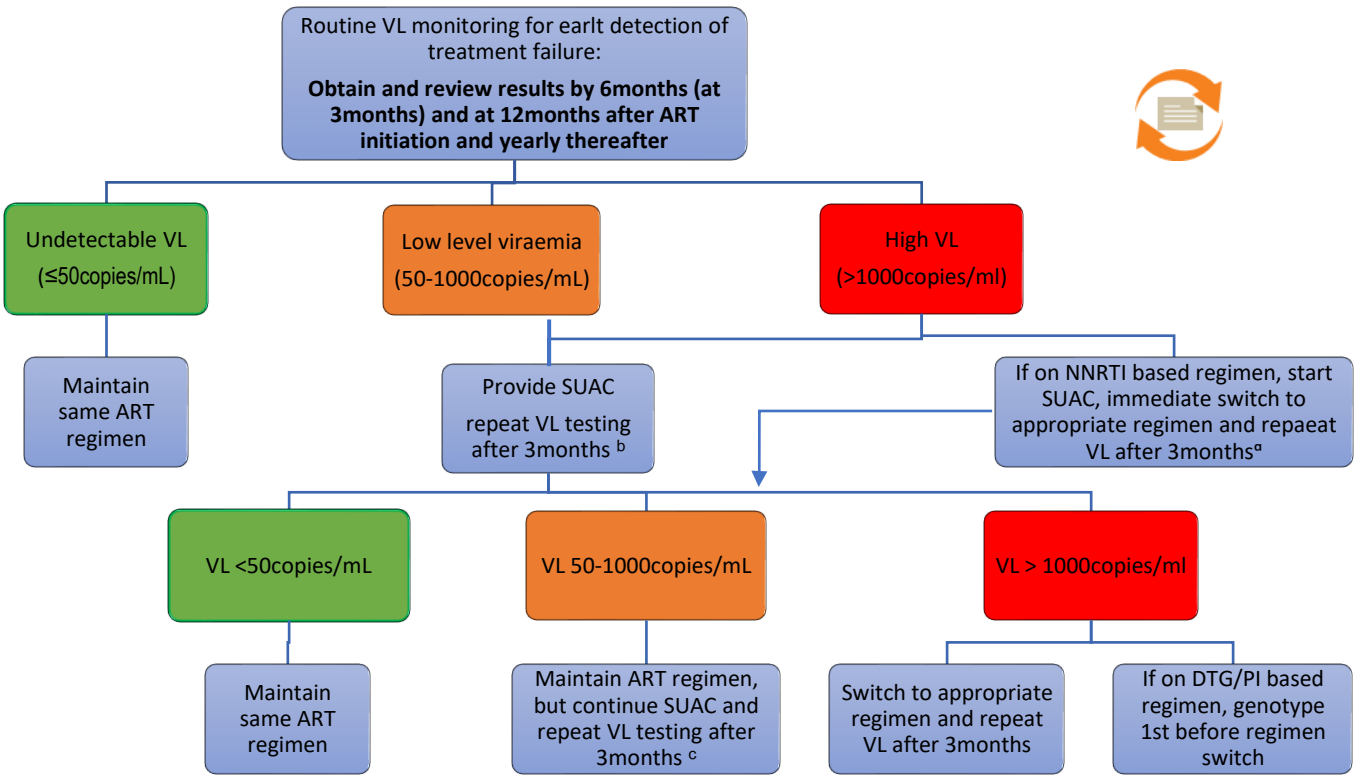


Figure 7.3 Viral load testing algorithm

Adherence counselling should be provided at all visits to ensure that viral suppression is maintained or given priority throughout the care

[a] If in NNRTI, immediately switch after a single elevated viral load

[b] Conduct same-day testing using point-of-care viral load testing for a repeat viral load test, where available, to expedite the return of results. If not available, viral load specimens and results for a repeat viral load test should be given priority across the laboratory referral process (including specimen collection, testing and return of results). See subsection 7.10.2 above on point of care viral load testing.

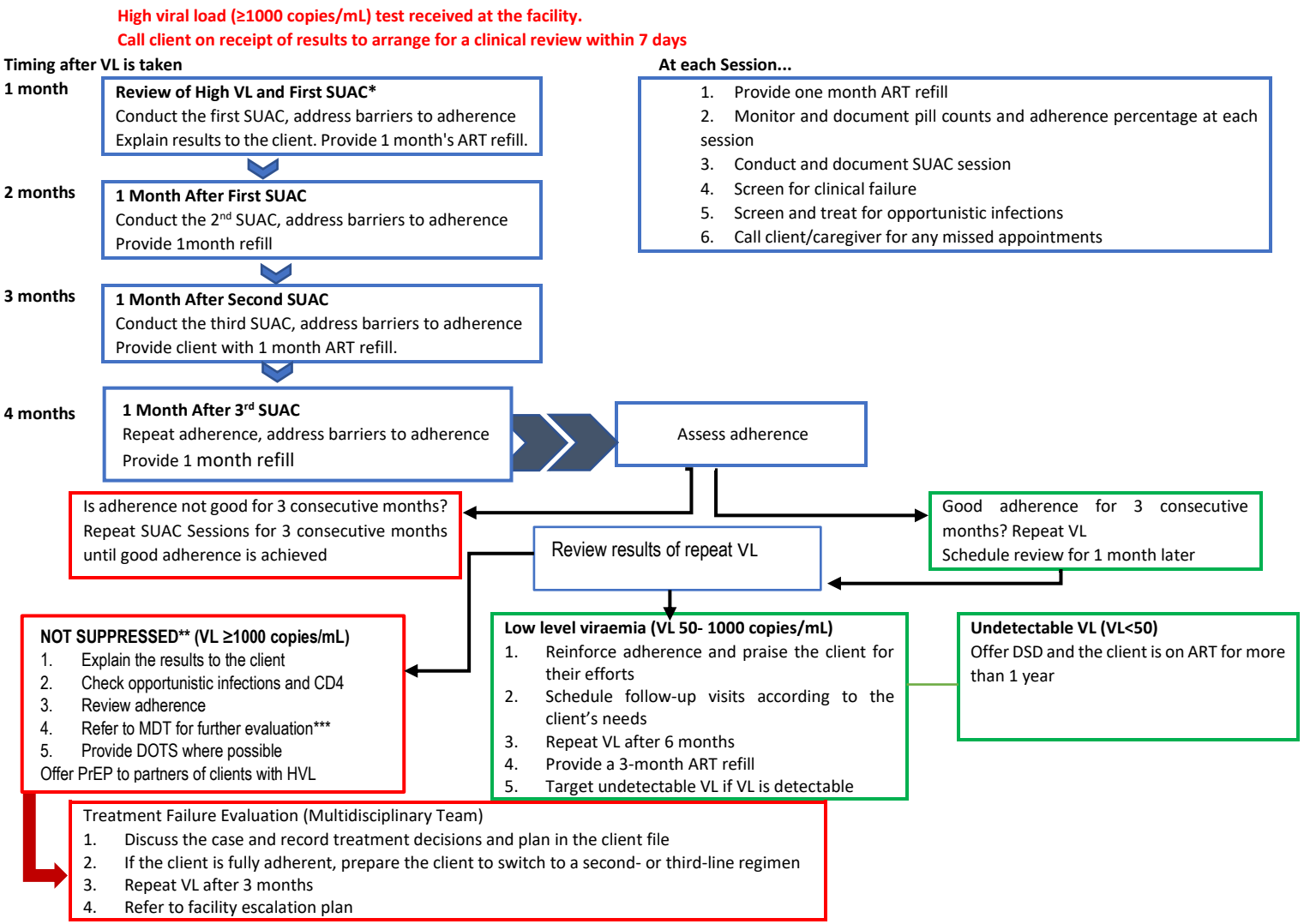
[c]Consider switching ART for those receiving NNRTI-based regimens based on clinical considerations and address any adherence concerns. Consult experienced clinician

Table 7.8 Viral Load Test Results Interpretation

VL Result	Interpretation		Action
< 50 copies/mL	Undetectable	Suppressed	• Maintain ART regimen • Praise the client for good adherence to treatment. • Remind the client they still have HIV. • Reinforce adherence messages. • Continue to test VL according to the timeline. • Offer and enrol into appropriate DSD
50 - 1000 copies/mL	Detectable (Low-level viraemia)		• Enquire about adherence challenges, possible DDIs or intercurrent mild and self-limited illnesses. • Emphasize ongoing adherence • Children and adolescents with VL > 400 copies/mL should be referred for SUAC • If on and NNRTI based regimen, immediate regimen switch while doing SUAC
≥ 1000 copies/mL	High viral load	Unsuppressed	• On top of the above: • Call the client to come to the facility within the next 7 days to begin stepped-up adherence counselling (SUAC) • Escalate client to SUAC. • Encourage DOTS • Reinforce dangers of continued viremia (e.g., HIV disease progression, opportunistic infections, death). • If on and NNRTI based regimen, immediate regimen switch while doing SUAC • Offer PrEP to partners of clients with a high viral load.

7.10.3 Management of a high viral load (VL >1000 copies/mL)

Receipt of a high VL test result should trigger immediate action within the facility. Clients should be called to come to the facility within the next 7 days to begin SUAC. *See Figure 7.*4 *below* for the management protocol.



**For clients on an NNRTI-based regimen, consider switching regimens after a single elevated VL. See Figure 7.3 above*

***For clients with VL≥ 1000 copies/mL provide index HIV testing to their partners with negative or unknown HIV status. Consult the doctor at the mother facilities or Baylor HIV/TB Hotline 7848 5571*

****Clients who despite adherence support have two consecutive high VL results while taking a DTG/PI-based regimen should be referred to the HIVDR clinical expert committee for consideration for genotype*

Figure 7.4 Management of Clients with VL >1000 copies/mL

7.11 Stepped Up Adherence Counselling (SUAC)

The goal of SUAC is to improve adherence and to lower a client's VL to an undetectable level. SUAC is also used to determine whether adherence is or is not the cause of the client's high VL and to accurately recommend an appropriate treatment option. The SUAC toolkit details the structure and steps to be undertaken when conducting SUAC sessions. In general, each session consists of the 7 steps highlighted in *Figure 7.5* below.

Figure 7.5 Structure of the Stepped-Up Adherence Counselling Session

For effective SUAC, all areas of psychosocial care have to be addressed as highlighted in the table below.

Table 7.9 Content of Stepped-Up Adherence Counselling Sessions

Psychosocial—How to address clients	• Have a positive, caring and engaging attitude towards the client and their supporters. • Address understanding of the chronic care issues by the client and their supporters. • Use the SUAC toolkit or job aids for counselling on difficult topics. Job aids can be pictures, photos or any other tool that the client can relate to. • Engage the family and other treatment supporters in the care of the client. Invite and counsel any new treatment supporter. Arrange family meetings if the situation allows. • Empowerment: Encourage questions/discussion. Listen to the client's own story. Focus on positive things and encourage a positive attitude to live with HIV. Address myths and misperceptions and spread knowledge. • Involve the client in important decisions to better understand why certain decisions are made. Make short-term plans, set up goals with the client and/or their supporters, and follow up on how goals were achieved. • Provide key messages at each step as outlined in the SUAC toolkit.

Table 7.9 Content of Stepped-Up Adherence Counselling Sessions (continued from the previous page)

Psychosocial—Other aspects of care	• Regularly, follow up on what time medicines are taken and adjust the time if necessary. • Encourage participation in support groups; map the closest ones and facilitate referrals. Start or support peer-support counselling groups at your facility. • For clients who may benefit, conduct a series of twice-a-month sessions facilitated by committed psychosocial support staff who know the clients well. • If possible, conduct home visits to help you understand the social environment and offer relevant support. • Engage community health care workers in supporting the client. • Screen for mental conditions (e.g., depression, alcohol or drug use, home-based violence, sexual violence, peer bullying). • Screen for other possible barriers to care or barriers to adherence—including transport costs, stigma, misconceptions or side effects and address them.
Clinical Follow up	• Regularly update or confirm clients' contact details (phone numbers and addresses) at every encounter (especially clients on 6MMD). • Actively rule out opportunistic infections or other medical conditions. • Provide adherence counselling and follow-up on issues at every visit. Encourage the use of an alarm, cell phone or watch for reminders for medication doses. Encourage the use of a pillbox and monitor use and maintenance if the client would benefit from it. Encourage keeping the medication stored safely. • Address potential medication side effects. Ensure the client receives adequate laboratory monitoring, • including CD4 and VL testing as per guidelines. Repeat VL only after at least 3 months of recorded good adherence according to the guidelines. Call the client if laboratory results are found to be abnormal and require immediate action. • Encourage the client to take medications even if late or on an empty stomach, rather than skipping pills. The recommended first-line regimens can be taken on an empty stomach. Have the client repeat doses that were spat out or vomited within 30 minutes. • Set up and use a system at your facility to avoid clients being lost to follow-up (both pre-ART and after defaulting from ART) and to call back clients who missed appointments.

Special clinic days for clients whose treatment is suspected to be failing is recommended

7.12 Viraemia/Challenge clinics

This is a model where clients with high viral load or treatment failure are booked and managed on a specific day(s) in the clinic. The viremia clinic model is advantageous to the clients, healthcare workers and the healthcare system

Advantages to the client

- Access to a multi-disciplinary team of health professionals (doctors, nurses, laboratory, pharmacy and psychosocial/adherence counsellors)
- Access to peers in similar situations where they can share best practices
- Rapid refills of medication and reduced time spent in the facility.
- Reduced movement in the facility since all services are brought to the clinic corner (?)

Advantages to the health care workers

- Easy booking schedule
- Ensures teamwork amongst health care workers
- Ensures collective responsibility and decision making
- Improves clients flow

Advantages to the health system

- Improved quality of care given to clients
- Reduction in costs accrued due to inaction on VL results
- Improved logistics in supply chain and sample transportation

Services offered in a viremia clinic:

- Pill counting and adherence monitoring
- Opportunistic infections screening e.g.: TB, cryptococcal meningitis
- Non-Communicable Diseases (NCDs) screening: diabetes mellitus (> 50 years), hypertension, cervical cancer
- Index testing listing
- Counselling
- ART refills, CTX, TPT, fluconazole when indicated
- Condom distribution
- PrEP for partners of clients with high viral
- Laboratory monitoring: VL, CD4 count, chemistry, FBC
- Switching to 2nd or 3rd line when indicated

Table 7.10 responsibilities of the multidisciplinary team in a viraemia clinic

Cadre	Responsibilities
Doctor	• Overall, in charge and guides client management • Available for consultations physically and also on the phone • Conduct thorough clinical assessment and management of clients • Collect samples for laboratory tests
Nurse	• In charge of the day-to-day running and overseeing of clinic activities • Refer and book clients for the doctor • Call the doctor for clients where immediate decisions need to be made • Conduct SUAC • Collect samples for laboratory tests
Expert client	• Book clients and follow up on missed appointments • Conduct SUAC • Refer clients to nurse for further assessment • Pill count and adherence assessment • Psychosocial assessment • Home visits • Screen clients due for VL, send them for testing and follow up on results • Index testing listing
HTS counsellor	• HIV testing for index client contacts
Laboratory staff, phlebotomist	• Collect and runs samples for laboratory tests
Pharmacy personnel -dispenser	• Prepack and dispense drugs • Drug ordering from mother sites or CMS
Social worker	• Review of clients with complicated psychosocial issues
Psychologist	• Provides counselling to clients with psychosocial issues

A client can be discharged from the viraemia clinic after viral achieving an undetectable viral load. HCWs should document the outcome in the high viral load register.

Treatment Failure

Treatment failure is defined as two consecutive VL ≥1000 copies/mL, with samples taken at least 3 months apart, irrespective of clinical and immunological findings, and with SUAC and good adherence between measurements.

Any client receiving NNRTI-based regimens with a single VL ≥1,000 copies/mL should immediately be switched to an appropriate optimised regimen based on their ART history.

Although plasma is preferred for VL testing, a dried blood spot specimen is an alternative, especially for children and clients who present outside the normal phlebotomy hours.

An individual must be taking ART for at least six months before it can be determined that a first line regimen has failed. A viral load threshold of ≥1000 copies/mL should be used to determine virological failure when using plasma or dried blood spot specimens.

VL should be used to diagnose and confirm treatment failure. CD4 count and clinical monitoring should not be used to diagnose treatment failure but as additional evidence for treatment failure

*See Annex **Error! Reference source not found.** for possible causes of treatment failure*

Management of Virological Failure

Clients failing treatment should be managed by a multidisciplinary team. Further discussions could be held with nurses or expert clients who are familiar with the client's family and adherence situations. The engagement of social workers and psychologists is necessary for psychosocial issues. Identify and manage the possible cause(s) of treatment failure as suggested then switch to an appropriate regimen**.**

For clientss with low level viraemia, maintain the same ART regimen and repeat VL every 3months

7.12.1 Second-Line ART for Adults and Adolescents

During SUAC sessions, identify and address the modifiable cause(s) of treatment failure, treat and control all intercurrent opportunistic infections, and then switch to an appropriate ART regimen.

Before Switching from non NNRTI based Antiretroviral Regimens:

Ensure optimal adherence (stepped up adherence counselling sessions have been completed)

Take a thorough history of previous antiretroviral drug use to help determine the appropriate second-line regimens.

What to Switch To

Clients who were previously treated with other regimens other that the standars first lne regimens must be individually evaluated before switching to a seconf line regimen

The recommended second-line ART should consist of two nucleoside reverse transcriptase inhibitors (NRTIs) plus an Integrase strand transfer inhibitor (INSTI) i.e., Dolutegravir (DTG) or Protease inhibitor depending on previous ART history

For clients who have failed a DTG-based first-line regimen, HIV resistance testing should be done before regimen switch, consult snapthirdline@mohcoag.org for genotype consideration. Using DTG, in combination with an optimized NRTI backbone among people for whom a non-DTG-based first-line regimen has failed, is generally safer and more effective than using a protease inhibitor (PI)– based second-line regimen.

Alternative second-line regimens should be used in case of contraindications to the preferred regimen.

For PI-based second-line regimens, two NRTIs) and a ritonavir-boosted protease inhibitor preferably Atazanavir (ATV/r) is recommended. Atazanavir/ritonavir (ATV/r) is preferred to Lopinavir/ritonavir (LPV/r) due to the reduced pill burden (1 tablet once a day), better tolerability and reduced cost.
ATV/r can be prescribed to clients who have the following characteristics:
Weigh more than 40kg

- Experiencing adherence issues from twice-daily dosing
- Experiencing side effects from LPV/r

Darunavir/ritonavir (DRV/r) can be used as an alternative PI for the ATV/r and LPV/r when available (see below).
In the rare instances in which a client cannot take DTG because of failure or intolerance, a regimen with DRV/r is preferred. For such clients, consult *snapthirdline@mohcoag.org* before prescribing.

Second-Line ART and TB Infection

See TB/HIV chapter 6, Table 6.15

Table 7.11 Recommended Sequence of Second-line NRTI Options

Current 1st line Regimen	Preferred 2nd Line Regimen	Alternative 2nd Line Regimen	Special Considerations
AZT + 3TC + EFV	TDF + 3TC + DTG	TDF+3TC+boosted PI**	Recycle the TDF/3TC backbone in chronic hepatitis B patients
ABC + 3TC + EFV	AZT + 3TC + DTG	AZT+3TC+boosted PI** TDF + 3TC + DTG***	
TDF +3TC + EFV	TDF +3TC + DTG*	AZT + 3TC + DTG AZT+3TC+boosted PI**	
TDF + 3TC + DTG ABC + 3TC + DTG AZT + 3TC + DTG	HIV resistance testing should be done for all clients failing on a DTG-based ART regimen. Only switch to 2nd line if the resistance test shows DTG resistance and the 2nd line regimen should be a **boosted PI + 2 NRTIs determined by the genotype results**		

**Studies have shown that for patients failing a TDF/3TC + NNRTI first-line regimen, recycling the TDF/3TC backbone in 2nd line was superior in viral suppression to switching to AZT/3TC*
*** For clients weighing ≥ 40kg, ATV/r is preferred over LPV/r as it can be taken once daily.*
****There is a 10% risk of TDF resistance in clients failing ABC, only use this option if twice-daily dosing will be a barrier to treatment success*

Clients who cannot tolerate ATV/r or LPV/r in 2nd line may be considered for DRV/r after reviewing genotype results. As DRV/r doses depend on previous PI exposure and resistance mutation pattern, use of DRV/r as part of a second-line regimen has to be approved by the HIVDR clinical expert committee. *snapthirdline@mohcoag.org*

Table 7.12 Options for Managing TB Clients

TB Client on Treatment	Action
LPV/r	Consult an experienced clinician or HIVDR expert committee (*snapthirdline@mohcoag.org*) before choosing the options below. • Super boost LPV/r to 400mg/400 mg by adding 300mg ritonavir to normal dose LPV/r and continue until 2 weeks after completion of TB treatment • Double-dose of LPV/r to 800mg/200mg twice daily and continue until 2 weeks after completion of TB treatment. Double dosing is only for clients >10 years of age. *See Annex 111.16* for dose adjustments in paeds • If evidence of VL suppression in the past 3-6months, switch to a DTG-based regimen and continue twice daily DTG until 2 weeks after completion of TB treatment
ATV/r and DRV/r	• Do not combine with RIF • Change to twice daily DTG or to LPV/r with adjustments as stated above • Use Bedaquiline with caution as there is a risk of QT prolongation
DTG	• Increase DTG dosing to 50mg twice daily until 2 weeks after completion of TB treatment. • Rifampicin is associated with hyperglycaemia so do monthly RBS

For all clients, maintain the same NRTI backbone provided there is no dose adjustment necessary, and clients are virally suppressed

Second-Line ART and Hepatitis B Virus Coinfection

Clients coinfected with HIV and HBV whose first-line regimen contained TDF + 3TC should be continued on TDF + 3TC in the second-line regimen for the anti-HBV activity to reduce the risk of hepatic flares.

Recommended Second-Line ART for Hepatitis B Virus Infection

If the failing regimen was TDF based, maintain TDF+3TC and add AZT to the NRTI backbone
If the failing regimen was AZT based, switch to TDF+3TC in the NRTI backbone

7.12.2 Third-Line ART for Adults and Adolescents

Treatment-Experienced Clients

Treatment-experienced clients are defined as those with loss or lack of virological response to at least 2 ARV regimens, including at least one member of each of the three drug classes (NRTI, NNRTI and PIs).

The goal of treatment for these clients is to re-establish virological suppression to undetectable. A treatment-experienced client should be assessed and managed by a multidisciplinary team. Sequencing of treatment in treatment-experienced clients and use of a third-line regimen should be supported by HIV drug resistance testing (genotype test) and in collaboration with the Eswatini National AIDS Program's third-line committee (snapthirdline@mohcoag.org)

- Ensure adequate adherence during SUAC before collecting sample for genotype. DOTS is advised.
- Order genotypic resistance testing while the client is still taking the failing second-line regimen OR no later than 4 weeks after discontinuing the failing regimen.
- Assess immune status (CD4 count) and need for: AHD package and prophylactic therapy.

- Review and document a full medical, laboratory and ARV history. A full physical examination is advisable to exclude any opportunistic infections or comorbidities.
- Ensure completion of SUAC.
- Order appropriate laboratory tests (including haemoglobin, ALT, CD4, bilirubin, fasting blood sugar, lipid profile, HbsAg, Creatinine).

Third-Line Regimens for Adults and Adolescents

Third-line regimens should include new drugs with minimal risk of cross-resistance to previously used regimens, such as integrase inhibitors, second-generation NNRTIs, and protease inhibitors. However, clients on a failing second-line regimen with no new ARV options should continue with a tolerated regimen.

Recommended third-line regimen:

Recommended third-line ART regimen for adults & adolescents (10-19 years) should be guided by genotype results and include the following combination

Potential Third-Line Regimens*
DRV/r + DTG ± one or two NRTIs
DRV/r + two NRTIs ± NNRTI**

*Construction of third-line ART regimens should be guided by HIV genotyping results; consult the HIVDR expert clinical committee on snapthirdline@mohcoag.org for guidance.

***Caution: high-level NNRTI resistance in Eswatini limits the use of Etravirine (ETR) 200 mg 12 hourly.*

DRV/r should not be used in children less than 3years of age

Who should receive Genotype testing?

HIV drug resistance testing (genotype) should be requested for all clients who after adequate adherence support have two consecutive viral load results above 1000copies/ml:

- while on drug-sensitive TB treatment during second-line treatment
- while taking a 2nd line regimen
- while taking a DTG-based ART first- or second-line regimen for less than two years

Paediatric clients <5yrs old failing on a PI-based (1st or 2nd line regimen) should be referred to the HIVDR committee for genotype without delay.

Initiate third-line regimen treatment only after reviewing results of resistance tests with the third-line committee and after satisfactory SUAC.

- Initiate third-line regimen treatment only after reviewing results of resistance tests with the third-line committee and after satisfactory SUAC.
- HIV drug resistance testing (genotyping) is accessible through the HIV drug resistance expert committee (third-line committee) at Eswatini National AIDS Program (SNAP), which reviews requests for genotyping. Email snapthirdline@mohcoag.org for guidance
- The National Molecular Reference Laboratory (NMRL) provides the necessary logistics to facilitate outsourced sample testing while the program facilitates requisitions from health facilities for such services.
- The turnaround time for lab results is 20days, call the lab focal person on +268 2404 2190 to make a follow-up. Always share results with the HIVDR committee on the email above even when no evidence of resistance mutations has been found

Monitoring of third-line clients

- Clients with pre-existing liver disease (chronic hepatitis, cirrhosis, elevated liver enzymes) should be monitored for elevated transaminases
- Follow-up VL, fasting blood sugar, cholesterol, and triglycerides at 3 and 6 months after starting 3rd line then at 6 monthly intervals for all third-line clients.
- Clinical visits may be spaced to 3 monthly intervals even after VL has re-suppressed

7.13 HIVDR surveillance

The country will for specified periods, collect data on early warning indicators for HIVDR.

To routinely conduct HIV drug resistance surveys, the country will adopt the use of remnant viral load samples (plasma or DBS) for HIVDR survey activities.

Remnant blood samples of all clients with high viral load may be stored and be used for surveillance purposes to guide program and policy changes.

7.14 Promoting Long-Term Care with PLHIV on ART

To achieve viral suppression for as long as possible, clients should be supported throughout care by promoting optimal adherence and reducing the client's economic burden associated with accessing ART long term. DSD and ongoing adherence and psychosocial support are key.

7.15 Adherence to care and treatment

The standard clinical definition of adherence has been taking >95% but < 105% of medications the right way, at the right time and includes: following a care plan, attending scheduled clinic appointments, picking up medicines on time and getting scheduled laboratory tests.

Pills remaining from last visit + pills dispensed last visit= pills given

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

Adherence is facilitated by a shared decision-making process between the client and the health care provider. Clients should be involved in treatment and should actively participate in establishing treatment goals (including support groups, keeping appointments, maintaining a healthy lifestyle, etc.)

Definition of appointment adherence

Adherence to appointments is an important measurement of the client's involvement and understanding of treatment.

Every facility should have a teen club, support groups, and caregiver focus groups to promote adherence and psychosocial support among peers.

Importance of adherence.

Adherence is a concern to clinicians, health care systems and other stakeholders because of evidence that non-adherence is associated with adverse outcomes and higher costs of care.

Clients who interrupt treatment are at increased risk of treatment failure; therefore, patient follow up should begin on the same day of not honouring an appointment to allow clients to return to care before being classified as having interrupted treatment.

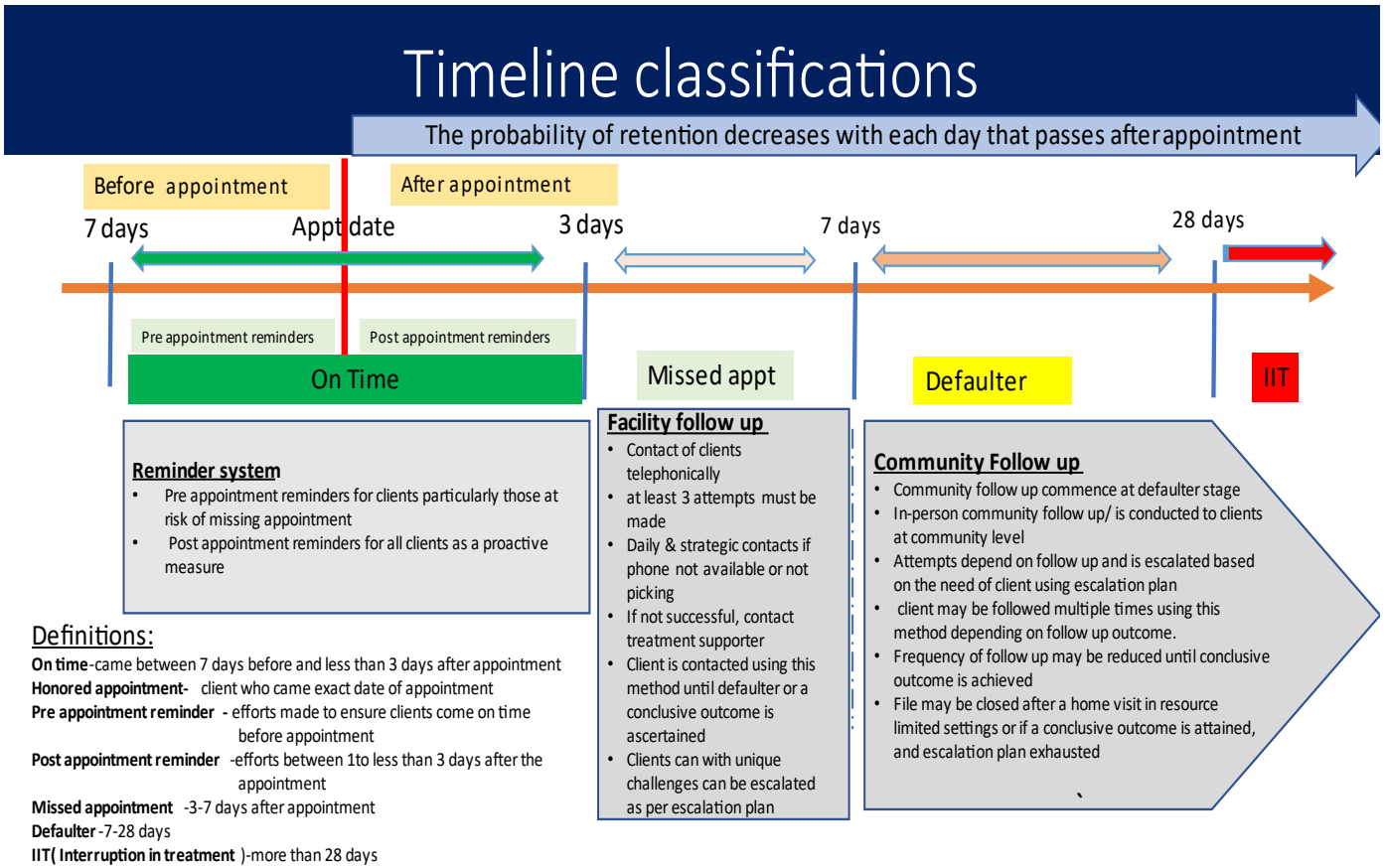


Figure 7.6 Defaulter tracing

For clients returning to care (RTT) after being classified as having interrupted treatment(IIT), document reasons for interrupting treatment as outlined in the *eLCM SOP.*

8 PREVENTION OF MOTHER TO CHILD TRANSMISSION OF HIV

DBS Hotline: 7687-9925

PMTCT Strategy

Strategically, the Prevention of mother-to-child transmission (PMTCT) is implemented through a 4-pronged approach as shown in *Table 8.1*. Details of services under each prong are outlined in the subsequent sections.

Table 8.1 PMTCT Prongs

Prong	Description	Target Population	Section
Prong 1	Primary prevention of HIV infection among women of childbearing age	Non-pregnant HIV-negative women of childbearing age including adolescents and their partners	*Section 8.1*
Prong 2	Prevention of unintended pregnancies among HIV-positive women and access to other Sexual and Reproductive Health (SRH) services	Non-pregnant HIV-positive women of childbearing age including adolescents and their partners	*Section 0*
Prong 3	PMTCT among HIV-positive pregnant and lactating women	Pregnant and lactating women	*Section 8.3*
Prong 4	Care, support and treatment for HIV-positive women and their families	HIV-infected women, their children, partners and families	*Section 8.4, Section 8.7*

8.1 Primary Prevention of HIV Infection among Women of Childbearing Age

Table 8.2 summarizes the HIV primary prevention services offered to non-pregnant women within maternal, new-born and child health (MNCH) settings and their partners.

Table 8.2 HIV Prevention Services for Non-Pregnant Women

Service	Description
HIV testing services (HTS)	• Provide routine HTS services for all women of childbearing age visiting the health facility and their male partners, and referral for prevention, care and treatment services. • Women currently in an active sexual relationship should ideally be tested as a couple where feasible. • Distribute HIVST kits for partners of women of childbearing age (15-49 years) • See Chapter 3 on HTS for more details
Provide sexually transmitted infection (STI) screening and management	• Provide STI screening for women and their partners and ensure all STIs detected are managed appropriately. • See National STI guidelines for more details.

Table 8.2 HIV Prevention Services for Non-Pregnant Women (continued from the previous page)

Service	Description
HIV prevention counselling and safer sex	• Provide information and counselling on HIV prevention and how to reduce the risk of sexual HIV transmission. • All clients should be offered PrEP at each visit. Inform clients of the safety and efficacy of PrEP • Promote correct and consistent use of female and male condoms for the woman and her partner, emphasizing the benefits of dual protection: ○ Give reasons and benefits for using condoms. ○ Dispel myths and misconceptions about condoms. ○ Demonstrate condom use and teach condom negotiation skills. ○ Promote/teach mutual assistance in using condoms and ensure both partners' involvement. ○ Encourage joint decision-making with both partners on visits to the health facility for care, condom usage, etc. *See Chapter 2* on Prevention for more details.
Provide gender-based violence (GBV) prevention and impact mitigation services	• Provide information to empower women on gender equality and equity—sexual and reproductive health rights. • Provide counselling, HTS, emergency contraception, HIV/STI post-exposure prophylaxis and psychosocial support, and screen for and manage Hepatitis B from survivors of gender-based violence. • Provide information on services and organizations specialising in gender-based violence. • Refer people who have experienced or are experiencing gender-based violence to appropriate services, including legal and psychological support services (e.g., Eswatini Action Group Against Abuse (SWAGAA) centres or One-Stop-Centres).
Provide men's minimum health care package to partners of the women visiting the health facility	• Emphasize the partner's role in HIV prevention (for himself, partner and child); including discussing gender-based violence, cultural norms and practices; and the importance of partner support. • Educate and counsel the client on men's health issues or refer the male client for sexual and reproductive health services • Advise on a healthy lifestyle—diet and exercise, alcohol, and substance use. • Provide prevention measures: • Offer HTS – couple testing and appropriate linkage to prevention or care and treatment services. ○ Screen and treat STIs, TB, NCDs, and other conditions as needed. ○ Demonstrate correct use of male and female condoms. Promote voluntary medical male circumcision (VMMC) for HIV-negative men and refer and link men to VMMC services. Emphasize dual protection: VMMC and correct and consistent condom use ○ Advise on available services for early infant medical circumcision (EIMC) for male new-borns and male siblings.

8.2 Prevention of Unintended Pregnancies in Women Living with HIV

Table 8.3 describes services provided to HIV-positive non-pregnant women to prevent unintended pregnancies. *See also National Family Planning Guidelines.*

Table 8.3 Services to Prevent Unintended Pregnancies

Service	Description
Provide information and services to support family planning and reproductive rights	• All PLHIV should be offered family planning services according to the National Guidelines on Integration of Family Planning in HIV Services. • Support women and couples to identify reproductive goals. • Counsel on the safety of and eligibility of the full range of contraceptives and family planning methods, including emergency contraception and permanent methods, in the context of HIV. • Provide adolescent-friendly family planning counselling. Adhere to confidentiality and encourage independent decision-making of adolescents. • Family Planning (FP) services should be integrated with all other HIV services (e.g., ART initiation and refill) • Encourage the use of long-term reversible contraceptive methods and dispel myths about side effects and return to fertility • All forms of family planning are appropriate for use with DTG in women and adolescents • Diagnose pregnancy early and inquire/document the last menstrual period in all women of childbearing age. • All HIV positive women should be on ART

8.2.1 Advice for Couples Considering Having a Child

The final decision to conceive depends on the couple. HCWs should provide accurate and unbiased information necessary to support their decision-making

Table 8.4 Advice for Couples Who are Considering Having a Child

Both are positive	• Provide adequate counselling around risks reduction, reinfection and risks of mother-to-child transmission of HIV • Before making recommendations, assess the couple clinically, immunologically and virologically. • If a woman is not on ART, she should be initiated on ART as soon as possible. • If a man is not on ART, he should be initiated on ART as soon as possible. • If the couple is already on ART, ensure undetectable viral load. • If the viral load is undetectable, advise on fertility days and timed ovulatory intercourse (condom use at all other times). • Prevent/treat STIs.

Table 8.4 Advice for Couples Who are Considering Having a Child (continued from the previous page)

Serodifferent couples	• Provide adequate counselling around risks of infection of the negative partner and risks of mother-to-child transmission. • Provide ART to the HIV-positive partner as soon as possible, if not already on ART. • If the positive partner is already on ART, ensure they have an undetectable viral load. • If the viral load is undetectable, advise on fertility days and timed ovulatory intercourse (use of condoms at all other times). • Advise the couple to wait until viral load is undetectable before trying to conceive on fertility days • Consider pre-exposure prophylaxis (PrEP) for the HIV-negative partner.

8.3 Antenatal Care for Pregnant Women to Prevent Mother to Child Transmission

Services for Pregnant Women in Antenatal Care

The first antenatal care (ANC) visit should occur as soon as the woman realizes she is pregnant, preferably within the first trimester (0-12 weeks of gestation).

Retesting schedule for Pregnant Women in Antenatal Care

Table 8.5 Retesting schedule for Pregnant Women in Antenatal Care

HIV-negative Women	• As part of efforts to achieve the elimination of MTCT, all HIV-negative pregnant and lactating women should be offered PrEP using the OPT OUT approach. If a woman deems herself low risk after complete discussion regarding PrEP benefits, clearly document refusal and offer PrEP again at the next visit. • Pregnant and lactating women on PrEP should be retested one month after initiation. PrEP refills and testing will align with the ANC or CWF/ MBP visits. • All HIV-negative pregnant women not on PrEP should be re-tested every 2 months (aligned with the ANC scheduled visits) with the most optimal time for retesting being during the third trimester visit (34 weeks gestation). • All HIV-negative lactating women should be re-tested at 6 weeks, 14 weeks, 6 months, 9 months, 12 months, 15 months and 18 months aligned with the MBP follow-up schedule. • For pregnant and lactating women with inconclusive results after HTS; conduct Nucleic Acid Amplification Tests (NAAT) – DNA PCR, and initiate ART immediately while waiting for NAAT results

Summary of Key Services for Pregnant Women in Antenatal Care

Table 8.6 Key Services for Pregnant Women in Antenatal Care

Service	Description
Comprehensive history-taking and examination 	• Take medical history including obstetric, family and psychosocial history. • IPV increases during pregnancy, in the event of reported or suspected cases of IPV, refer to the National GBV Guidelines for management. • Mental health screening
Tuberculosis screening 	• Screen all women regardless of HIV status for TB using the National TB/Covid-19 Screening Tool. • Refer or provide diagnostic and follow-up services according to National TB Management Guidelines. • All pregnant and lactating women are at high risk for TB and are eligible for TPT.
Nutritional assessment, counselling, and support	• Assessment: Assess nutritional status using mid-upper arm circumference. • Counselling: Counsel on a proper diet based on locally available foods. • Nutritional support and supplements: Provide ferrous sulphate, folic acid and multivitamins. For women with a mid-upper arm circumference of less than 23cm, enrol on or refer to food by prescription support.
HTS pregnant woman and her partner 	*See Chapter 3* for HTS Guidance including index testing and partner notification guidance. • Re-test all HIV-negative pregnant women every 2 months. The re-testing dates should be aligned to the woman's scheduled contact visits. Offer PrEP each visit. • Pregnant women declining HTS should continue receiving ongoing counselling at every subsequent ANC visit on the importance of knowing their status.
Laboratory investigations and treatment of identified conditions	• *See Chapter 5, Section 5.2* for routine tests. • Routine laboratory tests: Haemoglobin, blood group and Rh factor, urinalysis, HBsAg, malaria RDT and syphilis, and provide treatment for any anomaly according to national guidelines • Additional tests for HIV-infected pregnant women: CD4 cell count, liver function tests, and renal function tests (and calculate creatinine clearance); viral load for women on ART according to *Figure 8.1* ART initiation should not be delayed while awaiting results for these tests. • Any detectable viral load in pregnant women should be treated with urgency
Immunization	• Give tetanus toxoid and other immunizations according to National EPI Guidelines. • COVID-19 vaccination is of particular importance given the increased morbidity/mortality from SARS-Cov2 infection during pregnancy.

Table 8.6 Key Services for Pregnant Women in Antenatal Care (continued from the previous page)

Service	Description
Counselling and education	• Provide HTS for HIV-negative women as outlined in *Section 8.1* • Educate appropriately on: ○ Family Planning- emphasise dual protection ○ Pregnancy and Delivery (including danger signs) ○ Birth preparedness planning ○ Infant and young child feeding, *see sub-section 8.12* ○ Early Infant Male Circumcision, *see Chapter 2, section 2.4.* ○ Harmful habits * • Emphasize adherence to PrEP for the HIV-negative and ART for the HIV-positive. Emphasize that PrEP is safe for the baby throughout pregnancy and breastfeeding. • Provide psychosocial support, including partner and family support.
Refer high-risk pregnancies	Refer women with high-risk pregnancies to higher-level institutions. These include pregnancy-induced hypertension, diabetes, previous caesarean sections or pregnancy complications, multiple pregnancies, multiple miscarriages, heart disease, or any other pre-existing medical condition that should be referred. Women with viremia on 2nd or 3rd line ART are considered high risk

8.3.1 PMTCT Package for HIV-Positive Women in Antenatal Care

Table 8.7 Key Considerations for HIV-positive Women in Antenatal Care

Service	Description
ALL HIV-Positive Women	• All pregnant women testing HIV-positive should be re-tested for verification before initiation of ART. • All newly diagnosed HIV-positive pregnant women not yet on ART, regardless of gestational age, should be initiated on ART at the first ANC visit while maintaining ongoing counselling. • ART services for pregnant women should be provided within ANC settings. Virally suppressed mothers enrolled in a DSD model may continue to do so provided that all VLs are done on time (First ANC, 2nd trimester and 32-36 weeks). • Viral load testing should be done for all HIV-positive pregnant women already on ART at the first ANC visit, then follow the viral load schedule for subsequent tests • All HIV-positive pregnant and lactating women should be on ART with an undetectable viral load. A detectable viral load should be treated with urgency *See Table 8.9* • Initiate Co-trimoxazole 960 mg as outlined in section (*Chapter 5, Section 5.4*), TPT, and Vitamin B6 25mg PO daily for women who are eligible and not already taking it. *See Chapter 6, Section 6.1.5.* • Give enhanced infant prophylaxis (eIP): NVP (25ml bottle) and AZT(100ml bottle) with a syringe and provide instructions for the mother to give the baby 1.5 mL of NVP daily and 1.5 mL of AZT twice a day. Label bottles clearly to avoid confusion. AZT is given for 6 weeks post-partum. NVP is given a minimum of 14 weeks and/or until the mother is undetectable. Refer to *Table 8.10* for dosing

Table 8.7 Key Considerations for HIV-positive Women in Antenatal Care (continued from the previous page)

Service	Description
Newly positive OR known positive not on ART	• First-line ART regimen for pregnant women is TDF + 3TC + DTG. • Initiate ART as soon as possible at any gestational age, preferably on the same day and in the ANC clinic. CD4 Count should be done at initiation to identify AHD, however ART initiation should not be postponed in the absence of a CD4 count result • Ensure the mother understands the significance of ART adherence once initiated. If she adheres well to ART, reassure her that her baby will be HIV-free. • Schedule a follow-up visit for the woman in two weeks to review baseline tests and make any necessary ART changes if needed Monitor Viral load 3 months after initiation as per the VL schedule. *See Figure 8.1*

Already on ART	• Conduct viral load (VL) testing on the first ANC contact, regardless of prior VL testing dates and the subsequent VL test must be done at 34 weeks gestation. See Figure 8.1 below
	• If there is no evidence of treatment failure (VL <50copies/ml) continue the current ART regimen.
	• If VL is detectable (>50 copies/ml), initiate SUAC and refer to doctor, mother facility and/or Baylor
	• Any HIV positive pregnant woman with a detectable viral load at contact requires URGENT intervention:
	  ○ If VL is detectable (>50copies/ml) and on a DTG-based 1st line regimen, ART should be switched to a DTG-based 2nd line regimen with concurrent SUAC started on the same day. *See Table 7.11*
	  ○ If VL is detectable on a **DTG-based** first line should have expedited SUAC and follow-up VL in 6-8 weeks. **Do not wait 3 months.**
	  ○ Suspected 2nd line failures (DTG or PI-based) should have a genotype sent the same day and then be placed on a 3rd line holding regimen while awaiting further guidance from the HIVDR committee: Consult snapthirdline@mohcoag.org or Baylor for regimen selection and dosing

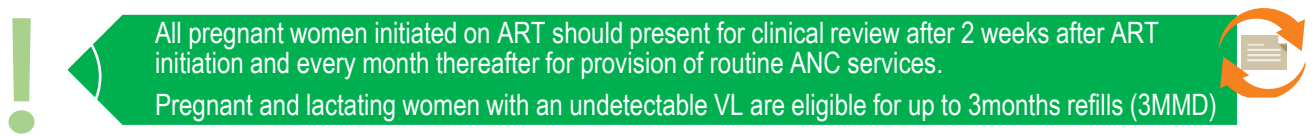
Not ready for ART	• Enrol into eLCM • Assure the patient's understanding and willingness to provide eIP. • Counsel women on the benefits of early initiation on ART for their health, for the child and partner(s). • Address any fears and/or barriers for the woman not ready to initiate ART, including partner support. • Follow-up in 2 weeks and initiate ART if she is ready. • If she is still not ready for ART, continue counselling at every visit. Discuss options for supplementary feeding of the infant. • Link client with Community Mentor Mother adolescent supporters and all local resources for additional counselling and support • Follow up with the woman in 2 weeks and initiate ART if she is ready. • If the woman is still not ready for ART, continue counselling at every visit. Assure her understanding and willingness to provide eIP.

8.4 Treatment for HIV-Positive Pregnant and Lactating Women

8.4.1 Recommended First-Line ART for HIV-Positive Pregnant and Lactating Women

The recommended first-line ART regimen for pregnant and breastfeeding women is the same as in non-pregnant/breastfeeding women;

Once-daily, fixed-dose combination of: TDF (tenofovir 300 mg) + 3TC (lamivudine 300 mg) + DTG (dolutegravir 50 mg)



8.4.2 Special considerations for ART Regimens in Pregnant and Lactating Women

TB/HIV coinfection: Refer to Chapter 6, Table 6.15 for further detail.

Renal insufficiency: Refer to *Section 7.7.4*

Moderate to severe anaemia: TDF + 3TC + DTG, treat for anaemia according to standard treatment guidelines

8.4.3 Follow-Up and Monitoring for HIV-Positive Pregnant Women

***HIV care*:** In addition to the routine ANC services, ensure HIV-positive pregnant women receive adherence counselling (and pill counting), psychosocial support, side-effect monitoring, clinical assessment, and laboratory assessment. ANC services should be linked with ART care appointments for the mother. PNC services should be linked to child welfare visits and ART visits as per the mother-baby pair schedule.

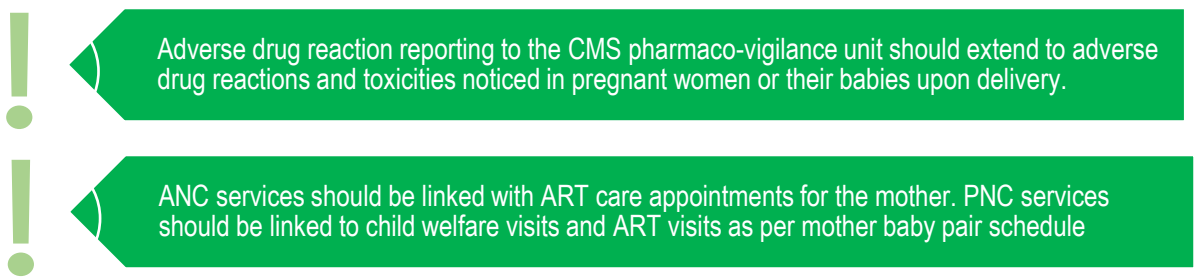


Table 8.8 Follow-up and Monitoring of HIV-positive Pregnant Women Summary

Time	Services to be provided during ANC	
	Pregnant women already on ART at entry into ANC	**Pregnant women newly identified as HIV-positive or known HIV-positive, but not yet on ART at entry in ANC**
First ANC Visit 	• Routine ANC including laboratory investigations • Check and reinforce adherence to ART • Viral load (VL) testing at 1st ANC irrespective of when prior VL was done • Provide enhanced infant prophylaxis (eIP) package (AZT/NVP syrups) • TB Screening: including Xpert TB-RIF Ultra and TB-LAM if symptomatic • Syphilis and viral hepatitis screening	• Routine ANC including laboratory investigations • Baseline tests (CD4, AST/ALT, syphilis screening, hepatitis B and C, renal function tests and calculate creatinine clearance) • Initiate ART, preferably on the same day if the woman is ready • Provide eIP package (AZT/NVP syrups) • TB Screening: including Xpert TB-RIF Ultra and TB-LAM if symptomatic
2 weeks after the first ANC	Not applicable	• Review baseline results and manage any abnormalities as needed • Check for side effects and manage accordingly • Check and reinforce adherence to ART
Each monthly visit before delivery	• Routine ANC • Check and reinforce adherence to ART • Check for any side effects and manage accordingly	
34 weeks gestation at ANC 	• Conduct VL testing and manage appropriately if detectable • Routine ANC • Check and reinforce adherence to ART • Check for any side effects and manage accordingly	

Table 8.8 Follow-up and Monitoring of HIV-positive Lactating Women Summary(continued from the previous page)

Time	Services to be provided during PNC	
	Lactating women already on ART	**Lactating women newly identified as HIV-positive or known HIV-positive, but not yet on ART at entry in PNC**
6 weeks after delivery	• VL testing is compulsory for all women on ART irrespective of when prior VL was done and manage appropriately if detectable. *Refer to Figure 8.1* • Offer mother family planning services	• For women starting ART during PNC the first viral load should be done 3 months after ART initiation** and the subsequent tests should be done every 6 months until the cessation of breastfeeding and aligned with the MBP schedule. *Refer to Figure 8.1* • Offer mother family planning services • For women starting ART during PNC, the first viral load should be done 3months after ART initiation and the subsequent tests should be done every 6months until the cessation of breastfeeding and aligned with the MBP schedule
Note: The 6-week VL is essential to decide EIP duration and to intervene early in women with a DVL while breastfeeding. **Therefore, ALL women on ART should have a VL at 6 weeks post-partum. The only women excluded from this are those starting ART during the 6 weeks post-partum visit.		

CD4 and VL monitoring in pregnant and breastfeeding women

Ensure that

- ALL pregnant have a Viral Load in the 3rd trimester preferably by 34weeks of gestation
- ALL lactating women have a VL by 6 weeks post-partum or every 6 months thereafter.

Ensure that all pregnant and lactating women who are on ART have a viral load test done during their first visit . All viral loads should be marked urgent and actively traced in the facility.

8.4.4 Viral load and CD4 testing schedule in pregnant and breastfeeding women

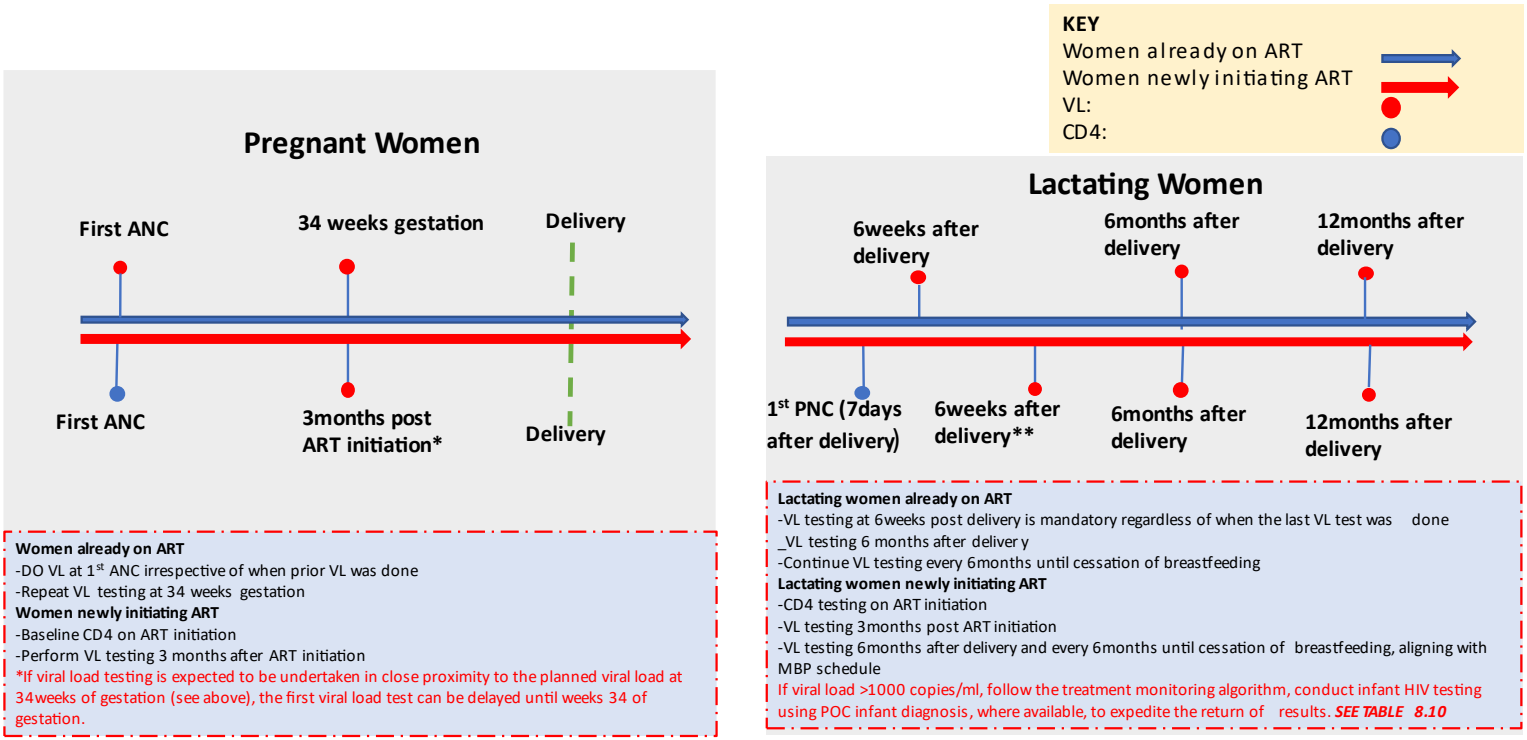


Figure 8.1 Timing of viral load and CD4 monitoring for pregnant and lactating women

Where available, pregnant and lactating women should be prioritised for point-of-care viral load testing

A detectable viral load at any point in time should be managed accordingly. *See Figure 7.3 and 7.4*

A detectable viral load in pregnant and lactating women should be treated as an emergency due to increased risk of mother-to-child-transmission. Healthcare workers are urged to utilize expert consultation from Mother Facility doctor and regional implementing partner focal doctors or the Baylor hotline in addition to the guidance below

Table 8.9 Action steps for management of a detectable viral load in pregnant and lactating women

Visit	Action steps for management
Immediately upon return of viral load result	Call the client and mentor the mother. Consider mentor mother DOT. If unable to reach the client, assure that outreach is done urgently. If non-DTG-based 1st line ART, call to change ART same day. If DTG-based 1st line ART, conduct telephonic SUAC if the client is unable to come to the clinic within 7 days. If DTG or PI-based 2nd line: Request mother to come for urgent genotype.
First visit after a detectable viral load	Begin SUAC today, document barriers to adherence and set goals. Ensure the mother understands the urgent need for an undetectable viral load. If the infant is breastfeeding and not on EIP. Restart NVP until the mother is undetectable. If the infant is breastfeeding and on EIP: Continue NVP beyond 14 weeks until the mother is undetectable. Call the Mother facility doctor or regional implementing partner Focal doctor or Baylor TB/HIV Hotline today while the client is present for specific guidance and to assure follow-up. Engage mentor mother today and arrange a home visit in 2 weeks. If the mentor mother is not available, call Baylor Hotline. Set an appointment for 4 weeks.
Second visit – 4 weeks later	1. Reassess and document barriers and complete SUAC 2. 2. **Collect VL and mark it as urgent. Ensure facility High VL focal person is aware of pending laboratory results**. 3. Ensure mentor mother has been involved. 4. Set an appointment for 4 weeks (or 2 weeks if nearing EDD).
Immediately upon return of viral load result	1. Call the client and mentor the mother. 2. If now undetectable, congratulate the mother and keep the previous appointment date. 3. If still detectable, call the mother facility doctor or regional Implementing Partner focal doctor for guidance and arrange for the client to visit the facility as soon as possible. 4. Continue NVP in the breastfeeding infant and plan for a repeat maternal VL in 1/12.

8.5 Services for Women and Infants during Labour, Delivery and Immediately After Delivery

Initiate ART in maternity for all women who are HIV-positive and not on ART regardless of WHO staging or CD4.
All HIV-exposed infants should be tested for HIV at birth or within 3 days of delivery. Assign a focal person to assure that all women receive the results within 3 days of testing. Be alert to infants born on weekends and holidays or who left the hospital early without the result.

All HIV-exposed infants testing HIV-negative at birth should be provided with enhanced infant prophylaxis (eIP):
- » Dispense AZT and NVP from birth for 6 weeks in maternity (if not given during ANC).
- » After stopping AZT at 6 weeks, Continue NVP until at least 14 weeks. This should be dispensed during the 6-week postpartum care visit.
- » Educate appropriately on family planning with emphasize on dual protection.

All HIV exposed infants testing HIV positive at birth should be initiated on ART (*Refer to table 6.10 and chapter 7* for appropriate regimen)

Table 8.10 Infant Dosing Regimens of NVP and AZT

Infant Weight	Dosing of NVP	Dosing of AZT
Birth to 6 weeks		
Birth weight 2000–2499g	10 mg once daily (1 mL of syrup once daily)	10 mg twice daily (1 mL of syrup twice daily)
Birth weight ≥ 2500g	15 mg once daily (1.5 mL of syrup once daily)	15 mg twice daily (1.5 mL of syrup twice daily)
Birth weight < 2000g	Call Facility Doctor or Baylor Hotline	
> 6 weeks to 6 months		
Any weight	20 mg once daily (2 mL of syrup once daily) or (½ a 50 mg tablet once daily)	STOP
6-9 months		
Any weight	3mL once daily	Not given
9-24 months		
Any weight	5mL once daily	Not given

8.6 The recommended regimen for new-born initiating ART

Refer to Chapter 9, Table 9.4, Table 9.5 and Table 9.6

Caesarean Section

A routine caesarean section is not recommended for PMTCT purposes. Newly diagnosed HIV-positive women must be initiated on ART at least 2 hours before an elective caesarean section for obstetric indications. The woman should continue her ART medication post-operatively (even during the "nil per os" period)

8.7 Services for Lactating Women and their Children

Retesting schedule for Lactating Women in Postnatal Care

Table 8.11 Retesting schedule for Lactating Women in Postnatal Care

HIV-negative Women	• As part of efforts to achieve the elimination of mother-to-child transmission (eMTCT) of HIV and syphilis, all HIV-negative lactating women should be re-tested at 6 weeks, 14 weeks, 6 months, 9 months, 12 months, 15 months and 18 months aligned with the MBP schedule. • Emphasize primary prevention of HIV (*see Table 8.2*) which includes the provision of PrEP using the opt-out approach • HIV-negative lactating women on PrEP should be retested based on the PrEP retesting schedule which can be aligned with planned child welfare/MBP schedules.

Follow-Up of Mother-Baby Pairs After Delivery

Mothers and their babies should be seen as a pair as much as possible from delivery. The mother-baby pair visits are aligned to the child immunization schedules. Figure 6.2 shows the timeline for the schedules of lactating mothers and their babies during the postpartum period. Mothers and their children should receive the mother-baby pair package of services outlined in *Figure 8.2*. ART care appointments for the mother and their babies should also be linked to the mother-baby pair visit schedules.

	Post-natal Care Using the MBP Model								
	7-14 days	6 weeks	10 weeks	14 weeks	6 months	9 months	12 months	15 months	18 months
Mother ART refill and baby services	✓	✓ Stop AZT Check VL	✓	✓ Decide on NVP	✓ Check VL	✓ DNA PCR	✓ DNA PCR	✓	✓ Rapid test baby. Plan next test if breastfeeding

Figure 8.2 Mother and Baby Appointment Schedule during Postpartum Care

All lactating mothers who are HIV-negative should be re-tested every 2 months (aligned with the mother-baby postpartum care visits) until the end of breastfeeding.

8.8 Services for HIV Exposed Infants

8.9 HIV testing approach for infants and children

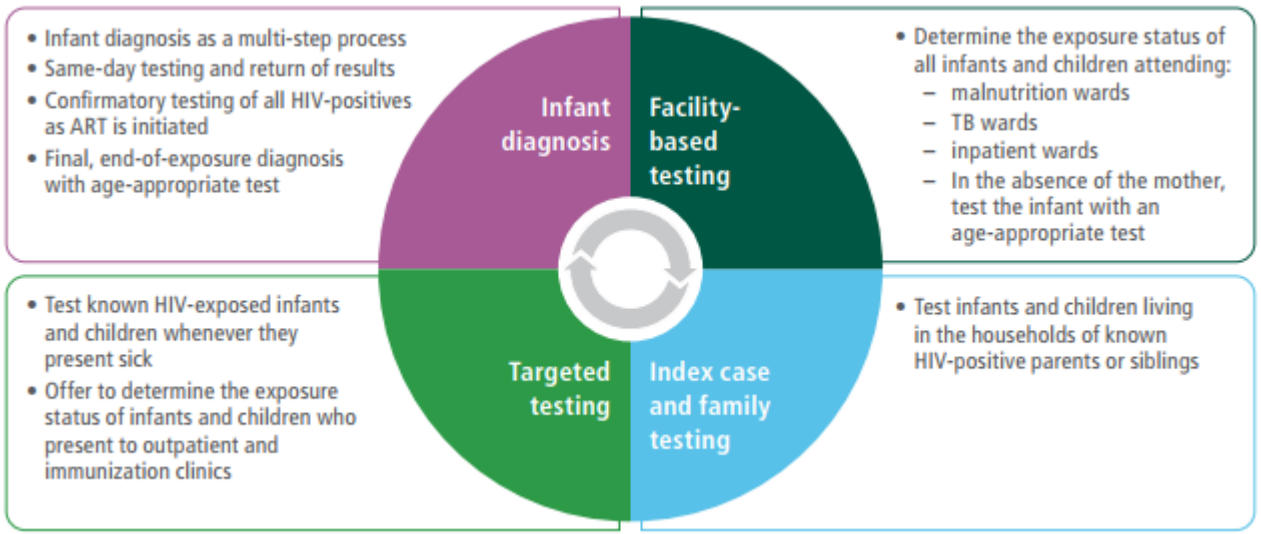


Figure 8.3 Comprehensive HIV testing approach for infants and children

A lactating woman that acutely seroconverts and/or is believed to have recent HIV infection is at very high risk of transmitting HIV to the infant. Please consult mother facility and/or Baylor for consideration of alternative EIP for the infant

8.10 Infant Diagnosis

All mothers should be tested to determine the HIV exposure of their infants.

Table 8.12 Infant Diagnostic Tests for Mothers of Varying HIV Statuses

Mother Status	Infant Diagnostic Tests
Mother Known HIV-Positive	• Nucleic acid tests-NAT (RNA and/or DNA PCR) for the child at birth (0-3days), 6-8 weeks, 9 months, and 12 months. The rapid test should be done at 18 months and if positive, should be confirmed with NAT before ART is initiated.
Mother HIV Status Unknown	• Conduct HIV rapid test for mother. • If the mother is positive conduct NAT (RNA and/or DNA PCR) for the child immediately, then follow the EID schedule if the child tests negative. If the child is less than 6 weeks, start AZT/NVP EIP. If the child is older than 6 weeks, start NVP until a minimum of 14 weeks and/or the mother is undetectable • If the mother is negative, the child is not HIV-exposed. Repeat HIV rapid test for mother every 8 weeks until the end of breastfeeding. Provide PrEP to the mother using the Opt-Out approach.
Mother is not Available	• NAT (RNA and/or DNA PCR) for the child immediately to ascertain HIV status, then follow the EID schedule if the child tests negative.

Table 8.13 Timing of HIV testing among exposed Infants and Young Children less than 18 months

Key	
	The child is HIV-negative and has never breastfed
	The child is HIV-negative and still breastfeeding
	Child is HIV-positive

Age of Infant	Eligible for Testing	Which Test to Use	Management
Birth (0-3 days)	HIV-exposed infants *(If exposure status is not known- test mother, if mother not available, test child using NAT)*	NAT (RNA and/or DNA PCR)	*If the child is negative and never breastfed:* inform mother that child is HIV-negative; start eIP; check and enforce ART adherence for mother; test child again at 6-8 weeks.
			If the child is negative and breastfeeding: start eIP; check and enforce ART adherence for mother; re-test child at 6-8 weeks or 2 months after stopping breastfeeding or if they present with symptoms suggestive of HIV (whichever comes first)
			If the child is HIV-positive: take blood for confirmatory NAT test; initiate child on ART (**do not await results of second NAT**; check and enforce ART adherence for mother and baby
6-8 weeks	HIV-exposed infants who tested HIV-negative at birth or missed birth testing. *(If exposure status is not known- test mother, if the mother is not available, test child using NAT)*	NAT (RNA and/or DNA PCR	*If the child is negative and never breastfed:* inform the mother that child is HIV-negative; continue eIP and stop at 14 weeks. Conduct an 18 months exit rapid test.
			If the child is negative and still breastfeeding: continue eIP; start Co-trimoxazole preventive therapy (CPT); check and enforce ART adherence for the mother; re-test the child at 9 months or 2 months after stopping breastfeeding or if they present with symptoms suggestive of HIV (whichever comes first)
			If the child is HIV-positive: stop eIP; take blood for confirmatory testing; initiate child on ART (do not await results of second NAT; start the child on Co-trimoxazole preventive therapy (CPT); check and enforce ART adherence for mother, continue breastfeeding. Breastfeeding is very important for an HIV-positive infant!

Table 8.13 Timing of HIV testing among exposed Infants and Young Children less than 18 months (continued from the previous page)

Age of Infant	Eligible for Testing	Which Test to Use	Management
9 months	HIV-exposed infants who tested HIV-negative at 6-8weeks or missed 6-8week test *(if exposure status is not known- test mother, if the mother is not available, test child using NAT)*	NAT (RNA and/or DNA PCR	*If the child is negative and never breastfed or stopped breastfeeding at least 2 months before the current test: inform the mother that child is HIV-negative; check and enforce ART adherence for the mother; Conduct an exit rapid test at 18 months*
			If the child is negative and stopped breastfeeding within 2 months of the current test: check and enforce ART adherence for the mother; re-test the child 2 months after cessation of breastfeeding (if positive- take blood for confirmatory testing and initiate ART; if negative- inform the mother that child is HIV-negative)
			If the child is negative and still breastfeeding: check and enforce ART adherence for mother; assure recent VL and re-test child at 12 months or 2 months after stopping breastfeeding or if they present with symptoms suggestive of HIV (whichever comes first)
			If the child is HIV-positive: take blood for confirmatory testing; initiate child on ART (do not await results of second NAT; start the child on CTX; check and enforce ART adherence for mother, Continue breastfeeding
12 months	HIV-exposed infants who tested HIV-negative at 9 months or missed test at 9 months *(If exposure status is not known- test mother, if the mother is not available, test child using NAT)*	NAT (RNA and/or DNA PCR)	Manage as above, however, if the child tests HIV-negative and is still breastfeeding re-testing should be done at 18 months or 2 months after stopping breastfeeding or if they present with symptoms suggestive of HIV (whichever comes first)
18 months	HIV-exposed infants who tested HIV-negative at 12 months or missed the 12 months test *(If exposure status not known- test mother, if mother not available, test child using Antibody test)*	HIV Antibody Test *(follow national algorithm)*	Manage as above, however; If child test tests HIV-positive, re-testing before ART initiation should be done using an antibody test instead of DNA PCR If the child tests HIV-negative and is still breastfeeding re-testing should be done 2 months after stopping breastfeeding or if they present with symptoms suggestive of HIV (whichever comes first)

Table 8.14 Package of care for HIV-Exposed Infants

Service	Description
Early infant diagnosis and treatment *Point-of-care testing is preferred due to its short turnaround time*	• *See* • *Table 8.*13 for HIV testing in infants and young children. • All HIV-exposed infants should be re-tested 2 months after cessation of breastfeeding. • Children presenting with symptoms suggestive of HIV infection should be tested at any point of contact. • Infants at high risk of infection (e.g., mothers with high viral load or seroconverted) can be tested outside of the routine time points to assure that they are diagnosed positive as quickly as possible. • Immediately initiate all HIV-positive infants for ART: » A second HIV test should be conducted for all infected children before ART initiation (do not wait for results of the second test before initiating ART). » *Refer to Chapter 9 section 9.5* for details on ART for children.
Growth and developmental assessment and immunization	• Follow the EPI assessment and immunisation schedule
Enhanced infant prophylaxis (eIP)	• *See Section 8.11*
Vigilance for HIV infection and re-testing	• Maintain a high level of suspicion for HIV infection. Watch for: • Growth failure (i.e., a child falling off the growth curve). • Poor development (i.e., delays in achieving or loss of developmental milestones). • Clinical signs or symptoms are suggestive of HIV infection. If HIV is suspected, the child should be re-tested, staged both clinically and immunologically, and presumptively enrolled in HIV care and treatment.
Cotrimoxazole preventive therapy (CPT)	• Give CPT to all HIV-exposed infants, starting from 6 weeks of age, to prevent PJP and other potentially fatal infections (*see Chapter 9, section 9.7*). • Continue treatment until HIV infection has been definitively ruled out AND the infant is no longer breastfeeding. • CPT is generally well tolerated by infants. However, parents should be counselled that if the child develops a severe rash (that includes sores in the mouth and red eyes), they should bring the child to the nearest health facility for evaluation. • In the rare circumstance that a child has a history of a severe (Grade IV) adverse reaction to CPT or other sulpha-containing drugs or known severe kidney disease (creatinine >3 times normal) and/or hepatic disease (liver function tests >5 normal), CPT should be avoided. Dapsone at a dose of 2 mg/kg once daily can be given as an alternative in these circumstances.

Table 8.14 Package of care for HIV-Exposed Infants (continued from the previous page)

Service	• Description
TB Preventive therapy for children with known TB contacts	• HIV-exposed infants who live with someone with active TB are at risk of TB infection. Please refer to Chapter 9, Section 9.7 for more information. • Investigate for TB and if TB is excluded, give TB preventive therapy (TPT) for 6 months at a dose of 10 mg/kg. • Pyridoxine (1–2 mg/kg) should be given to prevent side effects of isoniazid (INH). • See TB program guidelines for more details about TPT and dosing. • Children receiving TPT should be monitored closely for the development of active TB.
Early treatment of infections	• Be actively alert for infections and treat them early by following the guidelines for the integrated management of childhood illnesses (IMCI).
Infant feeding and nutrition counselling	• *See section 8.12* on infant and young child feeding recommendations.
Maternal and family health and well-being	• Assess the health and psychosocial well-being of family members and/or caregivers. The health of HIV-exposed infants is directly tied to the health of their caregivers. • At each visit, refer the child's mother for CD4 count, ART initiation if eligible and family planning. Ask all caregivers about TB symptoms. • Offer HTS for any family members who have not been tested. • Provide psychosocial support to the family.
Early infant male circumcision (EIMC) counselling	• Counsel parents on the importance of EIMC for their infant and refer infant for EIMC at facilities where services are available.

Steps to Successful Early Infant Diagnosis and Treatment

1. Record contact information of mother (cell phone or physical/ residential address).
2. Reinforce the importance of returning for test results.
3. Encourage woman to bring partner to discuss test results.
4. Emphasize that for all HIV-positive children, ART will be initiated urgently to keep the child alive and healthy.
5. Ensure that counselling and support are available to the family.

8.11 Enhanced Infant Prophylaxis (eIP)

All HIV-exposed infants should be given eIP (NVP and AZT syrup) from the time of birth. The duration of AZT is 6 weeks post-partum. The minimum duration of NVP is 14 weeks post-delivery. Please note that NVP should be continued beyond the minimum of 14 weeks if the mother is breastfeeding and has a detectable viral load. Only stop NVP once the mother is undetectable. Transmission of HIV during breastfeeding remains a significant source of HIV transmission in Eswatini. Close monitoring of maternal viral load and adherence throughout breastfeeding is essential to prevent transmission.

Prompt consultation is advised for women viremic on 2nd or 3rd line ART while pregnant or breastfeeding.

Table 8.15 Special Considerations for Enhanced Infant Prophylaxis in Exposed Infants

***Provide dosing clips and syringe**	
Mother diagnosed as HIV- positive during breastfeeding (acute seroconversion)	• The infant is at extreme risk of HIV transmission. Consult MD, mother facility, or Baylor for considerations of presumptive ART for the infant. Lacking specific same-day advice, test infant same day and start routine EIP. If < 6 weeks, start AZT/NVP. If > 14 weeks, start only NVP. • Start ART on the mother immediately. • Test infant on the same day
Mother diagnosed as HIV- positive during breastfeeding and refuses to be initiated on ART	• The infant is at extreme risk of HIV transmission. Consult MD, mother facility or Baylor for considerations of presumptive ART for the infant. Lacking specific same-day advice, test infant same day and start routine EIP. If < 6 weeks start AZT/NVP. If > 14 weeks, start only NVP. • Test the infant on the same day. • Continue counselling the mother on the benefits of ART for her health, the baby's and partner's health
The child defaulted from eIP before they are 14 weeks old	• Counsel on the importance of ongoing prophylaxis and restart AZT up until 6 weeks postpartum and NVP until 14 weeks of age or until the mother has undetectable VL
Mother is on 2nd or 3rd line	• Consult Baylor for guidance on appropriate Infant Prophylaxis. If lacking specific guidance start routine EIP with AZT/NVP

Note: Give AZT only up until 6 weeks post-partum regardless of the start date. Give NVP until at least 14 weeks of age but may continue for longer until the mother has a detectable VL.

8.12 Infant and Young Child Feeding Recommendations

All mothers, including those living with HIV:
- Should be counseled on the benefits of breastfeeding and be encouraged and supported to exclusively breastfeed for the first 6 months.
- Should continue breastfeeding for at least 12 months and may continue breastfeeding for up to 24 month or beyond, with complimentary feeding after 6 months, while being fully supported to adhere to care, maintain VL suppression and consistent condom use.
- Replacement feeding can be advised if the woman fulfils certain criteria. (*See Table 8.28* on replacement feeding)

Table 8.16 Recommendations for Infant and Young Child Feeding Based on HIV Status of Mother

Situation	Recommendations
Mother is known to be HIV-negative or whose HIV status is unknown	• Exclusive breastfeeding for the first 6 months with the addition of complementary feeding thereafter while breastfeeding continues for 24 months or beyond • HIV Testing should be offered for HIV-negative women and those of unknown status together with their partners at every PNC visit until the cessation of breastfeeding • Offer PrEP to all breastfeeding women at each visit.
Mother is known to be HIV-positive and on lifelong ART whose infant is HIV-negative or of unknown HIV status	• Exclusive breastfeeding for the first 6 months with the addition of complementary feeding thereafter • Mothers living with HIV should breastfeed for at least 12 months and may continue breastfeeding for up to 24 months or beyond (similar to the general population) while being fully supported for ART adherence. • All HIV exposed infants who are breastfeeding should be provided with eIP • » AZT and NVP for 6 weeks. This should be dispensed in maternity (if not given during ANC) • » NVP only from 6 weeks to a minimum of 14 weeks. This should be dispensed during the 6-week PNC visit • The mother should continue with her ART for life
Mother is known to be HIV-positive and whose infant is HIV-positive	• Mothers should be encouraged to exclusively breastfeed for the first 6 months of life and continue breastfeeding for up to two years or beyond • Complementary feeding should be introduced from six months while breastfeeding continues • HIV-infected infants should be started on ART as soon as possible. • The mother should continue with her ART for life
HIV-infected mothers who are well counselled but are considering not breastfeeding	• Health care workers should conduct a one-on-one discussion/counselling session with each woman on how to feed their infants and consider her circumstances • Replacement feeding can be advised if the woman fulfils certain criteria. See the replacement feeding section below • All HIV-exposed infants on replacement feeding should receive AZT and NVP prophylaxis from birth up to 6 weeks • The mother should continue with her ART for life
HIV-infected mothers who decide to stop breastfeeding	• When mothers known to be living with HIV decide to stop breastfeeding at any time, infants should be provided with safe and adequate replacement feeds to enable normal growth and development. • See below (under replacement feeding) for alternatives to breastfeeding • Mothers known to be living with HIV who decide to stop breastfeeding at any time should stop gradually within one month. • Infants who have been receiving eIP should continue prophylaxis for two weeks after breastfeeding is fully stopped. • Stopping breastfeeding abruptly is not advisable. • Mother should continue with ART for life

Replacement Feeding

- A mother who opts for replacement feeding from birth should be informed of the need to provide nutritionally adequate and safe replacement feeds to enable normal growth and development of the child. The mother should also meet the conditions outlined in *Table 8.17.* All HIV-exposed infants on replacement feeding should receive zidovudine (AZT) and nevirapine (NVP) prophylaxis from birth up to 6 weeks and then continue with NVP until 14 weeks as guided in *Table 8.10*
- Alternatives to breastfeeding (according to the age of the infant):

» For infants less than 6 months of age: Exclusive commercial infant formula milk should be given as long as home conditions in *Table 8.17* below are fulfilled.

» For children over 6 months of age: Appropriate commercial infant formula, or full cream/whole/undiluted animal milk (boiled for infants less than 12 months) should be provided as part of a diet adequate in micronutrients. Infant meals should be provided 6 times per day. All children need complementary foods from 6 months of age.

Expressing Breast Milk

Expressing breast milk is part of exclusive breastfeeding for mothers in circumstances where they cannot breastfeed on demand. In these instances, the HCWs must support the mothers.

Assessment for Replacement Feeding

Table 8.17 Assessment for replacement feeding

	Assess the following conditions for safe formula feeding	YES	NO
1	Are safe water and sanitation assured in the home and the community?		
2	Can the mother afford and reliably provide sufficient infant formula milk to support the normal growth and development of the infant (about E500 per month)?		
3	Can the mother/caregiver prepare formula milk cleanly and frequently enough so that it is safe and carries a low risk for diarrhoea and malnutrition?		
4	Can the mother exclusively give infant formula?		
5	Is the family supportive of exclusive replacement feeding?		
6	Can the mother or caregiver access health care that offers comprehensive child health services?		
• If YES to ALL, exclusive replacement feeding can be recommended. • If NO to ANY of the questions, recommend breastfeeding. Assure mother that ART and being undetectable makes breastfeeding safe			

Complementary Feeding

Complementary feeding is extremely essential from 6 months of age, while breastfeeding continues for 24 months or beyond. After 6 months of age, breast milk alone no longer provides complete nutrition to an infant but still contributes to approximately 50% of nutritional requirements between the age of 6 and 12 months. *See infant and young child feeding guidelines*

9 ART FOR CHILDREN AND ADOLESCENTS

Important Contacts:

- **DBS Hotline: 7687-9925**
- **Baylor HIV/TB Hotline: 7848-5571**
- **SNAP 3rd Line Committee e-mail:**

snapthirdline@mohcoag.org

9.1 Preparations of Children and Adolescents for ART

Clients and caregivers must be well-prepared for ART to ensure good adherence and treatment success.

Social Considerations for ART Initiation and Chronic Care

Identifying a parent or primary caregiver, plus a secondary caregiver whenever possible, is essential for children and adolescents initiating ART to ensure good adherence and treatment success. ART initiation should not be delayed while awaiting a secondary caregiver to be identified.

A psychosocial and readiness assessment should be conducted for both the child and their caregiver or treatment supporter.

Caregivers must be made aware of their responsibilities regarding the care of the child, as all care practices should be in the best interest of the child.

The parent or caregiver of a child or adolescent is responsible for:

- Directly observing treatment adherence and giving medications as prescribed.
- Accompanying/bringing the child or adolescent for scheduled medical visits.
- Providing ongoing care for the child and psychosocial support (e.g., nutrition, immunizations, disclosure).
- Ensure that the child's HIV status is fully disclosed by age 10.

Healthcare workers should inform parents and caregivers of the importance of notifying the health facility of change of caregivers. The new caregiver must receive counselling support and education to ensure continued quality care and support

Children and adolescents should be initiated on ART as soon as possible, preferably on the same day of testing positive for HIV diagnosis while adherence-counselling process is ongoing.

Adherence Counselling for Children and Adolescents

It is recommended that all caregivers and mature adolescents (they are a parent, the head of household, are pregnant or receiving treatment for an STI) clients who are aware of their status should receive counselling—group counselling or individual counselling—before or during ART initiation. These counselling sessions can happen on the same day as HIV diagnosis to encourage same-day initiation. Treatment supporters should be encouraged to attend counselling sessions. The parent or caregiver and mature client should be informed about the benefits of ART and that side effects are usually minor and transient, or manageable.

Develop a treatment plan with the client, specifying the drugs to be used (with names and details including the appearance of each drug, when and how they are to be taken and a brief indication of anticipated side effects and toxicity).

ART Readiness Assessments: *(See annexe 11.22*)

Assessing and supporting readiness for HIV chronic care offers the best opportunity for effective suppression of viral loads, immune recovery, and clinical benefit and that successful ART requires taking all medications as prescribed.

Readiness assessments should be conducted with the caregiver and the child/adolescent to assess and provide support for:

1. Willingness and readiness to start/initiate ART
2. Readiness to initiate ART
3. Level of caregiver and child/ adolescent treatment literacy (benefits, possible adverse effects and required follow-up and monitoring visits)
4. Mental health and substance use screening and support
5. Structured adherence support
6. Disclosure processes and necessary support (Assisted disclosure)
7. Individualized Linkage case management

ART readiness reassessment should be conducted:

- During clinical monitoring 6 at each visit
- When there is a change in the caregiver
- When adherence and/or another barrier is suspected or identified

Counselling on benefits of ART, adherence, disclosure, and maintaining an undetectable viral load (VL) should be provided during all client encounters because doing so on first ART regimen offers the best opportunity for effective life-long therapy.

Caregiver Literacy to Support paediatric and adolescent ART

Children should be viewed in the context of the family. Strengthening the understanding of the treatment of children and adolescents living with HIV by caregivers to ensure adherence to treatment and care is a key factor in good clinical outcomes for infants and children on treatment for HIV.

Educating caregivers will ensure long-term virological suppression, immune recovery, growth and development, and future treatment options for HIV-positive infants and children on treatment. This should include the importance of:

- A consistent primary and secondary caregiver
- Keeping scheduled appointments and regularly obtaining ARVs
- Administering the complete ARV regimen and correct weight-based dose
- Administering the age-appropriate formulation (syrup, granules, tablets, capsules) and progressive disclosure (disclosure is not a once of activity)
- Storage of ARVs and other prescribed medicines at home
- Fitting ART into the child's (or caregiver's) daily schedule(s) and setting reminders to support consistent dosing times
- Supporting adolescents to take more control over their health whilst still maintaining a relationship with the parent/carer
- Suppressed viral load
- Potential side effects (and what to do if they occur)

- Community and Peer to Peer support (children, adolescents and caregivers)
- Building self-management skills and health and HIV literacy

Strategies to optimize HIV treatment and care require regular review with the caregiver and child/ adolescent, and adaptation based on the individual needs and growth of a child.

Referral for community and peer support for children, adolescents and caregivers to ensure a continuum of care

Eliminating the divide between community and facility and providing seamless services will maintain CALHIV and their families on uninterrupted treatment and reduce co-morbidities and mortality through client-focused service provision. Children, adolescents, caregivers and their families, therefore, require coordinated, innovative and comprehensive interventions at the facility and community level.

Referral for Community support services will enable CALHIV, and their families to receive more services where they live, including:

- Adherence counselling and psychological support (Peer - Peer, individual or group) for children and /or caregivers
- Treatment literacy education and self-management skills
- Disclosure support
- Treatment refill appointment reminders
- Early identification, tracking and support for treatment interrupters to fast-track linkage back to treatment
- Family-based case management
- Support for enrolment and retention in school
- Support children, adolescents and their families with mental health problems
- Linkages to child protection and other social services
- Caregiver support with household economic strengthening initiatives
- Livelihood programs for AGYW to improve their economic empowerment
- Community access to contraceptives for AGYW
- U = U for adolescents

HCWs play vital roles in strengthening community support and are responsible for identifying, screening and facilitating appropriate bilateral referrals to community programs.

Developing an adherence plan is essential for long-term treatment success (*see Figure 9.1*)

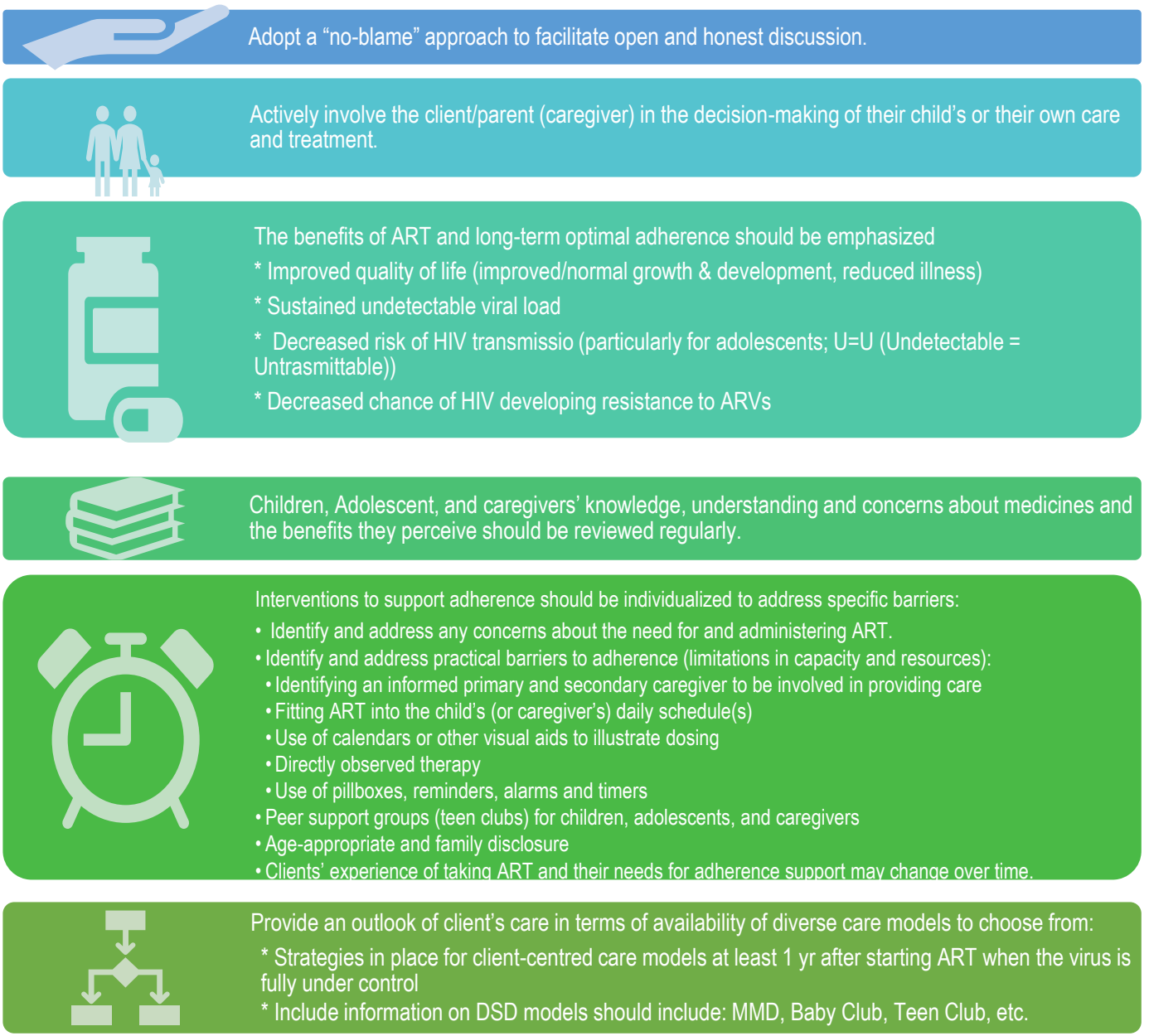


Figure 9.1 Steps to use when developing an adherence plan

9.2 Assessment of Children Before ART Initiation

See Table 5.11

9.3 When to Start ART for Children and Adolescents

All HIV-infected children and adolescents are eligible to start ART regardless of CD4 count or WHO clinical stage. It is imperative to confirm all presumptively diagnosed children with DNA PCR. against HIV.)

Assess the client's and caregiver's readiness and address barriers to ART initiation. Initiate ART as soon after diagnosis as possible (preferably 0–14 days).

Table 9.1 Timing of ART initiation (after HIV verification/confirmation and clinical assessment)

Clinical status	Timing of ART initiation
CALHIV with HIV with no signs and symptoms of TB	Rapid ART initiation on the same day should be offered to all people living with HIV (Test and Start)
CALHIV with suspected TB	Offer rapid ART initiation while rapidly investigating for TB, with close follow-up within 7 days to initiate TB treatment if TB is confirmed* *This is except for cases where the history and clinical examination indicate signs and symptoms of TB meningitis
CALHIV has already been diagnosed with TB but not receiving ART or treatment for TB	Initiate TB treatment first Initiate ART as soon as possible within 2 weeks of TB treatment
CALHIV with being treated for HIV-associated TB (including multi-drug-resistant TB (MDR))	Initiate TB treatment first Initiate ART within 2 weeks of initiating TB treatment, regardless of CD4 cell count
CALHIV being treated for HIV-associated TB meningitis (either clinically or with a confirmed laboratory test)	Initiate TB treatment first Delay ART initiation by at least 4 weeks (and initiated within eight weeks) after treatment for TB meningitis begins
CALHIV with cryptococcal meningitis	Immediate ART initiation is contraindicated because of the increased mortality presumed to be caused by immune reconstitution inflammatory syndrome in the central nervous system ART should be initiated between 4–6 weeks after beginning antifungal treatment
CALHIV who are hospitalized or severely ill	Acute management of the illness is the priority. ART should be initiated within 14 days, after medical stabilization of the coexisting illness.

ART should be deferred in a seriously ill child presenting with any of the following danger signs:

- Temperature ≥39°C
- Lethargy or unconsciousness
- Repeated vomiting
- Unable to drink or breastfeed
- Convulsions
- Tachycardia and/or tachypnoea

Children and adolescents with these danger signs require acute medical management +/- referral for admission and should not be initiated on ART until stable.

9.4 Advanced HIV Disease (AHD) in children and adolescents

All children with HIV who are younger than 5 years and have not been on treatment for at least 12months are considered to be a high-risk group and are therefore managed as having advanced immunodeficiency (advanced disease). Children above 2 years who have been on ART, and are stable, for at least one year may not be considered as having AHD.
For children aged 5 years and older *(refer to Table 9.2)*

Prioritize assessment (clinical and social) and rapid ART initiation in children and adolescents with advanced immune deficiency (advanced disease) as soon as possible (within 7 days) from the day of HIV diagnosis

Table 9.2 Definitions of Advanced Immunodeficiency and High-Risk Groups

	Advanced Immunodeficiency (Severe Immunodeficiency)	High-Risk Group (Very Severe Immunodeficiency)
Adolescents	• CD4 count ≤200 cells/mm³ or • WHO clinical stage 3 or 4	• CD4 count ≤100 cells/mm³
Children	**Children ≥5 years:** • CD4 count ≤200 cells/mm3 or CD4 less than 25% • WHO clinical stage 3 or 4 **Children < 5 years:** • Manage as clients with advanced immunodeficiency (Advanced disease)	**Children ≥5 years** • CD4 count ≤100 cells/mm3 or less than 25% **Children <5 years:** • CD4 count ≤100 cells/mm³ or <25%.

CD4 cell count is the best indicator of disease stage and immediate risk of death and thus should be used to identify children and adolescents with advanced HIV disease. Children and adolescents should be assessed for advanced HIV disease and should be offered the advanced HIV disease package as appropriate.

Children and adolescents at risk of Advanced HIV disease include those:

- Presenting to care for the first time following an HIV diagnosis
- Identified with treatment failure and consequent decline in CD4 cell count.

- Previously initiated ART and are re-engaging with care after a period of ART interruption

Package of care for children and adolescents with Advanced HIV Disease: Screen, Treat, Optimize and Prevent AIDS (STOP AIDS)

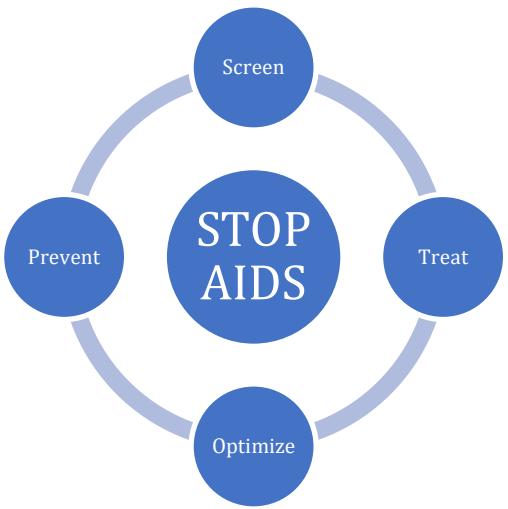


Figure 9.2 Elements of STOP strategy

Identify and treat opportunistic infections BEFORE initiating ART
Client with Active TB (other than TB meningitis): Initiate ART as soon as possible (within 2weeks) following initiation of anti - TB treatment
Client with Cryptococcal infection or Meningitis:ART initiation should be delayed for 6-8 weeks after starting treatment for meningitis

The elements for the implementation of the STOP strategy are outlined in Table *9.3* below.

Table 9.3 Stop AIDS strategy

	Screen for TB
Screen	• Use a clinical algorithm (see Figure 6.1) followed by an X-ray when indicated and if available • Use recommended diagnostic tests to confirm TB as applicable. 1. Rapid molecular diagnostic (Xpert® MTB/RIF or Ultra) on (induced) sputum, stool, gastric aspirate or nasopharyngeal aspirate or other extra-pulmonary samples if relevant 2. Lateral flow urine lipoarabinomannan (LF-LAM) assay

Table 9.3 Stop AIDS strategy (continued from the previous page)

<table>
<tr><td rowspan="9">Screen</td><td colspan="4">Indications for LF-LAM use in the diagnosis of active TB among CALHIV</td></tr>
<tr><td colspan="2">Indications for use in Inpatient settings
• With signs and symptoms of TB (pulmonary and/or extrapulmonary)
• With advanced HIV disease or who are seriously ill regardless of signs and symptoms of TB and with a CD4 count <200 cells/ mm³</td><td colspan="2">Indications for use in outpatient settings
• With signs and symptoms of TB (pulmonary and/or extrapulmonary)
• Seriously ill regardless of signs and symptoms of TB and with a CD4 cell count < 100 cells/mm³</td></tr>
<tr><td colspan="4">LF-LAM should not be used to assist in diagnosing active TB among children and adolescents in the following situations:
A. Children and adolescents without assessing TB symptoms
B. Children and adolescents without TB symptoms and unknown CD4 cell count or without TB symptoms and the CD4 cell count ≥200 cells/mm³
C. Children and adolescents without TB symptoms and with a CD4 cell count of 100–200 cells/mm³</td></tr>
<tr><td colspan="4">Screen for Cryptococcal infection among adolescents</td></tr>
<tr><td colspan="4">Serum or plasma or blood cryptococcal antigen screening followed by lumbar puncture if positive or symptomatic</td></tr>
<tr><td colspan="4">Screen for Malnutrition</td></tr>
<tr><td>Weight-for-height (Wt/Ht)</td><td>Height-for-age (Ht/Age)</td><td>Mid-upper arm circumference (MUAC)among children 2–5 years old</td><td>Weight for age (Wt./Age)</td></tr>
<tr><td rowspan="2">Treat</td><td colspan="4">Treat opportunistic infections</td></tr>
<tr><td colspan="4">This includes TB, severe pneumonia, severe bacterial infections, gastroenteritis, cryptococcal meningitis and severe acute malnutrition</td></tr>
<tr><td>Optimize</td><td colspan="4">• Rapid antiretroviral therapy initiation with optimal regimens (within 7 days)
• Antiretroviral therapy counselling
• Intensified adherence support interventions</td></tr>
<tr><td rowspan="4">Prevent</td><td colspan="4">Bacterial infections and Pneumocystis pneumonia - Co-trimoxazole prophylaxis</td></tr>
<tr><td colspan="4">TB - TB preventive treatment</td></tr>
<tr><td colspan="4">Cryptococcal meningitis among adolescents- Fluconazole pre-emptive therapy</td></tr>
<tr><td colspan="4">Vaccination (See National vaccination schedule Annex 11.33)</td></tr>
<tr><td>Pneumococcal vaccine</td><td>HPV (Adolescents)</td><td>Measles</td><td>BCG</td></tr>
</table>

9.5 What to Start: ART for Children and Adolescents

Children and adolescents are a priority population. In the absence of severe opportunistic infections like meningitis, initiate ART on the same day initiation and when not possible, as soon as the caregiver/child/adolescent is ready, preferably within 7 days (Test and Start) regardless of the availability of baseline results at the time of initiation.

Recommended First-Line ART for Children and Adolescents

Before initiating ART, conduct a comprehensive clinical and psychosocial assessment including adherence counselling. Initiate ART as outlined in Table 9.4 below.

Table 9.4 Recommended First-Line ART Regimens for Children and Adolescents

Recommended Regimens for Children and Adolescents			
Weight/Age	< 3.0 kg OR <4 weeks old	≥3-29.9 kg (AND ≥ 4 weeks of age)	≥ 30 Kg
Regimen	*AZT + 3TC + NVP (*Holding Regimen)	ABC + 3TC + DTG	TDF + 3TC + DTG
Special Considerations	Use Fixed Dose, once-daily combination pills whenever possible. ○ *If initiated at <4 weeks of age OR has weight <3 kg for ART initiation: ○ Transition to ABC + 3TC + DTG once ≥3kg AND ≥4 weeks of age *See Annex 11.20* for holding regimen dosing guidance or call the clinical mentor/Baylor Hotline If the neonate is UNWELL, or PREMATURE (<35 weeks gestation), call the clinical mentor/Baylor Hotline (7848-5571)		

See Annex 11.1 for additional information on antiretroviral (ARV) drugs. *See Annex 11.17* for the paediatric dosing chart, and *Annex 11.19* for Special Dosing Considerations in Birth Tested Infants.

Alternative First-Line ART Regimens for Children and Adolescents

Table 9.6 provide additional alternatives for special situations for ART initiation and substitutions in children when side effects occur to recommended first-line regimens. These situations include cases of children with side effects due to medication in recommended regimens for first-line treatment.

Table 9.5 Alternative First-Line ART Regimens for Children and Adolescents

Alternative Regimens for Children and Adolescents			
Weight/Age	≤3kg or <4 weeks	≥3-29.9 kg AND ≥4 weeks of age	≥ 30 kg
Regimen	AZT + 3TC + RAL	AZT + 3TC + DTG ABC (or AZT) + 3TC + LPV/r ABC (or AZT) + 3TC + EFV	ABC (or AZT) + 3TC + DTG TDF (or ABC) + 3TC + EFV 400mg
Special Considerations		• EFV should not be used in children < 3 years old OR ≤ 10kg • In line with ART optimization efforts, NNRTIs should be avoided whenever possible • LPV/r solid formulations (tablets) should be used as soon as the child can swallow • LPV/r tablets should never be cut, split, dissolved, chewed or crushed. • ATV/r can be used instead of LPV/r in children ≥40kg	
If the neonate is UNWELL, or PREMATURE (<37 weeks gestation), call the clinical mentor/Baylor Hotline (7848-5571)			

Table 9.6 Special Situations for Children and Adolescent

Special Situation	Age/Weight	ARV Recommended or Substitution	Comments
ABC hypersensitivity reaction (rare)	< 30 kg	AZT	Ensure Hb > 10 g/dL
	≥ 30 kg	TDF	Do not use TDF if: Confirmed and/or suspected renal dysfunction (CrCl <50 mL/min) Use with caution In the presence of nephrotoxic drugs
Anaemia while taking AZT (Hb<10 g/dL)	< 30 kg	ABC	Do not rechallenge if there is a history of ABC hypersensitivity and consult with an experienced clinician
	≥ 30 kg	TDF	See above
LPV/r (gastrointestinal side effects)	≥ 3 kg and 4 weeks of age	DTG*	Ensure VL suppressed in the previous 3-6months OR order urgent/POC VL first Case-by-case basis, consult with a doctor or call the Baylor HIV/ TB Hotline (7848-5571)
	≥ 3 years OR ≥ 10 kg	DTG (Preferred)* EFV*	
	≥ 40 kg	ATV/r	

Table 9.6 Special Situations for Children and Adolescent (continued from the previous page)

Special Situation	Age/Weight	ARV Recommended or Substitution	Comments
Caregiver unable to correctly dose LPV/r granules	≥ 3 kg and 4 weeks of age	DTG (Preferred) LPV/r Tablets	LPV/r Tablets can NOT be crushed, chewed or broken so only appropriate if the child can swallow them whole.
	≥ 3 years OR ≥ 10 kg	DTG (Preferred) EFV	Ensure VL suppressed in the previous 3-6 months OR Order urgent/POC VL first and consult Baylor HIV/ TB Hotline (7848-5571) OR snapthirdline@mohcoag.org
Unable to tolerate EFV (severe central nervous system side effects or moderate to severe rash); psychiatric history of EFV side effects	≥ 3 kg	DTG (preferred) LPV/r (granules/tablets)	Ensure VL is suppressed in the previous 3-6 months OR Order urgent/POC VL first. On a case-by-case basis, consult with a doctor or call the Baylor HIV/TB Hotline (7848-5571)
	≥ 40 kg	DTG (preferred) ATV/r *DRV/r	
Unable to tolerate DTG	< 3 years OR <10 kg	LPV/r granules	Ensure VL is suppressed in the previous 3-6months OR order urgent/POC VL first
	≥ 3 years OR ≥ 10 kg	LPV/r (granules or tablets) EFV *DRV/r	LPV/r Tablets CANNOT be crushed, chewed or broken so only appropriate if the child can swallow them whole.

Prescription of DRV/r is guided by genotype results, consult HIVDR clinical expert committee

9.6 Treatment Optimization

Children and adolescents living with HIV(CALHIV) must have access to effective, child-friendly, antiretroviral (ARV) treatment and formulations that will ensure good adherence and continuous viral suppression. Treatment optimization involves optimization of both regimens (ART) and formulations as highlighted below.

Treatment optimization occurs through the treatment of children and adolescents from initiation on ART through to long-term care.

Table 9.7 Strategies to Optimize ART

Optimal ART	Optimal formulations
Early therapy/ Treatment	Use of fixed-dose combinations (FDCs) e.g., ABC/3TC (120/60mg) or TLD for older children and adolescents
The optimal sequence of new drugs from birth to adolescence	Age-appropriate formulations (syrup, granules, dispersible tablets, solid tablets, capsules) depend on the age of the infant/child and their ability to swallow
Less toxic drug regimens with high barriers to drug resistance	Flexible administration e.g., dispersible tablets (e.g., pDTG10mg, ABC/3TC (120/60mg)) can be dissolved in liquid and administered to young infants, crushed and swallowed, chewed or swallowed whole
Simplified dosing by weight bands	Heat stable (e.g., LPV/r 125mg tablets)
Harmonizing Paediatric recommendations with adult regimens	Improved palatability (pDTG 10mg with strawberry taste)

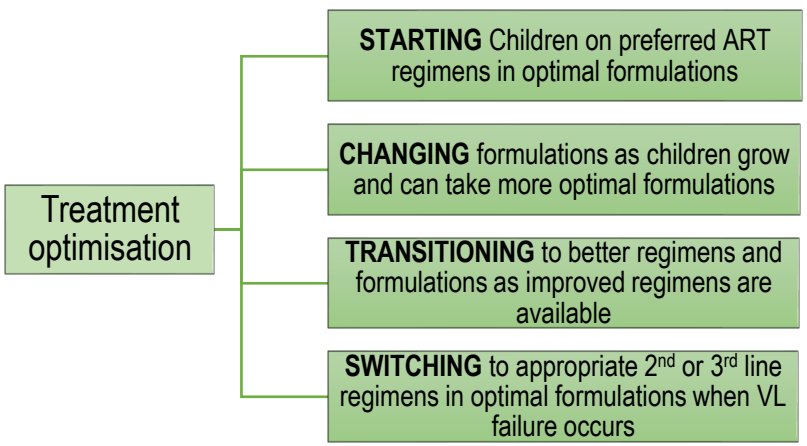


Figure 9.3 Key Components of Treatment Optimization

9.6.1 Transitioning regimens and formulations in children and adolescents

The country continues to promote optimization and sequencing from the first-line to second-line regimens to reduce toxicity and pill burden, ensure once-daily dosing, ensure minimal or no cross-class resistance and with a preference for regimens that can be used across populations.

- Transitioning to DTG-based regimens Children and adolescents:

DTG-based regimens provide a more efficacious and tolerated option that overcomes potential resistance to NNRTIs and provides the opportunity to fully harmonize regimens across children and adults. Transitioning to DTG for children and adolescents > 20 kg began in 2019 after WHO updated guidelines in 2018. In July 2021, the DTG 10mg dispersible tablet was introduced and children >3 kg could also benefit from transitioning to currently optimized regimens.

Paediatric DTG (pDTG) dispersible tablet (DT)

Paediatric dolutegravir 10 mg dispersible, scored tablets (pDTG) is a new generic formulation of DTG for CLHIV who are at least one month (4 weeks) of age and weigh at least 3kg and up to 20 kg. The dispersible tablet (DT) can be swallowed whole but is meant to be dissolved in water for younger children. The dispersible formulation allows pDTG to be easily administered to children by dispersing and drinking the medicine in a small amount of water, rather than having to swallow multiple pills, pellets, or granule formulations.

HCWs should guide caregivers to add the appropriate dose for the weight of pDTG to clean liquid, stir until the tablet(s) dissolves, and administer to the child. (See Annex 11.17 for paediatric dosing chart).

DTG 50 mg Film-Coated Tablets (FCT)

- The adult 50 mg tablet is a small, film-coated tablet that should be swallowed whole
- It should be used for children who weigh 20 kg or more

pDTG dispersible tablets are much better absorbed than DTG film-coated tablets. As a result, these two formulations should not be interchanged).

- <u>Transitioning to Paediatric ABC/3TC formulation:</u>

Children and adolescents transition to the preferred ABC/3TC 120/60mg tablets which are given once daily (OD) to reduce the pill burden.
Sequencing of ABC in first-line regimens allows for a more effective 2L treatment regimen using AZT.

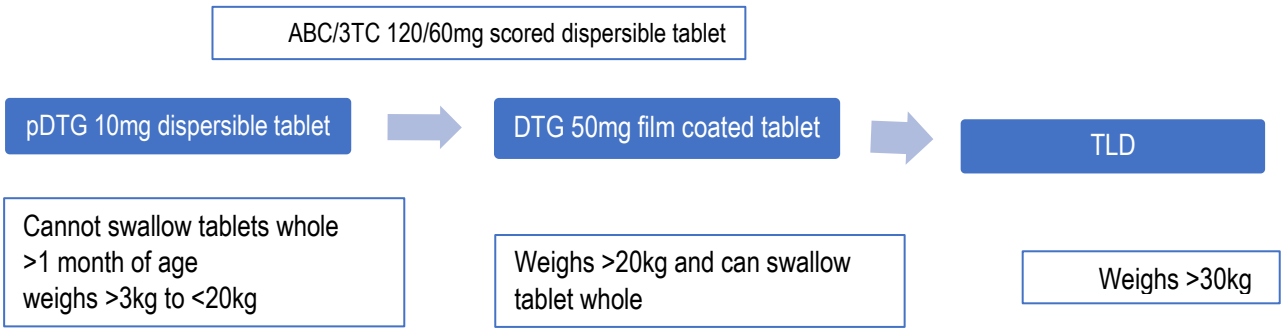
- <u>Transitioning away from LPV/r liquid to LPV/r solid formulations:</u>

Paediatric LPV/r 100mg/25mg tablets should be used once the child is safely able to swallow pills. LPV/r tablets cannot be chewed or crushed but must be swallowed whole. Infants and children also benefit from the use of LPV/r granules to ease the burden of LPV/r syrup administration

- <u>Co-administration with ABC/3TC 120/60mg DT (dispersible tablet):</u>

pDTG can be dispersed and administered in the same solution of clean water as ABC/3TC 120/60 mg DT. When dispersing both products together, use 10-20 mL (2-4 teaspoons) of clean water and ensure both medicines are properly dissolved before administering.

The sequence of transition to optimal ARV drug formulations for stable children and adolescents



It is NOT Recommended to co-administer DTG with anticonvulsants such as phenytoin or phenobarbital. (Consult expert or consider substituting DTG with EFV as alternative.)
Iron, aluminum, magnesium and calcium-containing medicines bind with and reduce absorption of DTG. If co-administered, DTG should be taken with food to enhance DTG absorption or taken at alternate times (6 hours apart).

Transition to optimal ARV drug regimens for stable children and adolescents

Table 9.8 General guidance on the use of VL results for clinical decision-making for treatment optimization for CALHIV on ART

VL Test Result in the past 6 months	Consideration	Action
Undetectable < 200 copies/mL	The client is adherent and doing well The client is eligible for substitution to an optimal regimen	Transition to an optimal regimen immediately
> 200 - 1000 copies/mL (detectable and ≤400 copies/mL)	The client may be experiencing adherence challenges and is at risk of treatment failure 	Provide a once-off special counselling session on the day of the visit and repeat the viral load in 3 months If repeat viral load is >200- 1000 copies/ml, manage as treatment failure (conduct 3 SUAC sessions and repeat viral load in 3 months) If third VL is still 200 - 1000 copies/mL, refer the client to the doctor/multi-disciplinary team for switching to second-line or third-line therapy
> 1000 copies/mL		Manage as treatment failure (conduct 3 SUAC sessions and repeat VL in 3 months)

Table 9.9 Treatment Optimization Recommendations for stable CALHIV

Current 1st Line Regimen	Weight	Optimal regimen for transition	Consideration
AZT + 3TC + EFV (or NVP) ABC + 3TC + EFV (or NVP) ABC + 3TC + LPV/r AZT + 3TC + LPV/r TDF +3TC+ EFV	<30Kg	ABC + 3TC plus DTG	If undetectable, transition immediately. If detectable, manage as treatment failure urgently. If <3kg, OR < 4 weeks of age refer to *Table 9.5* for treatment alternatives.
	>30Kg	TDF+3TC + DTG (TLD)	
Children and adolescents on 2nd Line PI-based regimens should be maintained on their regimens. If not suppressed, contact the national HIVDR clinical expert committee (snapthirdline@mohcoag.org) for evaluation of drug resistance and the need for genotyping urgently.			

Support for those not ready to transition

For clients not ready to transition to pDTG or any other optimal ARV, discuss the reasons behind their concerns and address those issues.

Refill ART for 1 month and advise the client to discuss and consider this and bring questions for the next visit. At the next visit, address questions and concerns.

Remember to be honest and understanding with caregivers as they are primarily concerned about the health and well-being of their child.

9.7 Prophylaxis Therapy for HIV-Exposed or -Infected Infants and Children

9.7.1 Cotrimoxazole Preventive Therapy (CPT)

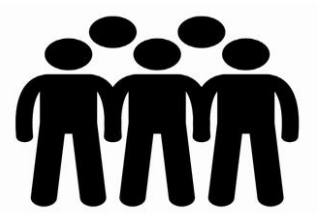
Table 9.10 Co-trimoxazole Preventive Therapy for Children and Adolescent Clients

Group	When to start Co-trimoxazole preventive therapy?	When to discontinue Co-trimoxazole preventive therapy? *
All HIV-exposed infants/ children	From 6 weeks of age (or at the first encounter with health services, if later than 6 weeks of age)	HIV-negative status has been confirmed and there is no longer exposure
All HIV-infected infants and children up to 5 years of age	Irrespective of WHO clinical stage or CD4 count or CD4 %	**≥5 years of age and after 1 year on ART if:** • WHO clinical T-stage 1 or 2 • CD4 count ≥350 cells/mm³ and • Viral load is undetectable

Table 9.12 Co-trimoxazole Preventive Therapy for Children and Adolescent Clients continued from the previous page)

Group	When to start Co-trimoxazole preventive therapy?	When to discontinue Co-trimoxazole preventive therapy? *
All HIV-infected children ≥ 5 years of age	WHO clinical stages 3 and 4 irrespective of CD4 OR CD4 ≤350 cells/mm³ irrespective of WHO clinical stage OR Detectable Viral Load irrespective of CD4 count	**≥5 years of age and after 1 year on ART if:** • WHO clinical T-stage stage 1 or 2 • CD4 count ≥350 cells/mm³ and • Viral load is undetectable
As secondary prophylaxis	After completion of treatment for Pneumocystis jirovecii pneumonia (PJP)	**<5 years old:** • Do not stop **≥ 5 years old, stop if:** • CD4 count ≥350 cells/mm³ and • Viral load is undetectable

Can also be stopped due to adverse drug reactions (See Chapter 5, Section 5.4)



9.8 Tuberculosis Preventive Therapy (TPT) for treatment of Latent TB infection (LTBI)

See Table 6.5 for TPT options in CALHIV dosing and *Table 6.11* TPT completion timelines

Infants, children and adolescents living with HIV should routinely be screened for TB as part of standard clinical care, whether they are receiving TB prophylaxis or ART. Treatment of LTBI is targeted to population groups at the highest risk for progression to active TB disease.

These include:

- Adults and adolescents living with HIV
- Children < 5 years, adolescents and adults who are household contacts of TB cases.
- Household contacts of DR-TB patients after an individualized risk assessment
- Other HIV-negative at-risk population groups

For children and adolescents living with HIV who are without active TB, TPT should be offered:

- Regardless of the degree of immunosuppression
- To CALHIV within 4weeks of ART initiation on ART
- To CALHIV that completed TB treatment
- To CALHIV that have been previously treated for TB

Special considerations for TPT

For children < 5 years, give TPT to

- All children < 5 years who are household contacts of TB patients if clinical evaluation shows no TB (regardless of HIV status).
- Children > 12 months living with HIV without active TB
- Children and infants < 1 year of age only if they have a history of household contact with a TB case and active TB has been excluded in investigations.

Provide vitamin B6 (1-2 mg/kg /day) to prevent peripheral neuropathy. This can be increased to 5-10mg/kg if peripheral neuropathy develops and is persistent.

3HP is only recommended in children >2 years of age. *Refer to Section 6.1.5*

Recent trials in an era of wide-scale access to ART, suggest that the protection offered by TPT even in high-burden settings can last as long as in low-/medium-TB burden settings. Repeat cycles of TPT should only be considered in patients exposed to household/close contact with TB after a TPT course.

9.9 ART for Children and Adolescents with TB/HIV Coinfection

Tuberculosis is a WHO clinical stage 3 or 4 condition. Screen all HIV-positive children for TB at every visit using the TB /COVID-19 screening questionnaire. Provide PT if TB screening is negative.

Recommended ART for Drug-Sensitive TB/HIV Coinfection

In children with TB/HIV coinfection, ART should be started as soon as possible within two weeks of initiating TB treatment, regardless of CD4 count.

See Annex 11.16 for regimen adjustments in PLHIV

For more information on the diagnosis and management of tuberculosis, see National Tuberculosis Guidelines.

Always consider prior regimens, adherence, and ensure that VL is undetectable when considering regimen changes, particularly one-drug substitutions. If the child or adolescent has a detectable viral load or adherence <95%, consult a doctor or call the Baylor HIV/TB Hotline (**7848-5571**).

9.10 Clinical Monitoring of Children and Adolescents on ART

ART monitoring in children will assist in:

1. Evaluating the child's response to therapy.
2. Diagnosing any new conditions.
3. Monitoring for short- and long-term treatment side effects.
4. Assessing changes in the family unit that might affect the child's care.
5. Addressing disclosure and ensuring that children's understanding of their condition evolves as they mature.
6. During the first 6 months after ART initiation, frequent visits are crucial to monitor for immune reconstitution inflammatory syndrome (IRIS) and acute ART toxicities and adherence issues.
7. The first follow-up visit should be scheduled 2 weeks after ART initiation. Thereafter, during the first 6 months of treatment, children and adolescents should be followed up monthly.

Immune Reconstitution Inflammatory Syndrome (IRIS)

Any opportunistic infection occurring during the first 6 months after ART initiation might have 2 causes:

- The immune system is not yet fully functional (the least likely scenario).
- IRIS has occurred. Typically seen when a client's impaired immune function is restored, IRIS is characterized by the paradoxical clinical worsening of a known condition or the appearance of a new condition. Infectious pathogens most frequently implicated in the syndrome include mycobacteria, varicella zoster, herpes viruses, and cytomegalovirus. At the clinic level, health care workers should refer clients with suspected IRIS to the doctor or the hospital.

Clients with severe immunodeficiency (advanced disease) are at greater risk for IRIS when initiating ART and should be closely monitored.

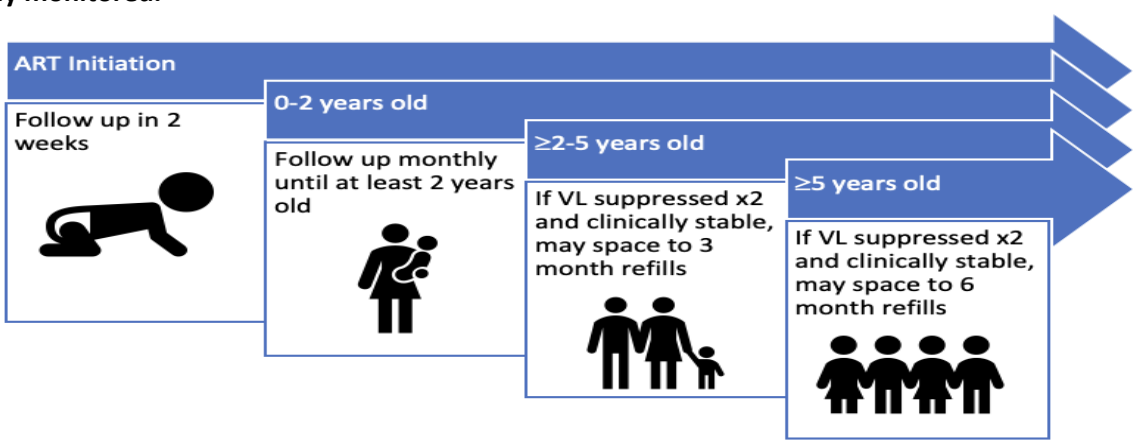


Figure 9.4 Key ART follow-up schedule for children and adolescents starting ART

Components of the Clinical Assessment

In addition to information in *Table 5.17*

- Assess timing of medication dosing:
» Missed doses should be taken immediately if not within 6 hours of the next dose for twice daily dosing
» Missed doses should be taken immediately if not within 12 hours of the next dose for once-daily dosing
- Pill counts/assessment of adherence and addressing barriers
- Continue ART readiness assessment (*Annex 11.22*)
- Enrol into DSD (*See Section 5.7*)

After the first 6 months of treatment, the frequency of clinical monitoring depends on the client's response to treatment and long- term follow-up focuses on toxicities, adherence and empowerment. Weight-based dosing must be practiced during refills.
Orphans and vulnerable children need special attention to assure good treatment outcomes. If social situations compromise adherence to treatment, consider engaging other caregivers or child welfare services.

9.11 Laboratory Monitoring of Children and Adolescents on ART

CD4 Count

CD4 count testing at baseline for all children living with HIV remains important to avoid the risks of missing children and adolescents with advanced immunodeficiency (advanced disease) who are at much higher risk of disease progression and mortality. After ART initiation, CD4 counts should be done at 6-month intervals. Once a client has 2 consecutive CD4 counts >350cells/mm^3 and undetectable viral load, CD4 monitoring can be stopped. If treatment failure is suspected, resume CD4 monitoring until the client has undetectable viral load and 2 consecutive CD4 counts >350 cells/mm^3.

Viral Load

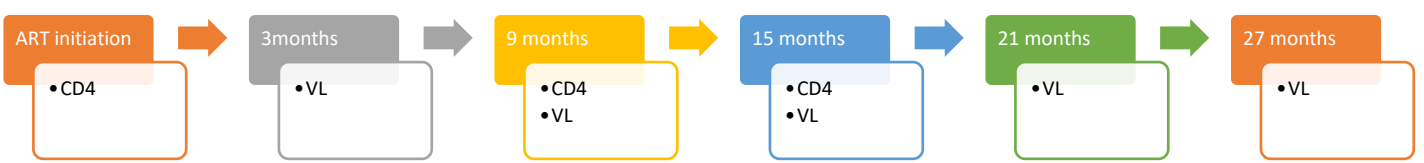
VL testing should be routinely conducted for all children and adolescents 3 months after initiation of ART and the second VL test repeated 6 months later. VL monitoring should be continued every 6 months for all children and adolescents 0-19 years old (see the schedule for VL monitoring in children and adolescents as shown in Figure 9.5). Children and Adolescents should have access to Point of Care VL testing when possible.

Table 9.11 Repeat VL Test After Initial Non-suppression

Repeat VL Test Result	Most Likely Reasoning	Recommendation
< 50 copies/mL (undetectable VL)	The client has improved adherence	• If VL is undetectable and the client is >2 years of age and on ART for more than 1 year, provide DSD models including MMD. • Address psychosocial issues which led to the initial detectable VL
50 – 1000 copies/mL (Low-level viraemia)	The client is still facing adherence challenges with treatment	Barriers to adherence should be evaluated and adherence should be reinforced through ongoing SUAC, and the VL should be rechecked after 3 months
≥1000 copies/mL (High viral load)	Diagnosis is virological treatment failure most likely due to a resistant virus or poor adherence	These clients should be considered switching to second-line therapy

Dried blood spot VL specimens can improve VL access/coverage in children (under 5 years) where paediatric phlebotomy is not routinely available and for hard-to-reach locations unable to maintain the cold chain required for plasma specimens.

VL testing schedule for clients 0-19 years old



Continue with VL monitoring every 6months until client is 19years then follow adult schedule

Figure 9.5 Timeline for VL and CD4 Monitoring in Children and Adolescents 0-19years

Management of Clients with Detectable Viral Load and Stepped-Up Adherence Counselling (SUAC)

See Figure 7.3 for the appropriate steps once a detectable VL test result is received. Children and Adolescents with VL >50 should be referred for SUAC.

For paediatric-specific information, continue to *Section 9.12* below.

9.12 Managing Treatment Failure in Children and Adolescents

ART failure is defined as a suboptimal response or a lack of sustained response to therapy using virological, immunological and/or clinical criteria. Treatment failure should be considered if the child has received the ART regimen for at least 6 months and demonstrated optimal adherence.

A viral load threshold of ≥1000 copies/mL should be used to determine virological failure when using plasma or dried blood spot specimens.

Note: Identification and management of treatment failure in children and adolescents should not be delayed.

Table 9.12 WHO Definitions of Types of Treatment Failure in Children and Adolescents

Failure	Definition	Comments
Virological Failure (preferred method of diagnosis)	Plasma viral load above 1000 copies/mL based on 2 consecutive viral loads taken at least 3 months apart, with stepped-up adherence support after the first viral load test and 3 consecutive months of good adherence support	An individual must be taking ART for at least 6 months before it can be determined that a regimen has failed Assessment of VL results should be carried out by a multidisciplinary team to give this final diagnosis
Immunological Failure	Younger than 5 years Persistent CD4 counts below 200 cells/mm3 or <10% 5–10 years Persistent CD4 counts below 100 cells/mm3 10 -19years CD4 count at or below 250 cells/mm3 following clinical failure, or persistent CD4 counts below 100 cells/ mm^3	These immunological criteria have low sensitivity and positive predictive value for identifying individuals with virological failure Exclude concomitant or recent infection to cause a transient decline in the CD4 cell count
Clinical Failure	Children (less than 10 years) New or recurrent clinical event indicating advanced or severe immune deficiency (WHO clinical stage 3 and 4 clinical conditions with exception of TB) after 6 months of effective treatment. Adolescents 10-19years New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 3 and 4 conditions except for TB) after 6 months of effective treatment	The new clinical condition must be differentiated from immune reconstitution inflammatory syndrome occurring after initiating ART For adolescents, certain WHO clinical stage 3 conditions (pulmonary TB and severe bacterial infections) may also indicate treatment failure These clinical criteria have low sensitivity and positive predictive value for identifying individuals with virological failure

How to Prevent and Manage Treatment Failure

If causes of failure remain unaddressed, ART resistance will eventually develop. Maximize adherence to retain children and adolescents on first-line treatment regimen.

A careful and systematic assessment, involving facility/regional multidisciplinary teams (or the Baylor clinical team through the Baylor HIV/TB Hotline) is required to evaluate the causes of treatment failure in a child or adolescent and to determine the appropriate management strategy to preserve the efficacy of first-line therapy in children.

Table 9.13 Prevention and Management of Treatment Failure in Children and Adolescents

Component	Interventions
Clinical Component	• Assure of correct weight-band-based doses of treatment at every visit • Assure adequate timing of dosing; children should not take the medicines to school unless adequate support is provided by a reliable teacher/other school staff • Monitor drug interactions • Inquire about how well the child is tolerating their medication • Identify previous ARV exposure (PMTCT and past treatments) • Identify suboptimal adherence and adherence barriers • Routine monitoring of VL • Encourage alignment of ART dosing within the family and employ DOTS when indicated
Psychosocial Component in Children, Adolescents and Caregivers	• Conduct ART readiness assessments ART baseline and at clinical visits • Identify psychological/mental conditions: depression, drug fatigue, substance abuse including alcoholism, self-stigma in the child and caregiver, and refer appropriately (*See Annex 0* for the PHQ-9 screening tool for depression) • Identify other structural care and adherence barriers (e.g., long travel times, school, parental refusal of consent, home conflicts) • Address HIV status disclosure with age-appropriate messages • Refer to teen clubs or children support groups where available • Establish a close, trustworthy and transparent relationship with the child/adolescent • Empower and educate the child/adolescent to be part of their treatment plan • Address gender-based violence and reproductive and sexual health needs

Barriers to adherence

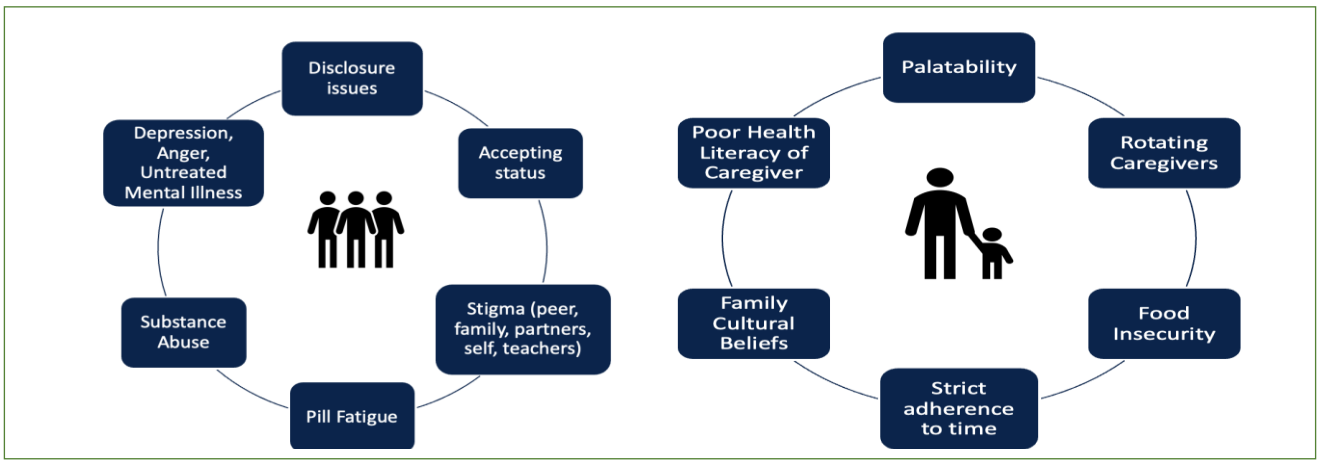


Figure 9.6 Barriers to Adherence for Children and Adolescents

Steps for Management of Treatment Failure in Children

All providers should consider the steps in *Figure 9.7* below when managing treatment failure in children/adolescents.

Before switching regimens:

Take a thorough ARV history to help determine the appropriate second-line regimen. Optimize adherence. Ensure client and caregiver have completed SUAC. Treat all inter-current opportunistic infections until they have resolved

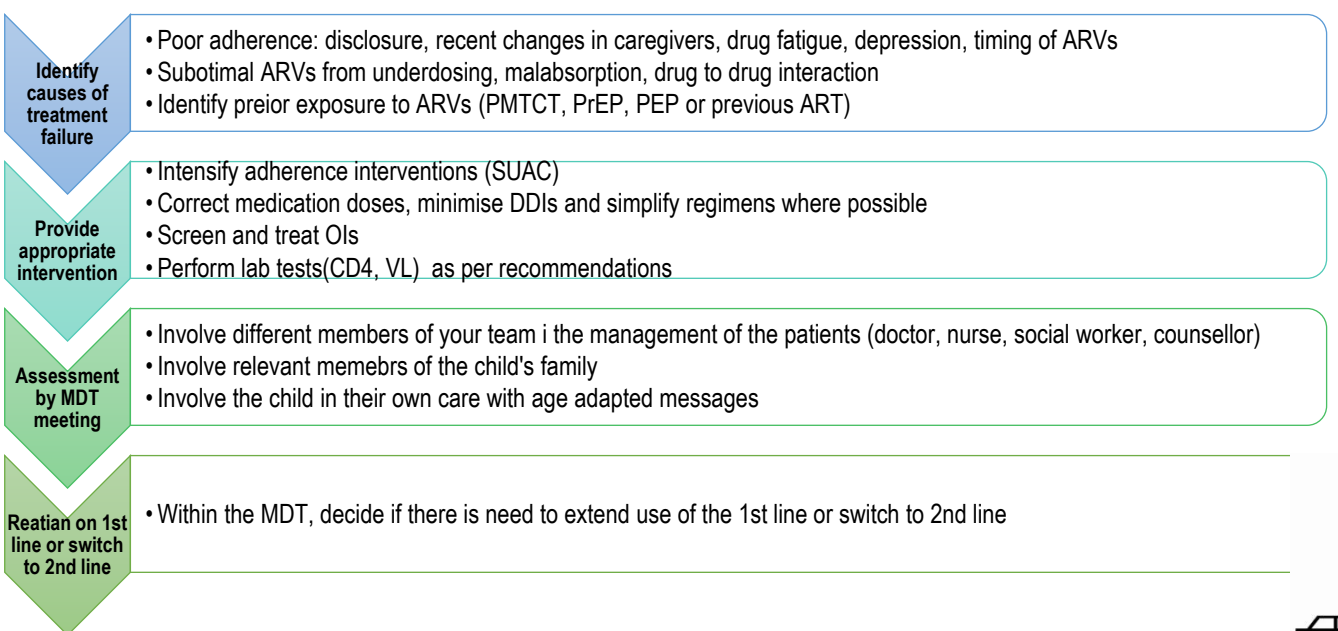


Figure 9.7 Steps for Management of Treatment Failure

Evaluation and support for children, and adolescents with treatment failure

For all children and adolescents, it is important to identify or re-engage caregivers/peers to support adherence. To ensure comprehensive social support children and adolescents should also be referred for additional community psychosocial support including Peer-Peer support and OVC/DREAMS programs.

Table 9.14 Evaluation and intervention for children and adolescents with treatment failure.

Assessment	Recommended evaluation	Proposed intervention
ART History	• Evaluate all previously used ART regimens including any previous PMTCT, PrEP and PEP exposures • Identify potential for past resistance	• Assess if the risk is still present
Comorbidities & malnutrition	• Assess and identify co-morbidities & malnutrition • Evaluate for ART side effects • Evaluate for drug-drug interactions	• Refer and /or treat co-morbidity & malnutrition • Mange possible ADRs • Minimize drug-drug interactions
Adherence to visits	• Assess appointments for refill visits from File/ electronic medical records (CMIS /APMR) • Assess electronic pharmacy records through LMIS	• Establish reminders for appointments • Document correct regimen in CMIS/APMR where applicable
Adherence to medication	• Interview patient/ caregiver/treatment supporter • Who gives the medications? • Who observes the medications? • When medications are given/ taken? • Timing of taking ARVs/ presence of reminders • Where medications are kept and administered • Assess potential sub-optimal ARV levels from under-dosing using therapeutic drug monitoring • Explore barriers to adherence	• Establish daily routines/ reminders for medication intake • Simplify the regimen where feasible to reduce the pill burden • Correct medication doses • Explore opportunities for home-based or facility-based directly observed therapy • Reconsider DSD/MMD where applicable
Psychosocial support	• Disclosure of HIV status • Recent changes in caregivers • Drug fatigue • Depression and substance abuse • Other mental health issues e.g., anxiety, depression etc	• Assisted age-appropriate disclosure • Refer to peer support, and social worker/ mental health nurses • Consider referral to a psychologist
Clinical MDT	• Involve different members of your team in the management of the child (expert client, nurse, doctor, social worker, psychologist, community health worker) • Involve relevant members of the child's family • Involve the child in his/her care with age-adapted message • Maintain/Optimize regimen to appropriate regimens line (1st, 2nd or 3rd)	

9.12.1 Second-Line ART for Children and Adolescents

When to Switch

Second-line ART in infants and children is more complex to manage. These children should undergo thorough clinical and psychosocial assessment to rule out inter-current illness or non-adherence as the reason for a detectable viral load.

Children and adolescents should be considered for second-line ART after 2 consecutive unsuppressed VL tests (above 1000 copies/mL) in a row are recorded in line with the National Viral load Algorithm. After the first elevated VL, the client and caregiver should receive a minimum of three SUAC sessions, each session being 1 month apart, to determine that adherence is not a contributing factor to the child's unsuppressed VL. VL testing should be repeated after at least 3 months after the regimen switch.

If the client is on an NNRTI-based regimen and has one detectable viral load (>1000), no need to repeat VL after 3 months, immediately change to optimized second-line treatment and begin SUAC.

See section 7.11 for details on stepped-up adherence counselling.

Switch to a second-line regimen when issues of adherence and treatment support have been addressed by a multidisciplinary team. Avoid delaying regimen switch while pursuing perfect adherence which may have worse outcomes. Disclosure should not be a prerequisite for starting second-line unless it is a primary barrier to adherence.

If CD4 < 25 % in children under 5 years of age OR < 100 cells/mm^3 in children over 5 years of age: Fast-track evaluation by MDT or consultation through Baylor HIV/TB hotline

Set up an Adherence Committee (MDT: doctor, nurse, expert client, social worker, etc.) at your facility for challenging cases and for internal referrals where clients with complex problems can be discussed and an action plan formulated.
Call the Baylor HIV/TB Hotline with any questions on Paediatric HIV/TB investigations, care and treatment

Table 9.15 Recommended Second-Line Regimens for Children and Adolescents

Weight	Current 1st Line	Preferred 2nd Line	Alternative 2nd Line
3-29.9 Kg	ABC + 3TC + DTG	Regimen guided by genotype	AZT + 3TC + [a]PI
	AZT + 3TC + DTG		ABC + 3TC + [a]PI
	ABC + 3TC + EFV	AZT + 3TC + DTG	ABC + 3TC + [a]PI
	AZT + 3TC + EFV	ABC + 3TC + DTG	ABC + 3TC + [a]PI
	ABC + 3TC + LPV/r	AZT + 3TC + DTG	Consult National HIVDR Expert Clinical Committee and/or Baylor Hotline.
	AZT + 3TC + LPV/r	ABC + 3TC + DTG	
≥30 kg	TDF + 3TC + DTG	Regimen guided by genotype results	TDF + 3TC + [a]PI AZT + 3TC + [a]PI
	ABC + 3TC + DTG		AZT + 3TC + [a]PI
	AZT + 3TC + DTG		TDF + 3TC + [a]PI
	TDF + 3TC + EFV	TDF + 3TC + DTG	AZT + 3TC + [a]PI ABC + 3TC + [a]PI
	AZT + 3TC + EFV		TDF + 3TC + [a]PI
	ABC + 3TC + EFV	AZT + 3TC + DTG	AZT + 3TC + [a]PI

[a]PI should be chosen based on availability and convenience:

- DRV can only be used for second line in cases of confirmed INSTI resistance on genotype. It must always be co-administered with ritonavir. It can only be given to children ≥3 years of age and 10 kg. Please see Annex 11.17 for DRV/r dosing which depends on prior PI exposure. DRV/r CANNOT be co-administered with rifampicin containing TB treatment. DRV should be used with caution in patients with known sulfonamide allergies.
- ATV/r can only be given if ≥40 kg.
- LPV/r is given twice daily for all clients >4 weeks and 3kg.

HIV resistance testing should be done for all clients failing on a DTG-based ART regimen. Only switch to 2nd line if the resistance test shows DTG resistance and the 2nd line regimen should be a boosted PI + 2 NRTIs determined by the genotype results

Use of ATV/r 300/100 mg in Second-line

TB treatment

ATV/r should NOT be used with clients on rifampicin. Adolescent clients with TB/HIV coinfection should use super boosted LPV/r or double-dose LPV/r (LPV/r 800 mg/200 mg twice daily). *See Chapter 7, Section 7.12.1*

Clinicians can substitute clients currently on an LPV/r-containing second-line regimen to an ATV/r containing regimen for all children or adolescents >40 kg

Pre-existing conditions: hepatitis and jaundice

ATV/r should NOT be used in clients with active hepatitis. Those with pre-existing jaundice and/or any pre-existing hyperbilirubinemia may be worsened by ATV/r which can also lead to neurological complications. LPV/r can be used with caution

Drug interactions

As with many protease inhibitor drugs (including LPV/r), caution must be used when prescribing ATV/r with several medications, including clarithromycin, hormonal contraceptives, antacids, inhaled steroids, proton pump inhibitors, H_2 blockers, and lipid-lowering agents. Avoid combination with etravirine, NVP (see Annex 11.2 for information on drugs that should not be used with selected ARV regimen

9.12.2 Third-Line ART for Children and Adolescents

Evaluation for third-line ART is currently supported by the Eswatini National HIVDR Clinical Expert Committee. The recommendation is to contact the Baylor clinicians in Mbabane, Manzini or Hlatikhulu for support should you have questions regarding management of paediatric or adolescent clients failing PI based ART regimens. It is highly recommended to refer or to call the Baylor HIV/TB Hotline or your clinical mentor to consult on each individual case.

Clients who fail second-line ART have limited ART options. Agents used to construct a third-line regimen are often more expensive, and will have increased pill burden and more side effects. These factors will exacerbate pre-existing poor adherence.

Before considering third-line therapy, adherence interventions should be intensified (e.g., stepped-up adherence counselling sessions), barriers to adherence addressed and then adherence assessed to be acceptable. If there is still no viral suppression, the client has been on second-line treatment for >2 years (or was on Anti TB treatment during second-line treatment), then a resistance test (genotypic/phenotypic) should be performed. Currently, genotyping is done for clients failing PI or DTG-based regimens with a viral load above 1000copies/ml and evidence of improved adherence. The resistance test is expensive and the client must be receiving the failing ART at the time, as wild-type HIV is more fit and outgrows the resistant mutant population, which therefore cannot be detected within some weeks after cessation of ART. If a client needs a genotype, please e-mail a request form to snapthirdline@mohcoag.org.

The decisions regarding treatment choices in third-line therapy are complex and need to be guided by resistance patterns found in resistance testing. It is essential that an expert, in conjunction with a full ART history, interprets resistance tests. Once a genotypic resistance test has been performed, the results are used to determine which combination of ARVs is most appropriate for a third-line regimen for the specific client. Each client on a third-line regimen requires individualized treatment based on HIV genotype results.

Table 9.16 Potential Third-Line Regimens for Children and Adolescents

Age	Potential Third-Line Regimens
Children (0-10 years)	DTG + 2 NRTIs
	DRV/r + 2 NRTIs
	DRV/r + DTG ± 1-2 NRTIs
Adolescents(10-19 years)	DRV/r + DTG ± 1-2 NRTIs
	DRV/r + 2 NRTIs ± NNRTI
	Optimize regimen using genotype profile

DRV/r should not be given to children below 3years of age

9.13 Special Considerations for Adolescents

Adolescence is a period of transitioning from childhood to adulthood and covers ages 10 to 19 years. Many physical, mental and emotional changes occur during these years that could potentially impact chronic conditions like HIV and ART treatment, regardless of whether the infection was acquired at birth or later in life.

Due to normal developmental processes, adolescence can be an especially challenging phase in life for those with chronic health conditions. Adolescence can be a particularly difficult time for adherence to ART and the risk for treatment failure is greatest among this age group.

Adolescents most commonly experience and need support to address:

1. Denial and fear related to their HIV diagnosis
2. Grief over the death of a sibling, parent or caregiver
3. Misunderstandings related to their status and health needs
4. Self-stigma
5. Lack of belief in the efficacy of ARV
6. Treatment fatigue
7. Distrust of family, practitioners and the health care system
8. Low self-esteem and chaotic, unstructured lifestyles
9. Limited family and social support
10. Long travel times to the clinic
11. Conflicts with school schedules and work Substance use and abuse
12. Substance use and abuse
13. Peer pressure
14. Depression (*PHQ-9 See Annex 0 a-c*)

Health Care Consent and Assent for Children and Adolescents

Anyone 12 years or older can give informed consent for medical care such as HIV testing services (HTS), PrEP, PEP, family planning, or medical male circumcision according to the 2012 Swaziland Child Welfare Act, but not for HIV treatment.

Children younger than 12 years can provide informed consent for treatment if they are considered an emancipated minor or mature adult (i.e., they are the head of a household, a parent, or if pregnant, they are being treated for a sexually transmitted infection (STI), are accessing family planning services, and/or are sexually active).

Although children and young adolescents less than 12 years may not give informed consent for HIV testing, their agreement should be sought via age-appropriate counselling.

Consent for health services, including HIV care, should be given by parents, guardians, caregivers, health care workers or social workers in the best interest of the child. See consent considerations in Chapter 3.

Disclosure of HIV status to the paediatric client

Disclosure is not a one-time event but a process that allows for clients to receive truthful information regarding their health at a developmentally and age-appropriate level, and that over time will include specific relevant details such as the name of the condition (HIV/AIDS), how it is transmitted, what is needed to avert progression, the role of ART, the importance of adherence, safe sex and reproductive choices.

Communication promotes honesty and trust within the adolescent-adult-family-clinical team relationships and facilitates dialogues about chronic treatment and positive prevention.

Benefits include improved self-esteem, a sense of autonomy and empowerment, and enhanced psychological adjustment.

The role of a healthcare worker in disclosure is to guide the family members and the child in the process, addressing the fears and barriers and ensuring protection and support.

Partial disclosure without naming HIV should begin early and be age and developmentally-appropriate. Children must be fully disclosed by age of 10 years.

In general, all adolescents should be linked to a regular ART support group (e.g., peer teen clubs) where issues relevant to their age group

are discussed and support is given. Home visits can be provided to ensure that the client adheres well to ART and to address challenges with insight into the home environment.

If the adolescent's adherence is repeatedly poor, treatment supporters, caregivers and supportive family members who are aware of the adolescent's HIV status can be called on for help.

When disclosing or counselling an adolescent, consider the client's social, family and medical histories, taking into account their age and psychosocial maturity, the mode of HIV transmission, prior knowledge of their infection, and past experiences.

Encourage adolescent clients to disclose their HIV status to trusted family members, peers or even teachers/mentor

Pregnancy Prevention in Adolescents Living with HIV

As children transition to adolescents and sexual maturation, sexual and reproductive health needs must be addressed. It is the role of the HCW to provide young people with the tools they need to live safe and productive life. All young people living with HIV should receive non-judgmental and confidential counselling from HCW regarding:

- Typical sexual Development/Maturation
- Sexual abuse including gender-based violence
- Sexual debut
- Information about PrEP for partners
- Contraception for adolescent boys and girls should be offered BEFORE and AFTER sexual debut in a safe, non-judgmental environment and include counselling on Emergency Contraception

WHO Recommends Long-Acting Reversible Contraception (IUD, Implants) as first choice for adolescent girls and young women wishing to prevent unwanted pregnancies. They are the most effective, safe and allow a swift return to fertility when a pregnancy is desired.

ALWAYS Counsel on the importance of dual protection for ALL methods of contraception.

Figure 9.8 Contraceptive Options available to all Adolescents in Eswatini

9.14 Transitioning to Adolescents to Adult Care

There are parallels between the maturation of adolescents into adults and the transition from paediatric to adult HIV programs.

As adolescents living with HIV grow into adulthood, it becomes necessary for them to transfer to adult care settings and take responsibility for their health alongside HIV management. The adolescent population comprises a mixed group of:

1) perinatally infected adolescents
2) horizontally infected adolescents.

Transition is the purposeful, planned movement of adolescents and young adults with chronic medical conditions from child-centred to adult-oriented care systems. Although the transition from adolescents to adulthood care occurs typically between 18 and 24 years of age, early preparation for transition is continuous from ages 10-19 years old supported by a multi-disciplinary team. Adolescents living with HIV may face challenges in their transition to adult care and learning to independently manage their care. These challenges affect both health care workers in paediatric and adult clinics as well as adolescents and their caregivers.

Adolescents living with HIV face unique challenges during the transition process to adult care, including:

- Stigma and the need to disclose their HIV status to friends, family and adult care providers.
- Neurocognitive impairments and mental health problems associated with HIV.
- Recognition that they face the risk of transmitting HIV to future sexual partners and possibly children.

Unsuccessful transition can result in:

- Poor adherence
- Viral rebound
- Teen pregnancies
- Higher rates of loss to follow-up in adolescents (lower retention in care and detectable viral load)
- Youth developing weaker immune systems
- Increased morbidity and mortality
- The possibility of youth developing drug resistance.

Goal of transition

The goal of the transition is to ensure the provision of uninterrupted, coordinated, developmentally and age-appropriate and comprehensive care before, during and after the transition.

Key components of support for adolescents living with HIV during the transition process

- Provision of adolescent-friendly services.
- Supporting self-management of medication and appointments.
- Understanding the goal of ART and a clear understanding of VL results
- Identification of developmental milestones and readiness for transition.
- Addressing issues of bullying, delinquency, teen pregnancies, substance abuse and obesity
- Provision of psychosocial support to enable the adolescent to cope with the typical changes, feelings and worries of adolescence (which may include relationships, employment and education).
- Supporting disclosure to enable sharing of their HIV status to other healthcare workers, peers and family.
- Encouraging them to become teen mentors
- The child must know that transition is inevitable.

Stakeholders in the transition of care

- Transition processes require active participation by a range of stakeholders, including the following:
- The child, adolescent, or youth client
- Caregivers (parents, guardians) and/or treatment supporters (partners, peers, etc.)
- Health care providers (clinicians, nurses, etc.)
- Other providers (counsellors, case managers, psychologists, pharmacists, etc.)
- Community health workers, school nurses or other school staff/advocates

The role of the health care worker in transitioning adolescents to adult care

The healthcare worker should help the adolescents set and achieve goals for independence and self-management of care as a way of recognizing their increasing maturation, capacity to make choices, and independence. A summary of general principles for effective transitioning is outlined in **Error! Reference source not found.** and a list of skills an adolescent should have before transitioning to adult care and a checklist for successful transition are outlined in

*Table 9.*17 Checklist for Successful Transitions to Adult Care

Paediatric (2-14yrs)	10- 24 yrs	15+ yrs
• Dependent on caregiver for care and ART adherence • Start and completion of disclosure to the child • Psychosocial support via art and games therapy • Self-care with a focus on hygiene, basic nutrition, and puberty	• Shift in responsibility, with client more accountable for adherence • Disclosure of HIV status • Participation in support/peer groups and clubs • Knowldege about HIV in relation to life and relationships • Establishment of own treatment goals and plans • Preparation for adult care and transition	• Completion of transition to independent clinical and self-care • Service options: young adult clubs, male adherence clubs, prevention of perinatal HIV transmission, mother-baby care, family clinics, and community antiretroviral therapy groups • Client-led psychosocial support: maintaining supportive networks via online groups and discussions sharing personal successes, job opportunities, HIV events, and more

Figure 9.9 Major components of different stages of transition

Benefits of transitioning

As children grow into adolescents, and adolescents grow into adults, their physical and emotional needs change. Health care workers must support children and adolescents as they grow into new roles, becoming increasingly able to manage their own life and health. —

Benefits of transitioning include:

- Promoting a positive self-image
- Promoting self-reliance
- Promoting a sense of competence
- Allowing for meaningful independent living
- Supporting social and emotional development
- Supporting long-term planning and working to achieve life goals
- Broadening systems of interpersonal and social support

Transition steps

Transition to adulthood occurs over years while the HCW, child or adolescent, and the caregiver work together to build the patient's knowledge and skills to manage their care in preparation for adult services. The transition should only occur when all parties have agreed that the child or adolescent has met the required criteria and is also mentally prepared (see **Error! Reference source not found.**)

Figure 9.10 Transition Steps

General Principles for Effective Transitioning

- Individualize the approach used (including identification of potential barriers, assessment of readiness to transition, flexible schedules
- for school children and adolescents/working adolescents).
- Identify adult care providers who are willing to care for adolescents and young adults.
- Begin the transition process early and ensure communication between the paediatric/adolescent and adult care providers before and
- during the transition.
- Develop and follow an individualized transition plan for the client in the paediatric/adolescent clinic; develop and follow an orientation plan in the adult clinic.

Transition plans should be flexible to meet the adolescent's needs:

- Use a multidisciplinary transition team, which should include peers who are in the process of transitioning or who have transitioned
- successfully.
- Address comprehensive care needs as part of the transition, including medical, psychosocial and financial aspects of transitioning.
- Allow adolescents to express their opinions.
- Educate HIV care teams and staff about transitioning.

Table 9.17 Checklist for Successful Transitions to Adult Care

Skills and Adolescent Should Have Before Transitioning to Adult Care	Checklist for Successful Transition
• Know when to seek medical care for symptoms or emergencies. • Identify symptoms and describe them. • Make, cancel and reschedule appointments. • Arrive at appointments on time. • Call ahead for urgent visits. • Can name/describe his/her medications and the doses • Request prescription refills correctly and allow enough time for refills to be processed before medications run out. • Knows when his/her last viral load test was done • Knows results of his/her last viral load test	• The client has accepted their chronic illness and is oriented toward future goals and hopes, including long-term survival. • The client has learned the skills needed to negotiate appointments and multiple providers in an adult practice setting. • The client has achieved personal and medical independence and can assume responsibility for his/her treatment and participate in decision-making. • The referring provider is familiar with the new provider and practice setting, and direct

• Understands what the viral load test results mean for his/her treatment • Establish a good working relationship with healthcare workers at the paediatric/adolescent site, which will enable the adolescent to work effectively with the healthcare worker at the adult site. • Negotiate multiple providers and subspecialty visits (for other services). • Condom use skills • Contraception access and usage • Readiness to join adult support groups	communication about an individualized plan for the client has taken place. • The client is receiving psychosocial support (peer, family, facility) and entitlements are in place (housing, home care, transportation). • Life skills have been addressed (e.g., educational goals, job training, parenting). • The client receives uninterrupted comprehensive medical care. • Sexual reproductive health and family planning. • Consistent and correct condom use.

Special consideration should be given to adolescents due to transition who have:

- Disclosed adherence challenges
- Unsuppressed viral load when due to transition
- Cognitive or developmental delays, all of which would require more intensive treatment support and/or caregiver roles.

Each plan should reflect on the following:

- Successes in HIV treatment so far
- Life and treatment goals in adulthood
- Anticipated challenges or barriers to be overcome
- Supportive people and places that can help this patient on their journey
- Steps to achieve goals
- Timeline for steps

9.15 Promoting Continuity of Care with Children and Adolescents on ART

To reach the goal of ART, which is to achieve undetectable viral load for as long as possible, it is very important to address challenges around adherence and retention that affect long-term health outcomes as children move from infancy, through childhood and adolescence, and into adulthood. Client and caregiver preparation for chronic care and ongoing adherence support, early age-appropriate disclosure and VL literacy, peer and psychosocial support, provision of integrated child and adolescent-friendly services and differentiated service delivery (including the successful transition to adult care) are critical components of effective long-term care for children and adolescents.

Adherence

Adherence requires the client and caregiver's active participation to establish treatment goals and the medical regimen.

For ART services, adherence includes both adherence to appointments and adherence to the prescribed regimen.
Adherence to ART means consistent action: taking the right medicine, at the right time, in the right dose, in the right way, and at the right frequency—consistently. This is known as the "five R's" (5 rights) of adherence. Adherence of ≥95% and ≤105% is accepted as optimal adherence. Levels of adherence below 95% and above 105% are considered suboptimal and could lead to a poor response to treatment.

Various factors influence adherence to ART which could include the drug regimen, patient and family factors, and the child/adolescent-provider relationship. Adherence to ART is an informed choice, so children and adolescents should participate in making the adherence plan. Though the physical role of looking after a child diminishes as the child grows older, caregivers need to be reminded that they remain critical in the child's care at every age.

9.16 Differentiated Service Delivery for children and adolescents

CALHIV have a lifetime of ART ahead of them. Implementation and support for differentiated ART delivery are strengthened by strong engagement with caregivers, peer providers and community platforms. For school-going stable children (5-9 years) and adolescents (10-19years), scheduling clinical visits during school holidays, particularly for those in boarding schools, can support continuity in care.

Multiple months dispensing (MMD):

After the age of two years, less intensive clinical follow-up is required for stable CALHIV and ART refills and clinical consultations can be extended to 3-monthly for younger children (ages 2-5 years) and 6 months for ≥5 years and adolescents. Refer to *Table 5.6*

Differentiated care models:

Differentiated ARV service delivery (including teen clubs, family-centred care models, and fast track, empowers children and adolescents to actively participate in their care, reduces client-related costs of accessing care, and enables client-centred access to services. See Section 5.7 for more information on DSD

Enrol children and adolescents living with HIV in these models whenever possible.

All facilities must have Teen Clubs.
Facilities should have dedicated days for children especially those that are failing treatment with a multidisciplinary team to review these failing clients whenever possible.

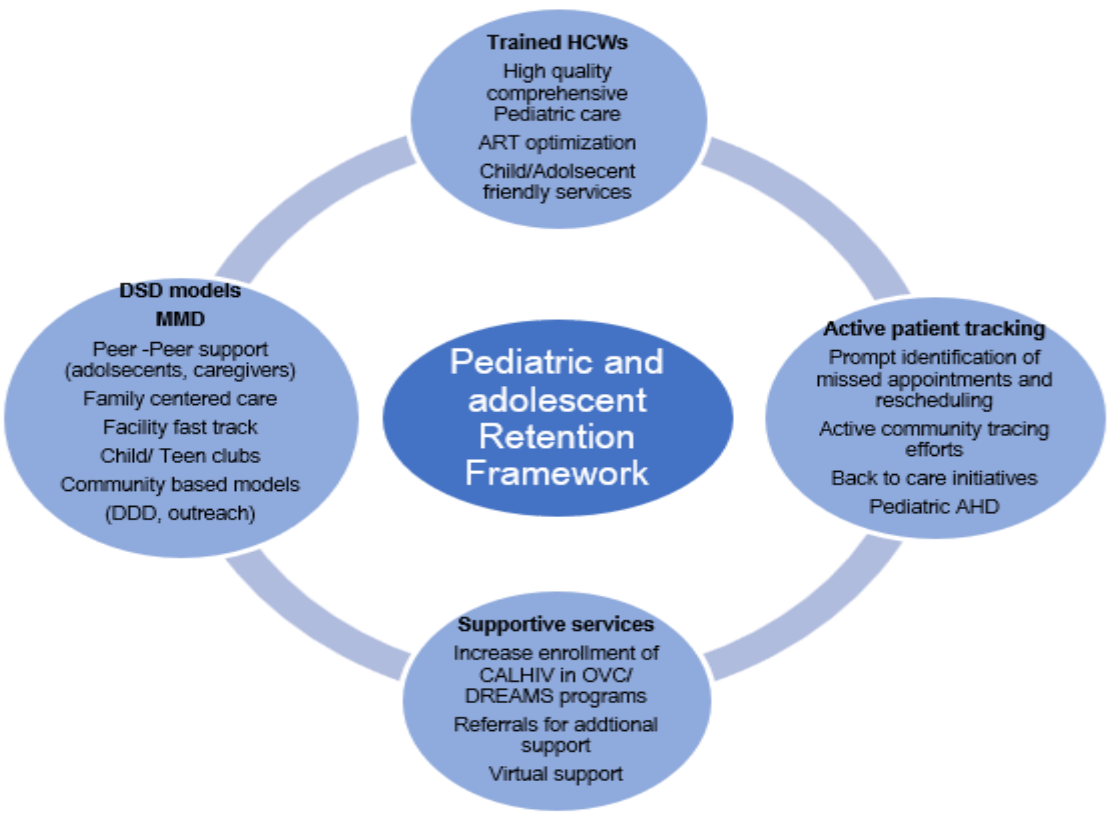


*Figure 9.11 Improving CALHIV continuity in care requires a mix of preventive and responsive strategies**

**Adapted from "Leveraging decentralized drug distribution models to meet the HIV treatment needs of children and adolescents living with HIV". Decentralized Drug Distribution (DDD) Learning Collaborative May 2021*

9.17 Elements of a Well-Functioning Paediatric HIV Program

Table 9.18 Elements of a Well-Functioning Paediatric HIV Program

Program Area	Specific Elements
Paediatric testing	• Dried blood spot kits, HTS kits • Disclosure materials
Care and treatment	• Paediatric ARV formulations • NVP clips and syringes • Pill cutters/pill boxes • Dosing charts • Adolescent services—family planning, cervical cancer screening • Access to clinical psychologist

Table 9.18 Elements of a Well-Functioning Paediatric HIV Program (continued from the previous page)

Program Area	Specific Elements
Client education	• Paediatric ARV formulations • Information, education and communication materials on paediatric ART • Disclosure counselling materials • U-report • Income generating skills development
Job aids	• WHO clinical stages posters • Neurological developmental stages • Dried blood spot posters • ART and ARV dosing guidelines • Stepped-up adherence counselling
Phlebotomy	• Blood collection tubes and Butterfly needles for phlebotomy • VL required materials (For plasma and DBS VL)
Differentiated Service Delivery	• Teen Clubs, paediatric-specific days, fast track, peer support, mother-baby clubs, family-centred models
Materials for teen clubs and other differentiated models of paediatric care	• HIV and sexual and reproductive health curriculum for teen clubs • Community-Centred Models of ART Delivery (CommART) Guidelines and SOPs • Tools and job aids • Condom demonstrations and distribution
Post-exposure prophylaxis paediatric materials	• Counselling tools • Post-exposure prophylaxis drugs package for partners • PrEP as per the need for partners

Marketing materials on our telemedicine options	• DBS hotline, Baylor HIV/TB Hotline (7848-5571), U-Report, Paediatric specific days

Hepatitis B screening in CALHIV

HbsAg screening should be done to

- All children and adolescents newly diagnosed HIV positive
- Adolescents with a history of exposure or at risk of hepatitis B virus (HBV) infection
- Children and adolescents with clinical signs and symptoms, or laboratory markers indicating chronic HBV
- Infants and children of close household contacts of clients with HBV infection

See Section 7.7.5 for more information on viral hepatitis

The following should be done at baseline and each clinical visit

- Growth and development of educational achievement and behaviour
- Adherence and correct dosing, Side effects/toxicity
- Opportunistic infections including TB
- Social history/ psychosocial factors including assessing family planning needs

9.18 Summary of Monitoring and Clinical Service Timelines for Paediatrics and Adolescents

Table 9.19 Summary of Monitoring and Clinical Service Timelines for Children and Adolescents

	Baseline	2 weeks	1 month	3 months	6 months	9 months	12 months	Thereafter
CD4 count or %	X				X			Every 6 months if detectable VL or when clinically recommended
Viral load	None				X		X	Every 6 months for ages 0–19 years
Haemoglobin	X	If clinically indicated (e.g., If on AZT, regimen, do Hb every 6 months)						
AST/ALT	As clinically indicated							As clinically indicated
Creatinine	TDF only				TDF only		TDF only	Every 6 months if on TDF
TB-LAM (TB symptoms present)	For children and adolescents with a CD4 count ≤ 100 cells/mm^3 or less than 25%.							For children and adolescents with a CD4 count ≤ 100 cells/mm^3 or less than 25%.
CrAg screening	For children (older than 10 years) and adolescents with a CD4 count ≤100cells/mm^3 or less than 25%.							Rescreen every child older than 10 years with CD4 count ≤100cells/mm^3 or less than 25% regardless of frequency

10 MANAGEMENT OF NON-COMMUNICABLE

10.1 Screening for Non-communicable Diseases

All HIV-positive clients should be screened regularly for non-communicable diseases and managed accordingly.

The prevalence of non-communicable diseases (NCDs) has been increasing as people living with HIV (PLHIV) are living longer due to ART. An increase in NCD prevalence is also seen in HIV-negative persons as they advance in age.

Despite the lifesaving role of antiretroviral therapy (ART), some antiretroviral (ARVs) such as PIs and INSTIs are associated with a propensity to develop metabolic complications. In addition, to the chronic immune activation lifestyle factors (tobacco smoking, obesity, physical inactivity, and unhealthy diet) and ageing, there is an ongoing interaction of NCDs with HIV infection. Consequently, all clients infected with HIV and/or tuberculosis (TB) should be screened for concomitant NCDs. The chronicity of both conditions provides the opportunity to assess, monitor and manage both conditions through the integration of clinical services.

10.2 Care and Management of Hypertension and HIV for patients 18 years and older

Hypertension is defined by the WHO as systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg on two measurements.

It is good clinical practice to always investigate possible causes of hypertension

Classification of hypertension

Table 10.1 The classification of BP for adults aged 18 years or older has been as follows

	Systolic BP	Diastolic BP
Normal	< 120 mmHg	<80mmHg
Prehypertension	120- 139 mmHg	80 – 89 mmHg
Stage 1	140 – 159 mmHg	90 – 99 mmHg
Stage 2	160 – 179 mmHg	100 – 109 mmHg
Stage 3	>180 mmHg	>110mmHg

Management of Hypertension for Patients 18 years and older

Always stage/grade hypertension according to the patient's presentation. Aim to reach target BP within 3 months. For more details on management, refer to the Eswatini Hypertension Guidelines.

See Table.10.2 Non-pharmacological management below shows high-risk features for patients presenting with an elevated BP

Non-pharmacological management of hypertension

The first step in managing uncomplicated hypertension is lifestyle modification

Table.10.2 Non-pharmacological management

Behaviour	Advice
Physical activity	• Engage in regular physical activity (e.g., aerobics) for at least 30mins/days Daily • Reduce and maintain BMI to 20-25kg/m² • Reduce and maintain waist circumference to <94cm in men and <80cm in females
Tobacco	• Encourage smokers to stop tobacco use and encourage them in their efforts • Encourage non-smokers not to start smoking
Harmful use of alcohol	• Limit alcohol to no more than 30ml of ethanol/day for men and 15ml/day for females and people of lighter weight • Avoid binge drinking (≥5 drinks on a single occasion for men or ≥4 drinks on a single occasion for women, generally within about 2 hours) • Avoid heavy drinking (≥15 drinks per week for men and ≥ 8 drinks or more per week for females)
Diet	• Eat a healthy diet low in saturated fats, Limit fatty meals, • Reduce high-calorie food • Reduce salt intake to not more than 5g of salt per day • Maintain adequate dietary calcium and magnesium for general health • Eat a diet high in fruits and vegetables
Adherence counselling	• Attend regular medical follow-up

When ≥2 of the above lifestyle modifications are maintained, BP is lowered, and cardiovascular disease risk is decreased

Alcohol consumption

There are no safe alcohol drinking limits, as even the drinking limits listed below may cause adverse health outcomes in certain individuals particularly if one consumes alcohol too quickly, if they have other health problems, if they are pregnant and if they are above the age of 65. Consumption of alcohol while pregnant is strongly condemned.

Low-risk drinking limits	Males	Females	1 drink is approximately equivalent to:
Maximum drinks per day	**4***	**3****	• 350ml of beer, • 150ml of wine, or • 50ml of 40% alcohol content - distilled spirits or liquor (e.g., gin, rum, vodka, whiskey).
	AND		
Maximum Drinks per week	14*	7**	

**A male who takes 3drinks on a given day, must not consume more than 11 drinks for the remainder of the week (must not take more than 4drinks on any given day)*

*** A female who consumes 2 drinks on a given day, must not drink more than 5 drinks for the remainder of the week (must not take more than 3 drinks on any given day.*

Pharmacological management of hypertension

If lifestyle modifications are inadequate to achieve the target BP, several drug options are available for treating Hypertension. Specific medications are available for contraindications and comorbidities e.g., heart failure, ischaemic heart disease, chronic kidney disease and diabetes mellitus

If medication is prescribed,

- Explain the difference between medicine for long-term control and medicines for quick relief
- Label and package medication clearly
- Explain the dose and how the medication must be taken
- Explain how to take the medication with the ARVs
- Explain the importance of keeping an adequate supply of medications and the need to take medicines regularly as advised even if there are no symptoms
- Explain the importance of refilling ARVs on the same day as ARVs
- Educate on possible side effects and that they need to be reported and managed

Table 10.3 High-risk features of hypertension

High Risk	Score	Interpretation:
Diabetes	2	Patients with a score of 2 or more points are considered high risk and warrant more aggressive treatment
Renal Failure creatinine ≥ 100 µmol/L (1.1 mg/dL)	2	
Age ≥ 65	1	
BMI ≥25	1	
Smoking	1	

Recommended Drugs to Initiate in Special Cases

Refer to national NCD guidelines

Never combine angiotensin receptor blockers (ARBs) with ACE inhibitors. Use ARBs if clients develop side effects to ACE inhibitors (e.g., cough or angioedema).Do not give ACE inhibitors in clients with hyperkalaemia.

Aspirin

• Prescribe ASA to clients adults 40-70yrs old who are at risk of atherosclerotic cardiovascular disease:

» Clients aged > 40 years

» Clients with cardiovascular risk factors

» Clients with a history of a previous cardiovascular event e.g., type 2 diabetes, diabetic nephropathy, coronary artery disease, transient ischaemic attack or stroke, or peripheral vascular disease

•Before prescribing aspirin, ensure BP is < 160/100mmHg to avoid intracerebral haemorrhage

•Ensure there are no contra-indications to aspirin use

Interactions of HIV and Hypertension

- PLHIV are likely to develop secondary hypertension due to renal vascular and glomerular pathology. This can be caused by the virus itself or after treatment with ARVs like tenofovir disoproxil fumarate (TDF)
- Routine screening of PLHIV enrolled in care for cardiovascular risks and risk reduction counselling on smoking, obesity, high blood pressure, sedentary lifestyle, and unhealthy dietary choices should be the standard of care in ART clinics across the country.

Interactions between antihypertensives and ARVs

- Calcium channel blockers like nifedipine and amlodipine may interact with protease inhibitors, producing increased serum levels of CCBs; hence, dose titration and electrocardiogram (ECG) monitoring are required.
- Several protease inhibitors can cause ECG changes, especially PR interval prolongation
  » Drugs used for hypertension with similar effects (e.g., beta blockers and calcium channel blockers) should be used with caution in clients receiving protease inhibitors,
  » ECG monitoring is recommended.
- Caution should also be exercised when combining diuretics with TDF; renal function could be impaired due to added risk for interstitial nephritis

Table 10.4 Drug Interaction. Source: University of Liverpool, HIV-druginteractions.org

Antihypertensive	TDF/TAF	AZT	3TC	FTC	EFV	NVP	DTG	LPV/r	ATV/r	DRV/r
Hydrochlorothiazide										
Amlodipine					↓	↓		↑	↑	↑
Enalapril										
Bisoprolol*					↓	↓		↑	↑	↑

**WHO Essential Medicines list includes atenolol, metoprolol, and carvedilol as alternatives.*

No interaction

Potential interaction with increased or decreased levels of antihypertensives which may require dose adjustment. Drug levels of ARVs are not affected by calcium channel blockers or beta-blockers and no dose adjustment is required.

Caution should also be exercised when administering B blockers and PIs due to the risk of QT prolongation. ***ECG monitoring is recommended.***

↑ *Increase in antihypertensive drug level* ↓ *Decrease in antihypertensive*

10.3 Care and Management of Diabetes and HIV

Diabetes Mellitus diagnosis:

- Fasting blood glucose >7.0mmol/L (126mg/dL)
- HBA1c ≥6.5%
- A 2hr post-oral glucose tolerance test plasma glucose ≥11.1mmol/L (200mg/dL)

Protease inhibitors (PIs) have a propensity to increase insulin resistance. The older PIs, especially indinavir, may cause diabetes. However, the newer PIs (ATV, DRV and LPV) do not. Frank diabetes is uncommon and rarely requires insulin treatment unless the clients are prone to develop diabetes (e.g., first-degree relative) among PLHIV.

- EFV, AZT and d4T are associated with small increased risks of dysglycaemia.
- Visceral fat gain, which occurs to a similar extent with all ART classes, is associated with insulin resistance. Blood glucose should be assessed serially in these patients as part of a cardiovascular risk assessment.
- Concerning DTG, several studies are ongoing to evaluate any associations with diabetes and metabolic syndrome. So far, no definite association between DTG exposure and insulin resistance has been established.
- In practical terms, clinicians should focus on individualized management of emergent or concomitant diabetes following current national guidelines. Such individualized management should be patient-centred, based on their needs, preferences, and tolerances. Annual symptom screening and baseline fasting blood glucose to rule out pre-diabetes and/or overt diabetes mellitus and routine random blood sugar test is recommended for early diagnosis of diabetes
- Diabetics have a potentially high risk of developing active TB because of the potential synergy of diabetes mellitus and HIV infection to suppress cell-mediated immunity.

Switching ART regimens should only be considered if a patient is on DTG, or LPV/r based regimen and their diabetes is out of control. Switching other ARV medications is of uncertain benefit.

As indicated below, special caution should be used when metformin is co-administered with DTG, as DTG significantly increases metformin concentration, leading to potential increased adverse events

1. If the patient is already on metformin and initiating dolutegravir, monitor closely for metformin adverse effects, glucose levels, and HbA1c, and adjust the dose as necessary.
2. In patients taking dolutegravir who are starting metformin, begin with a low metformin dose (250mg twice daily or 500mg once daily) and titrate up carefully. It is recommended to limit the dose of metformin to 1000 mg daily i.e., 500mg twice daily.

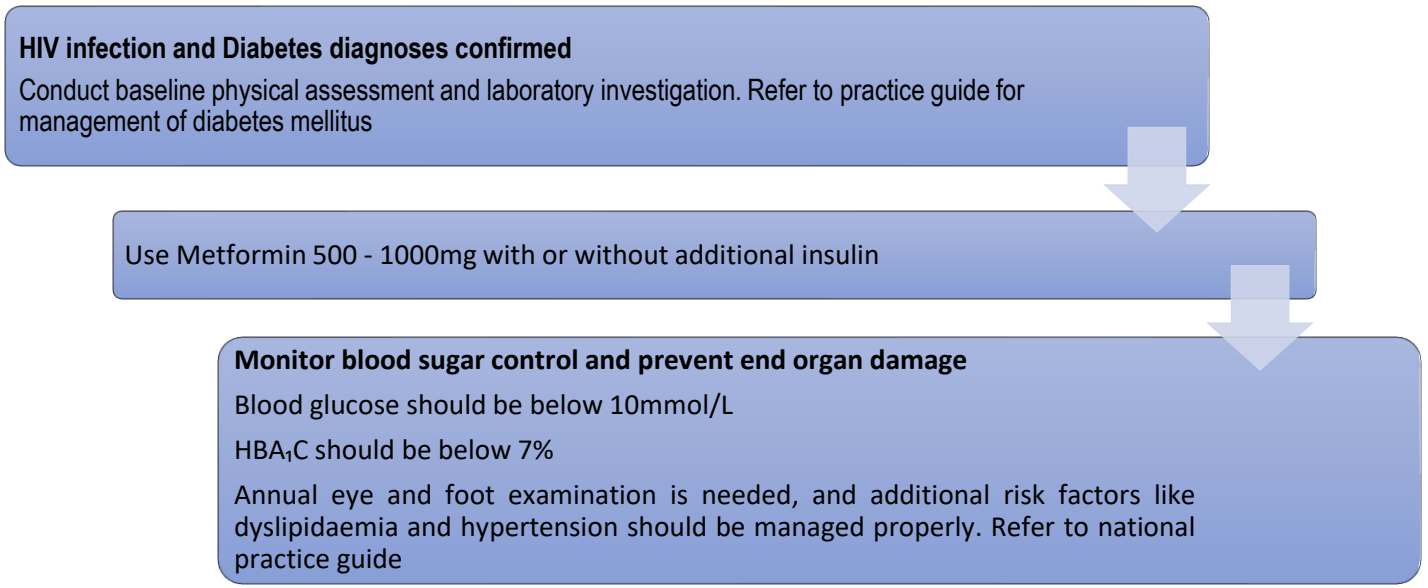


Figure 10.1 Evaluation of clients with Diabetes and HIV infection

Management of diabetes in a client with HIV follows a similar protocol for HIV-negative clients but with the following special considerations:

- Do not use sulphonylureas (e.g., glibenclamide) because of drug interaction with protease inhibitors that may result in profound hypoglycaemia; efavirenz (EFV) may also cause uncertain interactions with sulphonylureas, producing poor control or potentially protracted hypoglycaemia.
- Metformin is safe and effective in controlling blood sugar. It also has the additional advantage of reducing weight.
- Insulin is often required for tight control of blood sugar.

DTG And Diabetes Mellitus In PLHIV

Although an uncommon occurrence, hyperglycaemia is a potential side effect of dolutegravir. Healthcare professionals should be aware of this rare but serious event. Close monitoring of serum plasma glucose should be considered after initiation of an INSTI.

Recommendations when initiating or switching to an INSTI (DTG) regimen

- Health care workers should ensure that baseline fasting blood sugar and/or random blood sugar are measured and recorded for any client starting a DTG regimen or switching to a DTG regimen
- Family history and or current diabetes should be recorded for all clients.
- Health care workers should ensure that blood glucose levels in known clients with diabetes, are controlled (FBS<7mmol / RBS<10mmol)
- Blood glucose levels of newly DTG initiated/switched clients should be checked at baseline and monitored on the 2nd and 6th-week visits and 6 monthly thereafter.
- All clients should be educated on the signs and symptoms of diabetes (polyuria, polydipsia, polyphagia, fatigue and recurrent urinary tract infections etc.)
- Any client presenting with new-onset, random blood glucose levels >17mmmol and signs of diabetic ketoacidosis (DKA) or hyperosmolar hyperglycaemic state (HHS) [*previously hyperosmolar hyperglycaemic nonketotic coma (HHoNC)]* should be treated as emergencies and referred for prompt care.

Table 10.5 Guidance on ART and Diabetes

	Blood sugar values	Guidance for PLHIV newly initiating on/transitioning to DTG or PI-based regimens	Guidance for HIV-positive clients already on DTG or PI-based regimens
Step 1	Pre-diabetes FBS 5.6-6.9 mmol/l RBS7-11 mmol/l	▪ Check Blood Glucose at baseline ▪ Check Blood Glucose every 3 months ▪ Inform clients they may develop diabetes in future ▪ Advise lifestyle modifications ▪ The client can be on DTG or PI-based regimens	▪ Inform clients they may develop hyperglycaemia in future ▪ Advise lifestyle modifications ▪ Check blood glucose every 3 months if on ART regimen with risk of developing hyper-glycaemia ▪ The client can be on DTG or PI-based regimens
Step **2**	Diabetes FBS7-10 mmol/l RBS ≥11.1-17 mmol/l	▪ The client can be on DTG or PI-based regimens provided blood glucose is controlled by adjusting antidiabetic medications ▪ Lifestyle modifications if the person is committed ▪ If not controlled after 1-3 months, go to Step 3 ▪ If FBS >10 mmol/l or RBS >17 go to Step 3	▪ The client can be on DTG or PI-based regimens provided blood glucose is controlled by adjusting antidiabetic medications ▪ Lifestyle modifications if the person is committed ▪ If not controlled after 1-3 months, go to Step 3 ▪ If FBS >10 mmol/l or RBS >17 go to Step 3

Table 10.5 Guidance on ART and Diabetes (continues from the previous page)]

	Blood sugar values	Guidance for PLHIV newly initiating on/transitioning to DTG or PI-based regimens	Guidance for HIV-positive clients already on DTG or PI-based regimens
Step **3**	Failure at Step 2 OR FBS >10 mmol/l RBS >17mmol/l	▪ The client can be on DTG or PI-based regimens provided blood glucose is controlled by adjusting antidiabetic medications ▪ Lifestyle modification ▪ Metformin	▪ The client can be on DTG or PI-based regimens provided blood glucose is controlled by adjusting antidiabetic medications ▪ Lifestyle modification ▪ Metformin
Step **4**	Failure at Step 3 RBS > 17mmol/l	▪ Consider starting the client on or maintaining EFV based regimen then transition to DTG once blood sugar is controlled ▪ Lifestyle modification ▪ Metformin + Sulphonylurea	▪ Consider substituting ARV that could contribute to elevated blood glucose ▪ Lifestyle modification ▪ Metformin + Sulphonylurea
Step **5**	Failure at Step 4 RBS > 17mmol/l	▪ Consider starting the client on or maintaining EFV based regimen then transition to DTG once blood sugar is controlled ▪ Consider insulin ▪ Follow-up at hospital	▪ Consider substituting ARV that could contribute to elevated blood glucose ▪ Consider insulin ▪ Follow-up at hospital

10.4 Diabetes/Hypertension coinfection

The target blood pressure in diabetic patients with and without HIV is ≤130/80mmHg. It is ≤140/90mmHg in non-diabetic individuals. Low-dose thiazides (12.5 mg hydrochlorothiazide or equivalent) or ACE inhibitors are recommended as first-line treatment for hypertension in diabetic patients. They can be combined.

Beta blockers are not recommended for initial management of hypertension in diabetic patients but can be used if thiazides or ACE inhibitors are unavailable or contraindicated.

Who needs routine consultation with or referral to an experienced provider?

Consultation with or referral to an experienced provider is recommended in the following circumstances:

- FBS >14 mmol/l despite maximal doses of metformin and sulfonylurea
- Individuals with newly diagnosed diabetes and urine ketones 2+
- Severe infection and/or foot ulcers
- Recent deterioration in vision
- Gestational diabetes
- Blood pressure ≥130/80 mmHg despite treatment with 2 blood pressure-lowering agents

10.5 Care and Management of Dyslipidaemia and HIV

- HIV infection, indirectly through the effect of ART, causes an increase in low-density lipoprotein and triglyceride; thus, doubling the risk of coronary artery disease when compared with HIV-negative clients.
- ART also increases blood pressure and insulin resistance, contributing to the occurrence of coronary artery disease. These effects are more pronounced by protease inhibitors than nucleoside reverse-transcriptase inhibitors (NRTIs). The interactions can also result in dyslipidaemia that may accelerate the onset of coronary artery disease-related events, particularly in young men with the habit of smoking. However, HIV is an independent risk factor for cardiovascular disease events and ART can therefore reduce the rate of these events.
- Lifestyle modification, including an enhanced diet and switching to another ART regimen, may act favourably on dyslipidaemia. However, many clients on lopinavir/ritonavir (LPV/r) do require drug treatment with statins to achieve therapeutic goals for lipids.

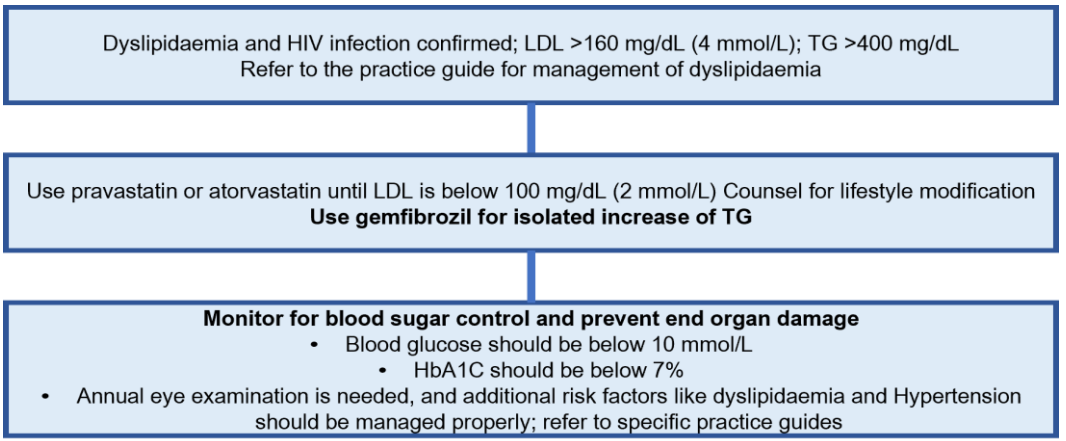
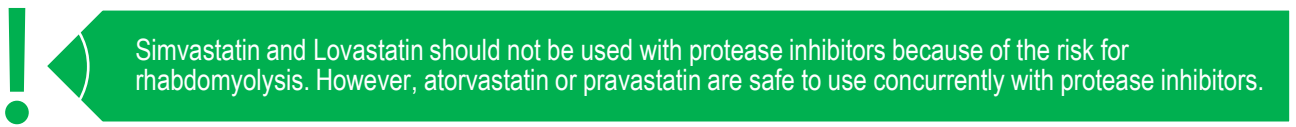


Figure 10.2 Evaluation of clients with dyslipidaemia and HIV infection



HMG-COA reductase inhibitors (statins) are indicated for patients with elevated LDL-C.
They reduce cholesterol synthesis, and very low-density lipoprotein production and Inhibit hepatic low-density lipoprotein receptors

Common side effects include joint and muscle pain with elevated transaminases

Table 10.6 Pharmacotherapy and Drug Information for Treatment of Hyperlipidaemia

Drug Name and Class	Starting Dose	Maximal Dose
Atorvastatin*	10 mg/day	80 mg/day
Simvastatin*	20 mg/day	40 mg/day
Lovastatin	20 mg/day	80 mg/day
Pravastatin	40 mg/day	80 mg/day
Fluvastatin	20 mg/day	80 mg/day
Rosuvastatin	10 mg/day	40 mg/day

**Available in the Eswatini National Essential Medicines List as lipid-lowering agents*

10.6 Care and Management of Depression and HIV

Health care workers must screen all clients testing HIV positive for mental health and substance use disoders and refer according to the facility referral system.

A higher prevalence of depression is reported among HIV-infected clients compared to the general population. Depressive symptoms have been associated with risky sexual behaviour, non-adherence to medications, and shortened survival.

Although sadness and grief are normal responses to many of the consequences of HIV infection, clinical depression is not.

Failure to recognize depression may endanger both the client and others in the community. Clients with depression are at higher risk for comorbid psychiatric abnormalities like alcohol and substance use-related disorders.

Depression is classified into 3 categories:

- Major depressive disorder with or without psychotic features
- Bipolar affective disorder—depressive phase with a previous diagnosis of bipolar mania
- Dysthymia—untreated depressive symptoms for more than 2 years

Nonpharmacological Management of Depression

- Psychotherapy—Provide non-judgmental and solution-focused counselling
- Basic counselling—Provide information about depression, potential side effects, adherence and prognosis (*see Annex 0* for the depression assessment in both English and Siswati)

Table 10.7 Clinical Diagnosis and Recommendations for Management of Depression

Clinical Diagnosis	Recommendation
Depression only	Use antidepressants (see *Table 10.8* below)
Depression with psychotic features	Use antidepressants + antipsychotic drugs
Bipolar affective disorder, (depressive phase)	Use a mood stabilizer + antidepressants (add an antipsychotic drug if the client has psychotic features).
If the client presents with persistent insomnia, consider Lorazepam tablet (1 mg at night) or Promethazine (25–50 mg at night). Use of Lorazepam should not exceed 2 weeks; antidepressants with some sedation effect can be substituted. Avoid DTG at night; it is advisable to take it in the morning to avoid sleep deprivation.	

Table 10.8 Drugs used to treat depression

Antidepressant Tablets	Initial Dosage	Max Dose/Day	Indication
Tricyclic Antidepressants (TCA)			
Amitriptyline	25 mg for 3/7, then 50 mg every night for 14 days then review	200 mg/day (increase dose by 25 mg at a time)	▪ If sedation is desirable ▪ Pregnant women ▪ Breastfeeding mothers
Selective Serotonin Reuptake Inhibitors (SSRIs)			
Fluoxetine	20 mg/day preferably in the morning	60–80mg /day (increase dose by 20 mg at a time)	▪ If sedation is not desirable ▪ Depression with suicide ideas/ attempt ▪ Elderly and children ▪ Physically ill clients; HIV with opportunistic infections, poorly controlled diabetes mellitus and hypertension, etc.
Sertraline	50 mg/day	200 mg/day (increase dose by 50 mg at a time)	

Drug Interactions: Antidepressants and ARVs

- Most first-line ARVs, including DTG, do not interact with antidepressants.
- Ritonavir increases levels of amitriptyline and fluoxetine.
- Darunavir decreases levels of sertraline.
- Fluvoxamine increases levels of protease inhibitors and non-nucleoside reverse-transcriptase inhibitors (NNRTIs).
- Use of efavirenz (EFV) can be associated with suicidal thoughts and attempts; regular screening for depression is essential. EFV should be avoided in clients with overt psychiatric symptoms, including depression and psychosis.
- The use of a high dose of amitriptyline with protease inhibitors can produce cardiac arrhythmia; electrocardiogram monitoring may be indicated when dose escalation is anticipated.
- DTG can cause insomnia. DTG should be given in the morning to avoid insomnia.

Table 10.9 Antipsychotic drugs

Antipsychotic tablet	Initial dose	Maximum dose
Haloperidol	3–5 mg 2 times daily	20 mg/day (Increase dose by 1.5-5 mg at a time)
Risperidone	1–2 mg 2 times daily	16 mg/day (Increase dose by 2 mg at a time)
Olanzapine	5 mg 2 times daily	25 mg/day (Increase dose by 5 mg at a time)
Olanzapine and Risperidone can cause impressive weight gain and also risk for diabetes.		

Mood Stabilizers

- Sodium valproate sodium 50mg–600mg twice daily (mostly preferred in PLHIV):
- Maximum therapeutic dose 2500mg/day in divided dose.
- Increase dose by 200–500mg.
- Check valproate levels yearly or every 6 months if the client is on the maximum dose.
- Lamotrigine 25mg for the first 14 days then increase by 25-50mg, maximum 500mg/day in divided doses.
- Carbamazepine is contraindicated as it increases levels of PIs and NNRTIs.

10.7 HIV related Malignancies

In PLHIV, all malignancies except Kaposi sarcoma, Non-Hodgkin's lymphoma and invasive cervical cancer are considered non–AIDS-defining malignancies. **AIDS-defining malignancies** occur in PLHIV with moderate to severe immunosuppression.

Other cancers found in HIV but are not AIDS-defining include

- Hodgkin's lymphoma (AIDS-related primary CNS lymphoma),
- Anal cancer
- Hepatocellular carcinoma,
- Squamous cell carcinoma and
- Leiomyosarcoma.

Hodgkin's lymphomas account for a minority of all malignant lymphomas. The advent of combination ART has greatly reduced the incidence of these malignancies. Chemotherapy and ART have increased the five-year survival of clients to over 80%. It is important to rule out underlying malignancies in clients who present with rapidly growing and bulky lymphadenopathy, splenomegaly, hepatomegaly, large abdominal mass, testicular mass, skin lesions and decreasing CD4 counts.

10.7.1 Non-Hodgkin's lymphoma (NHL)

AIDS-defining Non-Hodgkin's lymphomas include:

- Diffuse large B-cell lymphoma (DLBCL)
- Burkitt's lymphoma
- Plasmablastic lymphoma
- Primary effusion lymphoma

NHL symptoms include B symptoms (fever, unexplained weight loss, drenching night sweats); enlarged axillary, inguinal and cervical lymph nodes; and a sense of fullness in the chest. Other symptoms can include memory loss, seizures, and fatigue

Diagnosis

To diagnose Lymphomas, incisional or excisional biopsy for histopathological examination has to be made.

Treatment depends on

- Tumour stage,
- Phenotype (B-cell, T-cell, or natural Killer cell)
- Histology (low- intermediate or high grade)
- Symptoms
- Performance status
- Clients age
- Comorbidities

It is important to take note of potential drug-drug interactions between ARVs and cancer chemotherapy drugs. For patients on chemotherapy, INSTI (DTG) regimens which do not induce CYP3A4 are preferred. In clients with lymphomas who need to initiate ART, consider deferring ART and then introducing it soon after administration of the first cycle of chemotherapy. Likewise, in clients who need to modify ART, consider discontinuing concurrent ART and then reintroducing it soon after administration of the first cycle of chemotherapy

The chemotherapy drug options include a combination of corticosteroids, cytotoxic agents, antineoplastic agents, and monoclonal antibodies. *Refer to National Cancer Control Unit for more information*

10.8 Kaposi Sarcoma

Clients with Kaposi Sarcoma, as well as all PLHIV, should start ART regardless of CD4 count. Clients should be referred to designated facilities where there is a doctor and a pharmacist or pharmacy technician for treatment.

Clinical features of KS

Table 10.10 Symptoms of Kaposi Sarcoma

Mild or Moderate Kaposi Sarcoma Disease	Severe Symptomatic Kaposi Sarcoma Disease
Symptoms may include: ▪ Confined to skin and/or lymph nodes ▪ No symptoms of visceral disease ▪ The oral disease does not interfere with chewing or swallowing ▪ Oedema is not significant and does not affect normal function ▪ Condition not functionally disabling or immediately life-threatening	**Symptoms may include:** ▪ Symptomatic visceral disease (pulmonary[1] or gastrointestinal)[2] ▪ Extensive oral Kaposi sarcoma lesions which interfere with chewing or swallowing ▪ Painful or disabling tumour-associated facial/genital/peripheral oedema or ulcerated tumours ▪ Life-threatening or functionally disabling disease ▪ Progressive[3] or persistent Kaposi sarcoma despite ART

[1] Symptomatic pulmonary Kaposi sarcoma, suggested by shortness of breath, haemoptysis or moderate/severe cough which cannot be attributed to other pulmonary conditions.

[2] Symptomatic gastrointestinal Kaposi sarcoma, suggested by bleeding from mouth or rectum which cannot be attributed to other gastrointestinal conditions.

[3] Progressive disease is defined as an increase of 25% or more in the size of previously existing lesions and/or the appearance of new lesions or new sites of disease and/or a change in the character of 25% or more of the skin or oral lesions from macular to plaque-like or nodular. The development of new or increasing symptomatic tumour-associated oedema or effusion is also considered to represent disease progression.

Tumour staging criteria

Table 10.11 Staging Criteria and Prognosis for AIDS-Related Kaposi Sarcoma

	Good Prognosis (All of the Following)	Poor Prognosis (Any of the Following)
Tumour (T)	**(T_0)** Tumour confined to the skin and/or lymph nodes and/or minimal oral disease[1]	**(T_1)** Tumour-associated oedema or ulceration, extensive oral Kaposi sarcoma, gastrointestinal Kaposi sarcoma, Kaposi sarcoma in other non-nodal viscera
Immune system (I)	**(I_0)** CD4 count ≥200 cells/mm³ CD4 ≥20%	**(I_1)** CD4 count <200 cells/mm³ CD4 <20%
Systemic illness (S)	**(S_0)** No history of opportunistic infections and/or thrush; absence of "B" symptoms[2]; Karnofsky performance status score ≥70	**(S_1)** History of opportunistic infections and/or thrush; the presence of "B" symptoms[2] Karnofsky's performance status score is <70 (*See Annex 11.25*)

Adapted from Krown and colleagues (1989 & 1997).

[1]"Minimal oral disease" is defined as non-nodular Kaposi sarcoma confined to the palate.

[2] "B" symptoms: unexplained fever, drenching night sweats, >10% involuntary weight loss, or diarrhoea persisting for more than 2 weeks.

Kaposi sarcoma staging criteria

Table 10.12 Staging Criteria for Classic Kaposi Sarcoma

Stage	Cutaneous Lesions	Localization	Behaviour
I—Maculonodular	Macules or nodules or both	Lower limbs	Non-aggressive
II—Infiltrative	Plaques	Lower limbs	Locally aggressive
III—Florid	Angiomatous nodules and plaques	Extremities, particularly the lower ones	Locally aggressive
IV—Disseminated	Angiomatous nodules and plaques	Extremities, trunk, head	Disseminated, aggressive

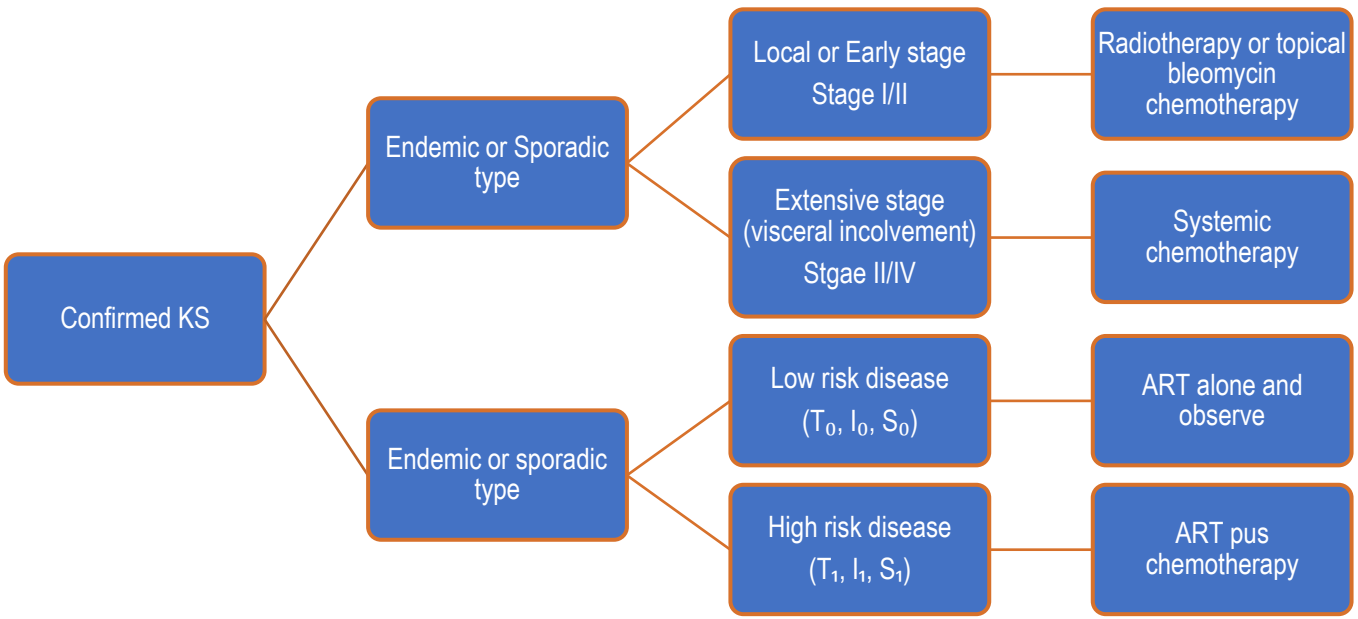


Figure 10.3 Treatment Guidelines for Kaposi Sarcoma

Table 10.13 Treatment of Kaposi Sarcoma

First-line regimen	Bleomycin 15 IU/m² IVD1 Vincristine 2 mg IVD1 Every 3 weeks for 6 cycles
Second-line regimen/recurrent Kaposi sarcoma	Paclitaxel 100 mg/m² * Every 3 weeks for 6–8 cycles Radiotherapy
First-line regimen among clients with pulmonary Kaposi sarcoma and poor PS	Vincristine 1.4 mg/m² IVD1 Repeat cycle every week for 6 weeks then transfer to a first-line regimen.

Clients requiring treatment for recurrent Kaposi sarcoma or non-responsive Kaposi sarcoma should be referred to the chemotherapy unit in Mbabane Government Hospital.

Special considerations

- Cap all clients at a body surface area of $2m^2$.
- Monitor for pulmonary fibrosis among clients receiving bleomycin (seen especially in elderly clients receiving a total dose of >300 units).

If a non-productive cough, dyspnoea, and pulmonary infiltrate develop, the drug should be discontinued and high-dose corticosteroids instituted, as well as empirical antibiotics pending culture. High doses of bleomycin should be given cautiously among clients with pulmonary Kaposi sarcoma.

- Vincristine is associated with severe peripheral neuropathy; the maximum dose for every cycle should not exceed 2 mg.
- In case of severe gastrointestinal side effects (e.g., loss of appetite, nausea and vomiting, diarrhoea, stomatitis, dry mouth, epigastric pain), postpone therapy until symptoms subside.
- Grade 3 or 4 vomiting or diarrhoea—reduce chemotherapy by 20% next cycle.
- Grade 3 or 4 mucosal ulceration—reduce chemotherapy by 20%.

Premedication

- Dexamethasone 20 mg orally 12 and 6 hours before treatment and 20 mg intravenous (IV) just before administration.
- Ranitidine 150 mg or cimetidine 300 mg IV 30 minutes before administration.
- Diphenhydramine orally 12 and 6 hours before treatment and 50 mg IV just before administration or Promethazine 12.5 mg IV.

10.8.1 Cervical cancer

Human papillomavirus (HPV) infection is the aetiology of most cervical cancers.
Screening for cervical cancer is of particular importance for women and adolescent girls infected with HIV.

When to suspect cervical cancer

Unfortunately, there are no early signs or symptoms of cervical cancer. As a result, most often, the cancer is diagnosed at an advanced stage. To reduce morbidity due to cervical cancer, screening to detect cervical lesions in the early (precancerous) stages is essential. Symptoms of cervical cancer may include the following:

- Unusual vaginal discharge, sometimes foul-smelling
- Irregular vaginal bleeding in women of reproductive age
- Postmenopausal spotting or bleeding
- Postcoital spotting or bleeding in women of any age, even in young women
- Lower abdominal pain

Screening for cervical cancer

The screening tests currently available in Eswatini include the following:

- HPV DNA typing
- Visual inspection with acetic acid (VIA)
- Cytology: conventional (Pap smear)

While both screening methods are available in Eswatini, VIA is the widely preferred screening option for identifying pre-cancerous lesions. If the screening result is negative, a follow-up screening schedule will be provided by the health care worker. Refer to the cervical cancer screening guidelines.

HIV- positive women should be screaned for cervical cancer at least once every year

Diagnosis of cervical pre-cancer

The definitive diagnosis of cervical precancer is confirmed by histopathological examination of tissue specimens taken from the lesion.

- VIA positive: acetowhite areas visualized after application of acetic acid are indicative of cervical pre-cancer and must be treated immediately. If an obvious abnormal/fungating lesion is noted, do not apply acetic acid but conduct a biopsy examination and histologically confirmed if it is cancerous.
- Pap smear: If the histology of the smear shows abnormal cells, conduct a biopsy of the abnormal area with a colposcope. Biopsy performed with the aid of colposcopy (colposcopy directed biopsy) is the standard method for diagnosis of cervical pre-cancer lesions and pre-clinical invasive cancer.

Treatment of cervical intraepithelial neoplasia (CIN)

Approaches

- "Screen-and-treat" approach: In this approach, treatment decisions are based on the results of the VIA(or HPV DNA) screening test. Women with a positive VIA screen can be treated with cryotherapy, thermal ablation or LEEP with histopathology depending on eligibility, at the primary or tertiary health care level.
- "Screen, triage and treat" Clients with a positive screen (on Pap smear, or HPV) can be examined with VIA, cytology or colposcopy triage. If a pre-cancerous lesion is detected, it can be treated immediately with cryotherapy, thermal ablation or LEEP.

Treatment methods

- Ablation with cryotherapy or thermal ablation
- Loop electrosurgical excision procedure (LEEP)
- Cold knife conization

Cervical cancer staging system

The classification by the International Federation of Gynaecology and Obstetrics, which is based on tumour size and the extent of spread of disease in the pelvis and distant organs, is recommended for staging invasive cervical cancer.

stage 0: cancer cells found only on the surface(epithelium) of the cervix

More-invasive cancers are separated into 4 stages:

stage 1: Cancer has not spread beyond the cervix

stage 2: Tumour has spread to the cervix

Stage 3: Tumour extends to the lower part of the vagina or the pelvic wall and may block urine flow.

Stage 4: Tumour has reached the bladder or rectum, or cancer cells have spread to other parts of the body.

Management and treatment of invasive cervical cancer

The presence of invasive cancer requires the engagement of a multidisciplinary team, and clients with invasive cancer must be referred to specialists.

Treatment options for cervical cancer

Treatment of cervical cancer depends on the staging and availability of treatment modalities which includes:

- Radiotherapy
- Chemotherapy
- Surgery
- Palliative care

10.9 Palliative Care and Management for PLHIV

Palliative care is an approach that improves the quality of life of clients and their families facing the problems associated with a life-threatening illness. Palliative care aims to prevent and relieve suffering through early identification, impeccable assessment and treatment of pain and other problems—physical, psychosocial, and spiritual.

PLHIV have palliative care needs at each stage, from diagnosis throughout the disease trajectory. As they are living longer, there is also a need to respond to HIV-related cancers.

Palliative Care Models

Good palliative care combines psychosocial, spiritual, and end-of-life care in addition to pain and symptom relief. It focuses on peace and dignity for the client, family, and care providers. Care should be provided where possible by a multidisciplinary team.

Palliative care can be provided at all levels of service delivery using different models:

- Community home-based care
- Facility levels
  »Outpatient
  »Outreach

Pain Assessment and Management

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Pain is a subjective experience that varies from person to person and from time to time. Pain is whatever the experiencing person says it is, existing wherever they say it does. The sensation of pain can be amplified when it occurs in the context of depression, anxiety and fear. Fear of injury can often produce pain even in the absence of actual injury.

Common Sources of Pain in PLHIV

Table 10.14 Common Sources of Pain in HIV and AIDS Clients

Cutaneous/ Oral	Visceral	Somatic	Neurological/ Headache
▪ Kaposi sarcoma ▪ Oral cavity pain ▪ Herpes zoster ▪ Oral/oesophageal candidiasis	▪ Tumours ▪ Gastritis ▪ Pancreatitis ▪ Infection ▪ Biliary tract disorders	▪ Rheumatological disease ▪ Back pain ▪ Myopathies	▪ HIV-related headaches: encephalitis, meningitis, etc. ▪ HIV-unrelated headaches: tension, migraine, etc. ▪ Iatrogenic (AZT) Peripheral neuropathy ▪ Herpes neuritis ▪ Alcohol, nutritional deficiencies

Pain Assessment

All clients should be evaluated for pain at every visit, supporting the claim that pain is the fifth vital sign. Pain is subjective and two clients may report severity differently from each other. Despite that pain is specific to each person, clients can usually accurately and reproducibly indicate the severity of their symptoms by using a scale.

Scientifically validated pain scales:

- Numeric Pain Rating: for adults
- Wong-Baker FACES® Pain Rating Scale: for children who can talk
- Observation-FLACC Scale: for children who cannot talk

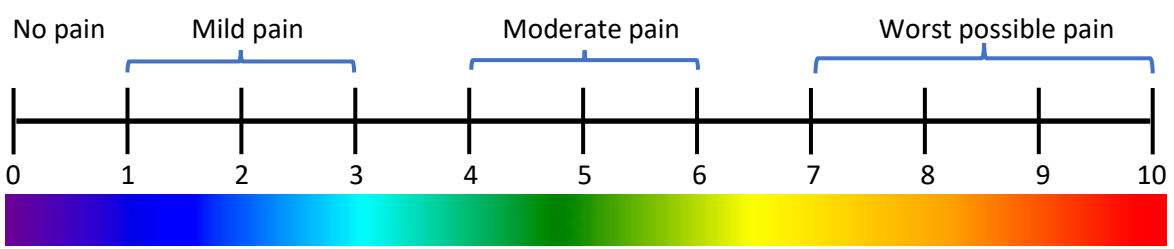


Figure 10.4 Numeric Pain Rating Scale

World Health Organization Analgesic Step Ladder

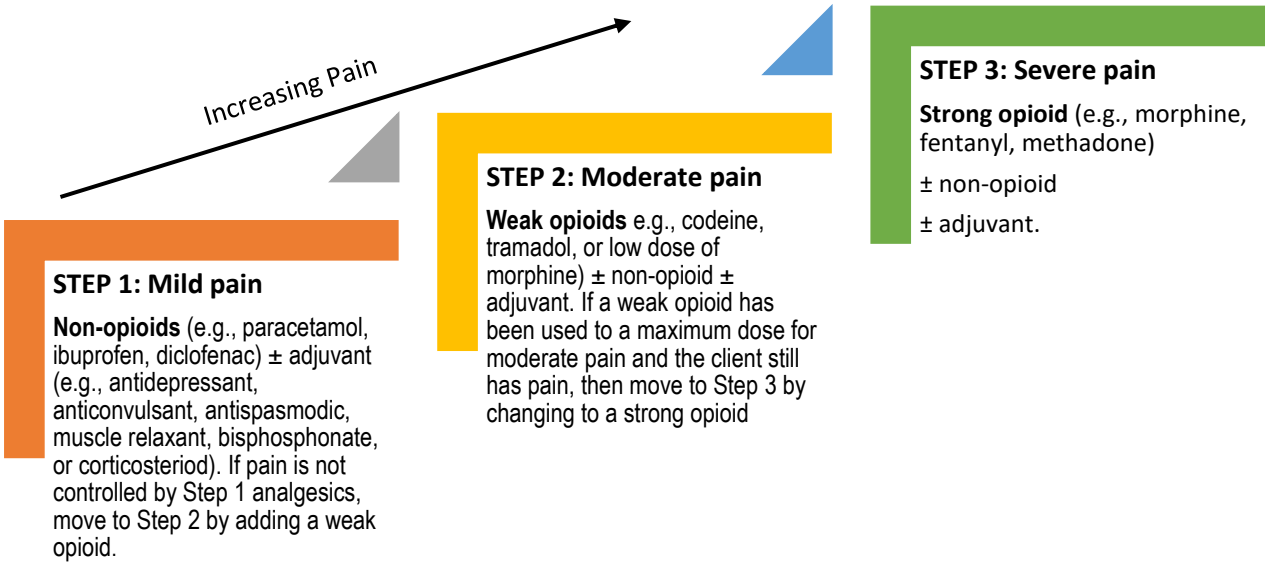


Figure 10.5 WHO analgesic step ladder

Combining an opioid and non-opioid is effective, but do not combine drugs of the same class. Paracetamol and NSAIDs can be used safely in combination. Time doses are based on drug half-life ("dose by the clock"); do not wait for the pain to recur. This allows for pain control instead of responding to active pain. For possible interactions between ARVs and pain management medicines *see Annex 11.4*

10.9.1 Specific Consideration for Pain Management in PLHIV

- Pharmacological pain management should follow the World Health Organization (WHO) analgesic ladder.
- Non-opioids (e.g., paracetamol, ibuprofen and other NSAIDs), adjuvants (e.g., tricyclic antidepressants and anticonvulsants) and nonpharmacological interventions are important in the control of pain in HIV/AIDS. Use NSAIDs with caution in clients with low platelets and those with a history of gastrointestinal disease such as peptic ulcer disease.
    - Many of the ARVs, especially the protease inhibitors, cause abdominal discomfort, nausea and vomiting. Headache and peripheral neuropathies are also common side effects of ART.

Some antiretroviral medicines interact with analgesics, so caution needs to be shown when giving analgesics to clients on ART. In particular:

- The main interactions occur with adjuvant analgesics such as phenytoin, carbamazepine, dexamethasone and amitriptyline.
- Potential interactions between ARVs and other drugs are set out in *Annex 11.3, 11.4 and 11.5*

Specific Considerations for Pain in Children

Table 10.15 Specific Considerations for Pain in Children

Condition	Consideration
Peripheral neuropathy	Peripheral neuropathy is more common in adults than children, but it does occur in children and is often underdiagnosed. When treating it, add adjuvant: carbamazepine for young children and amitriptyline for older children. It is best not to use carbamazepine and EFV together; if necessary, switch EFV to lopinavir/ritonavir (LPV/r).
Muscle spasm in HIV	Children with basal ganglia disease and abnormal movements may also experience considerable pain from muscle spasms.
Treatment-related problems with HIV and AIDS and cancer	For management of mucositis, use mouthwash as appropriate (e.g., in children, 10 mL lignocaine [1%], 30 mL Nystatin suspension and 15–30 mg morphine). Gargle and spit out.

Pain Management Strategy

Some people with HIV and AIDS also have cancer. It is therefore important to be aware of specific pain-related syndromes in HIV and cancer as well as those related to treatment interventions.

Table 10.16 Specific Pain-Related Syndromes in HIV

Clinical Presentation	Causes	Treatment
Peripheral neuropathy		
• Burning pain in hands and feet • Pins and needles • Allodynia (the experience • of pain from a stimulus that would not usually cause pain in a normal individual) • Pain relieved by local pressure	• HIV itself (distal sensory • neuropathy) • Cytomegalovirus Nerve • entrapments, carpal tunnel syndrome • Post-herpetic neuralgia • ARVs, especially • didanosine and stavudine • Other treatments: chemotherapy, Isoniazid, Metronidazole	• Remove offending agents if possible: change stavudine or didanosine to TDF • Treat herpes zoster early with acyclovir to limit post-herpetic neuralgia • Use WHO analgesic ladder—NSAIDs and opioids • Gabapentin in resistant cases • Try topical analgesics • For localized neuropathies-nerve block

Table 10.16 Specific Pain-Related Syndromes in HIV (continued from the previous page)

Clinical Presentation	Causes	Treatment
Abdominal pain in HIV		
Abdominal pain in HIV	• TB abdomen • Mycobacterium avium complex (MAC) • Pancreatitis • Peptic ulcer disease • Gastro-oesophageal reflux • disease • Gall bladder and biliary tract disease • Malabsorption syndromes • Drug side effects • Neuropathic abdominal pain (diagnosis of exclusion)	• Diagnose and treat the underlying cause if possible • Start ARVs if indicated • Treat pain according to the WHO analgesic ladder • Beware of ileus/constipation caused by opioids: can make the pain worse • Remember morphine causes contraction of • sphincter of Oddi, so pethidine is a better • choice in pancreatitis • For IRIS, try low-dose steroids • Beware of NSAIDs and gastritis
Muscle spasm		
Muscle spasm	• Caused by HIV itself in the form of HIV encephalopathy with increased tone • Secondary to cerebral insults from bacterial or tuberculosis meningitis	• ARVs • Levodopa (extrapyramidal dysfunction) • Analgesics (Step 2: non-opioid + weak opioid) • NSAIDs may help with musculoskeletal pain • Baclofen (for muscle spasm, can cause seizures) • Adjuvants, especially Clonazepam
Headache		
• Headache with focal neurological deficits	• Cryptococcal meningitis • Toxoplasmosis	• Treat pain according to the WHO analgesic ladder • Morphine and pethidine are contraindicated for raised intracranial pressure • Lumbar puncture is essential to control intracranial pressure from cryptococcal meningitis

General Principles of Treatment

Give palliative care medication by the mouth, by the clock, by the ladder

Control of Additional Symptoms

Dosing for Nausea

Prescribe an anti-emetic for 7–10 days, after which nausea should subside.

- Haloperidol: 1.5 – 5 mg, every night, for 5–7 days OR
- Metoclopramide: 10 mg, 3 times daily, for 5–7 days

Adjuvant Analgesics

Adjuvants, also called co-analgesics, are medicines that are not primarily used for analgesia. These are medicines that are administered alone or with non-opioids and opioids that may:

- Enhance the analgesic activity of the non-opioids or opioids.
- Have an independent analgesic activity for certain pain types (such as neuropathic or bone pain).
- May counteract the side effects of NSAIDs or opioids.

Management of Neuropathic Pain

Amitriptyline: Adults: 10–75 mg or 0.5–2 mg/kg at night (then increase slowly as needed).
Sodium valproate: Adults: 200 mg – 1.2 g once a day
Gabapentin: Adults: 300–400 mg in divided doses, increase gradually according to the response. Maximum 2400 mg/ day.

If sodium valproate and gabapentin are not available, carbamazepine can be used, but it should be noted that carbamazepine can interact with DTG and EFV. Carbamazepine: Adults: start at 100 mg twice a day and can be increased up to 800 mg twice a day.

Psychosocial and Spiritual Support

Caring for clients with chronic illness involves responding to their total needs, including:

- **Social needs**: an individual sense of belonging, role in family, community, society at large and friendships.
- **Physical needs**: basic needs such as food, shelter and clothing but also adequate health care and security and protection from physical pain.
- **Spiritual needs**: the individual's hope for the future, sense of trust, hope for survival and sense of meaning.
- **Emotional**: love, security, encouragement, motivation, care, self-care, trust, guidance and understanding.

11 ANNEXES

11.1 Overview of ARV Drugs

Generic Name	Standard Adult Dose	Adult Formulation	Paediatric Formulation	Food Restrictions / Special Considerations	Contraindications	Information on Use in Pregnancy
Nucleoside reverse-transcriptase inhibitors (NRTIs)						
Abacavir (ABC)	300 mg every 12 hours	300 mg tabs	20 mg/mL suspension	With or without food	Previous hypersensitivity reactions, kidney or liver disease	No evidence of human teratogenicity
Emtricitabine (FTC)	200 mg once a day	200 mg caps		With food	Kidney or liver disease	No evidence of human teratogenicity
Lamivudine (3TC)	150 mg every 12 hours or 300 mg once daily	150 mg tabs	10 mg/mL syrup	With or without food	Acute or chronic pancreatitis	No evidence of human teratogenicity
Nucleoside reverse-transcriptase inhibitors (NRTIs)						
Zidovudine (AZT)	300 mg every 12 hours	300 mg tabs	10 mg/mL syrup	With or without food, with adequate fluid (water)	Lactic acidosis Hypersensitivity to zidovudine or any of the components (e.g., anaphylaxis, Stevens-Johnson syndrome)	High placental transfer to the foetus
Nucleotide reverse-transcriptase inhibitors (NtRTIs)						
Tenofovir (TDF)	300 mg every 24 hours	300 mg tabs	Oral powder scoops 40 mg/scoop Tablets 150 mg or 200 mg	With or without food	Kidney or liver disease	—

Non-nucleoside reverse-transcriptase inhibitors (NNRTIs)						
Efavirenz (EFV)	400 mg at night	200 mg caps/tabs, 400 mg caps/tabs	50 mg caps/tabs, 30 mg/mL susp	Without food, at bedtime on an empty stomach	Psychosis	Potential foetal safety concern, no contraindication
Etravirine (ETV)	200 mg every 12 hours	100 mg caps, 200 mg caps		With food	Severe liver disease, history of Stevens-Johnson syndrome	—
Nevirapine (NVP)	200 mg every 24 hours for 14 days, then 200 mg every 12 hours	200 mg tabs	10 mg/mL syrup	With or without food	Severe liver disease, history of Stevens-Johnson syndrome	The potential risk of life-threatening hepatotoxicity in women with ≥250 cells/mm³ CD4 counts
Integrase strand transfer inhibitors (INSTIs) / Integrase inhibitors						
Raltegravir (RAL)	400 mg film-coated tablet orally, twice daily	400 mg tabs, 600 mg tabs	100 mg scored and 25 mg chewable tabs Single-use packet of 100 mg susp	With or without food	—	
Dolutegravir (DTG)	50 mg once daily	10 mg, 25 mg, and 50 mg tabs	40 mg tabs	With or without food	Previous hypersensitivity reaction to dolutegravir	
NRTI/NtRTI Fixed-Dose Combinations						
Tenofovir + Lamivudine	300mg + 300mg once daily	1 tablet every 24 hours	300 mg + 300 mg tabs	Indicated for children >35kg	See tenofovir, lamivudine	
Abacavir + Lamivudine		1 tablet every 24 hours	600mg + 300mg 300mg + 150mg	60mg + 30mg 300 mg + 150 mg tab	See abacavir, lamivudine	
Zidovudine + Lamivudine		1 tablet every 12 hours	300 mg + 150 mg tabs	60 mg + 30 mg tabs	See zidovudine, lamivudine	
Tenofovir + Lamivudine + Efavirenz		1 tablet every 24 hours	300 mg + 300 mg + 400 mg tabs		See tenofovir, lamivudine, efavirenz	

NtRTI/NRTI/NNRTI Fixed-Dose Combinations					
Tenofovir + Emtricitabine + Rilpivirine	1 tablet every 24 hours	300 mg + 200 mg + 25 mg tabs		See tenofovir, emtricitabine, Rilpivirine	
Protease Inhibitors					
Darunavir (DRV)	600 mg with 100 mg ritonavir every 12 hours or 800 mg with 100 mg ritonavir every 24 hours	400 mg tab, 600 mg tabs		With food	Liver disease
Protease Inhibitors					
Lopinavir (boost- ed with ritonavir) (LPV/r)	LPV + RTV (200 mg + 50mg) tabs every 12 hours	100 mg + 25 mg tabs 200 mg + 50 mg tabs	100 mg + 25 mg oral tablet 80 mg + 20 mg syrup Oral pellets 40 mg/10 mg	With food	Diabetes, liver or heart problems
Ritonavir (RTV)	To boost other protease inhibitors, 100–200 mg every 12 hours or 24 hours	100 mg caps		With food	
Atazanavir (boosted with ritonavir) (ATV/r)	ATV + RTV (300 mg + 100 mg) tabs every 24 hours	300 mg tabs		Better with food	Liver disease, heart problems, diabetes

11.2 ARV Drug Combinations to be Avoided

Drug Combination	Reason to Avoid
TDF + 3TC + ABC	High incidence of virological failure.
ETV + TPV/r	ETV concentration may be significantly reduced by RTV-boosted TPV.
FTC + 3TC	Similar resistance profiles; no potential benefit.
ATV + IDV	Overlapping toxicity—hyperbilirubinemia and jaundice.

11.3 Potential ARV Interactions with Other Drugs

ARV Drug	Potential Interaction With	Avoid Combination With
Zidovudine (AZT)	Codeine, Clarithromycin, Dapsone, Methadone, Rifampicin, Phenytoin, Phenobarbital, Valproate, amphotericin B, Fluconazole	• Ganciclovir—Increased zidovudine effects • Ribavirin—In vitro antagonism
Abacavir (ABC)	Rifampicin, Methadone, Metronidazole, Phenobarbital, Phenytoin	None
Lamivudine (3TC)	Amphotericin B, Co-trimoxazole	Chlorpropamide—Potentially increased serum glucose concentrations
Tenofovir (TDF)	Acyclovir, Amphotericin B, Co-trimoxazole, Cimetidine, Furosemide, Hydroxyurea, Streptomycin	• Lamivudine (3TC) + Abacavir (ABC)—High virological failure • Lamivudine (3TC) + Didanosine (ddI)—High incidence of virological failure; increased risk of side effects. • Didanosine (DDI) + NNRTI—High incidence of virological failure; increased risk of side effects. • Probenecid—Probenecid-induced inhibition of the renal tubular secretion of tenofovir
Nevirapine (NVP)	Artemisinin, Amiodarone, Buprenorphine, Carbamazepine, Clarithromycin, Codeine, Dexamethasone, Diazepam, Digoxin, Erythromycin, Oestradiol, Ethinyl Oestradiol, Fluconazole, Furosemide, Garlic, Gliclazide, Glipizide, Glitazones, Halofantrine, Haloperidol, Itraconazole, Ketamine, Ketoconazole, Levonorgestrel, Lorazepam, Medroxyprogesterone (intramuscular and oral), Methadone, Miconazole, Norethisterone, Milk Thistle, Phenobarbital, Phenytoin, Prednisolone, Quinine, Rifabutin, Rifampicin, Saint John's Wort, Simvastatin, Valproate	• Etravirine (ETV)—Co-administration decreases etravirine concentration and is contraindicated • Atazanavir (ATV)—Co-administration is not recommended: increases nevirapine exposure and decreases Atazanavir concentration • St. John's Wort—Decreased nevirapine effects. • Artemether/Lumefantrine—Potentially increased • treatment failure • Ketoconazole—Decreased ketoconazole effects • Ethinyl oestradiol/norethindrone acetate—Possible contraceptive failure due to the induction of CYP450 3A4 by nevirapine

ARV Drug	Potential Interaction With	• Avoid Combination With
Efavirenz (EFV)	Artemisinin, Codeine, Buprenorphine, Cimetidine, Clarithromycin, Diazepam, Ergometrine, Oestradiol, Ethinyl Oestradiol, Ketamine, Furosemide, Garlic, Gliclazide, Glipizide, Halofantrine, Haloperidol, Ketoconazole, Levonorgestrel, Lumefantrine, Lorazepam, Midazolam, Milk Thistle, Phenobarbital, Phenytoin, Prednisolone, Quinine, Rifabutin, Rifampicin, St John's Wort	• Etravirine (ETV)—Co-administration decreases etravirine concentration and is contraindicated • Atazanavir—Do not co-administer efavirenz with unboosted atazanavir • Boceprevir—Potentially decreased boceprevir effects • Carbamazepine—Decreased efavirenz and carbamazepine effects • Ergotamine—Potentially increased ergotamine effects (e.g., ergotism)
Lopinavir/ritonavir (LPV/r)	Amiodarone, Atorvastatin, Carbamazepine, Colchicine, Dexamethasone, Diltiazem, Ethinyl Oestradiol, Midazolam, Norethindrone, Oxycodone, Phenobarbital, Prednisolone, Rifampicin, Sildenafil, Simvastatin, St John's Wort, Tricyclic Antidepressants, Warfarin (monitor INR)	• Astemizole—Increased astemizole effects (e.g., cardiac arrhythmias) • Cisapride—Increased Cisapride effects (e.g., cardiac arrhythmias) • Darunavir—Decreased darunavir/ritonavir effects; increased lopinavir/ritonavir effects • Fluticasone—Increased fluticasone concentrations
Atazanavir/ritonavir (ATV/r)	Amiodarone, Antacids, Carbamazepine, Clarithromycin, Colchicine, Dexamethasone, H2 Receptor Antagonists, Midazolam, PPIs, Phenobarbital, Rifampicin, Sildenafil, Simvastatin, Tricyclic Antidepressants, St John's Wort, Warfarin (monitor INR)	• Etravirine, nevirapine • Cisapride—Increased Cisapride effects (e.g., cardiac arrhythmias) • Ergotamine—Increased ergotamine effects (e.g., ergotism) • Lansoprazole—Do not co-administer PPIs with unboosted atazanavir • Lovastatin—Increased lovastatin effects (e.g., myopathy, rhabdomyolysis) • Simvastatin—Increased simvastatin effects (e.g., myopathy, rhabdomyolysis)
Darunavir/ritonavir (DRV/r)	Amiodarone, clarithromycin colchicine, diltiazem, ethinyloestradiol, norethindrone, phenobarbital, simvastatin, rifampicin, midazolam, sertraline, St John's wort, tricyclic antidepressants, warfarin (monitor INR)	• Cisapride—Increased Cisapride effects (e.g., cardiac arrhythmias) • Lopinavir/ritonavir—Decreased darunavir/ritonavir effects; increased lopinavir/ritonavir effects • Phenobarbital and phenytoin—Decreased darunavir/ritonavir effects
Dolutegravir (DTG)	Carbamazepine, Phenobarbital, Phenytoin, Rifampicin - double dose of DTG	Use alternative anticonvulsant agent

11.4 Potential Interactions between ARVs and Pain Management Medicines

ARV	Analgesic	Effect	Time Course	Severity	Comments
Zidovudine (AZT)	Paracetamol	May rarely result in granulocytopenia and hepatotoxicity	Delayed	Minor	Intermittent use of paracetamol is considered safe; adverse effects not consistently reported
Nevirapine (NVP)	Phenytoin and carbamazepine	May decrease serum levels of NVP and anticonvulsants	Delayed	Moderate	Consider alternative anti-convulsant as an adjuvant analgesic
Efavirenz (EFV)	Phenytoin and carbamazepine	May decrease serum levels of EFV and anticonvulsants	Delayed	Moderate	Consider alternative anti-convulsant as an adjuvant analgesic
Ritonavir (RTV)	Benzodiazepines	Prolonged sedation due to accumulation of benzodiazepine	Delayed	Major	Monitor closely and adjust medication as needed
	Phenytoin and carbamazepine	May decrease serum levels of RTV; RTV may increase serum levels of anticonvulsants	Delayed	Moderate	Consider alternative anti-convulsant as an adjuvant analgesic
	Antidepressants	Increased serum levels of anti-depressants	Immediate	Major	Monitor closely and adjust the dose or change medication as needed
Lopinavir/ritonavir (LPV/r)	Benzodiazepines	Prolonged sedation due to accumulation of benzodiazepines	Delayed	Major	Monitor closely and adjust medication as needed
	Antidepressants	Increased serum levels of anti-depressants	Immediate	Moderate	May increase toxicities
	Phenytoin (also carbamazepine)	May significantly decrease serum levels of LPV/r	Delayed	Major	Consider alternative anti-convulsant as an adjuvant analgesic
Atazanavir (ATV)	Benzodiazepines	Prolonged sedation due to accumulation of benzodiazepines	Delayed	Major	Monitor closely and adjust medication as needed
	Phenytoin and carbamazepine	May decrease serum levels of ATV. ATV may increase serum levels of anticonvulsants	Delayed	Moderate	Consider alternative anti-convulsant as an adjuvant analgesic

11.5 ARV Interactions with Contraceptives

Family Planning Options		Antiretroviral Therapy					Rifampicin	HIV Stage III/IV (advanced HIV disease, CD4<200)		Untreated STI (Gonorrhoea and/or Chlamydia)	
		NNRTI		NRTIs (AZT, 3TC, ABC, TDF)	PIs (ATV/r, LPV/r, DRV/r)	Integrase Inhibitors (RAL, DTG)					
		NVP	EFV								
Male/Female Condoms											
Oral Contraceptive Pills (COCs/ POP)											
Implants (Jadelle or Implanon) *											
IUD (copper or hormonal IUD)								Don't initiate	Continuation	Don't initiate	Continuation
Progestin-only Injectables	Depo Provera										
	NST										
Emergency Contraception (ECP)											
Tubal Ligation/ Vasectomy								Case by Case basis		Delay	

Key	
	No Restrictions on use
	Generally, use: some follow-up may be needed
	Usually not recommended unless other more appropriate methods are not available or acceptable
	This method should not be used

11.6 Drugs That Should Not Be Used with Selected ARV Regimens

ARV	Anti-TB Agents to Avoid	Antiepileptic Agents to Avoid	Neurologic Agents
ATV/r or Atazanavir/cobicistat(ATV/c)	Rifampin Rifapentine	ATV/c only: Carbamazepine; Phenobarbital; Phenytoin	Lurasidone; Midazolam; Pimozide; Triazolam
Darunavir/cobicistat (DRV/c) or DRV/r	Rifampin Rifapentine	DRV/c only: Carbamazepine Phenobarbital; Phenytoin	Lurasidone; Midazolam; Pimozide; Triazolam
LPV/r	Rifampin Rifapentine	None	Lurasidone; Midazolam; Pimozide; Triazolam
EFV	None	None	None
ETV	Rifampin Rifapentine	Carbamazepine; Phenobarbital; Phenytoin	None
NVP	Rifapentine	None	None
MVC	Rifapentine	None	None
DTG	Rifapentine	Carbamazepine; Phenobarbital; Phenytoin	None

11.7 Most Common Adverse Drug Reactions to ARV Drugs

Generic Name	Adverse Reactions	Frequency	Signs and Symptoms	Management	Prevention
Zidovudine (AZT)	Minor symptoms	High	Nausea, vomiting, abdominal pain, diarrhoea, headaches; at the beginning of the treatment	Symptomatic treatment only if not subsiding or if leading to complication (dehydration)	Take AZT with food
	Lipodystrophy	High	Shrinking of lower limbs and buttocks, accumulation of fat around the abdomen, gynaecomastia, buffalo hump	If marked, switch to TDF	Regular exercise
	Myalgia	High	Intermittent muscle pain (usually lower limbs), cramps	NSAID, stretching, massages	None
	Leucopoenia	High	Leucopoenia < 750/mL	Follow-up, if high grade, with structured ART interruption, monitoring, and reintroduction of ART (TDF)	None
	Red cell megaloblastia	High	None	None—a good sign of adherence to AZT	None
	Nail discolouration	Medium	Black lines perpendicular to nail growth line (fingers, toes)	None	None
	Bone marrow* suppression	Medium	Anaemia, bicytopenia or pancytopenia	If high grade, implement structured ART interruption, monitoring, and reintroduction of ART (TDF)	None
	Hepatitis*	Low	Nausea, vomiting, jaundice, right flank pain, or asymptomatic + raised ALTs	Follow-up, if high grade, with structured interruption of ART, monitoring, and reintroduction of ART without AZT	Avoid alcohol and other hepatotoxic drugs

Generic Name	Adverse Reactions	Frequency	Signs and Symptoms	Management	Prevention
Zidovudine (AZT)	Lactic acidosis*	Low	Fatigue, rapid loss of weight, abdominal and limb cramps, nausea, in a very adherent client (more commonly female, obese, pregnant) Critical stage: dyspnoea	Stop all ART and follow up on the weight gain; usually, after one month, reintroduce ART with TDF. If dyspnoea: hospitalisation	Weight check at each consultation, client's education
	Myopathy	Low	Muscle weakness, muscle stiffness, muscular pain, cramps	Check creatinine kinase (CK); if high grade, switch AZT to TDF; massage, stretching	None
Lamivudine (3TC)	Pancreatitis	Low	Epigastric pain, loss of appetite	If high grade, implement structured ART interruption; when subsided, reintroduce regimen without 3TC, d4T, or ddI	Avoid alcohol and other pancreatotoxic drugs
	Paraesthesia/ peripheral neuropathy	Low	Numbness, pins and needles, burning sensation of the limbs	Pyridoxine, amitriptyline. If high grade, switch regimen to one without 3TC, d4T, and ddI	Avoid alcohol and other neurotoxic drugs
Abacavir (ABC)	Hypersensitivity reaction	Low	Fever, rash, headache, sore throat, cough, shortness of breath	Stop the medication immediately, treat symptoms Substitute with AZT or TDF	None
	Lactic acidosis	Low	Nausea, vomiting, abdominal discomfort, fatigue, muscle weakness in arms and legs	Stop the medication and treat the symptoms	None
	Minor symptoms	Medium	Loss of appetite, headache, malaise, nausea, vomiting, diarrhoea	Continue medication, symptoms improve within a few weeks of starting ART	None

Generic Name	Adverse Reactions	Frequency	Signs and Symptoms	Management	Prevention
Emtricitabine (FTC)	Lactic acidosis	Low	Nausea, vomiting, abdominal discomfort, muscle weakness and tiredness, shortness of breath	Stop all ART, treat symptoms and re-introduce ART with another NTRI e.g., TDF	None
	Minor symptoms	Low	Headache, diarrhoea, nausea, rash, stomach pain, indigestion	Continue treatment. Symptoms usually subside within a few weeks	None
Efavirenz (EFV)	CNS adverse effects	50% of clients (less common in kids)	Tiredness, dizziness, impaired concentration drowsiness, vivid dreams	Generally, resolve after 2-4 weeks. Avoid alcohol as may worsen CNS side effects.	
	Gynaecomastia		Enlargement of breast	Substitute with NVP or another therapeutic class (integrase inhibitors or boosted PIs).	
Tenofovir (TDF)	Reduction in bone mineral density	Low			Avoid concomitant corticosteroids
Nevirapine (NVP)	Rash	Females have a greater risk than males		If rash occurs in the first 14 days do not increase the dose until it resolves (up to 28 days). If the rash persists after 28 days choose an alternate ARV. Stop treatment if the rash is severe or Steven's Johnson Syndrome develops.	Do not use antihistamines or systemic corticosteroids to prevent rash, they will be ineffective and may increase the chance of rash occurring.
Lopinavir (LPV/r)	Rash, diarrhoea				
Atazanavir (ATV/r)	Unconjugated Hyperbilirubinemia		Jaundice - yellowing of the eyes and skin		

Generic Name	Adverse Reactions	Frequency	Signs and Symptoms	Management
	Cholelithiasis		Abdominal pain. History of kidney stones increases risk and clients may present with cholelithiasis and Kidney stones concurrently	Substitute with LPV/r or DRV/r. If boosted PIs are contraindicated and NNRTIs have failed in first-line ART, consider substituting with integrase inhibitors.
Darunavir (DRV)	DRV has a sulphonamide moiety which may predispose to Stevens-Johnson syndrome and erythema multiforme Hepatotoxicity Hyperlipidaemia	10%	Skin rash, Diarrhoea, nausea, Headache, Transaminase elevation, Fat maldistribution, Hyperglycaemia	
Ritonavir*	GI intolerance, Paraesthesia, Hyperlipidaemia, Hepatitis		Nausea, vomiting, diarrhoea, Fat maldistribution, Taste perversion, Hyperglycaemia	
Dolutegravir (DTG)	Hepatotoxicity Hypersensitivity reactions Insomnia		Rash	If DTG is used in first-line ART, and there are hypersensitivity reactions, substitute with another therapeutic class (EFV or boosted PIs).

*** (RTV)(as a pharmacokinetic booster)**

11.8 Grading of Severity of ARV Toxicities

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Severe and potentially life-threatening (Grade 4)
General Guidance on Estimating Severity / Grade				
Characterization of symptoms and general guidance on management	Symptoms causing no or minimal interference with usual social and functional activities	Symptoms causing greater than minimal interference with usual social and functional activities; may require minimal intervention and monitoring	Symptoms causing the inability to perform usual social and functional activities; require medical care and possible hospitalization	Symptoms causing an inability to perform basic self-care functions; requires medical or operative intervention to prevent permanent impairment, persistent disability or death
[a] Values are provided for children in general except where age groups are specified. [b] Usual social and functional activities in young children include those that are appropriate for their age and culture (e.g., social interactions, play activities, learning tasks). [c] Activities appropriate for age and culture (e.g., feeding self with culturally appropriate eating implement, walking or using hands).				
Haematology				
Absolute neutrophil count	750 - 1000/ mm^3 0.75 x 109 - < 1 x 10^9/L	500-749/ mm^3 0.5 x 109 - 0.749x10^9/L	250-500/ mm^3 0.25 x 10^9-0.5 x 10^9/L	<250/ mm^3 <0.250 x 10^9/L
Haemoglobin	8.5 - 10.0 g/dl 1.32 - 1.55 mmol/L	7.5 - 8.5 g/dl 1.16 - 1.32 mmol/L	6.5 - 7.5 g/dl 1.01 - 1.16 mmol/L	<6.5 g/dl <1.01 mmol/L or severe clinical symptoms attributable to anaemia (e.g., cardiac failure), refractory to supportive therapy.
Platelets	100,00 -< 125,000/mm^3 100 x 10^9 - 125 x 10^9/L	50,000- <100,000/ mm^3 50 x 109 - < 100 x 10^9/L	25000 - <50000/mm^3 25 x 10^9 - <50 x 10^9/ L	<25,000/ mm^3 <35 x 10^9/L or bleeding
Liver Function				
ALT (SGPT)	1.25 - 2.5 x ULN	2.5 - 5.0 x ULN	5.1 - 10.0 x ULN	>10.0 x ULN
AST (SGOT)	1.25 - 2.5 x ULN	2.5 - 5.0 x ULN	5.1 - 10.0 x ULN	>10.0 x ULN

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Severe and potentially life-threatening (Grade 4)
Gastrointestinal				
Bilirubin (>2 weeks old)	1.1 - 1.5 x ULN	1.6 - 2.5 x ULN	2.6 - 5.0 x ULN	> 5.0 x ULN
Lipase	1.1 - 1.5 x ULN	1.6 - 3.0x ULN	3.1 - 5.0 x ULN	> 5.0 x ULN
Pancreatic amylase	1.1 - 1.5 x ULN	1.6 - 2.0x ULN	2.1 - 5.0 x ULN	> 5.0 x ULN
Clinical				
Diarrhoea > 1 year of age	Transient or intermittent episodes of unformed stools OR increase of < 3 stools over baseline per day	Persistent episodes of un- formed to watery stools OR increase of 4-6 stools over baseline per day	Grossly bloody diarrhoea OR increase of > 7 stools per day OR intravenous fluid replacement indicated.	Life-threatening consequences (e.g., hypotensive shock) < 1 year of age
Diarrhoea < 1 year of age	Liquid stools (more unformed than usual) but the usual number of stools	Liquid stools with an increased number of stools OR mild dehydration	Liquid stools with moderate dehydration	Liquid stools resulting in severe dehydration with aggressive rehydration indicated OR hypo- tensive shock
Nausea	Not applicable	Symptomatic AND hospitalisation not indicated (other than emergency treatment)	Symptomatic AND hospitalization not indicated (other than emergency treatment)	Life-threatening consequences (i.e., circulatory failure, haemorrhage, sepsis).
Vomiting	Transient or intermittent vomiting with no or minimal interference with oral intake	Frequent episodes of vomiting with no or mild dehydration	Persistent vomiting	Life-threatening consequences (e.g., hypotensive shock)
Allergic / Dermatological				
Acute systemic allergic reaction	Localized urticaria (wheals) lasting a few hours	Localized urticaria with medical intervention indicated OR mild angioedema	Generalized urticaria OR angioedema with medical intervention indicated OR symptomatic mild bronchospasm	Acute anaphylaxis OR life-threatening bronchospasm or laryngeal oedema

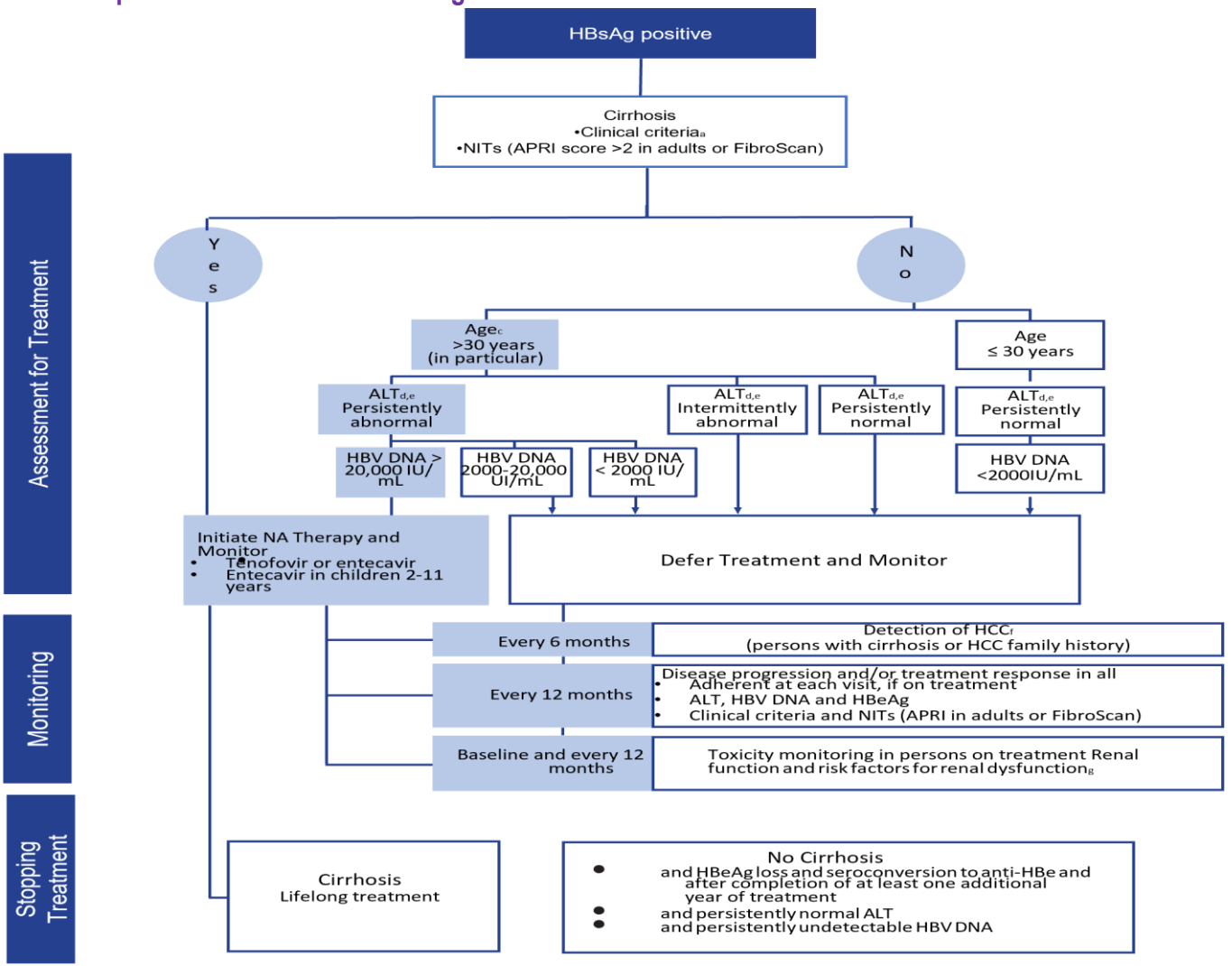
	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Severe and potentially life-threatening (Grade 4)
Dermatological				
Cutaneous reaction rash	Localized macular rash	Diffuse macular, maculopapular or morbilliform rash, OR target lesions	Diffuse macular maculopapular or morbilliform rash with vesicles or limited number of bullae OR superficial ulcerations of mucous membrane limited to 1 site	Extensive or generalized bullous lesions OR Stevens-Johnson syndrome OR ulceration of mucous membrane involving 2 or more distinct mucosal sites OR toxic epidermal necrolysis (TEN).
Neurological				
Alteration in personality behaviour or mood	Alteration causing no or minimal interference with usual social and functional activities [b]	Alteration causing greater than minimal interference with usual social and functional activities b	Alteration causing an inability to perform usual social and functional activities b AND intervention indicated	Behavioural potentially harmful to self or others OR life-threatening consequences
Altered mental status	Changes causing no or minimal interference with usual social and functional activities [b]	Mild lethargy or somnolence causing greater than minimal interference with usual social and functional activities b	The onset of confusion, memory impairment, lethargy or somnolence causing an inability to perform usual social and functional activities [b]	The onset of delirium obtundation or coma
Neurosensory alteration (including painful neuropathy)	Asymptomatic with sensory alteration on examination OR minimal paraesthesia causing no or minimal interference with usual social and functional activities	Sensory alteration or par- aesthesia causing greater than minimal interference with usual social and functional activities	Sensory alteration or par- aesthesia causing an inability to perform usual social and functional activities	Disabling sensory alteration or paraesthesia causing the inability to perform basic self-care functions [c]

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Severe and potentially life-threatening (Grade 4)
Neurological				
Neuromuscular weakness (including myopathy and neuropathy)	Asymptomatic with decreased strength on examination OR minimal muscle weakness causing no or minimal interference with usual social and functional activities [b]	Muscle weakness causing greater than minimal interference with usual social and functional activities b	Sensory alteration or paraesthesia causing greater than minimal interference with usual social and functional activities	Disabling muscle weakness causing an inability to perform basic self-care functions OR respiratory muscle weakness impairing ventilation.
[b] Usual social and functional activities in young children include those that are appropriate for their age and culture (e.g., social interactions, play activities, learning tasks) [c] Activities that are appropriate for age and culture (e.g., feeding self with culturally appropriate eating implement, walking or using hands)				
Other Laboratory Functions				
Cholesterol (fasting paediatric < 18 years old)	170-<200 mg/dl 4.40-5.15 mmol/L	200-300 mg/dl 5.16-7.77 mmol/L	>300 mg/dl >7.77 mmol/L	Not applicable
Glucose, serum, high: non-fasting	116-<161 mg/dl 6.44-<8.89 mmol/L	161-<251 mg/dl 8.89-<13.89 mmol/L	251-500 mg/dl 13.89 - 27.75 mmol/L	>500 mg/dl >27.75 mmol/L
Glucose, serum, high: fasting	110-<126 mg/dl 6.11-<6.95 mmol/L	126-<251 mg/dl 6.95-<13.89 mmol/L	251-500 mg/dl' 13.89 - 27.75 mmol/L	>500 mg/dl >27.75 mmol/L
Lactate	<2.0 x ULN without acidosis	2.0 x ULN without acidosis	Increased lactate with pH < 7.3 without life-threatening consequences or related conditions present	Increased lactate with pH < 7.3 with life-threatening consequences (e.g., neurological findings, coma, or related condition present)
Triglycerides (fasting)	Not applicable	500-751 mg/dl 5.65 - <8.49 mmol/L	751 - 1200 mg/dl 8.49 - 13.56 mmol/L	>1200 mg/dl >13.56 mmol/L

11.9 Supplementary Information on Dolutegravir

Dolutegravir (DTG) is an HIV Type 1 (HIV-1) integrase strand transfer inhibitor (INSTI) that can be used—in adults and children 12 years and older who weigh more than 40 kg—in combination with other antiretroviral medications for the treatment of HIV. Integrase inhibitors block HIV replication by preventing the viral DNA from integrating into the genetic material of human immune cells (T cells). This step is essential in the HIV replication cycle and is also responsible for establishing chronic infection.
DTG is approved for use in more than 90 countries across North America, Europe, Asia, Australia, Africa and Latin America.
DTG may be taken without food.
The most commonly reported adverse drug reactions are insomnia (3%), fatigue (2%) and headache (2%). **There have been reported cases of weight gain among patients taking INSTIs and the reasons are multifactorial: age, race, sex, AHD, CD4 count, VL, previous weight loss and previous ART regimen. More data is needed to allow the WHO to make evidence based recommendations.**
Hypersensitivity reactions characterized by rash, constitutional findings, and sometimes organ dysfunction, including liver injury, have been reported (in <1% or fewer clients). DTG is contraindicated in clients with a previous history of hypersensitivity. Discontinue DTG immediately if signs of hypersensitivity develop.
DTG inhibits OCT2 and MATE1, which are responsible for the tubular secretion of creatinine resulting in a mild increase in creatinine after initiation, which remains stable. No DTG dose adjustment is necessary for INI-naive subjects with mild, moderate or severe renal dysfunction.
Drugs that are metabolic inducers (e.g., ATT) may decrease the plasma concentrations of DTG.
Take DTG 2 hours before or 6 hours after taking cation-containing antacids or laxatives, sucralfate, oral supplements containing iron or calcium, or buffered medications. Alternatively, DTG and supplements containing calcium or iron can be taken together with food.
Co-administration of DTG with Dofetilide (an antiarrhythmic) is not recommended.
Plasma concentrations of metformin increase with co-administration of DTG. **Metformin requires a total daily dose limit of 1000 mg with co-administration**. When stopping DTG, the metformin dose may require an adjustment. Discuss with an HIV specialist before any adjustments.
Clients with underlying hepatitis B or hepatitis C may be at increased risk for worsening or development of transaminase elevations with the use of DTG. **Appropriate laboratory testing before initiating therapy, and monitoring for hepatotoxicity during therapy with DTG, are recommended in clients with underlying hepatic diseases such as hepatitis B or C.**
Redistribution or accumulation of body fat and immune reconstitution syndrome have been reported in clients treated with combination antiretroviral therapy.
The efficacy of DTG 50 mg is reduced in clients with an INSTI-resistance Q148 substitution plus 2 or more additional INSTI-resistance substitutions, including T66A, L74I/M, E138A/K/T, G140S/A/C, Y143R/C/H, E157Q, G163S/E/K/Q, or G193E/R.
Dolutegravir in pregnancy: DTG is classified as a B1 by the United States Federal Drug Administration. This category means that the drug has been taken by only a limited number of pregnant women and women of childbearing age, and there has not been an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus observed. Studies in animals have also not shown evidence of an increased occurrence of foetal damage.

11.10 Hepatitis B Virus[a] Treatment Algorithm



NITs: non-invasive tests,

ALT: alanine aminotransferase,

APRI: aspartate aminotransferase-to-platelet ratio index

[a] Defined as persistence of hepatitis B surface antigen (HBsAg) for six months or more. The algorithm does not capture all potential scenarios, but the main categories for treatment or monitoring. Recommendations for settings without access to HBV DNA testing are provided in the relevant chapters.

[b] Clinical features of decompensated cirrhosis: Portal hypertension (ascites, variceal haemorrhage and hepatic encephalopathy), coagulopathy, or liver insufficiency (jaundice). Other clinical features of advanced liver disease/cirrhosis may include hepatomegaly, splenomegaly, pruritus, fatigue, arthralgia, palmar erythema, and oedema.

[c] The age cut-off of >30 years is not absolute, and some persons with CHB less than 30 years may also meet the criteria for antiviral treatment.

[d] ALT levels fluctuate in persons with chronic hepatitis B and require longitudinal monitoring to determine the trend. Upper limits for normal ALT have been defined as below 30 U/L for men and 19 U/L for women, though local laboratory normal ranges should be applied. Persistently normal/ abnormal may be defined as three ALT determinations below or above the upper limit of normal, made at unspecified intervals during a 6 to 12month period or predefined intervals during a 12-month period.

[e] Where HBV DNA testing is not available, treatment may be considered based on persistently abnormal ALT levels, but other common causes of persistently raised ALT levels such as impaired glucose tolerance, dyslipidaemia and fatty liver should be excluded.

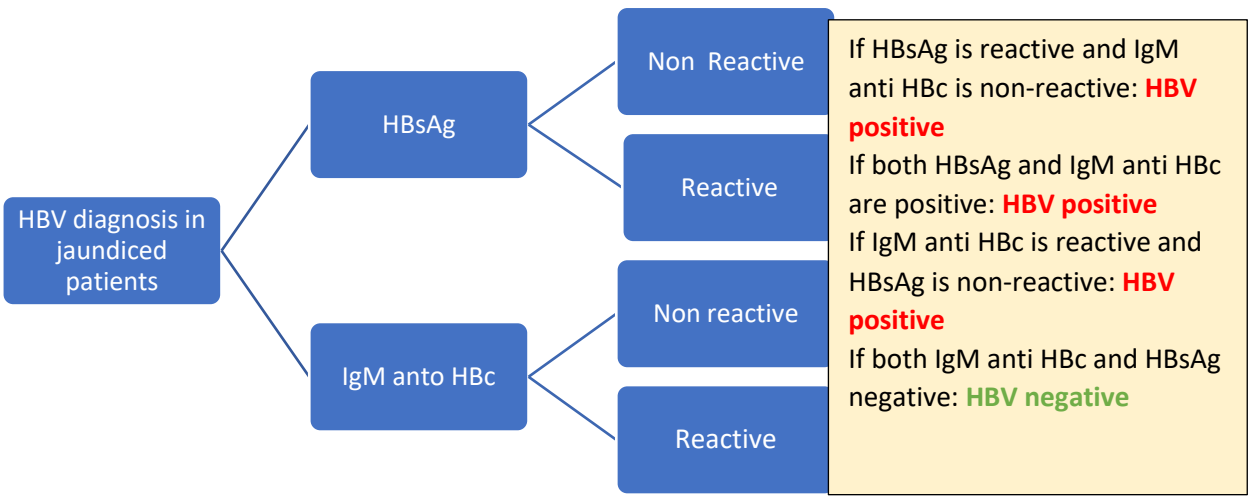
[f] All persons with CHB should be monitored regularly for disease activity/progression and detection of HCC, and after stopping treatment for evidence of reactivation. More frequent monitoring may be required in those with more advanced liver disease, during the first year of treatment or where adherence is a concern, and in those with abnormal ALT and HBV DNA levels >2000 IU/mL, not yet on treatment.

[g] Before initiation, an assessment should be done of renal function (serum creatinine level, estimated glomerular filtration rate, urine dipsticks for proteinuria and glycosuria, and risk factors for renal dysfunction (decompensated cirrhosis, CrCl <50 mL/min, poorly controlled hypertension, proteinuria, uncontrolled diabetes, active glomerulonephritis, concomitant nephrotoxic drugs, solid organ transplantation, older age, BMI <18.5 kg/m2 (or body weight <50 kg), concomitant use of nephrotoxic drugs or a boosted protease inhibitor (PI) for HIV). Monitoring should be more frequent in those at higher risk of renal dysfunction.

11.11 Interpretation of HBV laboratory tests

HBsAg	Total anti-HBc	IgM anti HBc	Anti-HBs	HBeAg	Anti-HBe	Interpretation
-ve	-ve		-ve			Never exposed
-ve	+ve	-ve	-ve			Past natural infection, cleared, anti-HBs levels have waned over time
+ve	+ve	+ve	-ve	+ve	-ve	Acute Hepatitis B, ongoing infection
+ve	+ve	-ve	-ve	+ve	-ve	Chronic Hepatitis B with active viral replication
+ve			-ve	-ve	+ve	Inactive HBV carrier state (low HBV DNA level) or HBeAg -ve chronic hepatitis B with active viral replication (high HBV DNA level)
+ve			+ve	+ or -ve	+ or -ve	Chronic hepatitis B with heterotypic anti-HBs (about 10% of cases)
-ve	+ve	+ve	+ve			Recent infection, recovered, immunity achieved
-ve	+ve	-ve	+ve	-ve	+ve or -ve	Immunity due to past infection
-ve	-ve	-ve	+ve	-ve	-ve	Immunity due to vaccination
-ve			-ve	-ve	-ve	False positive; less commonly, infection in remote past

IgM antibody to hepatitis B core antigen (IgM anti-HBc): is a specific marker for acute HBV infection and it decreases and disappears after 32 weeks.
Total hepatitis B core antibody (anti-HBc): IgM anti-HBc and total anti-HBc increase after 2 weeks of infection. IgM indicates acute infection. IgG persists for life
Hepatitis B surface antibody (anti-HBs): appears after acute infection signalling that the patient is cured from the infection
Hepatitis B surface antigen (HBsAg): increase within 2-10 weeks then decreases and disappears within 6 months, with acute infection.
Hepatitis B envelope antigen (HBeAg): Indicate HBV infectivity/replication
Hepatitis B envelope antibody (Anti-HBe)
Total anti-HBc, mainly IgG anti-HBc continues to be positive for life.



11.12 Hepatitis B Virus Treatment and Clinical Considerations

<table>
<tr><th></th><th>Population</th><th>Considerations</th></tr>
<tr><td>Who to treat</td><td>As a priority, all adults, adolescents and children with chronic hepatitis B infection (CHB) and clinical evidence of compensated or decompensated liver disease</td><td>APRI score >2 in adults
Start treatment regardless of alanine aminotransferase (ALT) level, HBeAg or hepatitis B virus DNA levels</td></tr>
<tr><td></td><td>Adults with CHB who do not have clinical evidence of cirrhosis</td><td>APRI score ≤2 and
More than 30 years old and
Has persistently abnormal ALT
And if available, there is evidence of high-level HBV replication (HBV DNA >20,000 IU/mL)</td></tr>
<tr><td>Who not to treat</td><td>Treatment is not recommended in HIV-negative clients without clinical evidence of cirrhosis; however, clinical monitoring should continue</td><td>APRI score ≤2 and
Persistently normal ALT levels and
Low level of HBV replication (HBV DNA <2,000 IU/mL)</td></tr>
<tr><td>What to treat with</td><td>Recommended agents and dosages
<table>
<tr><th>Weight</th><th>Dose</th><th>Agent</th></tr>
<tr><td>≥35</td><td>1 OD</td><td>TDF (300mg) + 3TC (300mg)</td></tr>
<tr><td>>30–35</td><td>10 or 0.5 mg</td><td>Entecavir (0.05 mg/mL)</td></tr>
<tr><td>>26–30</td><td>9</td><td>Entecavir (0.05 mg/mL)</td></tr>
<tr><td>>23–26</td><td>8</td><td>Entecavir (0.05 mg/mL)</td></tr>
<tr><td>>20–23</td><td>7</td><td>Entecavir (0.05 mg/mL)</td></tr>
<tr><td>>17–20</td><td>6</td><td>Entecavir (0.05 mg/mL)</td></tr>
<tr><td>>14–17</td><td>5</td><td>Entecavir (0.05 mg/mL)</td></tr>
<tr><td>>11–14</td><td>4</td><td>Entecavir (0.05 mg/mL)</td></tr>
<tr><td>10–11</td><td>2</td><td>Entecavir (0.05 mg/mL)</td></tr>
</table></td><td>Lamivudine (3TC) alone should not be used due to the rapid development of HBV resistance
Provide pre-treatment counselling about indications for treatment, likely benefits and side effects, the need for follow-up both on and off therapy, and the importance of full adherence to treatment</td></tr>
<tr><td>How to monitor</td><td>The following should be monitored at least annually:
• ALT (and aspartate aminotransferase [AST] for APRI)
• HBsAg, HBeAg
• HBV DNA levels
• Adherence to treatment at each visit</td><td>• More frequent monitoring is required for the following:
• Clients who do not meet the criteria for treatment
• Clients with advanced disease on treatment
• Clients who had their treatment discontinued</td></tr>
<tr><td>When to stop treatment</td><td>Discontinuation may be considered in the following:
• Persons without clinical evidence of cirrhosis (APRI score ≤2) and also
• Can be followed carefully and long-term for reactivation and also
• Have persistently normal ALT levels and persistently undetectable HBV DNA levels</td><td>• Lifelong treatment is required in all persons with cirrhosis based on clinical evidence (or APRI score >2 in adults)
• Do not discontinue antiviral treatment due to the risk of reactivation
• Relapse may occur after discontinuation, and re-treatment is recommended</td></tr>
</table>

11.13 Clinical Evaluation of a Client with High Blood Pressure and HIV Infection

HIV and hypertension confirmed; assess risk factors for cardiovascular disease

Investigate for end-organ damage; ask for an echocardiogram (ECG), creatinine, haemoglobin, low-density lipoprotein cholesterol, TC renal sonography and urine albumin.

Use conservative and/or pharmacologic treatment of hypertension:

- Use diuretics and angiotensin-converting enzyme inhibitors as appropriate.
- Avoid calcium channel blockers, or use them with caution.
- Monitor closely for the occurrence of Ischemic heart disease.

11.14 Baylor HIV/TB Hotline and Email Information

Paediatric HIV and TB hotlines are available to clinicians (nurses and doctors)

Baylor HIV/TB Hotline: 7848-5571

- The toll-free number, is available Monday through Thursday, 08:00 until 16:00, Friday 8.00 until 14.00
- Calls with questions on paediatric HIV care will be answered by a physician at Baylor
- Clinicians can use Short Message Service text messages or WhatsApp using the above number for assistance

Baylor clinic phone: 2409-6000

DBS Hotline: +268 7687-9925. To obtain dried blood spot results or for laboratory-related dried blood spot questions about TB/HIV email: *swazihivtb@gmail.com.* To address clinical questions to Baylor physicians

11.15 Initiation of Infants Less Than 4 Weeks old on Lopinavir/Ritonavir

Age	AM	PM
0–2 weeks	AZT + 3TC + NVP	AZT + 3TC + NVP
2 weeks–3 months	ABC + 3TC + LPV/r syrup	ABC + 3TC + LPV/r syrup
3–36 months	ABC + 3TC + LPV/r syrup or pellets	ABC + 3TC + LPV/r syrup or pellets

11.16 Alternative ART for Pediatric Clients on TB Treatment

Alternative ART for Paediatric Clients on TB Treatment			
Consideration		**Regimen**	**Comments**
Infants and children <3 years or < 10 kg			
Initiating ARVs while on ATT		**Recommended:** ABC+3TC+AZT while on ATT	Avoid in settings of severe immunosuppression, CD4 <15%. Check VL at the end of ATT. Change to LPV/r at TB treatment completion.
		Alternative 1: ABC(AZT)+3TC+LPV/r Super boosting with 1:1 ritonavir for the duration of TB treatment	Check VL at the end of ATT. Change back to LPV/r standard dosing after TB treatment. If VL is undetectable, conduct SUAC and consider genotyping.
		Alternative 2: ABC(AZT)+3TC+NVP for the duration of ATT	Check VL at the end of ATT
Initiating TB treatment while receiving ART	Child on standard first-line PI-based regimen (2 NRTIs + LPV/r)	**Recommended:** Substitute to ABC+3TC+AZT while on ATT	Check VL at the end of ATT. Change back to LPV/r after TB treatment.
		Alternative 1: Continue ABC (AZT)+3TC+LPV/r. Super-boosting with 1:1 ritonavir for the duration of TB treatment	Consider if the client currently tolerates standard dose LPV/r without a problem. If VL >1000 copies/mL: • Adherence counselling • Consider alternative formulations of LPV/r including pellets
		Alternative 2: Transition to ABC(AZT)+3TC+NVP	• Consider if poor tolerability is already limiting the efficacy of the LPV/r-based regimen • Adherence counselling • Check VL at the end of ATT or earlier if clinical deterioration • Continue NNRTI-based regimen if VL is undetectable at the end of ATT
	Child on standard NNRTI-based regimen (NVP)	**Recommended:** Continue ABC(AZT)+3TC+NVP	Check VL at the end of ATT and continue NNRTI based regimen if VL is undetectable

Children and adolescents 3 years and older			
Initiating ARVs while on TB treatment (ATT)	> 3 years, <10 kg	**Recommended** ABC(AZT)+3TC +EFV	
	> 12 years, >40 kg	**Recommended:** TDF+3TC+EFV	Check VL at the end of TB treatment. If VL is undetectable, substitute EFV with DTG
		Alternative: ABC+3TC+AZT while on ATT	Check VL at the end of ATT. Change back to LPV/r after TB treatment.
Initiating TB treatment while receiving ART	Child on standard first-line PI-based regimen (2 NRTIs + LPV/r)	**Recommended:** Substitute with EFV	Check that the child has no history of failure of an NNRTI-based regimen (VL<1000 copies/mL). Check VL at the end of ATT and continue the NNRTI-based regimen if VL is undetectable.
		Alternative 1: Substitute to ABC+3TC+AZT while on ATT	Consider if tolerability is leading to poor adherence with LPV/r or if not tolerating 1:1 ritonavir super boosting (see below) Check VL at the end of ATT. Change back to LPV/r after TB treatment.
		Alternative 2: Continue ABC(AZT)+3TC+LPV/r Super boosting with 1:1 ritonavir for the duration of TB treatment	Consider if the client currently tolerates standard dose LPV/r without a problem. If VL >1000 copies/mL: Adherence counselling Consider alternative formulations of LPV/r including pellets
	Child on standard NNRTI-based regimen (2 NRTIs + EFV or NVP)	**Recommended:** Continue the same regimen if the child is receiving EFV	In children with severe immunosuppression consider fast-track evaluation and initiation of second-line therapy while on ATT.
		Recommended: If the child is receiving NVP, substitute with EFV	Check VL at the end of ATT and continue the NNRTI-based regimen if VL is undetectable.
		Alternative 1: Substitute to ABC+3TC+AZT while on ATT	Check VL at the end of ATT and continue the NNRTI-based regimen if VL is undetectable.

Children and adolescents 3 years and older			
Initiating TB treatment while receiving ART	Adolescent on TDF-3TC-DTG	**Recommendation:** Substitute DTG to EFV	Check VL at the end of ATT, if VL < 100 copies, the client can switch back to DTG
	Current regimen LPV/r as second-line	**Recommended:** Continue ABC(AZT)+3TC+LPV/r Super boosting with 1:1 ritonavir for the duration of TB treatment	Consider if the client currently tolerates standard dose LPV/r without a problem. If VL >1000copies/ml: Adherence counselling Consider alternative formulations of LPV/r including pellets Consult doctor and Baylor HIV/TB Hotline for 3rd line evaluation *(See Annex 11.14)*
		Alternative 1: Substitute to ABC+3TC+AZT while on ATT	Avoid in settings of severe immunosuppression. Consider if tolerability of LPV/r is leading to poor adherence and will likely be made worse by increasing the ritonavir dose if not tolerating 1:1 dosing. Adherence counselling. Check VL at the end of ATT
	Current regimen ATV/r as second-line	**Recommended:** Substitute and double LPV/r dose for the duration of ATTs	Change back to ATV/r after TB treatment. If VL >1000 copies/mL: • Adherence counselling • Consider alternative formulations of LPV/r including pellets • Consult doctor and Baylor HIV/TB Hotline for 3rd line evaluation

11.17 Paediatric ARV Dosing Card

Any third line client with PI Resistance clinicians must consult with the National 3rd Line Committee for updated dosing and administrative guidance for 3rd line treatment options.

Any third line client with PI Resistance clinicians must consult with the National 3rd Line Committee for updated dosing and administrative guidance for 3rd line treatment options.

Paediatric ARV Formulation	**Weight in kg**							
	3 - 5.9	**6 - 9.9**	**10 - 13.9**	**14 - 19.9**	**20 - 24.9**	**25-29.9**	**30-39.9**	**>40**
ABC/3TC 120mg/60mg Tablet (dispersible)	1 OD	1.5 OD	2 OD	2.5 OD	3 OD			
ABC/3TC 600mg/300mg Tablet (Adult)	Not recommended					1 OD	1 OD	1 OD
AZT/3TC 60mg/30mg Tablet (dispersible)	1 BD	1.5 BD	2 BD	2.5 BD	3 BD			
AZT/3TC 300mg/150mg Tablet (Adult)	Not recommended					1 BD	1 BD	1 BD
DTG 10mg Tablet (scored/dispersible)	0.5 OD	1.5 OD	2 OD	2.5 OD	Change to Adult DTG 50mg tab OD			
DTG 50mg Tablet (Adult)	Not recommended				1 OD	1 OD	1 OD	1 OD
TDF+3TC+DTG 300mg/300mg/50mg TLD Tablet (Adult)	Not recommended						1 OD	1 OD
LPV/r 100mg/25mg Tablet	Not recommended			2 BD	2 BD	3 BD	3 BD	
LPV/r 200mg/50mg Tablet (Adult)	Not recommended				1 BD	2 AM 1 PM	2 AM 1 PM	2 BD
ATV/r 300mg/100 mg Tablet (Adult)	Not recommended							1 OD
TDF+3TC+EFV 300mg/300mg/400mg Tablet (Adult)	Not recommended							1 OD

Paediatric ARV Formulation	Weight in kg							
	3 - 5.9	6 - 9.9	10 - 13.9	14 - 19.9	20 - 24.9	25-29.9	30-39.9	>40
†Recommended DRV and ritonavir Dosing for PI Naïve Paediatric Patients ≥3 yrs & 10 kg In Need of 2nd Line								
†DRV75 mg Tablet (must add RTV)	Not recommended			8 OD	8 OD	8 OD	9 OD	
†DRV 150 mg Tablet (must add RTV)	Not recommended			4 OD	4 OD	4 OD		
†DRV 600 mg Tablet (must add RTV)	Not recommended			1 OD	1 OD	1 OD	675 mg OD (600mg tab +75mg tab)	
†DRV/r 400/50 mg Tablet	Not recommended							2 OD
Boosting RTV for children on DRV for 2nd Line								
Ritonavir 25mg Tablet	Not recommended			4 OD	4 OD	4 OD	4 OD	4OD
Ritonavir 100mg Tablet (Adult)	Not recommended			1 OD	1 OD	1 OD	1 OD	1 OD
Super boosting RTV for children on Rifampicin-containing TB Treatment								
Ritonavir (RTV) 80mg/ml Suspension	0.8ml BD	1.2ml BD	1.5ml BD	2ml BD	2.3ml BD			
Ritonavir 100mg Tablet (Adult)	Not recommended		1 BD	1 AM 2 PM	1 AM 2 PM	2 BD	2 BD	3 BD

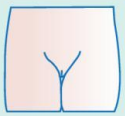
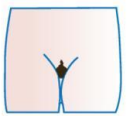
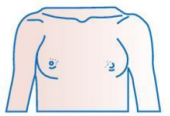
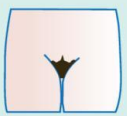
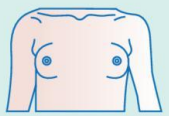
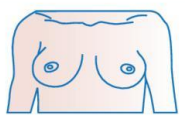
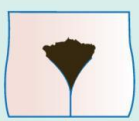
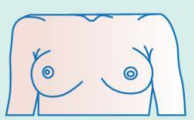
†DRV must be given with ritonavir (see chart above).

DRV/r CANNOT be co-administered with rifampicin containing TB treatment. DRV should be used with caution in patients with known sulphonamide allergies.

DRV/r can only be used in 2nd line in the following situations:

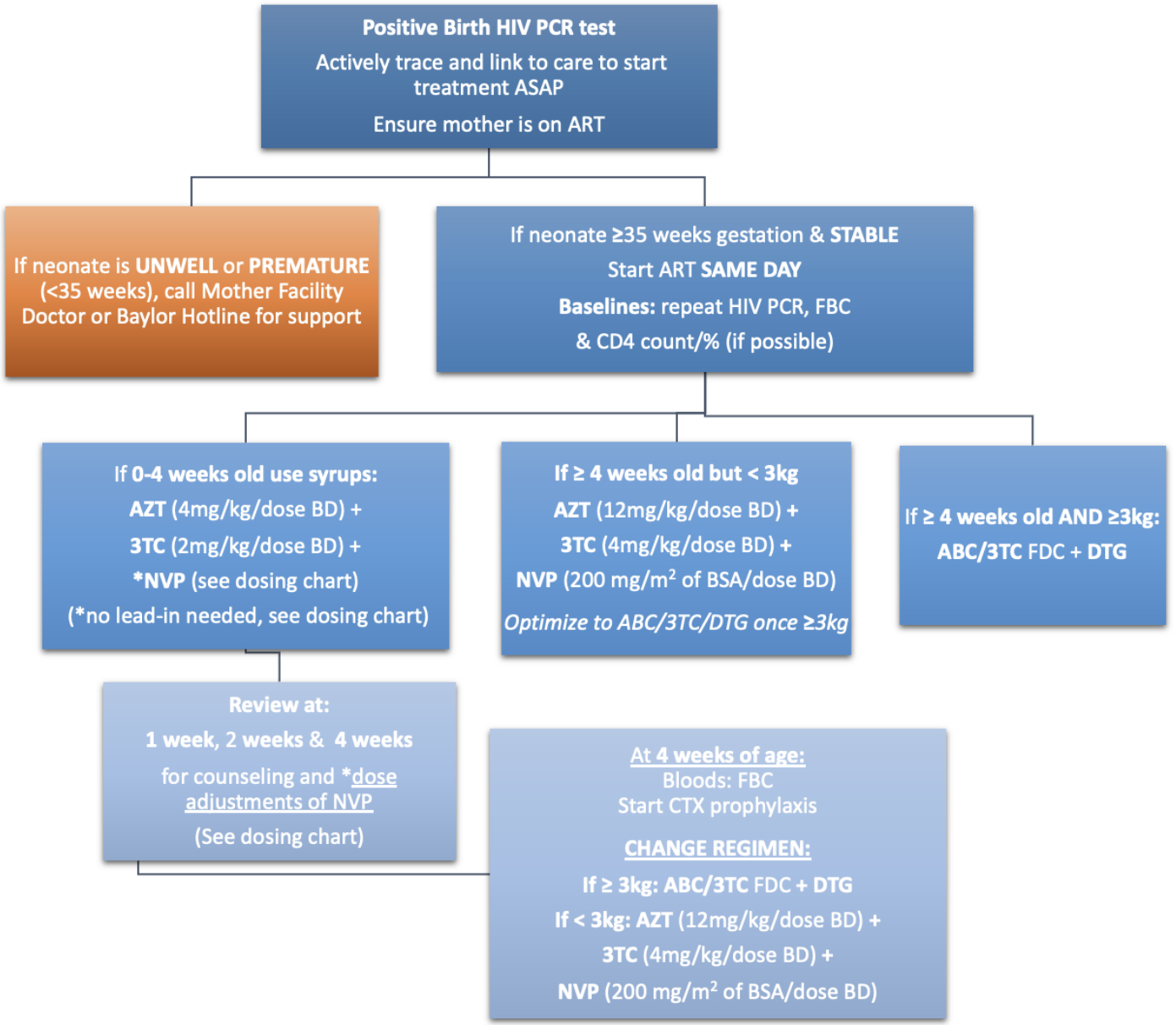
- **Children ≥3 years ≥10 kg**
- **PI naïve client**
- **Has INSTI resistance confirmed my genotype. (Any patient with PI exposure clinicians must consult National 3rd Line Committee prior to DRV use)**

11.18 Tanner staging

Tanner stage	Male genital appearance	Male genital description	Female pubic hair appearance	Pubic hair description	Breast appearance	Breast description
1		Testicular volume <3ml		No pubic hair		Elevation of papilla only
2		Testicular volume <3ml, change in texture to scrotal skin		Sparse growth chiefly along the labia/base of penis		Breast bud stage
3		Increase in size of penis with further testicular enlargement		Darker, coarser, more curled hair		Enlargement of breast and areola
4		Further enlargment of penis and testicles with development of glans penis		Adult type hair over a smaller area		Projection of the areola and papilla
5		Adult size and shape		Spread to the medial surface of the thighs		Recession of the areola to the contour of the breast, projection of papilla only

Source: *BMJ* 2020;368:l6597

11.19 Special Dosing Considerations in Birth Tested Infants.

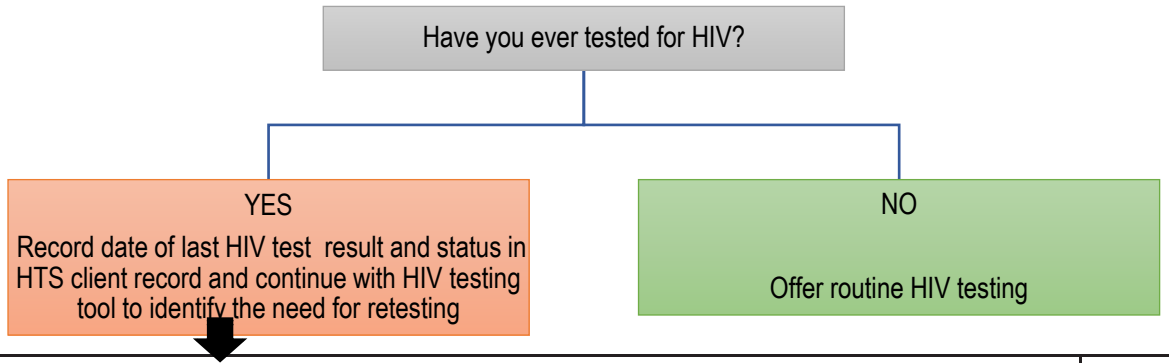


11.20 Holding Regimen Dosing for Birth Tested Infants

Holding Regimen Dosing for Birth Tested Infants 0-4 weeks old and ≥35 Weeks Gestation (Or after 4 weeks until ≥3kg)			
Drug	**Weeks Gestation at Birth**	**Current Age (weeks)**	**Dose**
AZT	≥35 Weeks	0-4 weeks	4 mg/kg/dose BD
		≥ 4 weeks	12 mg/kg/dose BD
3TC	≥35 Weeks	0-4 weeks	2 mg/kg/dose BD
		≥ 4 weeks	4 mg/kg/dose BD
*NVP	≥35 to <37 Weeks	0-1 week	4 mg/kg/dose BD
		1-4 weeks	6 mg/kg/dose BD
		≥ 4 weeks	$^{+}$200 mg/m^2 of BSA/dose BD
	≥37 Weeks	0-4 weeks	6 mg/kg/dose BD
		≥ 4 weeks	$^{+}$200 mg/m^2 of BSA/dose BD
*No NVP lead in dosing needed $^{+}$ Body Surface Area calculator can be found at: mdcalc.com/body-mass-index-bmi-body-surface-area-bsa			

11.21 HIV Testing Screening Tool

HIV screening tool for adults and adolescents



1. Have you had unprotected sex (sex without a condom) after a negative HIV test result with a partner with unknown HIV status?	[__] Yes	[__] No
2. Have you had unprotected sex with an HIV-positive partner who has a detectable viral load or who is not (yet) on ART? [If unknown VL, tick Yes]	[__] Yes	[__] No
3. Have you had sex while under the influence of alcohol or drugs?	[__] Yes	[__] No
4. Have you had more than 1 sexual partner in the last 12 months?	[__] Yes	[__] No
5. Have you ever come in contact with body fluids like blood or body secretions after a negative HIV test or in the past 2 months?	[__] Yes	[__] No
6. Have you had a sexually transmitted infection in the last 6 months?	[__] Yes	[__] No
7. Are you injecting drugs and sharing needles, syringes or other drug equipment with others?	[__] Yes	[__] No
Clients that answer "Yes" to one or more of the above questions should be re-tested for HIV. If the individual is requesting a test, provide it regardless of the screening result.		

HIV Testing Screening Tool for Children

Complete the tool for all children (age 6 - 15 years) with negative or unknown status.

If there is a single "Yes" the child needs HIV testing.

1. Are one or both parents of the child deceased or living with HIV?	[ ] Yes	[__] No
2. Has the child ever been admitted to the hospital before?	[__] Yes	[__] No
3. Does the child have reoccurring skin problems?	[__] Yes	[__] No
4. Has the child had poor health in the last 3 months?	[__] Yes	[__] No

11.22 ART Readiness and Psychosocial Assessment Form

Capacity Knowledge about HIV prevention and transmission and basic knowledge about the process of treatment and how treatment works, including side effects, is essential. A basic understanding is that treatment works by "reducing the virus" in the body and the need to maintain viral suppression. Patients should understand the importance of adherence to treatment, harm reduction and safe sexual practices. Patients need confidence in their ability to meet expectations of commitment to treatment, including coping strategies to maintain emotional stability.		
Basics of HIV		
What is HIV?	What is AIDS?	
How is HIV passed on / spread?	You CAN NOT Get HIV from…	
ART		
What do you understand by ART?		
What are the benefits of Early ART?		
What is your understanding of lifelong treatment?		
What are some side effects that may occur while taking ART?		
What should you do if any of these side effects occur?		
What are opportunistic infections, and can you list some you know?		
How can you prevent opportunistic infections?		
Would you continue ART if you would develop and opportunistic infections?		
Viral load and CD4		
What do you understand about the HIV viral load?	What is an undetectable/ lower than detectable viral load? What is a high/ unsuppressed viral load (>1000 copies/ml)?	
What do you understand about CD4?	Do you need to start ART with high CD4? What you need to do if your CD4 goes below 200 (ADM) (AHD)	
Adherence		
What do you understand by adherence?	What is adherence to ART? What happens when a patient does not practice adherence?	
Patient monitoring		
How will you be clinically monitored while on ART? Why is monitoring ART important?	What will be monitored during clinical visits?	
Do you know your laboratory monitoring schedule?		
Adults and children 0-10yrs	Pregnant and lactating	Adolescents
What other labs are monitored?		
Why is it important to come back to the clinic for review?		
Disclosure		
What is disclosure?		
When and to who can you disclose your HIV status and HIV Treatment		

Partner Children Family member Co-worker other	
Treatment support	
Treatment support for adults Do you have someone at home who can remind you about or make sure you are taking your HIV medications? Treatment support for children Who will give the child medication at home? What **reminders do you have for the child on ART?**	
Co-existing conditions	
Do you have any co-existing conditions? Hypertension Diabetics Anaemia Epilepsy Mental illness Other Are you taking medication for these conditions How well controlled **is your condition?**	
Potential barriers to adherence	
What potential barriers do you think could affect your treatment (ART)? Financial Work-related Family-related Transport related Migration/mobility Service provider related Facility related Mental health issues (substance use disorder and others) Others	How can these barriers be addressed?
Need The person initiating treatment must understand that treatment can extend health and productive life. The participants must trust that treatment will be helpful. This is one of the factors that could be bolstered by experienced expert clients on HIV treatment.	
Acceptance of HIV status and attitude towards ART	
How do you feel about starting ART? What do you expect from taking ARVs?	

What are your goals for the future? Do you think ARVs can help you achieve those goals? Do you feel confident that you can take ARVs as prescribed and adhere to treatment? If you change your residential place, what will you do to continue with treatment Are there any challenges that you foresee that can result in you stopping treatment?	
Review possible previous experience with ART (Defaulters, Back to care)	
Have you been prescribed ART before? If yes, under what circumstance was it prescribed? What issues or challenges made you stop taking your ARVs	
Client's Intention to start and adhere to ART	
Treatment plan (Adults) How and where will you store your medication? How will you remember to take your medication? Do you have a treatment supporter? What to do if you cannot make an appointment? How can you move to another facility?	Treatment plan (special considerations for children and adolescents) Have you identified a primary and secondary caregiver? How will you remember to give your child medication? How will your child receive additional support from the community?
Drive to live: This desire may be supported or discouraged by other aspects of life (family, children, partners, and friends). A component of the drive to live should include an assessment of shame, stigma, and how perceived or experienced discrimination is a force in the person's life. Understanding a person's drive to live may be guided by their expressions of fear of death. Within this context, assessing the presence and magnitude of anger, depression, and other emotionally distressing elements could be useful.	
Other aspects of PHDP (Positive Health, Dignity and Prevention)	
Index testing, prevention and treatment Do you know the status of your partners? Do you know the status of your children? Do you inject drugs? Have your social contacts tested for HIV? Is your partner or any of your children taking HIV treatment? What are safer sex practices you can use to protect yourself and your partner? Why is STI screening and treatment important? Are you using any family planning methods? Why is Family planning important? Do you experience stigma and discrimination? Where does this occur (work, school or home)? Feeling sad, down, or uninterested in life? Feeling anxious or nervous? Feeling stressed? Feeling angry? Do you feel stigmatized because of your HIV-positive status?	
Do you experience Intimate Partner Violence? Has your partner ever hit, kicked, slapped, or otherwise physically hurt you for taking HIV Treatment?	

Has your partner ever threatened to throw away or hide your HIV Medicine? Has your partner ever forced you to stop HIV treatment? Has your partner forced you to share your medicine with them or force you to collect his medicine for him?
Self-care and Treatment Success Measures The client should be given information on how they will know their treatment is working to be motivated to continue taking treatment. Other factors like multi-month dispensing should be included as benefits for treatment success. The following information on treatment success and self-care will be provided
Patient Self – care and treatment success measures
What can you do to ensure you stay well on ART? PLHIV Support groups Exercise Good Nutrition Healthy lifestyle How can you know the treatment is working? VL Suppression Increasing CD4 Reduced or no OIs Good growth and development (children) Do you know what U=U stand for? A sustained undetectable VL reduces the chance of you passing on HIV to your sexual partner, unborn child or breastfeeding child. This does not mean one has to stop using condoms What additional packages exist for you? Discuss DSD models available Longer refill intervals and convenient pick-up models Integrated care for HIV and other comorbidities

All clients must be enrolled for linkage case management for active follow-up and additional support.

11.23 Guidance on patients with low scores on ART readiness assessment

Assessment	Remedial action
From I- XVI	Additional counselling and patient education on identified knowledge gaps/ low scores to improve patient literacy and support by a nurse/ doctor or social worker Involve treatment/ Peer supporter for counselling for additional support Link to support group and community support structures
V- VI	Appoint re- counselling session with Treatment/ supporter ▪ Link to support group and other community support structures
VIII	▪ Counsel for assisted disclosure with EC, Peer supporter, Nurse or social worker
IX	▪ Identify treatment supporter ▪ Emphasize setting reminders
X	▪ Refer to nurse/ doctor for assessment, management and decision to initiate or delay ART
XI	▪ Assess the barrier ▪ Counsel on possible remedial actions ▪ Discuss, Agree and revise the treatment plan to address barriers ▪ Identify/ engage treatment supporter/ Peer supporter ▪ Assist and Arrange for referral to additional support structures (Nurse, social worker, Psychiatric nurse, OVC-DREAMS Linkage Case Assistants)
XII	If the Client is not ready for ART initiation ▪ Review potential barriers to ART initiation ▪ Additional counselling and patient education on identified knowledge gaps/ low scores to improve patient literacy and support by a nurse/ doctor or social worker ▪ Assist and Arrange for referral to additional support structures (Nurse, social worker, Psychiatric nurse, OVC-DREAMS Linkage Case Assistants) ▪ Engage Treatment supporter ▪ Reappoint patient for follow-up +/- ART initiation within 2 weeks.
XIII	▪ Review potential barriers to ART initiation ▪ Additional counselling and patient education on identified knowledge gaps/ low scores to improve patient literacy and support by a nurse/ doctor or social worker ▪ Assist and Arrange for referral to additional support structures (Nurse, social worker, Psychiatric nurse, OVC-DREAMS Linkage Case Assistants) ▪ Engage Treatment supporter
XVI	▪ Additional counselling and patient education on identified knowledge gaps/ low scores to improve patient literacy and support by a nurse/ doctor or social worker ▪ Involve treatment/ Peer supporter for counselling for additional support ▪ Link to support group and community support structures

11.24 Depression Assessment

(Siswati)

Sebentisa nalu luphawu V kuphendvula				
	Akukake kwenteka	**Emalanga lambalwa**	**Lokungetulu kweliviki (7 days)**	**Cishe onkhe emalanga**
Kuncishelwa ngumdlandla/inshisekelo ekwenteni tintfo letikuchazako/letikujabulisako	**0**	**1**	**2**	**3**
Kutiva uphansi emoyeni, ukhatsatekile noma ute litsemba	**0**	**1**	**2**	**3**
Bulukhuni bekwehlelwa butfongo noma kuphelelwa butfongo noma kuba nebutfongo lobuningi	**0**	**1**	**2**	**3**
Kutiva udziniwe noma uphelelwa ngemandla	**0**	**1**	**2**	**3**
Kungakhanuki kudla (inhlitiyo imnyama) noma kudla kakhulu	**0**	**1**	**2**	**3**
Kuva utisola/utenyanya noma usehluleki noma utentele **phansi noma wentele phansi umndeni wakho**	**0**	**1**	**2**	**3**
Kuba nebulukhuni kubeka umcondvo/kulandzelela etintfweni lotentako, letinjengekufundza liphephandzaba noma kubukela mabonakudze (TV)	**0**	**1**	**2**	**3**
Kuhamba kancane noma kunamula lokunakekako kulabanye bantfu. Noma kungahlaliseki kangangekutsi uhlala uphitsitela lokungetulu kwalokutayelekile	**0**	**1**	**2**	**3**
Kuba nemicabango yekutsi kuncono kufa, noma ucabange kutilimata.	**0**	**1**	**2**	**3**
SEKUKONKHE:				

Sisebenti setemphilo; kutfola inchazelo ngemphumela buka luhla lwetinchazelo ngemuva kuhlatiya umphumela.

- Nangabe ubeke luphawu kulenye yaletinkinga, kwente kwaba lukhuni kangakanani kutsi wente umsebenti, unakekele kahle likhaya noma uphilisane kahle nebantfuukabi nebulukhuni
- Kube lukhunyana
- Kube lukhuni kakhulu
- Kube lukhuni ngalokwecile

Depression Assessment (English)

Over the last 2 weeks, how often have you been bothered by any of the following problems?				
	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating (on things linked with your usual activities)	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed, or, on the contrary, being fidgety, restless, or moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or hurting yourself in some way	0	1	2	3
TOTAL:				

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all ☐ Very difficult☐

Somewhat difficult ☐ Extremely difficult ☐

Depression Assessment Score (English and Siswati)

Client Health Questionnaire Score (English and Siswati)	Provisional diagnosis	Recommendation
5–9	Minimal symptoms	Support and educate to call for support if symptoms get worse.
10–14	Minor to mild depression or chronic depression (symptoms lasting for 2 years)	Support and watchful waiting. Reassess in 1–2 weeks. Consider starting treatment for psychological support.
15–19	Major depression	Refer to social workers/psychologist/nurse. Needed for specific treatment.
>20	Severe depression	Major impairment, need for active treatment.

11.25 Karnofsky performance status

Status	Response
100%	• Normal, no complaints, no signs of disease
90%	• Capable of normal activity, minor symptoms or signs of disease
80%	• Normal activity with some difficulty, some symptoms or signs
70%	• Caring for self, not capable of normal activity or work
60%	• Requiring some help can take care of most personal requirements
50%	• Requires help often, requires frequent medical care
40%	• Disabled, requires special care and help
30%	• Severely disabled, hospital admission indicated but no risk of death
20%	• Very ill, urgently requiring admission, requires supportive measures or treatment
10%	• Moribund, rapidly progressive fatal disease processes
0%	• Death

11.26 Summary of the Uses of CD4 and Viral Load Monitoring

	CD4	VL
Baseline laboratory for clients diagnosed with HIV	X	
Disease progression for clients with HIV who have not initiated ART	X	
To determine immune status at enrolment—mild, moderate or advanced immunodeficiency	X	
To determine if LF TB-LAM testing and LF-CrAg screening should be conducted	X	
To assess treatment success or failure		X
To assess if a client is stable or unstable on ART	X	X
To assess adherence to treatment		X
To assess eligibility for DSD		X

11.27 Adverse Drug Reaction Report Form

The report can be returned to Central Medical Stores by Fax: 2518 6279 or via Whatsapp on +268 7655 7303
Email: cms@realnet.co.sz
Post: Adverse Drug Reaction, Central Medical Stores. P.O. Box 72, Kwaluseni

Section A: Patient Information

Patient initials or reference number:_____Sex: Male_____Female_Pregnant: No__Yes____Unknown_____ Weight (if known):___kg. Date of Birth: (*dd/mm/yyyy*), / / or age (at last birthday): _____

Section B: Medication History

All drug therapies/ vaccines before ADR (please use trade names and circle the suspected drug)	Batch number	Daily Dosage	Route	Date Begun	Date Stopped	Indication for Use

Allergies or other relevant histories (including medical history, liver/kidney problems, smoking, alcohol use, etc.)

Section C: About the Adverse Drug Reaction
Date of onset of ADR: (dd/mm/yyyy) / /
Description of event: _____

Category of ADR (please tick)
___ Suspect minor/major reaction from a drug (e.g., allergic reaction)
___ Adverse Event (e.g., congenital defects)
___ Product Use Error (e.g., use of antibiotic instead of NSAID)

Severity (can tick more than one if appropriate)
___ Life-threatening
___ Hospitalization (dd/mm/yyyy) / /
___ Hospitalization NOT required
Relevant laboratory result _

Adverse Drug Reaction Report Form (continued from the previous page)

Section D: Treatment and Outcomes

Treatment of ADR:_No____Yes
Details (including dosage, frequency, route, and duration):
_____
_____
Outcome:
___ Recovered on (dd/mm/yyyy) / /
___ Not yet recovered
___ Unknown
___ Died on (dd/mm/yyyy) / /
___ Persistent disability
___ Birth defect
___ Medically significant events
Details: __
_____

Section E: Reporter Details

Name:____Director of the service:_Private_Public
Occupation:_Doctor_Dentist_Pharmacist_Nurse_ Other:_____Correspondence Address: _____Telephone number: _____Fax Number: ___Email: _____Also report to: Manufacturer___ Distributor/Importer___ Others: _____
Date of this report: (*dd/mm/yyyy*) / /

Instructions/ Notes

1. ADR can be briefly described as a noxious and unintended response to a drug or vaccine when the normal dose is used
2. This report form is used for voluntary of all suspected ADR
3. There is no need to put down the full name of the patient
4. Please provide information to every section, information of individual reporter will be treated with strict confidence
5. Please use another page for additional information if necessary
6. For further enquiries, please contact the Pharmacist at Central Medical Stores at 2518 4111

*Completion of this form is not an admission of guilt or negligence

11.28 Causes of treatment failure

Medical conditions	Intervention
Comorbidities Malabsorption Inter-current illnesses Advanced immunodeficiency (AHD)	Consult experienced clinician Treat current illness following national guidelines Conduct thorough screening of OIs before ART initiation Follow AHD guidelines Assure of correct doses of treatment at every visit
Substance use disorder Depression *	Consult social worker/psychologist Consult the psychiatrist and refer if necessary
Transmitted resistance	Counsel patient and trace index contacts Switch to an appropriate regimen Identify previous ARV exposure before ART initiation
Toxicity or side effects Drug-drug interactions	Manage according to the severity of the side effect (*see chapter 5, Section 5.12* on pharmacovigilance) Stop offending drug(s) if necessary Follow national guidelines when prescribing Ask about drug history at each refill
Psychosocial factors	**Intervention**
Forgetfulness Absence of social support Stigma Lack of disclosure	Engage treatment supporter Home visits Engage community health care workers
Migration and relocation Unfavourable working hours	Ensure adequate supply when travelling Enrol into DSD if eligible
Misinformation from the community	Document presented issues and engaged the APS/health promotion focal persons
Poor storage conditions	Ensure optimal storage conditions of the drug formulations before prescribing MMD
Health System Factors	**Management**
Drug stockouts Incorrect regimen and drug doses VL regimen stock out	Capture correct patient medical data in the correct data collection tools. Verify M&E data before quantification
Service Accessibility	Encourage patients to access services at their nearest health facilities Conduct ART readiness assessment before ART initiation Aim to provide patient-centred care Conduct routine VL monitoring and use the HVL register effectively

Follow the PHQ9 screening tool on *Annex 0* for Depression screening and manage appropriately

11.29 Revised WHO clinical staging

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 Seborrheic dermatitis	Unexplained persistent hepatosplenomegaly Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis) Herpes zoster Linear 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 leucoplakia 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), neutropenia (<0.5 x 10^9/l) and/or chronic thrombocytopaenia (<50 x 10^9/l)	Unexplained moderate malnutrition not adequately responding to standard therapy Unexplained persistent diarrhoea (14 days or more) Unexplained persistent fever (above 37.5°C, intermittent or constant, for longer than one 1 month) Persistent oral candidiasis (after the first 6 weeks of life) Oral hairy leucoplakia Lymph node tuberculosis Pulmonary tuberculosis Severe recurrent bacterial pneumonia Acute necrotizing ulcerative gingivitis or periodontitis Unexplained anaemia (<8 g/dl), neutropenia (<0.5 x 10^9/l) or chronic thrombocytopaenia (<50 x 10^9/l) Symptomatic lymphoid interstitial pneumonitis Chronic HIV-associated lung disease, including bronchiectasis

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

- 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.
- 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.
- 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 <115mm or the presence of oedema.

11.30 Developmental milestones- The First 24 months of life

Age	Psychosocial	Gross motor	Fine motor and visual	Communication and hearing
1 month	Follows faces to the midline	Moves all extremities equally. Lifts head while lying down on stomach	Opens hands spontaneously	Startled by loud sounds Cries Quiets when fed and comforted
2 months	Follows faces past the midline Smiles responsively	Lifts head at 45 degrees when on stomach	Looks at their own hand	Makes baby sounds (cooing, squealing, gurgling)
3 months	Recognizes mother Smiles responsively	Can support head for a few seconds when held upright	Opens hand frequently	Responds to voices Laughs
4months	Follows an object with the eye for 180degress Regards own hand Anticipates food on sight	Bears weight on legs Good neck control when pulled to a sitting position Lifts chest and supports self on elbows when lying on stomach	Claps hands Grabs objects e.g., a rattle Reaches for objects	Turns head to sound
6 months	Reaches out to familiar people	Rolls from stomach to back or back to stomach Sits with anterior support	Plays with hands by touching them together Sees small objects e.g., breadcrumbs	Responds to name Babbles
9 months	Indicates wants Waves “bye-bye” Has stranger anxiety	Can sit without support Creeps or crawls on hands and knees	Looks for a toy when it falls from his/her hand Takes a toy in each hand Transfers a toy from one hand to the other	Responds to soft sounds e.g., whispers
12months	Has separation anxiety Social interactions are intentional and goal-directed	Pulls self-up to a standing position Walks with support	Points at objects with the index finger	Says 1-word Makes mama or dada sounds Locates sounds by turning head
15 months	Imitates activities Finds a nearby hidden object	Can take steps on own Can get up from a sitting position to a lying position	Can stack one cube on top of another	Able to say mama and dada to respective parents (Sounds to identify caretakers)
18 months	Initiates interactions by calling an adult	Walks without help	Can take off their own shoes Feeds self	Says at least 3 words
2 years	Does things to please others Engages in imitative play	Runs without falling	Looks at pictures in a book Imitates drawing a vertical line	Combines 2 different words

11.31 Nutritional Assessments

BMI-for-Age Table, BOYS 15–18 years

Age (Years: months)	Severe acute malnutrition < –3 SD (BMI)	Moderate malnutrition ≥ –3 to < –2 SD (BMI)	Normal ≥ –2 to ≤ +1 SD (BMI)	Overweight > +1 to ≤+2 SD (BMI)	Obese > +2 SD (BMI)
15.0	<14.7	14.7- 15.9	16.0- 22.7	22.8 -27.0	>27
15.6	<14.9	14.9- 16.3	16.3 -23.1	23.2 – 27.4	>27.4
16.0	<15.1	15.1-16.4	16.5 -23.5	23.6 -27.9	>27.9
16.6	<15.3	15.3- 16.6	16.7 -23.9	24.0 -28.3	>28.3
17.0	<15.4	15.4-16.8	16.9 -24.3	22.4 -28.6	>28.6
17.6	<15.6	15.6- 17.0	17.1 -24.6	24.7 -29.0	>29.0
18	<15.7	15.7- 17.2	17.3 -24.9	25.0 -29.2	>29.2

Adapted from WHO 2007

BMI-for-Age Table, Girls 15-18 years

Age (Years. months)	Severe acute malnutrition < –3 SD (BMI)	Moderate malnutrition ≥ –3 to < –2 SD (BMI)	Normal ≥ –2 to ≤ +1 SD (BMI)	Overweight > +1 to ≤+2 SD (BMI)	Obese > +2 SD (BMI)
15.0	<14.4	14.4- 15.8	15.9- 23.5	23.6 -28.2	>28.2
15.6	<14.5	14.5- 15.9	16.0 -23.8	23.9 – 28.6	>28.6
16.0	<14.6	14.6-16.1	16.2 -24.1	24.2 -28.9	>28.9
16.6	<14.7	14.7- 16.2	16.3 -24.3	24.4 -29.1	>29.1
17.0	<14.7	14.7-16.3	16.4 -24.5	24.6 -29.3	>29.3
17.6	<14.7	14.7- 16.3	16.4 -24.6	24.7 -29.4	>29.4
18	<14.7	14.7- 16.3	16.4 -24.8	24.9 -29.5	>29.5

Adapted from WHO 2007

11.32 Differential diagnosis of a child presenting with cough and respiratory distress

Diagnosis	Common signs and symptoms	
Pneumonia	Cough with fast breathing Lower chest wall in-drawing Fever Coarse crackles on auscultation	Nasal flaring Grunting Head nodding
Tuberculosis	Cough Poor growth/wasting or weight loss Positive contact history with tuberculosis patient Diagnostic chest x-rays such as primary complex or miliary tuberculosis	
Pneumocystis pneumonia	A 2-6-month-old child with central cyanosis Hyper-expanded chest Fast breathing Finger clubbing	Chest x-ray changes, but chest clear on auscultation Enlarged liver, spleen, lymph nodes Wasting
Pneumothorax	Sudden onset Hyper-resonance on percussion on one side of the chest Shift in mediastinum	
Empyema	Stony dullness to percussion	
Severe anaemia	Severe palmar pallor Haemoglobin <6 g/dl	
Foreign body	History of sudden choking Sudden onset of stridor or respiratory distress Focal areas of wheeze or reduced breath sounds	
Cardiac failure	Gallop rhythm Raised jugular venous pressure Basal fine crackles	Apex beat displaced Enlarged palpable liver Heart murmur
Congenital heart disease	Central cyanosis Difficulty in feeding or breastfeeding Enlarged liver Heart murmur	
Malaria	Fast breathing in a febrile child Blood smear: high parasitaemia Lives in or travelled to a malaria endemic area In severe malarial deep (acidotic) breathing/lower chest wall indrawing Chest is clear on auscultation	

Adapted from World Health Organization. Management of the child with a serious infection or severe malnutrition. Guidelines for care at the first-referral level in developing countries, 2000

11.33 Eswatini Immunization Schedule

Antigen & Supplements	No. of Doses	Age for Administration of Vaccine
BCG & OPV 0	1	At birth
OPV	5	6,10,14 weeks, 18 months & 5 years
DTP-HepB-Hib	3	6,10,14 weeks
PCV13	3	6,10,14 weeks
Rotarix	2	6,10 weeks
IPV	1	14 weeks
Measles-Rubella (MR)	2	9, 18 months
DPT	1	18 months
Td	1	5, 9 years
Td for women of childbearing age (15-49 years)	5	First contact; 4 weeks after 6 months after;1 year after; 1 year after respectively
Hepatitis B adult	3	First contact, 4 weeks, 6 months
Yellow fever	1	Travellers to at-risk countries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