Ministry Of Health
Kingdom of Swaziland

SWAZILAND INTEGRATED HIV MANAGEMENT GUIDELINES

2018

World Health Organization

Swazis and Americans
In partnership to fight HIV/AIDS
PEPFAR

Preface

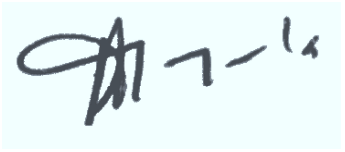
Swaziland has made significant strides towards achieving the UNAIDS 90-90-90 goals by 2020 and the 95-95-95 epidemic control goal by 2030. This is evidenced by the recent Swaziland HIV Measurement Survey 2 (SHIMS2) of 2016. SHIMS2 was a two-stage cluster randomised survey with a nationally representative sample. It showed that Swaziland has diagnosed 85% of all people living with HIV (PLHIV), 87% of which are currently taking antiretroviral therapy (ART), and 92% of those on ART are virally suppressed. At the population level, Swaziland has achieved viral suppression of at least 90% of the population on ARVs, with 73% viral suppression of all PLHIV regardless of ART status. Therefore, Swaziland is in a good position to achieve epidemic control by 2022 as envisioned by His Majesty, King Mswati III.

Deeper analysis of the SHIMS2 data, however, shows that there are sub-population differences with regards to service coverage and clinical outcomes. There are certain sub-populations exhibiting disparities in testing, treatment, viral suppression and prevention interventions. For example, adult and adolescent males and young people aged 15-24 years were found to have lower levels of awareness of their HIV status (77.5% and 66% respectively). Additionally, young people aged 15-24 years demonstrated low rates of ART uptake (76%) and lower levels of viral load suppression (VLS) (76%). This calls for targeted interventions to address these gaps in testing, treatment and VLS by sub-populations, geographies and modalities. Results also show that it is also essential to integrate HIV services with prevention and main stream health service delivery such as non-communicable diseases and mental health. As services expand, attention should be given to the quality of services provided. This is partly addressed by implementation of the National HIV Services Standards as well and the Site Improvement Monitoring Systems (SIMS) implemented at PEPFAR supported sites.

As we approach epidemic control, there is a greater emphasis on the need to sustain the success of the National HIV response. This requires a clear understanding of donor funded program and intervention components that are critical for the country to achieve and sustain epidemic control and how these components can be transitioned to government if not already within government structures. Additionally, healthcare workers across all cadres should maintain up to date on these innovated approaches, incorporating them into daily practice.

These guidelines address new innovations like HIV self-testing (HIVST), Pre-Exposure Prophylaxis (PrEP) for HIV prevention, a package of care for clients with advanced immunodeficiency and the introduction of better drugs and formulations (e.g. tenofovir, lamivudine, dolutegravir (TLD) a fixed dose combination (FDC) formulation) including differentiated ART delivery models (CommART). The guidelines will also bring clarity on quality related issues like re-testing for verification for clients who are initiating on ART and guidance to strengthen pharmacovigilance systems. These guidelines provide the standards and recommendations to move Swaziland forward in achieving the Government of the Kingdom of Swaziland's vision of zero new HIV infections (including elimination of Mother to Child Transmission of HIV) and ending AIDS. 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.

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



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Chapter 9: Annex (continued)

3TC	lamivudine
ABC	abacavir
ACEI	angiotensin-converting enzyme inhibitor
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-Guérin
BDQ	bedaquiline
CAGs	community ART groups
CCB	calcium channel blocker
CIHTS	client-initiated HIV testing services
CommART	community-centred models of ART delivery
CPT	co-trimoxazole preventive therapy
CrAg	cryptococcal antigen
DBS	dried blood spot
DMA	delamanid
DSD	differentiated services delivery
DTG	dolutegravir
ECP	emergency contraception
EFV	efavirenz
EIMC	early infant male circumcision
eIP	enhanced infant prophylaxis
EPI	expanded programme on immunization
FDC	fixed-dose combination
FTC	emtricitabine
GBV	gender based violence
HBV	hepatitis B virus
HCTZ	hydrochlorothiazide
HCV	hepatitis C virus
HCW	healthcare worker
HIVST	HIV self-testing
HPV	human papillomavirus
HTS	HIV testing services
IPT	isoniazid preventive therapy
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, newborn and child health
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
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
RIF	rifampicin
STI	sexually transmitted infection
SUAC	stepped-up adherence counselling
TB	tuberculosis
TDF	tenofovir
VIA	visual inspection with acetic acid
VL	viral load
VMMC	voluntary medical male circumcision
WHO	World Health Organization

Figures

Chapter 1:

Introduction

1.1 Background

The 2018 Swaziland 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 the use of antiretroviral drugs for treating and preventing HIV infection (June 2016), and Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy (July 2017). These Guidelines replace the 2015 Integrated HIV Management Guidelines.

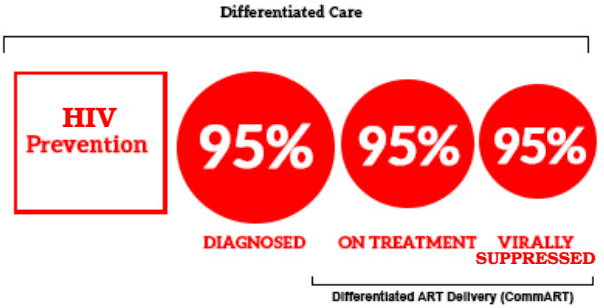
The Care and Treatment TWG led the development of these guidelines, providing leadership, coordination and critical reviews. Sub-Technical working groups, such as HTS, PMTCT and Pediatric Care and Treatment created specialized content for each chapter. Experts from the Ministry of Health, bilateral, multilateral, and implementing partner organizations drafted the respective sections of the guidelines. Additional input was received from WHO and other international experts.

The aim of these guidelines is to standardize and promote continued provision of comprehensive, quality, and client-centered prevention, care and treatment services. The goal of these new guidelines are 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.

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-centered 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, high quality care, and been shown to improve uptake of services and retention. See figure 1 below.

All health facilities that provide HIV services in Swaziland 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 knowledge to facilitate uptake of HIV services as well as strengthen linkages and client follow-up systems.

Figure 1: Differentiated service delivery as a tool to help achieve 95-95-95 by 2022



1.2 How to Use These Guidelines

The following images will appear throughout the guidelines to highlight:

Updates and changes to guidelines	
Outside reference	
Important messages	
Tools	
Dosing information	

1.3 Summary of Major Changes

Chapter 2: Prevention	• At every visit, assess knowledge and skill of condom use in all populations. • Early infant male circumcision is recommended for all male infants and can be done immediately after birth and up to 60 days after birth. • Voluntary medical male circumcision is recommended for all men/boys. Priority groups include men/boys aged 10-19 and all sexually active men. • Pre-Exposure Prophylaxis (PrEP) can be offered as an additional prevention choice for people at substantial risk of HIV infection, as part of a combination of prevention approaches. • All persons exposed to HIV accidentally, occupationally, sexually or otherwise should be prescribed Post-Exposure Prophylaxis (PEP) (as early as 1 hour and within 72 hours) by any Registered nurse or doctor, to minimize the risk of transmission of HIV and other blood-borne pathogens. » Adults/adolescents at low risk: TDF + 3TC » Adults/adolescents at high risk: TDF + 3TC + ATV/r [Strongly recommended for all penetrative sexual assault cases.] » All children (<40 kg): AZT + 3TC + LPV/r
Chapter 3: HIV Testing Services	• HIV testing service should be offered to all clients with unknown HIV status at every point of contact in 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.

Chapter 3: HIV Testing Services	• 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. • 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 are outlined in Table 3.15.
Chapter 4: Basic Care Package for HIV-Positive Individuals	• The basic HIV chronic care package must be provided to every client and differentiated based on client's baseline CD4 count and clinical assessment findings at presentation (mild, moderate or advanced immunodeficiency). • Baseline laboratory samples should be collected on the same day as HIV diagnosis • All clients diagnosed with HIV should start on cotrimoxazole (CTX) at enrolment into HIV chronic care. Clients should continue CTX until clinically stable on ART, with evidence of immune recovery (i.e. CD4 counts > 350 cells/mm^3 and an undetectable viral load. • All HIV-positive clients who do not have active TB should be started on isoniazid (INH) treatment for latent TB infection (LTBI) from one month after ART initiation for a duration of 6 months and should be repeated every two years from date of completion. • Clients who are over 5 years old with a CD4 count ≤200 cells mm^3 (or a CD4 count less than 25% for children), or WHO clinical stage 3 or 4, or, children with HIV who are younger than 5 years old are classified as, and must receive the advanced immunodeficiency package. • Clients with advanced immunodeficiency and CD4 ≤100 cells/mm^3 receive Cryptococcal antigen (CrAg) screening, and if positive, receive fluconazole prophylaxis for 6 weeks. • Clients diagnosed with Cryptococcal meningitis should initiate ART 6 weeks after commencement of antifungal treatment. • Clients who are TB-presumptive or are seriously ill with danger signs of advanced immunodeficiency, CD4 ≤100 cells/mm^3 or are seriously ill with danger signs, receive LF TB-LAM testing and if positive, start DS-TB treatment. • After one year on ART, adult clients who are clinically stable can receive ART refills every 3 months, and clinical assessments every 6 months. • The basic HIV chronic care package includes routine screening and management of non-communicable diseases, mental health and palliative care services. • All HIV-positive women should be screened at least once every year for cervical cancer. • Family planning needs should be assessed and family planning commodities offered to every HIV-positive woman at every visit. • All PLHIV should be assessed for symptoms of STIs at every clinical visit. • Index testing of among PLHIV should be done at least annually. • Treatment of Kaposi Sarcoma (KS) has been updated.

1.3 Summary of Major Changes (continued)

Chapter 5: Antiretroviral Therapy	• Test and Start means all PLHIV are eligible to initiate ART as early as possible preferably within 2 weeks of HIV diagnosis. • Every client should complete an individualized ART readiness assessment and counselling before ART initiation. Same-day initiation is encouraged for clients who are ready to start ART. • Clients who are diagnosed with advanced disease, under 5 years old, pregnant or lactating, have TB, HIV-positive in a sero-discordant relationship, have hepatitis B co-infection or have HIV-associated nephropathy should be prioritized for rapid/early ART initiation. • ART in TB clients should be started as soon as possible, preferably within 2 weeks of initiating TB treatment. • The recommended first line ART regimen is (Tenofovir (TDF 300mg) + Lamuvidine (3TC 300mg) + Dolutegravir (DTG 50mg) taken as a fixed dose combination (TLD) once daily preferably in the morning. • Clients initiating on DTG should be closely monitored for IRIS for the first 6 months. • Clients on a DTG-based regimen require active pharmacovigilance monitoring and reporting. » Viral load (VL) should be undetectable when switching from TLE to TLD. • For second line ART regimen: Initiate adults and adolescents on an ATV/r- based regimen. Clients can be switched from LPV/r regimens if they meet the requirements outlined in Chapter 5, Section 10. • VL should be measured 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 • 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 5.3 for the management protocol. • A viral load threshold of ≥1000 copies/mL should be used to determine virological failure when using plasma or dried blood spot specimens. • HIV drug resistance testing (genotyping) requests should be submitted to SNAP for review for clients suspected to be failing second line regimen after completion of SUAC. • Contact email for HIVDR support: snapthirdline@gmail.com. • To promote long term adherence for children and adolescents every facility should have a teen club, support groups, and caregiver focus groups. • After 1 year on ART, stable clients with undetectable viral load should be offered an opportunity to choose one of five ART service delivery models (or CommART/ Differentiated Service Delivery) for continued adherence • For methods and reporting on pharmacovigilance, refer to Annex 9.1.

Chapter 6: Prevention of Mother to Child Transmission of HIV (PMTCT)	• The recommended First-Line ARV for HIV-positive pregnant and lactating women is a once daily, fixed dose combination: TDF (Tenofovir 300 mg) + 3TC (Lamivudine 300 mg) + DTG (Dolutegravir 50 mg) » For methods and reporting on pharmacovigilance, refer to Chapter 9 • Initiate ART in maternity for all women who are HIV-positive regardless of WHO staging or CD4 count • Viral load monitoring schedules specific for pregnant and lactating women are: » All newly initiated on ART should receive first viral load test 3 months after starting ART. » Women on ART enrolling for ANC should receive a repeated viral load test if the last VL is more than 3 months old. A subsequent viral laod test shoudl be conducted after 3 months. » All lactating women should have a viral load at 6 weeks post-delivery regardless of previous viral load date. • All HIV-exposed infants should be provided with enhanced infant prophylaxis (eIP): » HIV-exposed infants should receive AZT and NVP until 6 weeks. This should be dispensed in maternity (if not given during ANC). » HIV-exposed infants should receive NVP only from 6 weeks to 14 weeks. This should be dispensed during the 6 week postpartum care visit. • Early infant diagnosis: » All mothers should be tested at ANC and PNC to determine the HIV exposure of the infants. » All HIV-exposed infants must be tested using DNA PCR at 6 weeks, 9 months, and 12 months. A rapid test should be done at 18 months. • All mothers, including those living with HIV: » Should exclusively breastfeed for the first 6 months. » Should continue breastfeeding for at least 12 months and may continue breastfeeding for up to 24 months or beyond, with complimentary feeding after 6 months, while being fully supported to adhere to care and consistent condom use.
Chapter 7: Paediatric Antiretroviral Therapy	• All HIV-infected children and adolescents are eligible to start ART 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. » For methods and reporting on pharmacovigilance, refer to Annex 9.1. • 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.

1.3 Summary of Major Changes (continued)

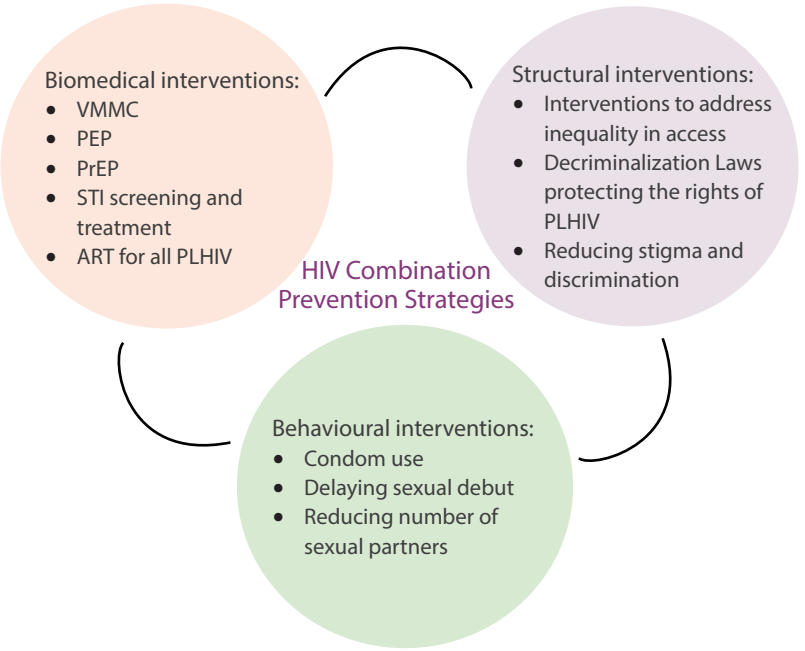
Chapter 7: Paediatric Antiretroviral Therapy	• Paediatric and adolescent clients with advanced immunedeficiency should be screened for cryptococcal meningitis using a serum Cryptococcal antigen (CrAg) test and TB presumptive adolescents and children should receive an LF TB-LAM test. • Children and adolescents with a VL > 400 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: Initiate adolescents on Atazanavir (ATV/r) regimens to reduce pill burden. Clients can be switched from LPV/r regimens if they meet the requirements outlined in Chapter 5 Section 10. • Third line ART: Each child or adolescent should receive individualized treatment regimens based on HIV resistances 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 successful transition is provided in Table 7.15 and Table 7.16. • 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 8: 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 level 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 Chapter 8, Section 3. • A high prevalence of depression is reported among PLHIV. 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 Chapter 8, Section 4. • All clients should be evaluated for pain at every visit using a validated pain scale. • For methods and reporting on pharmacovigilance, refer to Annex 9.1.

Chapter 2:

Prevention of HIV

2.1 HIV Prevention Approaches

This chapter reviews the major recommended biomedical HIV prevention approaches in Swaziland. Preventing new HIV infections is critical to controlling the HIV epidemic in Swaziland. Combination HIV prevention is an approach that seeks to achieve maximum impact on preventing new HIV infections by combining biomedical, socio-behavioral 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 HIV prevention services.

2.2 Condoms

Consistent and correct use of condoms reduces sexual transmission of HIV, other STIs by up to 94%, and prevents unwanted pregnancies. Male and female condoms should be available at all health facilities and in communities.

Table 2.1: Recommendations for Consistent and Correct Use of Condoms

Priority Groups	Key Actions
Heterosexuals who engage in anal sex	• Counsel and demonstrate on correct and consistent condom use • Provide adequate condoms and condom-compatible lubricants • 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-discordant couples Specific couselling for couples who are trying to conceive, please refer to Chapter 6, Section 2	
Adolescents (sexually active or not)	

At every visit, assess knowledge and skill of condom use in all populations (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. The treatment of STIs is the same for HIV-negative and HIV-positive individuals. For treatment of common STIs in Swaziland, see Chapter 4, Section 7.

2.4 Medical Male Circumcision

Medical male circumcision should be offered to all men/boys, 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

VMMC is recommended for all men/boys.

Voluntary medical male circumcision (VMMC) in Swaziland is provided by trained HCWs at health facilities or during outreach programs to adolescent and adult males. Priority groups include men/boys aged 10–49 and all sexually active men.

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:

- Emphasize correct and consistent use of condoms (dual protection).
- HIV testing services (HTS) and, if positive, linkages to care and treatment services.
- Prevention screening and treatment for STIs and, if positive, referrals to STI treatment and PrEP; see Section 2.4 and 2.5.
- 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.

2.5 Post-Exposure Prophylaxis

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

Post-exposure prophylaxis (PEP) is the use of ARVs by HIV-negative people after an exposure to HIV to prevent infection with HIV.

All persons exposed to HIV accidentally, occupationally, sexually or otherwise should access PEP as early as 1 hour and within 72 hours to minimize the risk of transmission of HIV and other blood-borne pathogens.

All Registered doctors and nurses at all health facility levels can prescribe ARV-drugs for PEP for any individual who presents with a history of exposure to HIV in the past 72 hours.

Recommended ARV Regimen for Post-Exposure Prophylaxis

Adults/Adolescents at low risk: Tenofovir (TDF)* + lamivudine (3TC)
Adults/Adolescents at high risk: Tenofovir (TDF)* + lamivudine (3TC) + atazanavir/ritonavir (ATV/r)
All children (<40 kg): Zidovudine (AZT) + lamivudine (3TC) + lopinavir (LPV/r)

*AZT can be used as an alternative.

Considerations for Post-Exposure Prophylaxis

PEP to be initiated without police form (RSP88) in all health care facilities.

Table 2.2: Recommendations for Post-Exposure Prophylaxis

Consideration	Recommendation
Eligibility	Must meet all of the following criteria: • Exposed individual is HIV-negative at baseline. • Exposure occurred within the past 72 hours. • Risk assessment conducted: » High risk (must be high-risk type AND source AND material): * High-risk type of injury: Mucous membrane, non-intact skin, or percutaneous injury. * High-risk source: HIV-positive or of unknown HIV status. * High-risk material: Blood or bloody body fluids; breast milk; semen; vaginal secretions; synovial, pleural, pericardial or amniotic fluids; cerebrospinal fluid; or HIV cultures in laboratory. » Low risk: * All other exposures not classified as high risk.
Management at initial contact	• Counsel on risks and benefits of PEP and obtain verbal consent 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 1 hour and within 72 hours) and 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). • Test women of childbearing age for pregnancy. • Do not delay administration of PEP while waiting for laboratory results. Special laboratory considerations: Creatinine (if TDF-containing regimen and diabetic or hypertensive) and haemoglobin (if AZT-containing regimen and suspect clinical anaemia); however, PEP should be offered even when laboratory tests are not available.
ARV regimen for PEP	Adults/adolescents at low risk: TDF* + 3TC Adults/adolescents at high risk: TDF* + 3TC + ATV/r [*Strongly recommended for all penetrative sexual assault cases.*] All children (<40 kg): AZT + 3TC + LPV/r **AZT can be used as an alternative*

Table 2.2: Recommendations for Post-Exposure Prophylaxis (continued from previous page)

Consideration	Recommendation
Dose of PEP	Same as indicated for ART; use weight-based dosing for children.
Time of initiation	Initiate PEP within the first hour or as soon as possible after exposure, but no later than after 72 hours. More than 72 hours: Conduct HTS and then repeat HTS after 8 weeks, but do not initiate on ART for PEP. If confirmed HIV-positive, the client should be referred to care and treatment.
Duration of PEP	28 days (dispense all 28 days of treatment at the first visit).
Follow-up	• Follow up with client at 7 days, 14 days, and 28 days after starting PEP. • Provide follow-up HIV testing 8 weeks after exposure. For HTS guidelines; see Chapter 3, Section 2. • Assess for and manage side-effects due to PEP.
Counselling	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 victims of sexual assult, 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. • Offer emergency contraception for non-pregnant women not on any contraceptive method or not compliant/adherent to 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, pre-exposure prophylaxis (PrEP) should be discussed as an option.

2.6 Pre-exposure Prophylaxis

PrEP is the use of ARVs by HIV-negative people who are at increased risk for acquiring HIV to prevent acquisition of HIV during periods of high risk.

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, male and female condoms, lubricants, ART for all HIV-positive people, and VMMC.

Priority Populations for PrEP

Populations who may benefit most from PrEP include:

- Serodiscordent couples
- Adolescents girls and young women (aged 16 - 25)
- Pregnant and lactating women
- Clients with STIs
- MSM
- Sex workers
- Clients who perceive themselves to be at high risk (please refer to Annex 9.18 for the HIV testing screening tool)

Eligibility for pre-exposure prophylaxis:

Clients determined to be at substantial risk for HIV infection must meet the following eligibility criteria before initiating PrEP.

- Confirmation of HIV-negative status.
- Determined to be at substantial risk for HIV by a HCW.
- No clinical symptoms or signs of acute HIV infection (e.g., flu-like symptoms, sore throat, lymphadenopathy, fever, skin rash) in combination with a preceding high-risk exposure for HIV in the previous 14 days.
- Ready to adhere to PrEP and willing to attend follow-up visits, including repeat HIV testing and monitoring for side-effects.
- No contraindication to use of tenofovir disoproxilfumarate (TDF) plus either emtricitabine (FTC) or lamivudine (3TC).

Recommended ARV Regimen for Pre-exposure Prophylaxis

Tenofovir (TDF) 300 mg and lamivudine (3TC) 300 mg by mouth daily (given as a fixed-dose combination).
Tenofovir (TDF) 300 mg and emtricitabine (FTC) 200 mg by mouth daily (given as a fixed-dose combination).

Effectiveness and safety of pre-exposure prophylaxis

PrEP and condom use have been shown to reduce the overall HIV transmission risk by more than 90% when clients are adherent. PrEP requires daily usage to be effective. PrEP must be taken for 7 days before it becomes fully effective followed by daily use for the duration of possible exposure to HIV in order to maintain full protection.

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.

Contradictions for pre-exposure prophylaxis

PrEP should NOT be provided to people with the following characteristics:

- 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 client.
- Creatinine clearance <60 mL/min.
- Body weight <40 kg.
- Age <16 years.

Side-effects

TDF-based PrEP is safe. 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 do not require discontinuation of PrEP. Elevated creatinine clearance happens but is a rare occurrence. Refer to the PrEP Implementation Guidance from the Ministry of Health on how to monitor and manage evaluated TDF-induced creatinine clearance. Refer to Annex 9.4 for potential ARV interactions with other drugs.

When to stop pre-exposure prophylaxis

Clients can safely stop PrEP when they feel they are no longer at substantial risk of HIV exposure. PrEP must be continued for 28 days after the last risky exposure, in order to be protected. Clients can safely re-start PrEP during a new episode of high risk if meeting eligibility criteria.

PrEP is not for everyone and not forever. PrEP is for times when people are at substantial risk for HIV infection.

2.7 ART for People Living with HIV

Treating PLHIV with ART has been shown to be the most effective strategy for preventing new HIV infections. All people living with HIV are eligible to start ART regardless of CD4 count or WHO staging and HCWs should promote early ART initiation see Chapter 3.

For additional information on the core package for HIV Prevention, HCWs can refer to the Core Package for HIV Prevention Guidelines for Implementers developed by National Emergency Response Counsel on HIV/AIDS (NERCHA).

Chapter 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 referred and linked to support, prevention and treatment services. It is ideal that clients receive a same-day diagnosis, as well as same-day referrals and linkages to prevention and treatment services.

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

3.1 HIV Testing Services Approaches

Client-Initiated HIV Testing Services

In client-initiated HTS (CIHTS), a client voluntarily seeks HTS. This approach emphasizes individual risk assessment and management by counsellors, and the development of an individualized risk reduction plan. CIHTS is available in the settings detailed in Section 3.5.

Provider-Initiated HIV Testing Services

In provider-initiated HTS (PIHTS), the healthcare worker (HCW) takes the initiative to offer HTS to clients with an unknown HIV status at all entry points. Routine testing maximizes the number of individuals who know their HIV status and is important in removing the stigma associated with taking an HIV test.

Routine testing, or opt-out HIV testing, should be conducted for clients presenting at the facility or in the community, prioritizing those with unknown HIV status. Targeted testing should direct HIV testing services to persons who are unaware of their HIV status and at higher risk of HIV acquisition.

Targeted testing

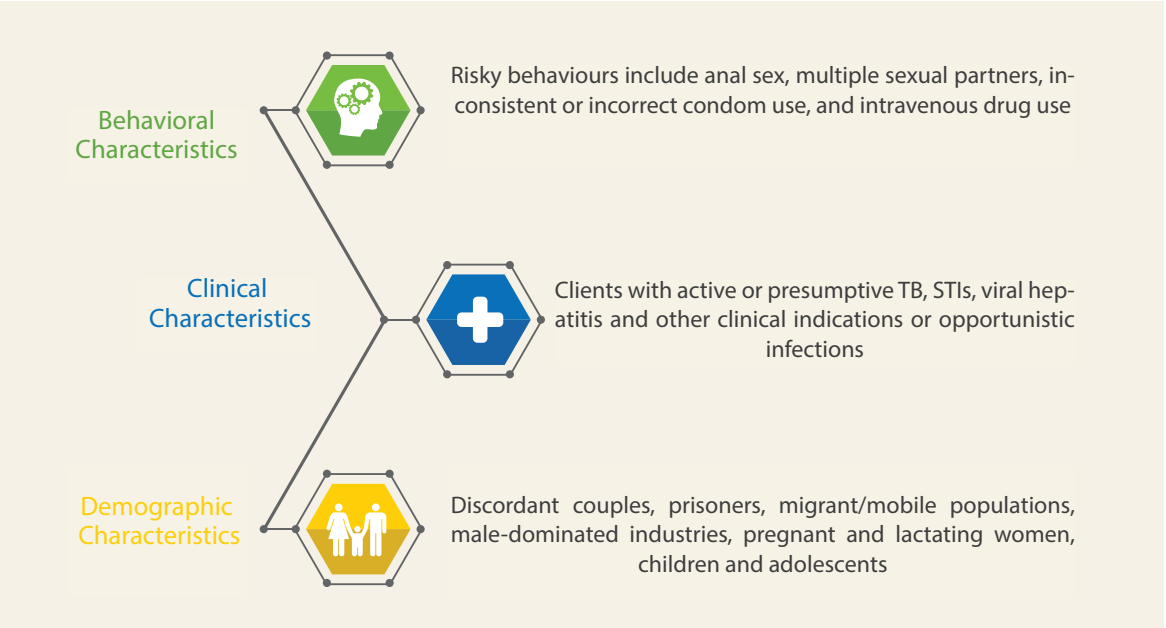
Targeted testing is intended to reach high risk populations typically defined on the basis of behaviour or clinical characteristics and includes priority groups such as:

- Men
- Children and adolescents (ages 0 - 19)
- Key populations

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

Figure 3.1 shows targeted testing approaches.

Figure 3.1: Targeted Testing



Some targeted testing approaches that have been shown to be cost-effective and produce high-yield include index testing/assisted partner notification, hot spot site testing, street-testing, offering HIV testing in shebeens (bars/taverns) and after-hours testing (moonlighting).

Index HIV testing as a targeted HIV testing approach

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 targeted HIV testing approach

A social network-based approach to HIV testing is recommended for key populations and is an approach in which HIV testing services are offered to sexual partners 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.

Partner Notification Services

The aim of notification is to encourage the contacts of the index clients with unknown HIV status to be tested.

1. Passive partner notification services:
   - 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 services:
   - Provider referral: with the consent of the HIV-positive client, a trained provider confidentially contacts the person's partner(s) directly and offers the partner(s) voluntary HTS.
   - Contract referral : when HIV-positive clients enter into a contract with a trained provider to refer their partner(s) to HTS)within an agreed time period, after which the provider contacts the partner(s) directly and offers voluntary HTS.
   - Dual referral: when a trained provider accompanies HIV-positive clients when they disclose their status to their partners. The provider also offers voluntary HTS to the partner(s). (For more information, see the WHO 2016 Guidelines on HIV self-testing and partner notification).

Every HIV-positive client should be given a partner/client invitation slip.

Assisted notification is always voluntary and methods may include face-to-face conversations by the index clients, invitation slips, phone calls, text messages and Internet-based messaging systems. 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 links and contacts that may also have HIV (see Figure 3.2).

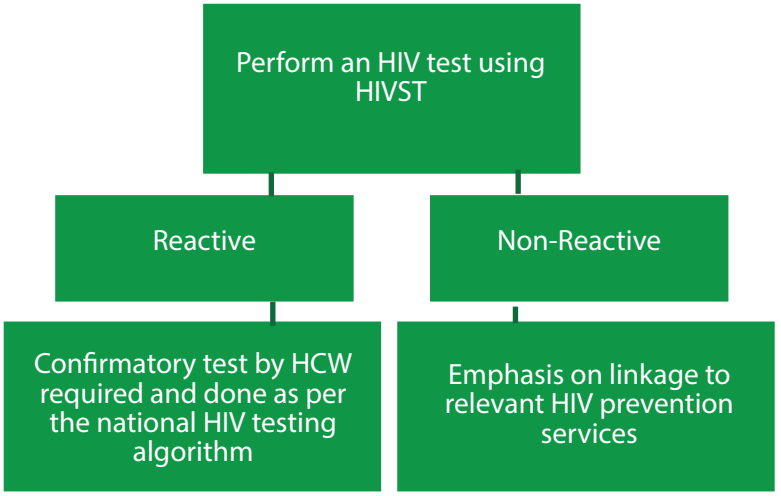
HIV Self-Testing

HIV self-testing (HIVST) is a process in which the client collects his or her own specimen and then performs an HIV test and interprets the result by him/herself, either alone or with someone he or she trusts. Any positive HIV result must be confirmed by a HCW in accordance with 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 Swaziland is 16 years. (For more information, see HIVST SOP)

Table 3.1: 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	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.

Figure 3.2: HIV Self-Testing Flowchart



3.2 Guiding Principles of HIV Testing Services

Both PIHTS and CIHTS, including HIVST, are voluntary and the "5 Cs" outlined below must be respected and adhered to by all HTS providers in all settings.

Table 3.2: The 5 Guiding Principles of HTS

Guiding Principles	Key Points
Informed Consent	• 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 request HTS and verbal consent is obtained to conduct the HIV test.
Confidentiality	• Testing results and any discussions between the HTS provider and the client should not be disclosed to anyone without the expressed consent of the person being tested. • Shared confidentiality among HCWs to promote linkages and further client management should be explained to the client.
Counselling	• 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 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 testing algorithm prior to ART initiation.
Connections and linkages to prevention, care and treatment	• Increased efforts to refer and link all clients to appropriate HIV prevention, treatment, and other support services, according to their result.

Ethical Considerations for HIV Testing Services

Informed consent

Individuals 12 years or older may give informed verbal consent for facility- or community-based HIV testing. In the case of minors, under 12 years of age, unconscious clients or those who are mentally challenged, the HCW and/or guardian may give consent in the best interests of the client.

For HIVST, either assisted or unassisted, the age of consent is 16 years and older.

Mandatory testing

Mandatory HIV testing is not endorsed in Swaziland. It may be considered only in special circumstances where the good of others is in jeopardy, for example, for blood donation and legal matters pertaining to rape cases. In such cases where clients require the results, the testing shall be accompanied by counselling.

Ethical disclosure

HIV test results should be disclosed in person and only to the client or client's guardian. Disclosure of results to anyone else should be done only with the client's or guardian's consent. HCWs are permitted to access a client's HIV status when it relates to care and treatment of the client. With that said providers should encourage clients to notify/disclose their status to sexual partners and family members or trusted others, where beneficial.

Messages should be tailored to the client's needs and focused on encouraging notification/disclosure of HIV status. Clients who are reluctant or fearful to disclose their results should schedule a disclosure counselling session with the counsellor to facilitate disclosure.

Partner notification

All HIV-positive clients should be offered assistance by the provider to help with notifying sexual and/or drug-injecting partners.

A partner invitation slip should be provided to HIV-positive clients to give to their partners with active follow-up. In no case may a testing provider or HCW notify a partner without that client's consent.

Issues relating to sexual violence

All persons who have been sexually violated should be offered HTS services. For victims who are HIV-negative, post-exposure prophylaxis (PEP) should be offered as soon as possible after exposure (within 72 hours); (see Chapter 2, Section 3 on PEP). If the client is HIV-positive, they must be referred to HIV care and treatment services. Mandatory testing and counselling for the sexual violence perpetrators can be performed only with a court order and the results can only be disclosed to the magistrate or judge handling the case.

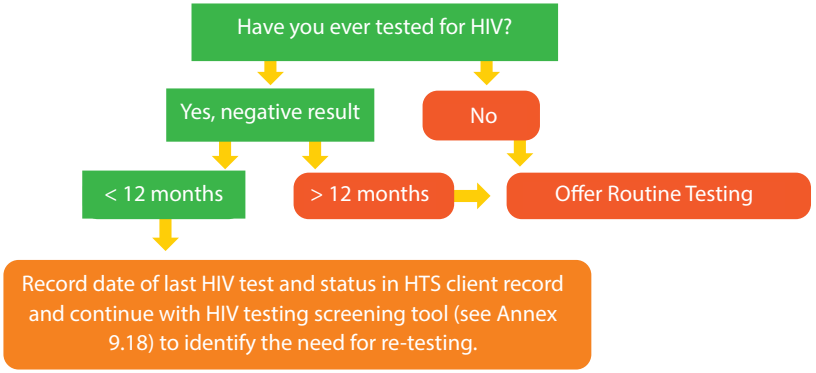
Who Can Perform an HIV Test?

Nurses and doctors registered with the Nursing Council or Medical & Dental Council in Swaziland can perform HIV testing. All other cadres need to receive training from a Ministry of Health- approved institution prior to performing or distributing an HIV test, including HIVST kits. These institutions are recognized by the Ministry of Health as providing quality training so that they can certify HTS providers to deliver HTS.

3.3 HIV Testing Screening Tool

The HIV Testing Screening tool is important in determining how often a client with a previous HIV-negative test will need to be re-tested for HIV. Re-testing will vary on risk of specific population groups and according to individual risks identified through a risk assessment. See Annex 9.18 for the HIV testing screening tool for Adolescents and Adults to assess the need for re-testing.

Figure 3.3: HIV Screening Tool



3.4 Timing of HIV Re-Testing and Key Points for Targeted Groups

Table 3.3: Population-Specific HTS Guidelines

Population	Key Points	When to re-test
General Population	• People should be offered an HIV test at first contact with a health facility and through other CIHTS approaches outlined in this chapter.	Based on HIV testing screening tool
Couples and partners	• HTS, with support for mutual disclosure, should be offered to married and cohabiting couples, premarital couples, polygamous unions and any other sexual partnerships. • Be aware of intimate partner violence and support individuals when they do not want to test with their partners. • HIV-positive clients should be offered assistance with notifying sexual partners periodically and at a minimum given an invitation slip to their partner for HIV testing (See Section 3.2 on partner notification).	Based on HIV testing screening tool
Negative partner in sero-discordant relationship	• Support the positive partner to initiate ART and remain adherent until they achieve an undetectable viral load. • Refer for PrEP when possible until partner has an undetectable viral load. • Promote correct and consistent condom use.	Re-test every 2 months unless there is evidence of undetectable viral load. Once partner maintains an undetectable viral load, re-test based on HIV exposure or annually.

Table 3.3: Population-Specific HTS Guidelines (continued from previous page)

Population	Key Points	When to re-test
Pregnant and lactating women	• At the initial antenatal care (ANC) visit, if a client is tested as HIV-negative, repeat HIV test at 8 weeks and every ANC visit throughout pregnancy. • For women who are not bringing their children for immunization, arrange to re-test them every 8 weeks pending result of the risk assessment (see Annex 9.18 for the HIV testing screening tool).	At delivery: Test women with unknown HIV status and/or those who have not been tested by the third trimester. After delivery: Encourage testing at the 6-week postpartum care visit and every 8 weeks, aligned with mother and infant visits thereafter.
Key and priority populations	• Key population groups and vulnerable populations are at higher risk for HIV. Key population groups include sex workers and their clients, injecting drug users, men who have sex with men, prisoners, and vulnerable populations include mobile populations and young women aged 15-24 years. • Healthcare providers should be especially aware to uphold standards of informed consent and confidentiality for these groups, as well as stigma- and discrimination-free service delivery throughout the health sector. • Refer for PrEP when possible (see Chapter 2, Section 4 for more information on PrEP).	Re-test every 8 weeks or as per HIV exposure, as these groups are at a particularly high risk for HIV infection.
People with disabilities	• Provisions should be made for people with disabilities to access HTS in a manner that meets their specific needs. For individuals unable to consent for themselves, the process of obtaining consent for other medical procedures and diagnostic tests should apply.	Based on HIV testing screening tool
Person with a recent HIV exposure	• Test at initial presentation (recommend PEP if exposure is within 72 hours).	Re-test every 8 weeks.
Symptomatic STI client	• Test at initial presentation; re-test pending ongoing risk as per risk assessment.	Re-test every 8 weeks or as per HIV exposure, as these groups are at a particularly high risk for HIV infection.
Client on PrEP	• Test at PrEP initiation, then as per PrEP follow-up schedule.	Refer to PrEP Implementation Guidelines.

Table 3.3: Population-Specific HTS Guidelines (continued from previous page)

Population	Key Points	When to re-test
Children and adolescents	• Paediatric HIV testing should be conducted in all HTS settings and applicable entry points such as Child Welfare Departments, paediatric outpatient departments or paediatric wards as well as in adult testing points. • Return of results (for DNA PCR) should be within 4 weeks and rapid initiation of treatment is essential. • For children under 18 months of age, HIV infection can only be definitively confirmed using a DNA PCR test on dried blood spot samples because of the presence of persisting maternal HIV antibodies. • Infants with an initial positive virological test result should be initiated on ART immediately while a second specimen is collected to confirm initial positive test result. • The guiding principle is that "the best interests of the child shall be the primary consideration" in all actions concerning children. • Adolescents should be tested in all HTS settings where adults are tested based on an HIV testing screening tool. The frequency of testing is based on the risk assessment results.	HIV-exposed infants should be tested within 6 to 8 weeks of birth. Subsequent tests are detailed in Section 3.8 within the early infant diagnosis algorithm. All HIV-exposed infants should undergo HIV testing routinely at 9 and 12 months using dried blood spot samples for DNA PCR to determine HIV status. All HIV-exposed children should undergo HIV testing at 18-24 months using HIV rapid tests to determine HIV status.

3.5 Settings for HIV Testing

HIV testing must be provided at all entry points within the health facility as well as in the community and households.

Facility-Based Testing

Routine opt-out PIHTS should be offered to all clients (including infants, children, adolescents and adults) visiting health facilities who do not know their HIV status, regardless of the reasons for their contact with the health facility. PIHTS should be integrated at all service delivery points as a standard of care in all units, but not limited to those listed below:

- Adult and paediatric inpatient and outpatient facilities
- Outpatient units
- Maternal and child health clinics
- Gender-based violence care units
- Tuberculosis (TB) clinics
- Sexually transmitted infection (STI) services
- Sexual and reproductive health/family planning services
- Antenatal, delivery and postpartum health services
- Child welfare services
- Home-based HTS through index clients
- National blood transfusion service

Community-Based Testing

Community-based HTS includes a number of strategies, for example, testing in homesteads, workplaces, parks, bus terminals, places of worship and educational establishments. It is an important approach for increasing early diagnosis, reaching first-time testers and people who seldom use clinical services, including men and adolescents in high-prevalence settings and people from key populations.
Community- based testing includes:

- Mobile and outreach services: Services provided from fully equipped mobile caravans/vehicles and other movable structures. This includes testing services offered at or nearby the workplace and educational institutions.
- Integrated sites: Services integrated or co-located within the health care system in government and nongovernmental facilities.
- Home-based HTS through door-to-door services: Services provided in a home setting with a family focus to increase access to and uptake of HTS.
- Stand-alone HTS sites: Sites where only HTS is provided, with referral and linkages to other services as needed.

All clients testing in community settings must be linked to appropriate care based on their HTS results.

HIV Self-Testing

Services provided by HIVST distributors and performed by individuals in a private setting. Distribution can occur in a facility setting to increase testing coverage, particularly in high-volume sites, or delivered through community-based or peer/sexual partner methods.

3.6 Pre-Test Information

Informed Consent

Obtain informed verbal consent according to Table 3.2: The 5 Guiding Principles of HTS.

Summary of Pre-Test Information

Table 3.4: Summary of Pre-Test Information

<table>
<tr><th colspan="3">Pre-test information included in both CIHTS and PIHTS</th></tr>
<tr><td colspan="3">

The benefits of HIV testing (highlighting the positive benefits).
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 prevention options and encouragement of partner testing.
» The fact that the test result and any information shared by the client is confidential.

The fact that the client has the right to refuse to be tested 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 provider questions.
Clinical and prevention benefits of HIV testing.
Benefits of ART and the Test and Start approach (starting treatment within 2 weeks of diagnosis).
Encourage voluntary notification of partners and disclosure of status.
Confidentiality of testing and results.
An offer to answer any question the client may have.
Condom use demonstrations (male and female condoms).
HIV testing screening tool (Annex 9.18)
Gender-based violence assessments for adolescent girls and young women

</td></tr>
<tr><th>CIHTS should also include:</th><th>PIHTS should also include:</th><th>HIVST should also include:</th></tr>
<tr><td>

Preparation for testing and receiving results
Suicide assessment and coping skills
Development of a risk reduction plan

</td><td>

Information on shared confidentiality
Reassurance that refusal to test will not result in the client being denied care for their current health problem

</td><td>

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

</td></tr>
<tr><td colspan="3">Inform client about HTS Hotline in case client wants to ask questions.</td></tr>
</table>

Table 3.5: Specific Pre-Test Information for Different Populations

Population	Specific Pre-Test Information Points
General Population	• HTS may provide information about testing and the need for consent in a group setting, such as group health education, but clients should give consent in an individual and private manner. • In settings such as PIHTS sites, where HIV testing is routinely offered, HCWs should carefully explain how a client can decline testing and ensure that each person has a private opportunity to opt out of testing, as informed consent remains essential. • People who are under the influence of drugs or alcohol or otherwise mentally impaired should not be tested, as they are not able to give informed consent. • HTS should ensure that no one coerces clients into being tested. • There are different methods to prevent HIV infection including male and female condom use, reduction of number of sexual partners, treatment of STIs, VMMC, PrEP and PEP.
Couples	• Possibility of discordant results and ongoing risks of reinfection. • For sero-discordant couples: in addition to messages on prevention, also emphasize ways for HIV-negative partner to stay negative (e.g. ART for HIV-positive partner, PrEP and condoms). • Importance of partner testing and notification services, as well as mutual support and disclosure.
Infants and children	• Briefly assess the child's knowledge and understanding of HIV/AIDS. • Counsel according to the level of development and knowledge using age-appropriate language. • Address both the child and the guardian's questions. • Ascertain the HIV exposure status of all infants with unknown or uncertain HIV exposure being seen in health care facilities at or around birth or at the first postpartum care visit—usually 7 days, 4–6 weeks or other child health visits in line with the Expanded Programme on Immunization (EPI) schedule.
Adolescents	• Prevention methods including delaying sexual debut, reducing number of sexual partners, male and female condom use, treatment of STIs, VMMC, PrEP and PEP. • Importance of partner notification services, as well as mutual support and disclosure.
Key populations	• Counselling on harm reduction programs and services. • Importance of partner testing, partner notification services, as well as mutual support and disclosure. • Availability of VMMC, PrEP and PEP for HIV-negative clients.
Pregnant and lactating women	• Risk of acquiring HIV from a male partner during pregnancy and breastfeeding. • Importance of partner testing, couples testing and partner notification services, as well as mutual support and disclosure of HIV status with emphasis on possibility of sero-discordancy results. • Measures that can be taken to reduce mother-to-child transmission, including the provision of ART to benefit the mother and prevent HIV transmission to the infant. • Potential risk of transmitting HIV to the baby or infant. • Counselling on infant feeding practices to reduce the risk of HIV transmission. • Consistent ART use during pregnancy and through breastfeeding can prevent mother-to-child transmission of HIV. • The benefits of early HIV diagnosis for mothers and infants.

3.7 Types of HIV Tests for Diagnosis

Types of Laboratory Tests

Table 3.6: Three Types of Laboratory Tests for HIV Diagnosis

Test Type	Test Name	Test Image	
Antibody (serological) tests	Rapid tests	Determine ™ 	While antibody testing provides a definitive diagnosis in adults and children over 18 months, virological testing is needed for definitive diagnosis in children younger than 18 months because the presence of maternal antibodies confounds the results of the antibody test.
		UniGold ™ 	
Antibody test (saliva) HIV Self Test (HIVST)	OraQuick		
Virological tests	DNA PCR for early infant diagnosis		

Antibody testing

Rapid tests detect antibodies to HIV and can be used to definitively diagnose adults and children 18 months of age or older. The 2 rapid tests approved for use in Swaziland are a sensitive test—Determine HIV1/2 and a specific test—UniGold HIV1/2. In Swaziland, rapid HIV testing is done serially one after the other (see Figure 3.4 for testing algorithm). If the result of the first test (Determine) is non-reactive, report as HIV-negative. If the result of the first test (Determine) is reactive, continue with the second test, UniGold. If both test results are positive, report as HIV-positive.

If results of both tests are discordant—Determine test positive and UniGold test negative or Determine test negative and UniGold test positive—repeat the testing strategy immediately but test both tests at the same time (parallel). If both tests are positive, report as HIV-positive. If both tests are negative, report as HIV-negative. If repeat tests remain inconclusive (i.e., Determine test is reactive and UniGold test is non-reactive, or vice versa) send sample to the National Reference Laboratory for DNA PCR testing. If DNA PCR results are reactive, the result is interpreted and communicated as HIV-positive. If DNA PCR results are non-reactive, the result is interpreted and communicated as HIV-negative.

Virological testing

- DNA PCR testing using the dried blood spot technique is used to definitively diagnose children less than 18 months of age.
- DNA PCR testing is also used in case of an inconclusive result for HIV re-testing or verification of HIV-positive result prior to ART initiation (see Section 3.7).
- DNA PCR testing can also be used as the last step to confirm HIV status in case of an inconclusive test result in adults and children older than 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 the serum/blood. The individual is highly infectious during the window period. The length of the window period varies from individual to individual, and also depends on the HIV test used.

Table 3.7: Summary of HIV Tests Performed

	Antibody Test		Virological Test
Test Name	Rapid Test	HIVST	DNA PCR
Sample Type	Blood	Saliva	Blood
Collection Site	Finger*	Mouth	*Heel/Toe for infants and venepuncture for adults
Window Period	8 weeks	8 weeks	2-6 weeks
Indication	Diagnosis 18 months or older	Self-screening	Diagnosis under 18 months or inconclusive test results
Turnaround Time	20 minutes	20 minutes	2-6 weeks

*In certain circumstances, venepuncture may need to be done instead of finger-prick (e.g., if other tests need to be run concurrently)

3.8 HIV Testing Algorithm

Every test that is conducted must follow the National HIV Testing Algorithm for children and adults.

Infants and Children Less Than 18 Months

All HIV-exposed infants less than 18 months old should be diagnosed with DNA PCR testing. Table 3.8 outlines the algorithm for HIV testing for infants and young children.

Table 3.8: Algorithm for HIV Testing for Infants and Young Children (continued on next page)

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

Age of Infant	Eligible for Testing	Which Test to Use	Management
6-8 weeks	HIV-exposed infants *(if exposure status not known- test mother, if mother not available, test child using DNA antigen test)*	DNA PCR	*If child is negative and never breastfed:* inform mother that child is HIV-negative; stop eIP; check and enforce ART adherence for mother; no need to test child again
			If child is negative and still breastfeeding: continue eIP; start CTX; check and enforce ART adherence for mother; re-test child at 9 months or 2 months after stopping breastfeeding or if they present with symptoms suggestive of HIV (whichever comes first)
			If child is HIV-positive: stop eIP; take blood for second DNA PCR testing; initiate child on ART (do not await results of second DNA PCR test; start child on CTX; check and enforce ART adherence for mother
9 months	HIV-exposed infants *(if exposure status not known- test mother, if mother not available, test child using DNA antigen test)*	DNA PCR	*If child is negative and never breastfed or stopped breastfeeding 2 months before current test*: inform mother that child is HIV; check and enforce ART adherence for mother; no need to test child again
			If child is negative and stopped breastfeeding within 2 months of current test: check and enforce ART adherence for mother; re-test the child 2 months after cessation of breastfeeding (if positive- take blood for second DNA PCR testing and initiate ART; if negative- inform mother that child is HIV-negative)
			If child is negative and still breastfeeding: check and enforce ART adherence for mother; 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 child is HIV-positive: take blood for second DNA PCR testing; initiate child on ART (do not await results of second DNA PCR test; start child on CTX; check and enforce ART adherence for mother

Table 3.8: Algorithm for HIV Testing for Infants and Young Children (continued from previous page)

Age of Infant	Eligible for Testing	Which Test to Use	Management
12 months	HIV-exposed infants *(if exposure status not known- test mother, if mother not available, test child using DNA antigen test)*	DNA PCR	Manage as above, however; • If 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 *(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 antibody test instead of DNA PCR • If 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)

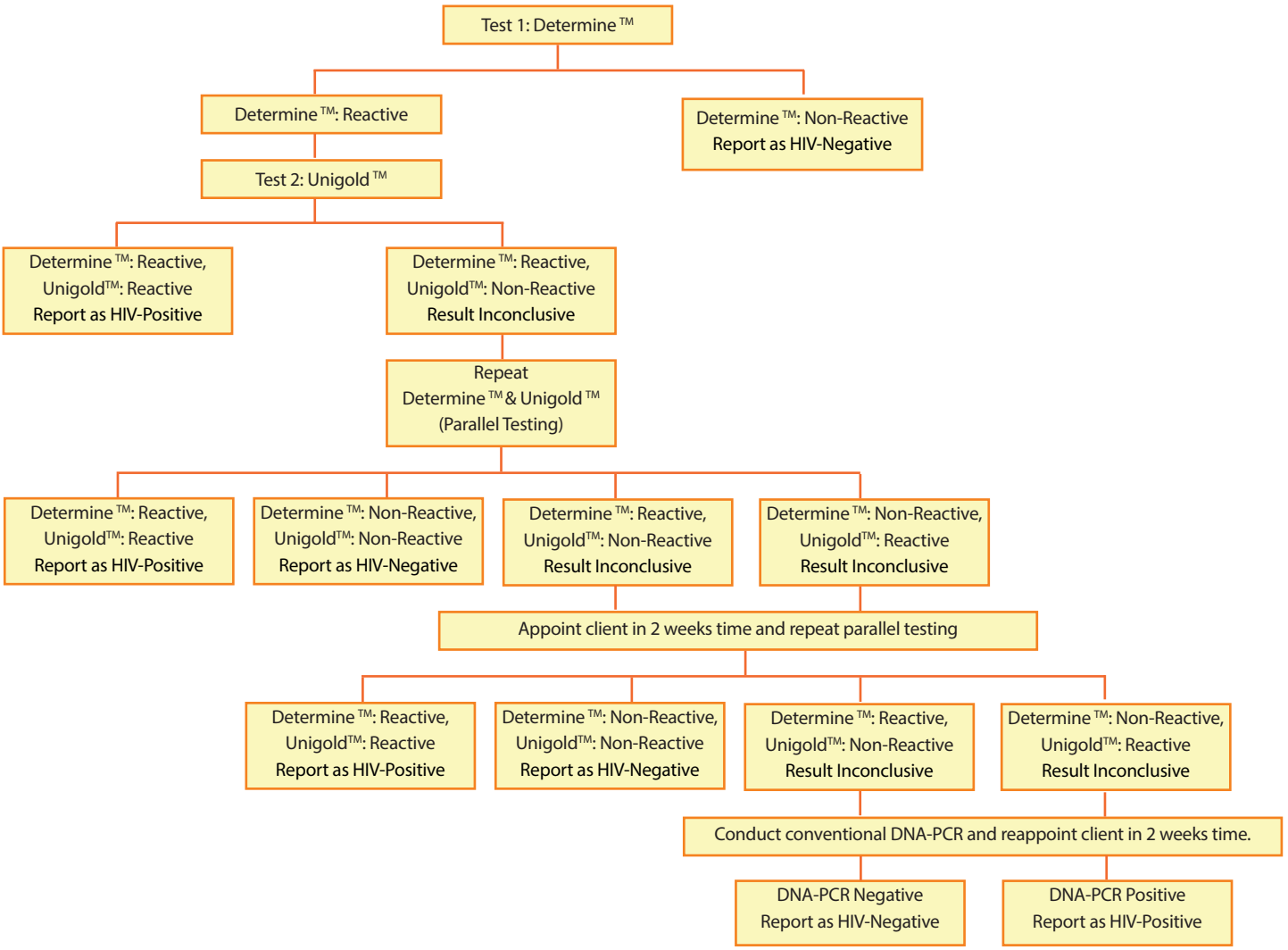
Adults, Adolescents and Children More Than 18 Months

Swaziland follows a serial testing algorithm as depicted in Table 3.9 and Figure 3.4.

Table 3.9: Serial HIV Testing Steps for Rapid Testing in Adults and Children Over 18 Months

Perform HIV Testing as Follows:
1. Perform testing with the 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 client in two weeks time 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) send sample to the National Reference Laboratory for DNA PCR testing. All specimens referred to the National Reference Laboratory should be accompanied by a Laboratory Request Form. Then appoint clients in two weeks time to receive results of DNA PCR.
12. If DNA PCR results are reactive, the result is interpreted and communicated as HIV-positive.
13. If DNA PCR results are non-reactive, the result is interpreted and communicated as HIV-negative.

Figure 3.4 Serial HIV Testing Algorithm—Rapid Testing in Adults and Children Over 18 months



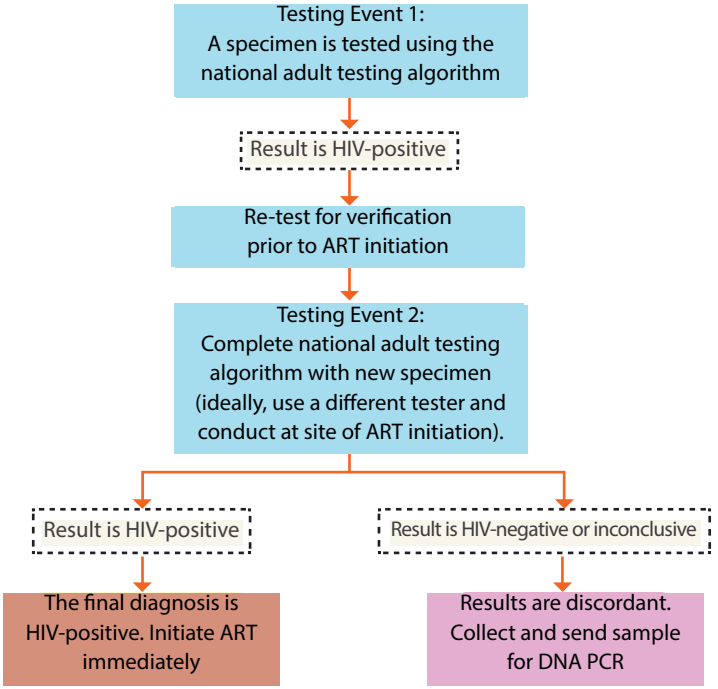
Verification of HIV-Positive Result Prior to ART Initiation

Re-testing for verification of HIV-positive diagnosis is part of quality assurance procedures to assure clients of their HIV-positive status classification before initiation on lifelong ART.

Re-testing for verification is *not* recommended for clients already on ART.

All clients with positive HIV test results presenting for ART initiation will be re-tested, with a second specimen, preferably with a different tester, before ART initiation (including immediate initiation of ART for all pregnant women to prevent mother-to-child transmission). This also includes clients with positive HIV test results willing to start ART the same day they are diagnosed, the Test and Start approach. This means the client will have both testing events conducted the same day and then initiated on ART same day (see Figure 3.5). Refer to 2017 Re-testing for Verification SOP for further details.

Figure 3.5: Re-testing for Verification Flow Chart



*Re-testing should not be performed on people who are already established on ART.

Source: Re-testing for Verification SOP, 2017

Re-testing for verification before ART initiation follows the same national algorithm as described in National Re-testing Algorithm.

What to do in case of a discordant result (if re-testing results in inconclusive or negative):
If the re-testing for verification result is negative or inconclusive, the client is classified as "Discordant": • Refer the blood specimen to the National Reference Laboratory for further confirmatory testing using DNA PCR. All specimens referred to the National Reference Laboratory should be accompanied by a Laboratory Request Form. Mark the form as urgent and the reason for test should be "confirmatory test." Advise the client to return after 2 weeks for their definitive HIV diagnostic test results from the laboratory.

3.9 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:

- ART is available and is recommended for everyone confirmed as HIV-positive.
- Starting treatment as soon as possible (preferably within 2 weeks of testing HIV-positive) reduces the chance of clients' illness getting worse or passing HIV to others.
- If you take ART properly and do not miss pills, you can expect to live a long and productive life and significantly minimize the risk of passing HIV to sexual partners and unborn children.
- Encourage partner notification and disclosure.

Table 3.10: Summary of Post-Test Counselling

Post-test counselling for both positive and negative results should include:
• Simple and clear communication of test results • Check clients' 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

Table 3.10: Summary of Post-Test Counselling (continued from previous page)

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 number of sexual partners. • Scheduling of ongoing supportive counselling sessions as per client need. Referral for prevention and other health services where indicated.	• Supporting the emotions arising from test result. • Discussion of any immediate concerns. • Informing 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.

Counselling for Special Populations

Table 3.11: 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. • Family planning. • Partner and family testing. • Sero-discordancy and how to stay negative, including availability of PrEP for the negative partner in a sero-discordant couple.
Pregnant and lactating women	Counsel on the following points: • Childbirth plans. • Family planning. • 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 own health and for PMTCT should be promoted as well as the importance of HIV testing for the infant reviewed.

Table 3.11: Additional Key Counselling Messages for Special Populations (continued from previous page)

Special Population	Specific counselling messages to be included:
Children	• Younger children should be told their status incrementally to accommodate their cognitive skills and emotional maturity in preparation for full disclosure.
Adolescents	• Listen and address adolescents' concerns. • Focus on risky behaviour and develop risk reduction plans. • If test is positive, reassure 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 on the modes of transmission of HIV. • Provide condoms and lubricants, and referrals for prevention, treatment and care, including availability of PrEP, STI testing and treatment, and needle and syringe programmes. • Discourage reuse of needles, razors and syringes. • Encourage partner testing, notification and disclosure. • Early treatment of STIs • Encourage VMMC

3.10 Documentation and Reporting

All HIV test results should be documented in a standard way.

- Positive test result: Reactive
- Negative test results: Non-reactive
- Inconclusive test results: Inconclusive

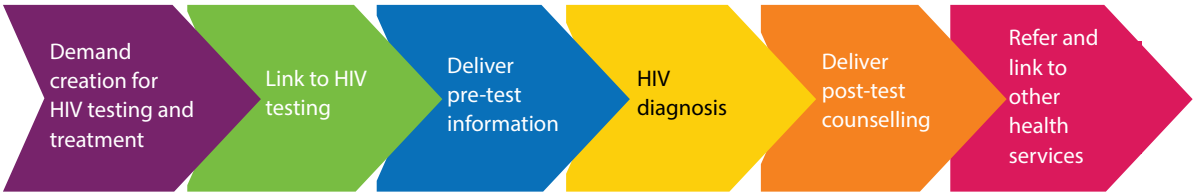
HIV test results should be documented in the following places:

- Client prescription sheet
- HTS register
- HTS client record
- Re-testing for verification register
- Chronic care file

3.11 Referral and Linkages

Linkage or connection to HIV care for PLHIV refers to the period beginning with demand creation for HIV testing, HIV diagnosis and ending with enrolment in care or treatment and other health services.

Figure 3.6: Linkages to HIV Care for PLHIV



Source: Adapted from WHO Guidelines on HIV Testing Services, July 2015

Written results should be provided to the client in all cases. All referrals should be made using the national referral forms.

Linkage to services can be to and from different levels as explained in Table 3.12:

Table 3.12: Types of Linkage to Services

Linkage Point	HCW Responsibilities
Linkages within same facility	HCWs should always escort clients to the next point of service. Individuals diagnosed with HIV in a facility must be entered into a chronic care (pre-ART or ART) register after treatment services have been offered.
Linkages from community to facility	Individuals testing HIV-positive 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.
Linkages between 2 facilities	Clients tested in a facility and referred to another facility for care must have an appointment set for them in the receiving facility so that follow-up can take place if they miss their appointment.

The responsibilities of HCWs at the testing site, with regard to linkage and referrals, include:

- Staff members working in health care facilities and community-based and outreach settings should be trained on how to implement and manage effective referrals.
- Understanding the service needs of their clients.
- Ensuring the referral is made and that the receiving site is aware that a client is expected.
- Awareness of available referral services (both clinical services and community resources).

A referral directory or guide should be used to help staff members make appropriate referrals.

Table 3.13: Summary of Referral and Linkages

Referral and linkages for both HIV-positive and HIV-negative clients should include	
• Same-day referral, if services offered onsite or close to a health facility. • Referral to another facility that is conducive to the care of the client.	
Referral and linkages for HIV-negative clients should also include: • Referral for re-testing based on ongoing HIV risk • Referral to other supportive care services/prevention services (e.g., condoms, male circumcision and family planning)	**Referral and linkages for HIV-positive clients should also include:** • Enrolment into care • Referral to other supportive care services including ongoing counselling and support groups

3.12 Quality Assurance in HIV Testing Services

Table 3.14: Quality Assurance in HTS

HTS Provider
• Conduct quality control tests every time a new batch is opened. • Participate in all proficiency panel testing and document reports. • Store test kits in a temperature controlled environment (e.g., a refrigerator). • Ensure samples are stored and transported appropriately. • Adhere to HIV testing SOPs (rapid and HIVST) and national HIV testing algorithms. • Ensure information and testing aids are given to clients using the HIVST kits. • Ensure strong linkages and strong after-care mechanisms for clients.
Supervisor
• Ensure the facility has the capacity for cold chain management. • Ensure samples are stored and transported appropriately. • Oversight of testing performed by HTS providers. • Ensure compliance to HIV testing/HIVST SOPs and national HIV testing algorithms. • Monitor stock management of HIV testing commodities.

Table 3.14: Quality Assurance in HTS (continued from previous page)

Laboratory/National HTS Program
• Conduct regular onsite supportive supervision for laboratory, point of testing sites and individuals distributing HIVST kits. • Conduct HTS trainings and refresher trainings regularly. • Regularly conduct and distribute proficiency panel testing and ensure facilities receive feedback and develop corrective action plans as appropriate. • Ensure documentation and dissemination of quality assessment reports. • Review HIV testing registers and HIVST registers. • Ensure samples are stored and transported appropriately. • Review HIV testing SOPs and national HIV testing algorithms. • Disseminate information on HIV testing and monitoring compliance with recommended testing algorithm(s). • Evaluate the performance of new HIV tests kits at the national level. Only approved kits may be used for routine testing. • Engage all HIV testing points in an external quality assessment program of the Swaziland Health Laboratory service through participation in quarterly proficiency testing. • Conduct competency assessments of testers at least once a year.

Table 3.15: Quality Assurance for Counselling

HTS Provider
• Administer counsellor reflection forms. • Administer client satisfaction measuring tools (i.e., client exit forms). • Document and disseminate quality assurance assessment report.
Supervisor
• Regular site visits. • Conduct regular sit-ins with HTS providers. • Supportive supervision for counsellors. • Counsellor care. • Client intake record and review procedures. • Documentation and dissemination of quality assurance assessment report.
Laboratory/ National HTS Program
• Oversight of HIV testing quality assurance and control (e.g., accreditation of HTS training partners and the standardization of the HTS curricula). • Refresher trainings. • Quality assurance tools.

Chapter 4:

Basic Care Package for HIV-Positive Individuals

4.1 Basic HIV Chronic Care Package

All clients who test HIV-positive should be linked to and enrolled into 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 (see Summary Table 4.2) for people living with HIV (PLHIV) includes:

- Initial clinical evaluation and categorization of clients.
- Opportunistic infection screening and management, including provision of prophylactic treatment (cotrimoxazole [CTX], isoniazid preventative therapy [IPT], fluconazole).
- Adherence and psychosocial support services.
- HIV index testing.
- Laboratory tests.
- 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 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
- Routine and structured clinical follow-up visits.

The basic HIV chronic care package should be differentiated based on the client's laboratory and clinical evaluation findings.
See Table 4.2 for definitions of relevant categories.

HIV care should be differentiated according to clinical evaluation, laboratory evaluation and client needs. This approach will ensure that services are client-centred to address the client's needs and expectations and improve efficiencies as well as client outcomes at health facilities

Figure 4.1: Differentiated HIV Care and Treatment Services

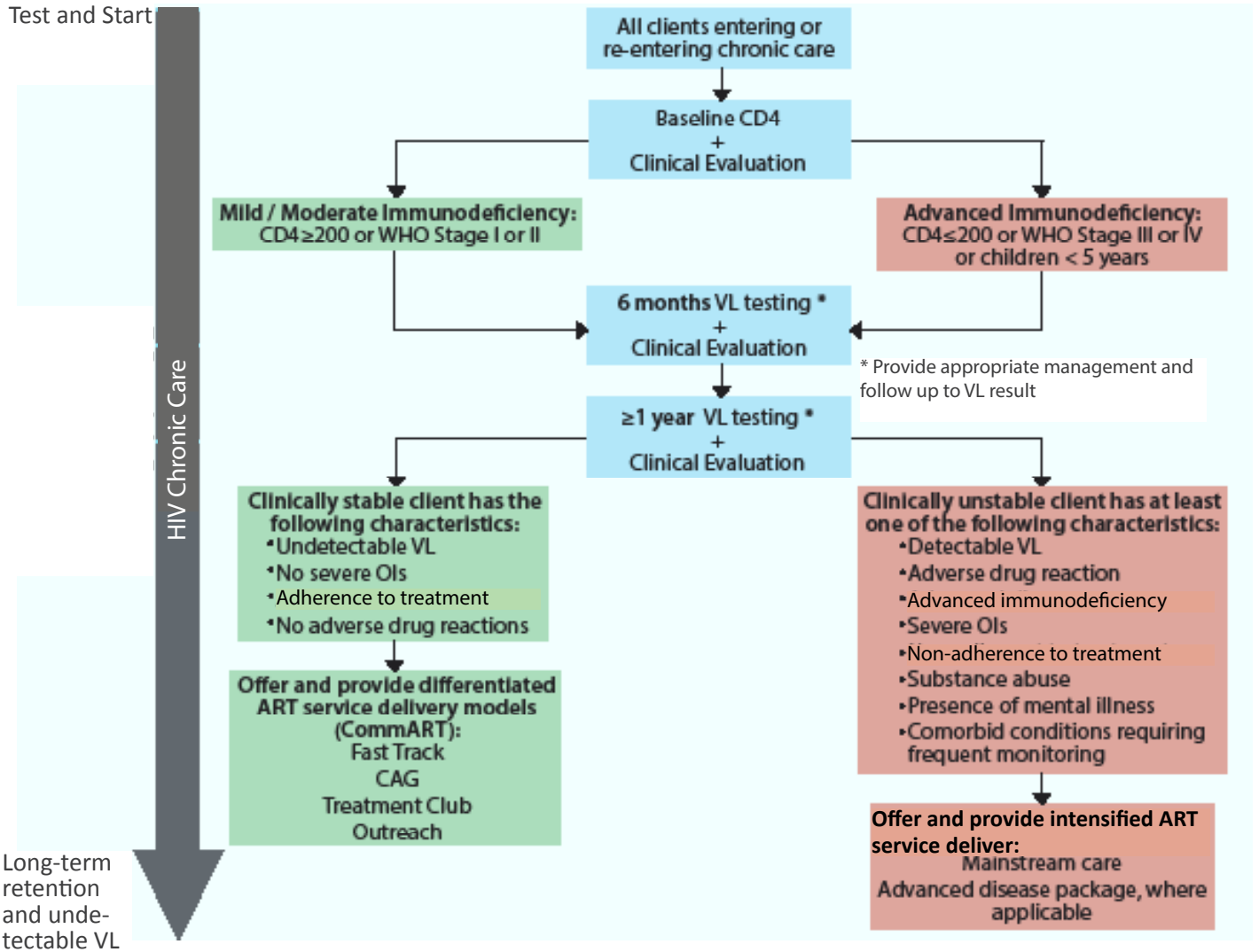


Table 4.1: Definition of Client Categories for Differentiated HIV Service Delivery

All People Living with HIV (PLHIV)			
Clients initiating or reinitiating ART or on ART for <1 year		Clients on ART for >1 year	
Clients with Advanced Immunodeficiency (Advanced Disease)	Clients with Mild or Moderate Immunodeficiency (Clinically Well)	Clients Clinically Stable on ART	Clients Classified as Unstable on ART
Adults: • Presenting or returning to care with advanced HIV disease (WHO stage 3 or 4 disease and/or CD4<200 cells/mm^3) • Such individuals may be ART naïve, interrupted treatmen, or failing treatment Children 5 years and older: • Same as adults plus those with CD4 count less than 25% Children under 5 years: • All children less than 5 years old are managed as clients with advanced immunodeficiency (advanced disease)	Mild immunodeficiency: • Presenting or returning to care when clinically well (absence of WHO clinical stage 3 or 4 disease and/or CD4 cell count ≥350 cells/mm^3) • Such individuals may be ART naïve, may have interrupted treatment, or failing treatment Moderate immunodeficiency: • Presenting or returning to care when clinically well, absence of WHO clinical stage 3 or 4 disease and/or CD4 cell count between 200-350 cells/mm^3 • Such individuals may be ART naïve, may have interrupted treatment, or failing treatment	• Undetectable viral load • No severe opportunistic infections • CD4 ≥200 cells/mm^3 • Treatment adherent • No adverse drug reactions • 5 years of age or older	If a client has 1 or more of the following characteristics: • Detectable viral loadFailing ART regimen • CD4 <200 cells/mm^3 • Adverse drug reactions • Active opportunistic infections • Non-adherent to treatment • Substance use • Comorbid conditions requiring frequent monitoring • Child under 5 years of age

Table 4.2: Differentieted HIV services : Package of care for the different client categories

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?
Entering chronic care and/ or <1 year on ART	Presenting or returning with mild or moderate immunodeficiency (clinically well)	Basic chronic care package including (refer to Section 4.1 for the basic care package): • Client readiness assessment prior to initiating ART • Early ART initiation • Adherence support • Prophylaxis (isoniazid (INH) preventive therapy [IPT] and Co-trimoxazole (CTX) preventive therapy [CPT]) • Management of possible side-effects • Index HIV testing • Provision of condoms	Health Facility	Soon after HIV diagnosis, • ART initiation within 2 weeks to 1 month • CTX from enrolment; see Section 4.6 on when to stop • IPT from 1 month post-ART initiation see Section 4.6 ART refill: • 2 weeks after ART initiation • Monthly refills through the first 6 months • Every 3 months after first 6 months on ART if an undetectable VL is achieved *For more information on the ART refill schedule, see Chapter 5, Section 7*	Nurses Doctors Expert clients Laboratory teams Pharmacy teams
	Presenting or returning with advanced immunodeficiency (advanced disease)	Basic chronic care package as listed above. Emphasis is on the advanced immunodeficiency package: • CrAG screening • LF TB-LAM testing • Management of OIs • See Section 4.5 for the full Advanced Disease package	Health Facility	Soon after HIV diagnosis, • ART initiation within 2 weeks to 1 month • CTX from enrolment; see Section 4.6 on when to stop • IPT from 1 month post-ART initiation see Section 4.6 ART refill: • After initiating ART: 2 weeks • First 6 months on ART: every 1 month • After 6 months refer to Chapter 5, Section 7	Nurses Doctors Expert clients Laboratory teams Pharmacy teams

Table 4.2: Differentieted HIV services : Package of care for the different client categories (continued from previous page)

Client Category		HIV Chronic Care Package			
		What is included in the basic care package?	Where is care provided?	When is it provided?	Who will provide it?
On ART for > 1 year	Clinically stable on ART	Basic care package including: • Differentiated ART delivery models—see Chapter 5, Section 6 for CommART • HIV Index testing • Provision of condoms	Health facility and community	Clinical assessment: • Every 6 months ART refill: • Every 3 months	Doctors Nurses Expert Clients Laboratory teams Pharmacy teams
	Clinically unstable on ART	Basic care package emphasis is on: • Stepped Up Adherence Counselling • If there is evidence of treatment failure timely switching to 2nd or 3rd line regimen is necessary • Advanced Immunodeficiency package (if CD4 <200); see Section 4.5 • Management of other comorbidities and adverse drug reactions to common first-line ARVs (see Annex 9.8) • Special clinic days for clinically unstable clients e.g. targeting clients suspected to be failing treatment • HIV Index testing • Provision of condoms	Health Facility	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 Multi-disciplinary team approach

4.2 Clinical Evaluation for PLHIV

All clients should be clinically evaluated for the elements described in Table 4.3.

Table 4.3: Elements of Clinical Evaluation for PLHIV

History	Current and past medical history	• Document current presenting complaints and symptoms. • Screen for opportunistic infections (see Section 4.6) such as TB, cryptococcal meningitis, toxoplasmosis, Pneumocystis jeroveci 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). • 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 sulfonamidesanilamide drugs). • Family history of HIV testing
	Psychosocial history	• Establish and document social support structures. • Establish possible presence of mental health concerns, depression, substance abuse, etc. • Encourage disclosure to trusted significant others and sexual partners. • Elicit and begin to address possible barriers to adherence to treatment. • Link to additional facility and community support resources.
	Sexual and reproductive history	• Discuss secondary prevention and avoidance of reinfection with STIs, including combined prevention approaches. • Ask about HIV and ART status of sexual partner(s). • Encourage index testing and 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. • 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 Exam	General examination	• Check vital signs (respiratory rate, temperature, heart rate, and blood pressure) • Look for cyanosis, clubbing, jaundice, dehydration, pallor and oedema. • Calculate body mass index; use mid-upper arm circumference for pregnant women and children. • Refer client for further management if malnourished (e.g., Food by Prescription or Integrated Management of Children Illnesses Guidelines).

Table 4.3: Elements of Clinical Evaluation for PLHIV (continued from previous page)

Physical Exam	General examination	• Look for signs of cryptococcal meningitis and TB as these illnesses will affect the timing of ART initiation; see Section 4.6. • Provide STI screening and management.
	Systems examination	• Examine other systems
	Summary	• Assign and document the initial WHO clinical stage and manage presenting illnesses: prompt treatment of inter-current illness contributes to the success of ART and reduces early mortality. • Identify and prioritize care for clients with advanced immunodeficiency to improve client outcomes.

4.3 Baseline Laboratory Evaluation of PLHIV

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

Table 4.4: Baseline Laboratory Evaluation Differentiated by Client Category

		Baseline Test	Comments
All PLHIV: Mild/ Moderate or Advanced Immunodeficiency	All PLHIV	Re-testing for verification	• Required; refer to Chapter 2 on HIV testing services (HTS).
		CD4 count	• Required to make management decisions for people presenting with advanced immunodeficiency (advanced disease) (especially those with CD4 count ≤100 cells/mm^3.)

Table 4.4: Baseline Laboratory Evaluation Differentiated by Client Category (continued from previous page)

	Baseline Test	Comments
All PLHIV	Alanine aminotransferase / aspartate aminotransferase (AST/ALT)	• If not available, look for signs of liver disease prior to ART initiation.
	Creatinine	• Recommended for clients being initiated on TDF. • If not available, rule out renal dysfunction clinically prior to ART initiation, especially in clients with hypertension and diabetes, and run creatinine when later available.
	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 client on a tenofovir (TDF)-based regimen.
	Pregnancy test	• Recommended for women of childbearing age.
Clients with CD4 ≤100 cells/mm^3	Lateral flow urine lipoarabino-mannan assay (LF TB-LAM)	• LF TB-LAM is an additional diagnostic tool to supplement the national TB algorithm and encourage same-day results. • LF TB-LAM is for HIV-positive, TB-presumptive clients who also have a CD4 ≤100 cells/mm^3 or are seriously ill with danger signs. • If LF TB-LAM positive, start DS-TB treatment and follow-up sputum results. • See Figure 4.2 for LF TB-LAM testing algorithm.
	Cryptococcal antigen (CrAg) screening	If CD4 ≤100 cells/mm^3, see Section 4.6 for the CrAg screening algorithm • If positive and symptomatic for meningitis, refer client to hospital for further investigation • If positive and asymptomatic, refer to Section 4.6 for fluco-nazole pre-emptive treatment. • Reflexive test following CD4 result of ≤100 cells/mm^3

Baseline laboratory samples should be collected on the same day as the HIV diagnosis although absence of results should not delay ART initiation.

4.4 Changing Role of CD4

CD4 remains a valuable laboratory test that is used to determine a client's chance of developing opportunistic infections. However, clients stable on ART with undetectable viral load and CD4 count ≥350 cells/mm^3 do not require routine CD4 count monitoring.

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
- Evaluating the need for routine screening of opportunistic infection
  - » If CD4 ≤100 cells/mm^3, then then LF TB-LAM testing and LF CrAg screening should be completed
- If CTX prophylaxis should be started, stopped or re-started
- Disease progression, for clients with HIV who have not initiated antiretroviral therapy (ART)

See Annex 9.22 for the use of CD4 and VL tests.

4.5 Differentiated Service Delivery for Clients with Mild or Moderate Immunodeficiency

Assessment of PLHIV at Initial Contact

PLHIV present at different stages of disease progression. Upon presentation, clients should be assessed using baseline CD4 count, clinical evaluation, including WHO clinical stage (see Section 4.1) to determine whether the client has mild, moderate or advanced immunodeficiency. Clients must be offered differentiated service delivery according to their clinical presentation. For differentiated service delivery for clients on ART, see Chapter 5, Section 12.

The following populations should be given close medical attention and initiated on ART as a priority:

- Clients with advanced immunodeficiency (CD4 ≤200 cells/mm^3 or WHO clinical stage 3 or 4)
- Infants and young children ≤5 years old
- Pregnant women
- Clients with Tuberculosis (TB)
- HIV-positive individuals in a sero-discordant relationship
- Clients with hepatitis B virus (HBV) coinfection
- Clients with HIV-associated nephropathy

Clients diagnosed at WHO clinical stage 1 or 2 or who have a CD4 count above 350 cells/mm^3 (adults) or 25% (children 5 years and older) are considered as presenting with mild immunodeficiency. These clients should be supported to initiate ART as soon as possible (preferably within 2 weeks) after HIV diagnosis to avoid disease progression. Clients who have a CD4 count between 200 and 350 cells/mm^3 have moderate immunodeficiency and are at high risk for progressing to advanced immunodeficiency. These clients should also be initiated on ART as soon as possible and monitored closely.

4.6 Differentiated Service Delivery for Clients with Advanced Immunodeficiency

Definition of Advanced Immunodeficiency

1. Adults, adolescents and children over 5 years who have a CD4 count ≤200 cells/mm^3 (or a CD4 count of less than 25% for children) or a WHO clinical stage 3 or 4

2. All children with HIV who are younger than 5 years are considered to be a high-risk group and are therefore managed as having advanced immunodeficiency (advanced disease).

Table 4.5: Definitions of Advanced Immunodeficiency and High-Risk Groups

	Advanced Immunodeficiency (Severe Immunodeficiency)	High-Risk Group (Very Severe Immunodeficiency)
Adults and Adolescents	CD4 count ≤200 cells/mm^3 or WHO clinical stage 3 and 4	CD4 count ≤100 cells/mm^3
Children	Children 5 years and older: • CD4 count ≤200 cells/mm^3 or CD4 less than 25% • WHO clinical stage 3 or 4 Children under 5 years: • All children less than 5 years old are managed as clients with advanced immunodeficiency (advanced disease).	Children 5 years and older: • CD4 count ≤100 cells/mm^3 or CD4 less than 25% Children under 5 years: • CD4 count ≤100 cells/mm^3 or CD4 less than 25%

Management of Clients with Advanced Immunodeficiency

Clients with advanced immunodeficiency are at high risk of opportunistic infections including TB, cryptococcal meningitis, toxoplasmosis, PJP, and other bacterial infections. Clients may also progress to advanced immunodeficiency (advanced disease) while on treatment, especially during the first year of treatment or if client has a detectable viral load.

Package of Care for Clients with Advanced Immunodeficiency

- Rapid ART initiation (within 7 days) is recommended to restore immune functioning and prevent further decline of CD4 cells.
- The following considerations should be noted:
  - » ART should be deferred for 6 weeks if client is diagnosed with cryptococcal meningitis
    - * Immediate ART in clients newly diagnosed with cryptococcal meningitis is not recommended due to risk of life-threatening immune reconstitution inflammatory syndrome (IRIS)
  - » In TB diagnosed clients, ART should be started within 2 weeks of starting TB treatment when client can tolerate treatment.
    - * Caution is needed for people living with HIV with TB meningitis, since immediate ART is associated with more severe adverse events
  - » See below sections on TB and cryptococcal meningitis for more information.
- After ART initiation, clients need to be monitored closely for the following:
  - » Clinical response
  - » Development of IRIS
  - » Non-adherence to ART
- Enhanced psychosocial counselling and adherence support.

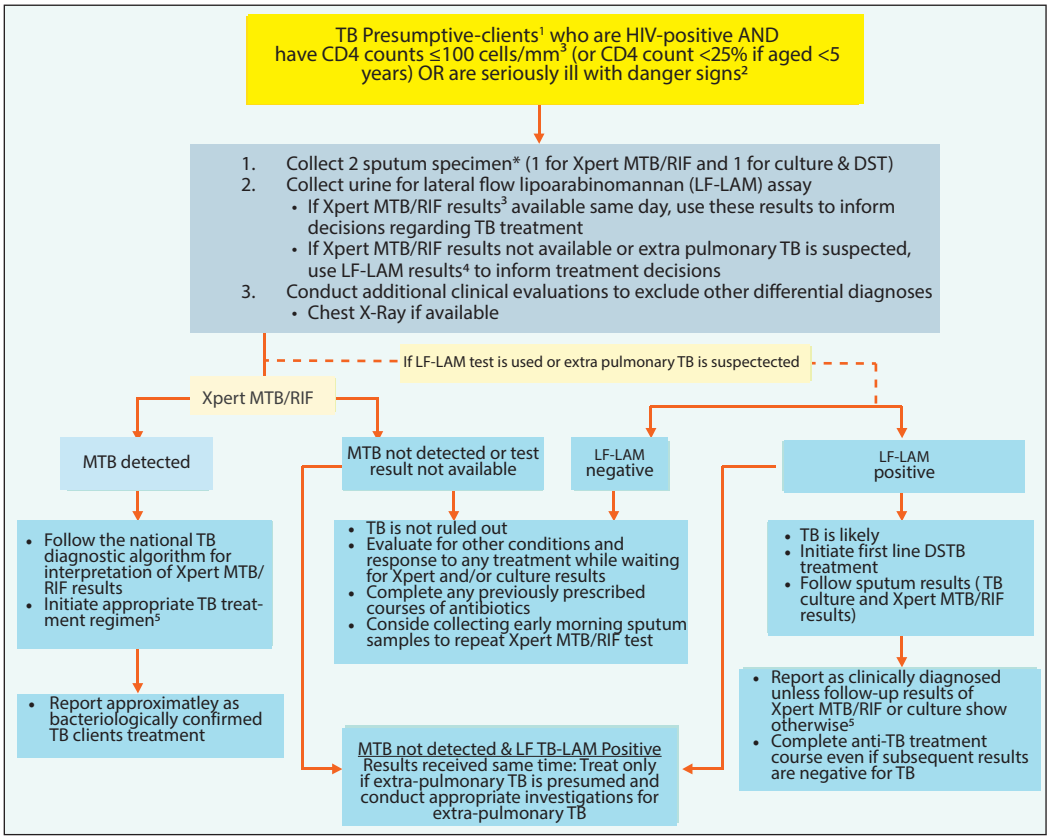
Laboratory Tests for Clients with CD4 ≤100 cells/mm^3

Clients with advanced immunodeficiency (advanced disease) require additional laboratory tests:
1. CrAg screening—for all clients with CD4 ≤100 cells/mm^3.
2. LF TB-LAM testing—for HIV-positive, TB-presumptive clients with CD4 ≤100 cells/mm^3 or are seriously ill with danger signs.

LF TB-LAM testing is used to assist in the diagnosis of TB in HIV-positive clients with signs and symptoms of TB and CD4 count <100 cells/mm^3 or <25%. See Figure 4.2.

Lateral flow urine lipoarabinomannan assay testing in PLHIV with advanced immunodeficiency

Figure 4.2: LF TB-LAM Testing for PLHIV with Advanced Immunodeficiency

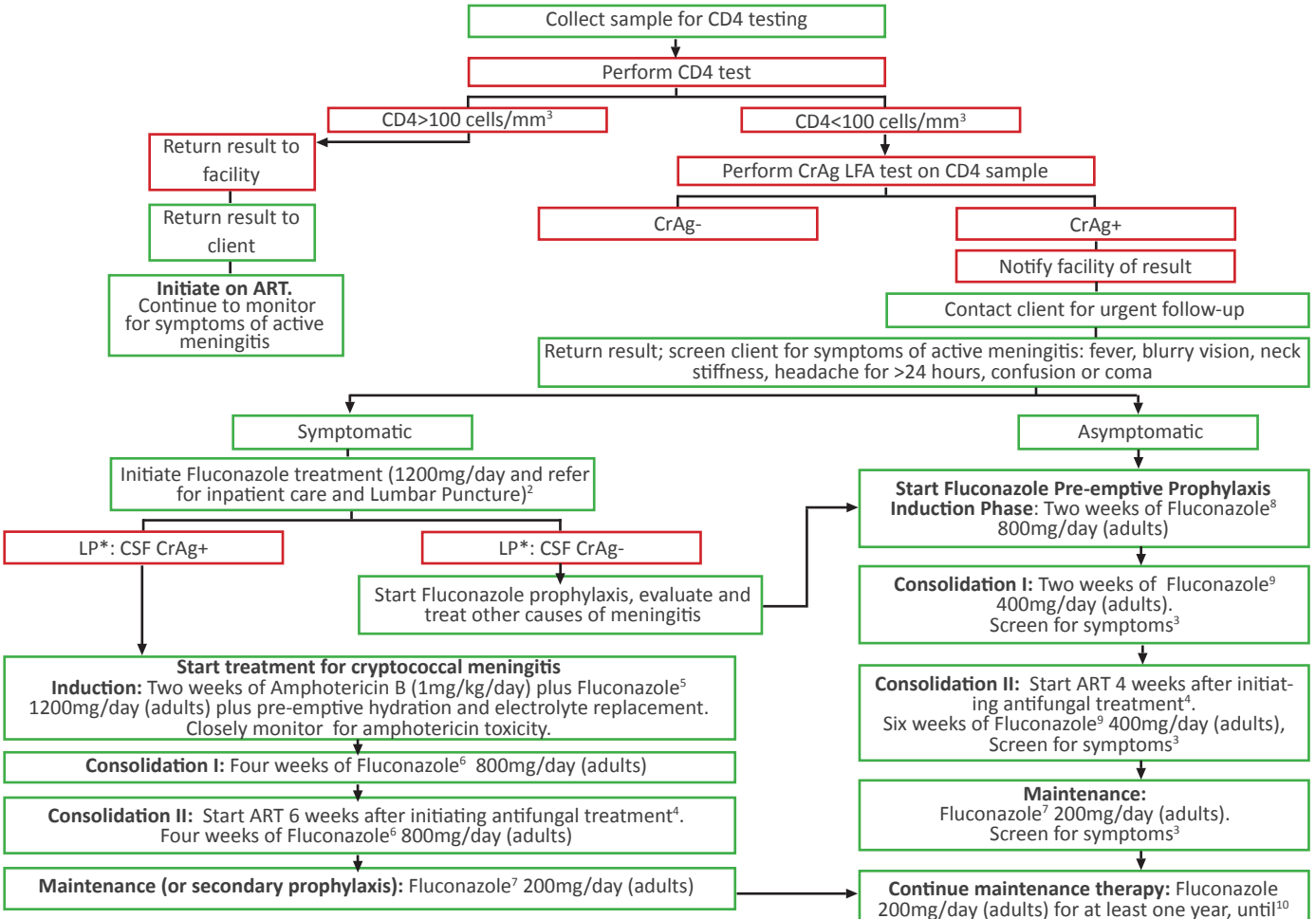


1. Clients evaluated for TB include adults and children with signs and symptoms of TB. #For children <5 years, use CD4 count <25%.
2a. Danger signs for adults can be any one of the following: respiratory rate >30 per minute, temperature >39°C, heart rate >120 beats per minute, or unable to walk unaided. This excludes danger signs that can be explained or are a result of other diagnosed conditions e.g. cardiac failure, other bacterial infections, or malaria.
2b. Danger signs for children (fast breathing with chest-in-drawing, severe wasting or oedema, lethargy or convulsions): Parameters vary by age; refer to IMCI tables.
3. Xpert MTB/RIF test is the preferred initial diagnostic test. For clients being evaluated for pulmonary TB; sputum is the preferred specimen.
4. LF TB-LAM assay can be used can be used to assist in diagnosing active TB in HIV-positive clients (both inpatient and outpatient) with symptoms presumptive of TB and CD4 counts ≤ 100 cells/mm³ or those who are seriously ill with danger signs. LF TB-LAM can also aid in the diagnosis of extra-pulmonary TB where samples are not readily accessible in the same target population. Clinicians can initiate TB Treatment immediately based on the positive LF TB-LAM and their clinical judgement while awaiting other TB results.
5. Initiate TB treatment with first line or second line TB drugs based on the Xpert MTB/RIF results (refer to national TB diagnostic algorithm).
*Prioritize sputum culture if unable to get two sputum specimens.

If a client is identified as positive by LF TB-LAM, see Section 4.3 for treatment and clinical considerations.

Cryptococcal antigen screening in PLHIV with advanced immunodeficiency

Figure 4.3: CrAg Screening for PLHIV with Advanced Immunodeficiency



[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 at 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.

4.7 Prevention, Screening and Management of Common Opportunistic Infections

All PLHIV should be screened for opportunistic infections and treated appropriately. Common opportunistic infections among HIV clients, especially clients in Swaziland 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 Swaziland Standard Treatment Guidelines.

Co-trimoxazole Preventive Therapy (CPT)

CPT is used to prevent many common opportunistic infections among PLHIV.

Indications

All adults (including pregnant and lactating women), adolescents and children diagnosed with HIV should receive CPT.

When to start

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.

Dosing

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

Table 4.6: Co-trimoxazole Prophylaxis Dosing for Adults, Adolescents and Children

Age	Weight	Suspension 200 mg 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 yrs to 14 years	15–30 kg	10 mL	4	1	--
>14 years	>30 kg	--	--	2	1

Adverse events

Table 4.7: 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 Section 4.6 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 9.1).

When to stop

Clients should continue CPT until clinically stable on ART (see Section 4.1) with evidence of immune recovery (i.e., CD4 counts >350 cells/mm^3 and an undetectable viral load). Continue CD4 monitoring as per viral load schedule while a client remains on CPT.

Clients can stop CPT when any of the following occurs:

- Client has full immune recovery evidenced by CD4 >350 cells/mm^3, an undetectable viral load and no history of PJP or toxoplasmosis or other opportunistic infections.
- Severe (Grade 3 or 4) adverse reaction to CPT or any other sulphfur-containing medication.
- Severe kidney disease (creatinine clearance <50 mL/min)
- Severe liver disease (aspartate aminotransferase/ alanine aminotransferase [AST/ALT] >5 times 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.

Alternatives to Co-trimoxazole Prophylaxis
Adults and adolescents: Dapsone 100 mg once daily (with food)
Children: Dapsone 2 mg/kg once daily (with food)

Co-trimoxazole desensitization in adults and adolescents

In instances of Grade 3 reactions to CPT, consider desensitization as described below.

Desensitization should be performed only under the supervision of a medical doctor.

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 4.8: 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 doble-strength tablet

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

Co-trimoxazole oral suspension
(200 mg sulfamethoxazole + 40 mg trimethoprim) / 5 mL

Tuberculosis

All HIV-positive clients (adults, adolescents, children and pregnant women) should be screened for tuberculosis (TB) at every clinical visit using the national TB screening tool.

All pregnant women should be screened for tuberculosis at every antenatal care visit.

Prevention of TB among PLHIV

Counselling on risk reduction behaviour to reduce the risk of TB transmission at home and in health facilities should be included in HIV care.

The following activities should be implemented at all entry points that provide HIV and TB care:

1. Prevention and treatment of TB among PLHIV (Three I's strategy)

   i. Intensified TB case-finding
      - Screen all clients for TB and refer for TB prophylaxis or TB treatment services.

   ii. Isoniazid preventive therapy (IPT)/treatment of latent TB infection (LTBI)
      - To prevent development active TB, offer IPT to all clients who screen negative for TB unless there are contraidications to IPT.

   iii. Infection prevention and control of TB
      - Refer clients with active TB to a TB clinic if available; separate people in facility waiting areas and ensure airflow.
      - Provide rapid triage of clients with cough in waiting areas.
      - Ensure that facilities have an up-to-date infection control plan.

2. Prevention and treatment of HIV infection in clients with active TB
   - Provide HTS to all clients with presumptive or diagnosed TB.
   - Ensure HIV prevention interventions for HIV-negative TB clients and early ART initiation for TB clients living with HIV.
   - Provide IPT for TB/HIV coinfected clients who have successfully completed their TB treatment.

For more information, please refer to the National Policy guidelines on TB/HIV Collaborative Activities, 2015.

FDC (CTX/INH/pyridoxine) is a prefered option to clients indicated for both INH and CTX, when available.

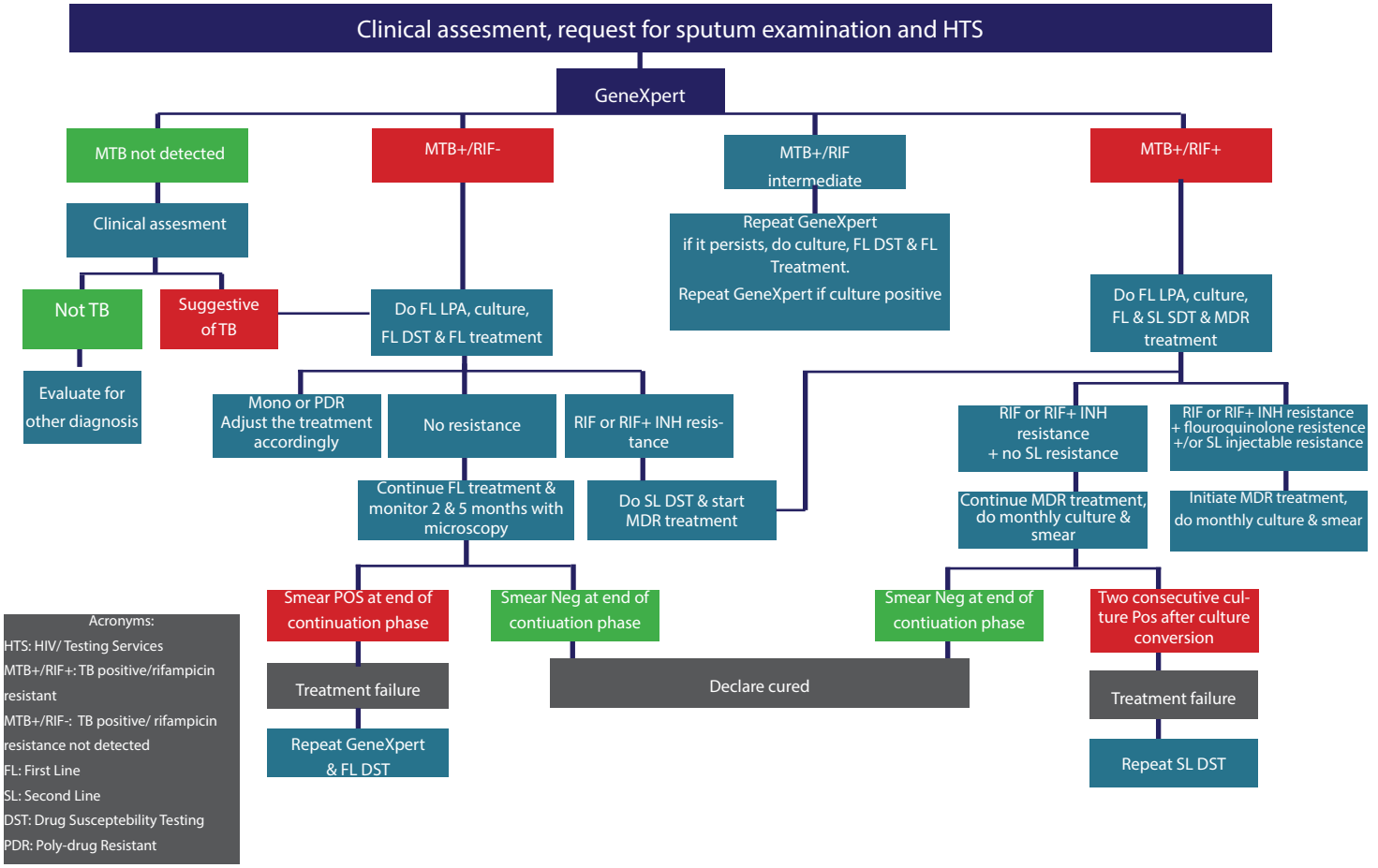
Diagnosis of pulmonary TB

For more information on the diagnosis and management of TB, refer to the National Tuberculosis Guidelines.

Evaluation for Other Diagnoses

- When treating empirically for a lower respiratory tract infection, use antibiotics that cover both typical and atypical pneumonias (but do not use fluoroquinolones).
- To decrease the number of visits and speed up diagnosis, further investigations should be done at the same time.
- Advise the client to return for reassessment if symptoms recur.

Figure 4.4: Laboratory TB Diagnostic Algorithm



For diagnosis of paediatric TB, reference the algorithm shown in Figure 4.4. However, when sputum cannot be collected, clinical symptoms and positive TB contact are enough to start TB treatment.

For management of TB/HIV coinfection among adults, see Chapter 5, Section 4.

For management of TB/HIV coinfection among children and adolescents, see Chapter 7, Section 6.

Diagnosis of TB among clients with advanced immunodeficiency

See Chapter 5, Section 8 for use of LF TB-LAM for HIV-positive clients with presumptive TB and CD4 <100 cells/mm^3 (or <25% in children) or seriously ill with danger signs.

Presumptive treatment of latent TB infection with INH

Indications

All PLHIV who do not have active TB disease (i.e., screened negative using the TB symptom screening tool or tested negative after TB investigations) should receive isoniazid (INH) treatment for LTBI for at least 6 months.

Timing

Table 4.9: When to Start INH for LTBI in PLHIV, by Client Category

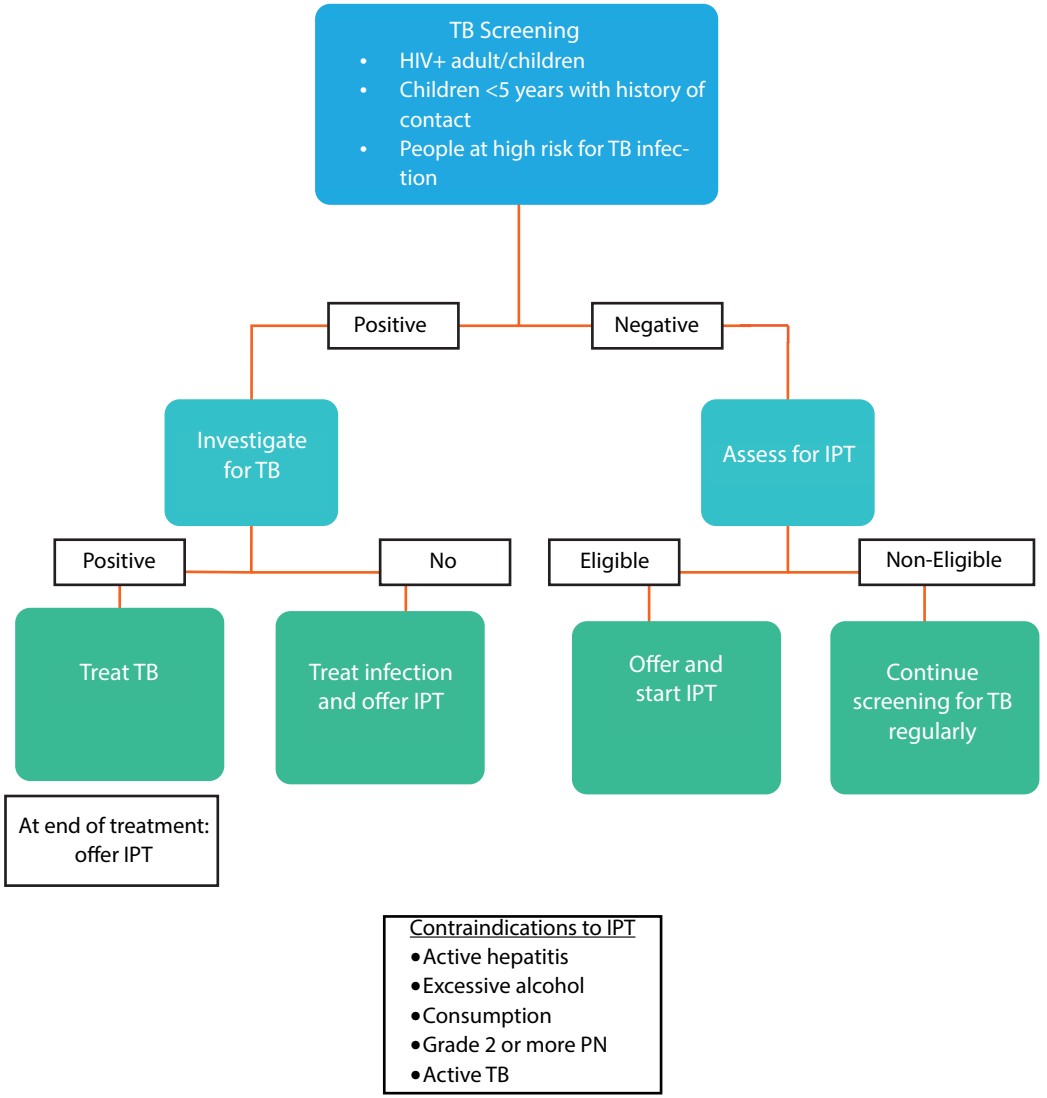
Client Category	When to Start INH
Adults, adolescents and children >12 months	Initiate LTBI treatment after 1 month on ART
Children <12 months and with a history of TB contact	
Clients on TB treatment	Initiate LTBI treatment on day of TB treatment completion
Clients with presumptive TB	Initiate LTBI treatment after TB is ruled out and after 1 month on ART
Pregnant and lactating women	Initiate LTBI treatment after 1 month on ART

IPT can be started from 1 month after ART initiation and should be repeated every 2 years from the date of completion.

Contraindications

- Active TB
- Children <12 months with no history of TB contact
- Acute/ chronic liver disease
- History of poor adherence to treatment
- Excessive consumption of alcohol (defined as alcohol intake of >21 units per week for men/boys or 14 units per week for women/girls)

Figure 4.5: TB Screening Flowchart



Dosing

Table 4.10: INH Dosing for Adults and Children

Weight Bands (kg)	Dose Given (mg)	Number of 100 mg INH tablets per dose
>5	50	½ tablet
5.1–9.9	100	1 tablet
10–13.9	150	1½ tablets [or ½ adult 300mg tablet]
14–19.9	200	2 tablets
20–24.9	250	2½ tablets
>25 to adult	300	3 tablets [or 1 adult 300mg tablet]
Isoniazid is taken once daily for 6 months. Best absorbed when taken on an empty stomach (1 hour before or 2 hours after a meal).		
Pyridoxine 1–2 mg/kg daily (25–100 mg for adults) with each dose of isoniazid is recommended to reduce the risk of peripheral neuropathy.		

Monitoring

INH refill dates must be synchronized with ART refill or clinic visits. At each clinical visit, assess for the following:

- TB symptoms, including cough, fever, night sweats and weight loss (if a person on INH develops TB symptoms, discontinue INH and promptly evaluate for TB disease)
- Toxicity (e.g. hepatitis, neuropathy, rash)
- Adherence to LTBI treatment
- If client is suspected to have liver toxicities than conduct AST/ALT test for liver enzyme

Discontinue isoniazid (INH) if either of the following occurs:

- Symptoms of acute hepatitis and elevation of ALT 3 times the upper limit of normal
- No symptoms of acute hepatitis but ALT increases to 5 times the upper limit of normal
- Worsening peripheral neuritis despite treatment
- Other uncommon neurotoxic effects such as psychosis

Addressing treatment defaulters

- Clients who miss up to 1 month of therapy (30 days) should have the length of LTBI treatment extended to accommodate the missed doses.
- Clients who miss doses frequently (i.e., 2–3 times per week) should stop LTBI treatment and receive adherence counselling. Re-initiate the LTBI treatment only if client is committed to the medication schedule and dosing. The number of doses missed should be added to the length of treatment already received, but total treatment duration should not last longer than 9 months (270 days).
- Clients who miss medication doses for up to 60 consecutive days should have LTBI treatment stopped and should be counselled on medication adherence. Clients who are to re-initiate treatment of LTBI should be registered as new clients and given a new course of treatment.

Client education and counselling

Symptom awareness

All PLHIV should be educated on the importance of seeking medical care promptly if they—or any person they live with—develop symptoms suggestive of TB (e.g., cough with sputum and blood at times, chest pains, weakness, weight loss, fever, night sweats) or develop recognized side-effects of INH (e.g., yellowing of eyes, itchy skin rash, abdominal pain with vomiting).

Client's household members

Household contacts of the person with TB should be evaluated for TB and offered HIV testing and counselling. INH should be offered to all household contacts who are HIV-positive or are children under 5 (regardless of HIV status) and do not have symptoms and signs of TB.

Cryptococcal Infection and Meningitis

Clients with cryptococcal infection may present with symptoms (symptomatic) or without symptoms (asymptomatic) of meningitis. Both symptomatic and asymptomatic cryptococcal infection have a high mortality rate and should be treated immediately. Clients with symptoms of meningitis should be referred to a doctor for further management as soon as the condition is suspected.

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

Initiate antiretroviral therapy for clients diagnosed with cryptococcal meningitis after there is evidence of sustained clinical response to antifungal therapy and completion of at least 6 weeks of treatment.

When to suspect

Table 4.11: Reasons to Suspect Cryptococcal Meningitis

Cryptococcal Meningitis	Asymptomatic Cryptococcal Antigenemia
Symptoms include fever, fatigue, headache, blurred vision and confusion. Symptom onset is often sub-acute and progressively worsens over several weeks.	Clients with CD4 ≤100 cells/mm^3 (adults) or less than 25% (children). See Section 4.6 for CrAg screening in advanced immunodeficiency (advanced disease).

Diagnosis

Table 4.12: Diagnosis of Cryptococcal Meningitis

Diagnostic Tests for Cryptococcal Meningitis
• CSF CrAg • CSF India ink The gold standard test is culture of cerebrospinal fluid for *Cryptococcus neoformans.* For clients with advanced immunodeficiency and with positive blood CrAg an LP should be preformed, if feasible and no contraindications, to rule out cryptococcal meningitis.

Management

Table 4.13: Management of Cryptococcal Meningitis and Antigenemia

Cryptococcal Meningitis	Asymptomatic Cryptococcal Antigenemia
If cryptococcal meningitis is suspected in the primary health care setting, the client should be urgently referred to a hospital for admission and further management.	Clients with CD4 ≤100 cells/mm^3 who screen positive on the CrAg lateral flow assay (LFA) test but do not have symptoms or signs of cryptococcal meningitis can receive fluconazole preventive therapy at the health facility under close supervision. See Table 4.14. Consider LP if feasible and if there are no contraindications.

Treatment

Table 4.14: Treatment of Cryptococcal Meningitis

Treatment	Cryptococcal Meningitis	Asymptomatic Cryptococcal Antigenemia
When to start	Positive CrAg with or without signs or symptoms of meningitis.	Clients with CD4 <100 cells/mm^3 screening positive for CrAg LFA and not presenting symptoms of meningitis. See Section 4.6 for screening algorithm.
When to stop	Secondary fluconazole prophylaxis can safely be stopped after one year in clients on ART who have undetectable viral loads and have two consecutive CD4 counts >350 cells/mm^3 taken 6 months apart.	Maintenance therapy of fluconazole prophylaxis can safely be stopped after one year in clients on ART who have undetectable viral loads and have two consecutive CD4 counts >350 cells/mm^3 taken 6 months apart.
Adult Dosing	**Induction phase:** Intravenous amphotericin B* (1.0 mg/kg/day) combined with fluconazole (1200 mg/day) for two weeks. **Therapeutic cerebrospinal fluid tapping:** Recommended if opening pressure >250 mm H_2O, persistent headache, recurrent vomiting, or altered mental state. *Note: If flucytosine is available: a short course of 1 week amphotericin B plus flucytosine (100 mg/kg/day, divided into four doses per day) followed by 1 week of fluconazole (1200mg/day) is preferred.* **Consolidation phase:** 800 mg fluconazole once daily for 8 weeks. **Secondary prophylaxis:** 200 mg fluconazole once daily for at least 1 year until client is stable with CD4 > 350 cells/mm^3 (or 25% for children 2-5 years) and undetectable viral load is achieved. See Section 4.6 for fluconazole prophylaxis *Lipid formulations of amphotericin B are superior. Dosage: 4–6 mg/kg/day.	**Induction phase:** 800 mg fluconazole once daily for 2 weeks. **Consolidation phase:** 400 mg fluconazole once daily for 8 weeks. **Maintenance therapy:** 200 mg fluconazole until client is stable with CD4 > 350 cells/mm^3 (or 25% for children 2-5 years) and undetectable viral load is achieved.
Child Dosing	**Induction phase:** The recommended treatment is intravenous amphotericin B (0.7–1.0 mg/kg/day) combined with oral flucytosine (5FC) 100 mg/kg/day in 4 divided doses. If 5FC is not available, fluconazole 12 mg/kg/day (up to 800 mg) should be used with amphotericin B. **Therapeutic cerebrospinal fluid tapping:** Recommended if opening pressure >250mm H2O, persistent headache, recurrent vomiting, or altered mental state. **Consolidation phase:** Fluconazole 6-12 mg/kg/day (up to 800 mg/day) for 8 weeks. **Secondary prophylaxis:** Fluconazole 6 mg/kg/day (up to 200 mg/day) until 2 consecutive CD4 counts (6 months apart) with results >350 cells/mm^3 (<25% for children 2-5 years) and viral load is undetectable. See Section 4.6 for fluconazole prophylaxis.	**Induction phase:** Fluconazole 12 mg/kg/day (up to 800 mg/day) once daily for 2 weeks. **Consolidation phase:** Fluconazole 6–12 mg/kg/day (up to 400 mg/day) once daily for 8 weeks. **Maintenance therapy:** Fluconazole 6 mg/kg/day (up to 200 mg/day) until clinically stable (i.e., CD4 >350 cells/mm^3 (<25% for children less than 5 years) for 6 months and viral load is undetectable.
Contradictions		• History of hypersensitivity to fluconazole or other azole medicines. • Pregnancy. • For potential interactions between ARVs and other drugs, see Annex 9.4

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

Table 4.15: 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 • Oral disease does not interfere with chewing or swallowing • Oedema not significant and not affecting 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% of 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 4.16: Staging Criteria and Prognosis for AIDS-Related Kaposi Sarcoma

	Good Prognosis (All of the Following)	Poor Prognosis (Any of the Following)
Tumour (T)	(T0) Tumour confined to skin and/or lymph nodes and/or minimal oral disease[1]	(T1) Tumour-associated oedema or ulceration, extensive oral Kaposi sarcoma, gastrointestinal Kaposi sarcoma, Kaposi sarcoma in other non-nodal viscera
Immune system (I)	(I0) CD4 count ≥200 cells/mm^3 CD4 ≥20%	(I1) CD4 count <200 cells/mm^3 CD4 <20%
Systemic illness (S)	(S0) No history of opportunistic infections and/or thrush; absence of "B" symptoms[2]; Karnofsky performance status score ≥70	(S1) History of opportunistic infections and/or thrush; presence of "B" symptoms[2] Karnofsky performance status score <70 (See Annex 9.21)

Adapted from Krown and colleagues (1989 & 1997).

[1] "Minimal oral disease" 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 more than 2 weeks.

Kaposi sarcoma staging criteria

Table 4.17: 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 4.6: Treatment Guidelines for Kaposi Sarcoma

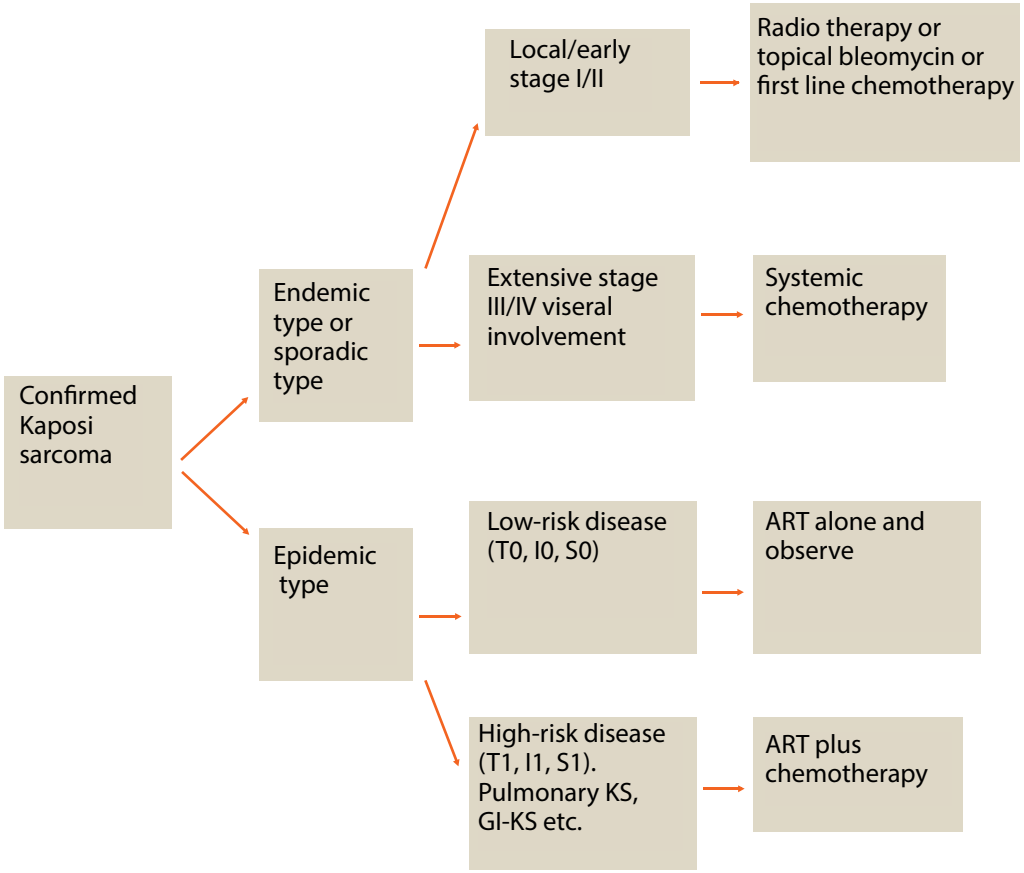


Table 4.18: Treatment of Kaposi Sarcoma

First-line regimen	Bleomycin 15 IU/m^2 IVD1 Vincristine 2 mg IVD1 Every 3 weeks for 6 cycles
Second-line regimen/recurrent Kaposi sarcoma	Paclitaxel 100 mg/m^2 * Every 3 weeks for 6–8 cycles Radiotherapy
First-line regimen among clients with pulmonary Kaposi sarcoma and poor PS	Vincristine 1.4 mg/m^2 IVD1 Repeat cycle every week for 6 weeks then transfer to 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 body surface area of 2 m^2.
- Monitor for pulmonary fibrosis among clients receiving bleomycin (seen especially in elderly clients receiving a total dose of >300 units). If a nonproductive 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 prior to administration.
- Diphenhydramine orally 12 and 6 hours before treatment and 50 mg IV just before administration or Promethazine 12.5 mg IV.

Cervical Cancer

Human papillomavirus (HPV) infection is the etiology 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. Most often, the cancer is diagnosed at an advanced stage. This is why screening is essential. Symptoms 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

It is recommended that women who have initiated sexual activity should be screened every 2 years and those who are HIV-positive should be screened at least once every year. The available screening tests include the following:

- Cytology: conventional (Pap smear)
- Visual inspection with acetic acid (VIA)

Both methods are available in Swaziland, but VIA is the widely used Screening Option for Pre-Cancerous Lesions. If the screening result is negative, a follow-up screening schedule will be provided by the health care worker and will depend on the client's HIV status. Refer to the cervical cancer screening guidelines.

HIV-positive women should be screened for cervical cancer at least once every year.

Diagnosis of cervical pre-cancer

The definitive diagnosis of cervical cancer is confirmed by histopathological examination of tissue specimens taken from the lesion.

- VIA positive: acetowhite areas visualized after application of acetic acid. This is 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 to confirm if cancerous.
- Pap smear: If histology of smear shows abnormal cells, conduct a biopsy of abnormal area with colposcopy. 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 screening test, without a prior diagnostic test. Women with a positive VIA screen can be treated with cryotherapy, depending on eligibility, at the primary health care level.
- Colposcopy-based "see-and-treat" approach/digital cervicography: Clients with a positive screen (on Pap smear, VIA, or HPV) can be examined with colposcopy. If a pre-cancerous lesion is detected, it can be treated immediately with cryotherapy.

Treatment methods

- Cryotherapy
- 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.

Stages of Cervical Cancer

Stage 0: Cancer cells found only on the surface (epithelium) of the cervix.

More-invasive cancers are separated into 4 stages:

Stage I: Cancer has not spread beyond the cervix.

Stage II: Tumour has spread to the upper part of the vagina or the parametrium.

Stage III: Tumour extends to the lower part of the vagina or the pelvic wall and may block urine flow.

Stage IV: Tumour has reached the bladder or rectum, or cancer cells have spread to other parts of the body.

Management and treatment of invasive cancer

The presence of invasive cancer requires engagement of a multidisciplinary team, and clients with invasive cancer must be referred to specialists.

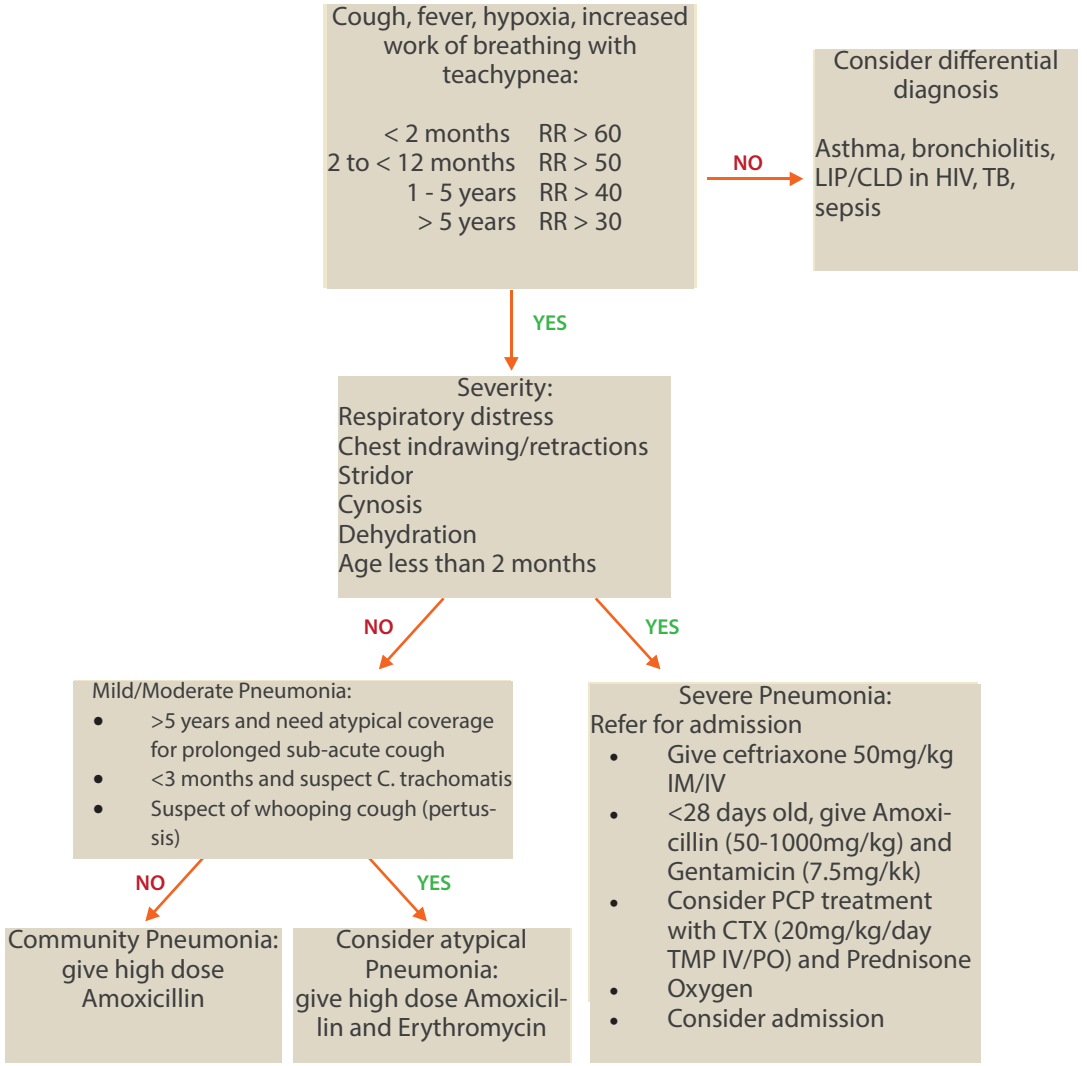
Treatment options for cervical cancer

Treatment of cervical cancer depends on the staging and availability of treatment modalities which includes:

- Radiotherapy
- Chemotherapy
- Surgery
- Palliative care

4.8 Special Considerations: Opportunistic Infections in Children

Figure 4.7: Opportunistic Respiratory Infections in Children



Pneumonia

Follow up in 2 days. If not improving on amoxicillin and/or erythromycin, consider screening for TB, lymphoid interstitial pneumonitis, PJP or asthma.

Table 4.19: Pneumonia Treatment for HIV-Positive Paediatric Clients

Amoxicillin			Erythromycin	
High dose (80–100 mg/kg/day)			(30–50 mg/kg/day)	
Give twice daily for 5 days			Give three times a day for 7 days	
Weight	Tablet	Syrup	Tablet	Syrup
	(250 mg)	(125 mg/5 mL)	(125 mg/5 mL)	(125 mg/5 mL)
<4	½	5 mL	¼	2.5 mL
4 to <6	1	10 mL	¼	2.5 mL
6 to <10	1.5	15 mL	½	5 mL
10 to <15	2	20 mL	½	10 mL
15 to <25	3	30 mL	1	10 mL
≥25 kg	4	N/A	2	N/A

4.9 Sexual and Reproductive Health

STIs in PLHIV

All PLHIV should be assessed for symptoms of STIs. Syphilis screening using rapid plasma regain should be performed as a baseline investigation for all PLHIV. Sexual partners of clients with STIs should be contacted and treated as well. Early diagnosis and effective treatment of STIs can contribute significantly towards reduced STI 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

HIV testing services should be offered routinely for all STI clients. 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 STI clients should receive individual counselling on risk reduction and prevention of transmission to partners, together with provision of commodities.

Table 4.20: STIs Commonly Found as Coinfection with HIV

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: erythromycin 500 mg orally 4 times daily for 7 days. • For HIV clients with donovanosis: gentamicin 1 mg/kg IV 3 times a day should be added if improvement is not evident within the first few days of therapy.
Genital herpes	• Persistent and/or severe mucocutaneous ulcerations involving large areas of perianal, scrotal or penile skin is 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.
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 clients. • See Standard Treatment Guidelines.
Candidiasis	• Candidiasis affecting multiple sites, including vulva and vagina, glans, and prepuce, often occurs in HIV disease. • Relapses of candidiasis are frequent.	• Ketoconazole 400 mg orally BD for 14 days • Clotrimazole, 500 mg intravaginally, weekly for 6 months. • Fluconazole 150 mg orally as a single dose, weekly for 6 months.
Genital warts	• There is a high prevalence of genital warts in persons with HIV. • The warts may be multifocal, extensive and poorly responsive to treatment. • There is a greater likelihood of malignant transformation in HIV-positive clients.	• Screen for cervical cancer • See Standard Treatment Guidelines

STIs in Children and Adolescents

With the exception of neonatal infections and congenital syphilis, the occurrence of STIs in children invariably indicates sexual abuse. If identified, both emotional and legal support are recommended for the child as part of comprehensive management of STIs in children and adolescents.

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

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

4.10 Family Planning

Family planning needs should be assessed and family planning resources offered to every HIV-positive woman at every visit.

The following family planning services are offered within Swaziland:

- Condoms (both male and female)
- Oral contraceptives
- Injectable contraceptives
- Subdermal implants
- Intrauterine contraceptive devices (IUCDs)
  - » Copper-bearing IUCDs, widely available in public health facilities
  - » Hormone-release IUCDs, available in some private facilities
- Tubal ligation - bilateral tubal ligation
- Vasectomy
- Natural methods

Pregnancy history, including last menstrual period, should be documented at every visit.

Some family planning methods are contraindicated with antiretroviral drugs (ARVs). See Annex 9.6 for interactions between ARVs and hormonal contraceptives.

For prevention of mother-to-child transmission of HIV (PMTCT) for women living with HIV, see Chapter 6, Section 3.

For additional information regarding family planning counselling, refer to the 2015 National Family Planning Guidelines.

4.11 Monitoring Clients in Chronic Care

Monitoring Clients Initiating on ART

All clients diagnosed with HIV should be assessed and managed according to the appropriately differentiated care package (see Sections 4.4 and 4.5). Clients are eligible to initiate ART regardless of CD4 count or WHO clinical stage and preferably within 2 weeks of HIV diagnosis. Same-day initiation is encouraged for clients who are ready to start ART.

Clients presenting with advanced immunodeficiency (advanced disease) should be prioritized for initiation of antiretroviral therapy within 2 weeks.

For guidance on initiation of ART for adults, see Chapter 5. See Chapter 6 for PMTCT and Chapter 7 for ART for children and adolescents.

Managing Clients Not Initiating ART on Same Day as Diagnosis

Clients who fail to initiate ART on the day of HIV diagnosis should be enrolled for pre-ART services and scheduled for further counselling to address barriers to ART initiation or for treatment of opportunistic infections. The goal is to initiate ART within 2 weeks of diagnosis for better health outcomes.

Table 4.21: Differentiated Care for Clients Who Are Not Yet on ART

	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 immunodeficiency (advanced disease) (CD4 <200 cells/mm^3 or WHO clinical stage 3 or 4)	Weekly clinical review until client initiated on ART.	Prioritized for ART initiation within 2 weeks.	Screen for opportunistic infections (including TB). For clients with CD4 <100 cells/mm^3, see Section 4.5, Screening for Advanced Immunodeficiency. Schedule additional counselling sessions if necessary. Provide CPT.	Clinical review dates to be scheduled following the opportunistic infection treatment plan.	Aim to initiate on 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.	At each visit, prepare client to be ready to start ART and to manage opportunistic infections. • Conduct readiness assessment for beginning ART. • Review clinical symptoms and signs, medication use, and side-effects. • Assess adherence and psychosocial status 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 pretreatment CD4 count at 6 months.
Presenting with mild or moderate immunodeficiency (clinically well) (CD4 >200 cells/mm^3 or WHO clinical stage 1 or 2)	Clinical review every 2 weeks until client initiated on ART.	Aim to initiate on ART within 2 weeks of diagnosis.	Screen for opportunistic infections (including TB). Provide CPT. Provide IPT.	Clinical review dates to be scheduled following the opportunistic infection treatment plan.	Aim to initiate on 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.	

4.12 Summary of Basic Care Package for PLHIV

Table 4.22: Basic Care for PLHIV

		Clients Presenting with Mild or Moderate Immunodeficiency (clinically well) (CD4 >200 cells/mm^3 or WHO clinical stage 1 or 2)		Clients Presenting with Advanced Immuno-deficiency (advanced disease) (CD4 <200 cells/mm^3 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
	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
Counselling focus	Preparation for early ART initiation	X	X	X	X
	Promotion of benefits of early ART initiation	X	X	X	X
Baseline Laboratories	All clients:				
	Re-testing for verification	X	X	X	X
	CD4 count	X	X	X	X
	LF TB-LAM (If TB screening is positive)			X If CD4 ≤100 cells/mm^3	X If CD4 ≤100 cells/mm^3 or less than 25%
	CrAg			X If CD4 ≤100 cells/mm^3	X If CD4 ≤100 cells/mm^3 or less than 25%
	Clients initiating ART:				
	AST/ALT	X	X	X	X
	Creatinine	X	X	X	X
	HB/FBC	X	X	X	X
	Hepatitis B surface antigen	X	X	X	X

Table 4.22: Basic Care for PLHIV (continued from previous page)

		Clients Presenting with Mild or Moderate Immunodeficiency (clinically well) (CD4 >200 cells/mm^3 or WHO clinical stage 1 or 2)		Clients Presenting with Advanced Immuno-deficiency (advanced disease) (CD4 <200 cells/mm^3 or WHO clinical stage 3 or 4)	
		Adults	Children/ Adolescents	Adults	Children/ Adolescents
Sexual and reproductive health	Family planning counselling and services	X		X	
	STIs	X	X	X	X
Prophylaxis	CPT	X	X	X	X
	IPT	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			X If CrAg+ and asymptomatic.	X If CrAg+ and asymptomatic.
Opportunistic 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 adolescent only	X	X Sexually active adolescent only
	Respiratory infections	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

Chapter 5:

Antiretroviral Therapy

5.1 Preparing Clients for ART

Clients must be well-prepared for antiretroviral therapy (ART) to promote good adherence to treatment. Good adherence reduces the risk of development of drug resistance and treatment failure.

Table 5.1: Preparing Clients and Providers for ART

Client Readiness	Provider Readiness
Health care providers should discuss the following topics with their clients before initiating ART: • Understanding of HIV diagnosis • Understanding of ARVs » How they work » What to do when experiencing side effects • Understanding of the benefits of starting ART early • Expectations when on ART » Undetectable viral load and healthy life free of opportunistic infections • Can explain the importance of CD4 count and viral load monitoring • Understanding their role in the treatment plan » Adherence to treatment plan » Reporting side effects/ adverse events » Reporting concurrent medicine use • Knowledges about different ART service delivery models available to them • Ablility to identify potential barriers to adherence and has solutions to address them » Transport costs » Transport availability » Getting time off work » Disclosure » Absence of a treatment support » Stigma and discrimination » Substance abuse • Self-motivated » Ability to state additional motivating factors to start ART outside health benefits • Willingness and readiness to initiate ART • Understanding their role in HIV prevention	Provider readiness is determined by their capacity to provide the following: • Comprehensive client assessment: » Complete psychosocial and ART readiness assessment » Complete clinical assessment » Complete assessment of baseline laboratory tests * Lack of availability of laboratory tests should not delay ART initiation. • Utilization of routine tools and complete documentation, including: » chronic care files and registers » electronic records: CMIS and APMR » client booklets • Provider skills: » Competence in the implementation of HIV management guidelines and standards

Adherence Counselling Prior to ART Initiation

It is recommended that all adult clients participate in at least one individual counselling session prior to initiating ART. This counselling session can happen on the same day as 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 is an ongoing process aiming to motivate clients to achieve and sustain treatment goals.

Adherence and psychosocial counselling can be individualised or in groups but every client should have completed individualised counselling and an ART readiness assessment before ART initiation.

General Guidance on Adherence Counselling

- 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 oppostunistic infections
  - » Decreased risk of HIV developing resistance to ARVs
  - » Decreased risk of HIV transmission e.g. in pregnant and lactating women and , serodiscordant couples
  - » Better overall health outcomes
- Individualize the counselling interventions to identify and address specific barriers to initiating and adhering to treatment, such as the following:
  - » Concerns about personal need for ART
  - » Specific concerns about taking ARVs and prophylactic treatment e.g. fear of side effects
  - » Practical barriers to adherence including disclosure challenges
- Use interventions to overcome any specific practical problems. Interventions might include the following:
  - » Empower clients to monitor their own compliance to treatment and to remain motivated to their treatment and life goals
  - » Simplifying the dosing regimen (once-daily regimens and fixed-dose combinations are preferred)
  - » Using adherence aids such as pill boxes and phone alarm reminders
  - » If side-effects are a problem:
    - * Discuss benefits, long-term effects and options for dealing with side-effects
    - * Consider adjusting the dosage, substitution, or try other strategies such as changing the dose timing or formulation
  - » Facilitate disclosure of HIV status to trusted other such as partner, family members or friends.
  - » Engage treatment supporter in care plan

- 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
- Provide an overview of the client's care in terms of the availability of client centered ART delivery models (CommART) to choose from.
  - » Emphasize the importance of correct and consistent condom use to maintain viral suppression
  - » 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 non-communicable diseases (Hypertension, Diabetes, Cervical Cancer, Prostate pathology, etc.)
- Mental health and psychological wellbeing.
- Importance of comprehensive health e.g. prevention of TB, family planning (dual protection), NCD screening, management and risk reduction, mental health and STI screening and management.

5.2 When to Start ART

All People living with HIV (PLHIV)—children, adolescents and adults—are eligible to start ART regardless of CD4 count or WHO clinical stage. Healthcare workers (HCWs) should promote early initiation of ART by all PLHIV, even when feeling healthy. ART can be started on the same day of diagnosis.

Test and Start means all people living with HIV (PLHIV) are eligible to initiate antiretroviral therapy (ART)—preferably within 2 weeks 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 prioritized for rapid/early ART initiation:

- Clients with advanced immunodeficiency (advanced disease) (CD4 ≤ 200 cells/mm^3 or WHO 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-discordant relationship*
- Clients with hepatitis B coinfection**
- Clients with HIV-associated nephropathy

*Relationship refers to individuals who identify themselves as sexual partners.

**If laboratory tests for hepatitis B surface antigen is positive.

Table 5.2: Early Versus Delayed ART Initiation

Rapid/Early ART Initiation	Delayed ART Initiation
Within 0–14 days of diagnosis, including same-day initiation. *Same day initiation of ART means client is initiating ART on the same day as the HIV diagnosis*	More than 14 days after HIV diagnosis

For clients who do not initiate ART on the same day as their HIV diagnosis, see Chapter 4 for recommended packages of care.

Table 5.3: Timing of ART Initiation Definitions

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

5.3 What ART Regimen to Start

An optimal ART regimen is a combination that is the most effective, durable, safe, well-tolerated, and affordable treatment. To accomplish this, Swaziland has prioritized fixed-dose combinations and once-daily regimens for ART. These facilitate better adherence, tolerance, and viral suppression.

Basic Principles of Antiretroviral Therapy (ART)

- ART regimens for treatment-naïve clients should contain 3 ARV drugs.
  - » Preferably, 2 nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) and 1 integrase inhibitor - [2 NRTIs + 1 INSTI]
  - » Alternatively, 2 nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) and 1 non-nucleoside reverse transcriptase inhibitor (NNRTI) – [2 NRTI + 1 NNRTI]
- Regimen selection and dose should take into consideration factors such as age, weight, comorbid conditions (e.g., tuberculosis, hepatic dysfunction, renal dysfunction, and other chronic non-communicable diseases) and potential interactions with other medications.
- Fixed-dose combinations are preferred for use in first-line ART.

See Annex 9.2 for an Overview of ARVs.

Recommended First-Line ART for Adults and Adolescents

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

Benefits of Dolutegravir (DTG)

- Tolerance:
  - » DTG has a low toxicity or side effects profile.
  - » DTG has less neuro-psychiatric adverse events.
  - » Available in fixed-dose combination (FDC)
    - * Smaller size pill
- Rapid viral suppression:
  - » DTG is linked to rapid viral suppression within the first 4 weeks of initiation
- High genetic barrier to resistance
  - » DTG is durable
- Fewer drug interactions
  - » Simplifies management of concomitant diseases

Known Side-Effects of Dolutegravir (DTG)

- Insomnia (DTG is best taken in the morning)
- Other minor side effects include: nausea, diarrhea, dizziness, and headache

See Annex 9.10 for supplementary information on DTG.

Clients on a DTG based regimen require active pharmacoviligence monitoring and reporting.

Alternative First-Line ART for Adults

Table 5.4 Alternative First-Line Regimens

Scenario	Alternative Regimen
• Active TB/HIV coinfection[a] in client initiating on ART • DTG induced insomnia	• TDF (tenofovir) + 3TC (lamivudine) + EFV (efavirenz)
• Confirmed and/or suspected renal dysfunction (creatinine clearance <50 mL/min)[b] • Presence of nephrotoxic drugs • Other disease-associated nephropathy	• ABC (abacavir) + 3TC + DTG • See Table 5.5 for revised dosing schedule for clients with renal dysfunction.

Table 5.4: Alternative First-Line Regimens (continued from previous page)

Scenario	Alternative Regimen
Other Special Circumstances	
• TB/HIV coinfection[a] with renal dysfunction[b]	• ABC + 3TC[b] + EFV • AZT (zidovudine) + 3TC[b] (lamivudine) + EFV (efavirenz)
• Hypersensitivity to ABC with renal dysfunction[b]	• AZT + 3TC[b] + DTG

[a] Clients with 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 5.5 for the dose reduction of 3TC to be used when clients have renal dysfunction.

For dosing of other regimens refer to Annex 9.2.

Abacavir Hypersensitivity Reaction

Abacavir (ABC) is associated with hypersensitivity symptoms, especially in clients with the HLA B*5701 allele. Stop treatment immediately if a client has 2 or more of the following symptoms or signs of hypersensitivity:

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

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 hypersensitiry, substitute ABC and do not reinitiate on an ABC-based regimen at any time in the future. Be sure to document visibly the client's hypersensitivity to ABC and inform the client.

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.

Risk factors for renal disease:

- Known underlying renal disease
- Age >50 years
- Body mass index <18.5
- Diabetes mellitus
- Hypertension
- Receiving nephrotoxic drugs

Creatinine Clearance Calculation (Cockcroft-Gault Formula)

Men:

(140 – age) x weight in kg x 1.23
serum creatinine (in µmol/L)

Women:

(140 – age) x weight in kg x 1.04
serum creatinine (in µmol/L)

If 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 (see Table 5.5).
- If ABC cannot be used, the TDF and 3TC dose can be adjusted according to the creatinine clearance, as described in Table 5.5.

Table 5.5: Dose Reduction Guidelines for TDF and 3TC in Clients with Renal Dysfunction (CrCl <50 mL/min)

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

5.4 ART for Clients with TB/HIV Coinfection

Alternative First-Line ART for Adults with TB/HIV Coinfection

Clients already on TB treatment when initiated on ART:

TDF (300 mg) + 3TC (300 mg) + EFV (600 mg) once daily FDC

Check VL at the end of TB treatment. If 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 viral load is detectable, start SUAC.

Clients developing TB while on a DTG based ART regimen:

TDF (300 mg) + 3TC (300 mg) once daily + DTG (50 mg twice daily)

Clients must return to DTG 50 mg once daily 2 weeks after completing TB treatment.

All clients must be substituted to a DTG-based regimen upon completion of TB treatment.

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

Clients Diagnosed with TB and HIV at the Same Time

Initiate TB treatment as a first priority (see the National Tuberculosis Guidelines), then initiate ART (in all TB clients, regardless of CD4 count) when TB treatment is tolerated—preferably within 2 weeks of starting TB treatment.

Clients Who Develop TB While on ART

Review ART treatment for any necessary changes to the regimen or dosage, and move the client from the ART clinic to the TB clinic for the duration of TB treatment. The client should return to the ART clinic after finishing TB treatment.

- Client on dolutegravir (DTG): Increase DTG dosing to 50 mg twice daily, then, 2 weeks after the completion of TB treatment, return to standard DTG dosing 50 mg once daily.
- Client on efavirenz (EFV): Continue on EFV. Two weeks after the completion of TB treatment, check VL. If viral load is undetectable, the client can be transitioned to a once-daily FDC of TDF+3TC+DTG. If viral load is detectable, start SUAC.
- Client on nevirapine (NVP): Change to EFV. Two weeks after the completion of TB treatment, check VL. If viral load is undetectable, the client can be transitioned to a once-daily FDC of TDF+3TC+DTG. If viral load is detectable, start SUAC.

Potential Interactions of TB Treatment Drugs

Table 5.6: TB Treatment Drug Interactions

Drug Combination	Considerations
Rifampicin (RIF) and nevirapine (NVP)	• Clients must be substituted to an EFV-based regimen for duration of TB treatment. See Annex 9.2 for EFV-based regimen dosing.
RIF and lopinavir/ritonavir (LPV/r)	• LPV/r can be used with RIF. • Super boost the LPV/r (1:1 lopinavir and ritonavir) by adding ritonavir. • Closely monitor client for toxicity (especially gastrointestinal intolerance) and virological failure.
RIF 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 estrogen (50 mcg) 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 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 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 client has completed TB treatment. This may increase the occurrence of DTG side effects.

Table 5.6: TB Treatment Drug Interactions (continued from previous page)

Drug Combination	Considerations
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. • NVP is the preferred NNRTI for clients receiving BDQ.
Delamanid (DEL) and ARVs	• DEL is generally considered safe to administer with ART. Evidence shows safety with EFV, TDF and LPV/r. • No long-term studies have been done on potential drug-to-drug interactions with DEL and ARVs

Multidrug-Resistant TB and ART

- Treatment with TDF and other nephrotoxic drugs can increase the risk of renal dysfunction. Many second-line TB drugs (e.g., amikacin, capreomycin, cycloserine, imipenem, kanamycin, para-aminosalicylic acid) are nephrotoxic, thus the combinations should be used with caution and renal function should be closely monitored.
- Liver function should be monitored for hepatotoxicity when using ethionamide and prothionamide with hepatotoxic ARVs. Refer to Annex 9.9.
- Consider the increased potential for neuro-psychiatric side-effects in clients taking EFV with terizidone.

For more information on multidrug-resistant TB (MDR-TB), refer to the MDR-TB guidelines.

5.5 Clients with Viral Hepatitis Coinfection

HIV-positive individuals should be routinely tested for hepatitis B infection. HIV-positive individuals who test positive for hepatitis B surface antigen should be prioritized for rapid ART initiation. Clients who are changing from a TDF and/or 3TC based regimen should be tested for hepatitis B virus infection.

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

- TDF and 3TC is preferred in hepatitis B coinfected clients in order to control a hepatitis B viral load.
- If ARVs need to be changed due to HIV drug resistance, follow these guidelines:
  - » 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.

Use of ARVs to Treat HIV-Negative Clients with Chronic Active Hepatitis B Virus Infection

Hepatitis B virus (HBV) infection can occur independently of HIV. In such cases, the following guidance should be used:

- Active ongoing hepatic damage, more than 6 months, should be an indication for initiating HBV treatment. (Hepatic damage includes symptoms of liver disease, persistent elevation of ALT and abnormal ultrasound).
  - » APRI (aspartate aminotransferase [AST] to platelet ratio index) is recommended as the preferred non-invasive test to assess presence of liver fibrosis/cirrhosis at baseline and during follow-up.
  - » Adults with an APRI score > 2 should be given treatment as an priority

    See Annex 9.11 for WHO recommended algorithm for managament of persons with chronic hepatitis B infection
- See treatment and clinical considerations for HBV in Annex 9.12.
- Risk of HIV aquisition should be assessed at every refill visit and clients must be counselled on HIV prevention.
- HIV testing should be done according to the HIV testing screening tool (see Chapter 3, Section 3).
- Review the client's need for treatment annually (VL for HBV should be done if available). If hepatitis B viral suppression is achieved for 3 years, HBV treatment can be stopped.

APRI score calculation:

$$\text{APRI} = \frac{\left(\frac{\text{AST level}}{\text{AST upper limit of normal}}\right) \times 100}{\text{Platelet count } (10^9/\text{L})}$$

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

- All HIV-positive individuals should be screened for hepatitis C virual (HCV) infection.
- All clients with HIV/HCV coinfection should be evaluated for treatment of HCV.
- Use the national recommended first-line ART regimen for HIV/HCV coinfected clients (FDC of TDF + 3TC + DTG).
- 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 a physician when managing HIV/HCV coinfected clients).

*Health providers should be aware of clients who may be HIV-negative and on TDF + 3TC regimen for treatment of hepatitis B and therefore should not receive the full ART regimen (3 ARV agents) given to HIV-positive clients.

5.6 Monitoring of Clients on ART

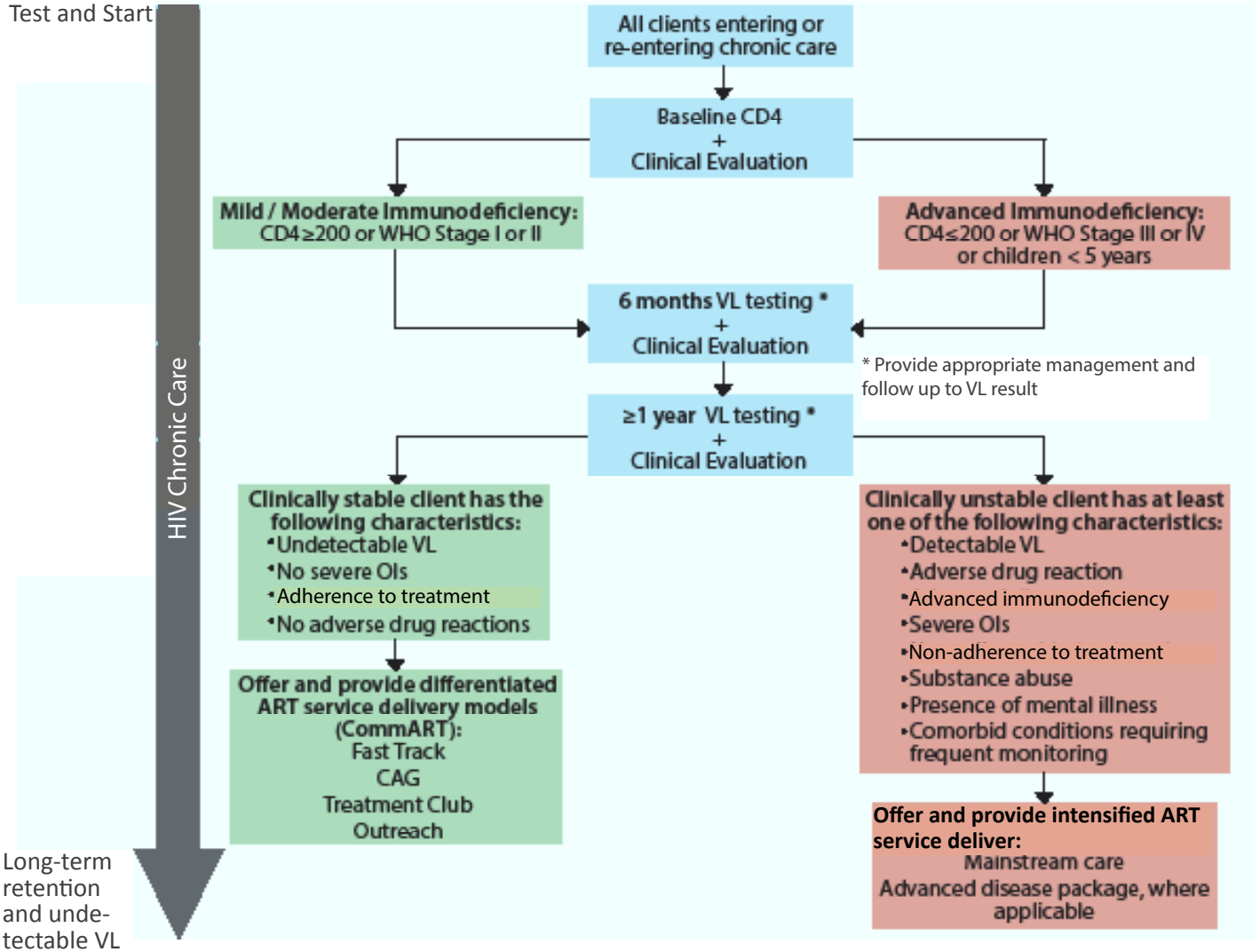
When clients are initiated on ART they are monitored through clinical and laboratory assessment. Clients on ART should be monitored for adherence, toxicity and treatment failure. The aim is to achieve the following:

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

To achieve the above, routine monitoring, timely response to clients' needs and appropriate clinical management is necessary.

Differentiated care is offered based on the findings of the clinical and laboratory monitoring. Refer to Chapter 4, Section 5.

Figure 5.1: Differentiated HIV Care and Treatment Services



All clients in their first year on antiretroviral therapy are considered to be unstable.

5.7 Clinical Monitoring of Clients on ART

During the first 6 months of treatment, clients should be reviewed monthly. The first review should be scheduled not more than 14 days after ART initiation.

Table 5.7: Clinical Review Schedule for the First Year on ART

	2 Weeks After Initiation	4 Weeks After Initiation	Monthly	Every 3 Months
Mild/moderate immunodeficiency (clincally well) CD4 count ≥200 cells/mm^3	X		X	After 6 months on ART and VL is undetectable
Advanced immunodeficiency (advanced disease) CD4 count <200 cells/mm^3	X	X	X	After 6 months on ART and VL is undetectable

If the client has mild or moderate immunodeficiency (clinically well) at first clinical review and is adherent to treatment with no side-effects at the 2-week review, then 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.

During the first 6 months of treatment, clients should be reviewed monthly. ART refills should follow the clinical review schedule.

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.
  - » Conduct screening for TB and opportunistic infections.
  - » Provide acute care, if necessary.
  - » Manage symptoms.
  - » Manage comorbid conditions (e.g., diabetes, hypertension).
  - » Resupply ART.
  - » Resupply Co-trimoxazole preventive therapy (CPT) and treatment for latent TB [isoniazid preventive therapy (IPT)] if indicated.
- And other services as required (refer to Chapter 4, Basic Care)

Any opportunistic infection occuring during the first 6 months after initiation of ART may be due to immune reconstitution inflammatory symdrome (IRIS).

IRIS is 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 (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 to the hospital for further management.

Clients with advanced immunodeficiency (advanced 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 on DTG should be closely monitored for IRIS.

5.8 Laboratory Monitoring

Once a client has initiated ART, laboratory monitoring will be routinely done at pre-determined intervals to determine immunological and virological response to ART as well as liver and renal function (See Table 5.8).

Table 5.8: Schedule for Laboratory Monitoring of Clients who have Initiated ART

Laboratory Tests	All Clients at Baseline	If CD4 <100 cells/ mm^3	6 months	12 months	After 12 months
CD4 count or %	X		X	X	If viral load is detectable, monitor CD4 to assess immune status and need for prophylaxis or advanced immunodeficiency package (see Chapter 4, Section 5)
Viral load*			X Return VL result	X Return VL result	• If second VL is undetectable, repeat VL every year. • If VL is detectable and < 1000, see Table 5.9 and Table 5.10 • If second VL ≥ 1000, see Chapter 4, Section 5
Haemoglobin (Hb) or Full Blood Count (FBC)	X		X	X	• Repeat according to clinical requirements • Repeat annually if on AZT regimen

*For adolescents, pregnant and lactating women, see the Paediatric and PMTCT chapters for viral load monitoring schedules.

Table 5.8: Schedule for Laboratory Monitoring of Clients who have Initiated ART (continued from previous page)

Laboratory Tests	All Clients at Baseline	If CD4 <100 cells/ mm^3	6 months	12 months	After 12 months
Urea and Creatinine	X		X (TDF regimen)	X (TDF regimen)	Every 6 months (if on TDF) All visits (if known renal dysfunction)
Aspartate aminotransferase (AST)/ alanine aminotransferase (ALT)*	X				If stable, repeat every 12 months or if clinically indicated
Hepatitis B surface antigen (HbsAg)	X				Perform HBsAg any time TDF is being discontinued
Lateral flow TB- lipoarabinomannan assay (LF TB-LAM)		X (if TB-presumptive)			Repeat test at any point when CD4 drops to <100 cells/mm^3 and TB-presumptive
Cryptococcal antigen lateral flow assay (CrAG LFA)		X			Repeat test at any point when CD4 drops to <100 cells/mm^3
Pregnancy Test	X (women/girls)				As required
Non-communicable diseases screening • Blood glucose • Lipid Profile » Total cholesterol » Triglyceride	X (Clients >50 years old, risk of diabetes, or with cardiovascular event)			X (Clients on LPV/r or DRV/r regimen; clients >50 years old, risk of diabetes, or with cardiovascular event)	Annually for clients on LPV/r or DRV/r or clients >50 years old, risk of diabetes, or with cardiovascular event
Cervical cancer screening • VIA or Pap smear every 12 months	X			X	Annually

CD4

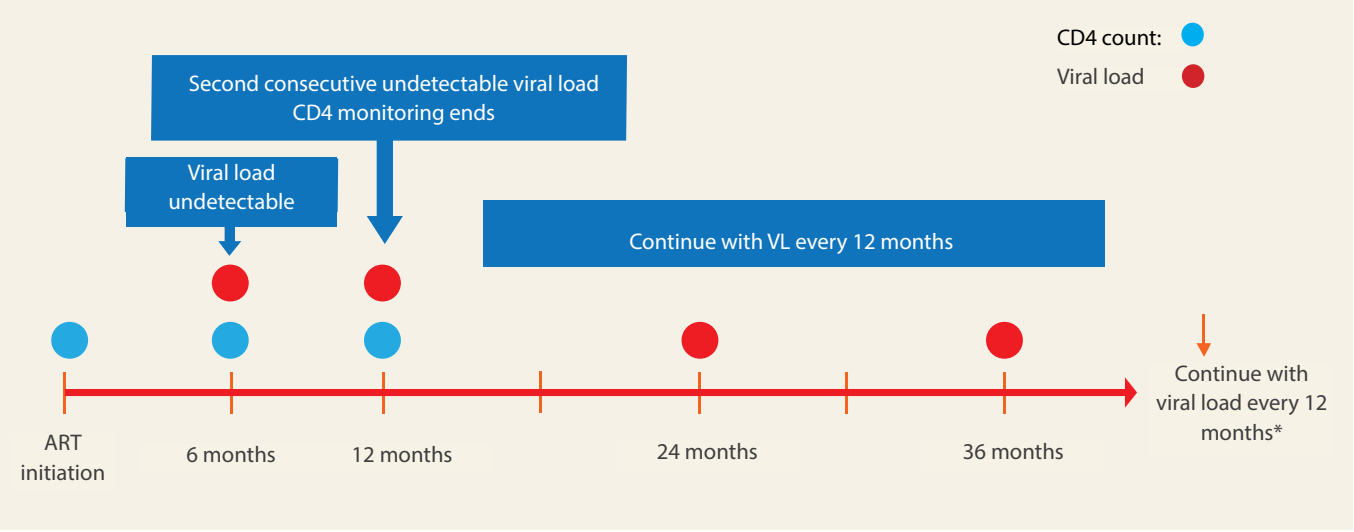
CD4 count testing should be done at baseline as well as 6 and 12 months after ART initiation. Once the client has 2 consecutive undetectable viral loads (see the second on VL below), CD4 monitoring can be stopped. If treatment failure is suspected, resume CD4 monitoring until client has an undetectable viral load. For more details on role of CD4 count, refer to Chapter 4, Section 3.

Viral Load

The goal of initiating people living with HIV on ART is to achieve an undetectable viral load.

VL should be measured 6 months after ART initiation to confirm virological response to ART. After 2 consecutive undetectable VL results 6 months apart, VL monitoring can be done annually. A detectable viral load may indicate non-adherence, drug-drug interaction and/or possible treatment failure.

Figure 5.2 Adult Viral Load Monitoring Algorithm



*For women clients, cervical cancer screening should also be done a the time of VL testing every 12 months.

If VL ≥1000 copies/mL, start Stepped Up Adherence Counselling. 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.

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.

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

Interpretation and utilization of viral load test results

Table 5.9: Viral Load Test Results

Result	Terms		Action
< 20 copies/mL	Undetectable	Suppressed	• Praise client for good adherence to treatment. • Remind client they still have HIV. • Reinforce adherence messages. • Continue to test VL according to timeline.
20 - 1000 copies/mL	Detectable		• Enquire about adherence challenges or inter-current mild and self-limited illnesses. • Emphasize ongoing adherence (especially for clients who have VL > 400 copies/mL) • Children and adolescents with VL > 400 copies/mL should be referred for SUAC
≥ 1000 copies/mL	Detectable	Unsuppressed	• Call client to come to the facility within the next 7 days to begin stepped up adherence counselling (SUAC) • Escalate client to SUAC. • Reinforce dangers of continued viremia (e.g., HIV disease progression, opportunistic infections, death).

How to interpret repeat viral load tests after initial detectable viral load result

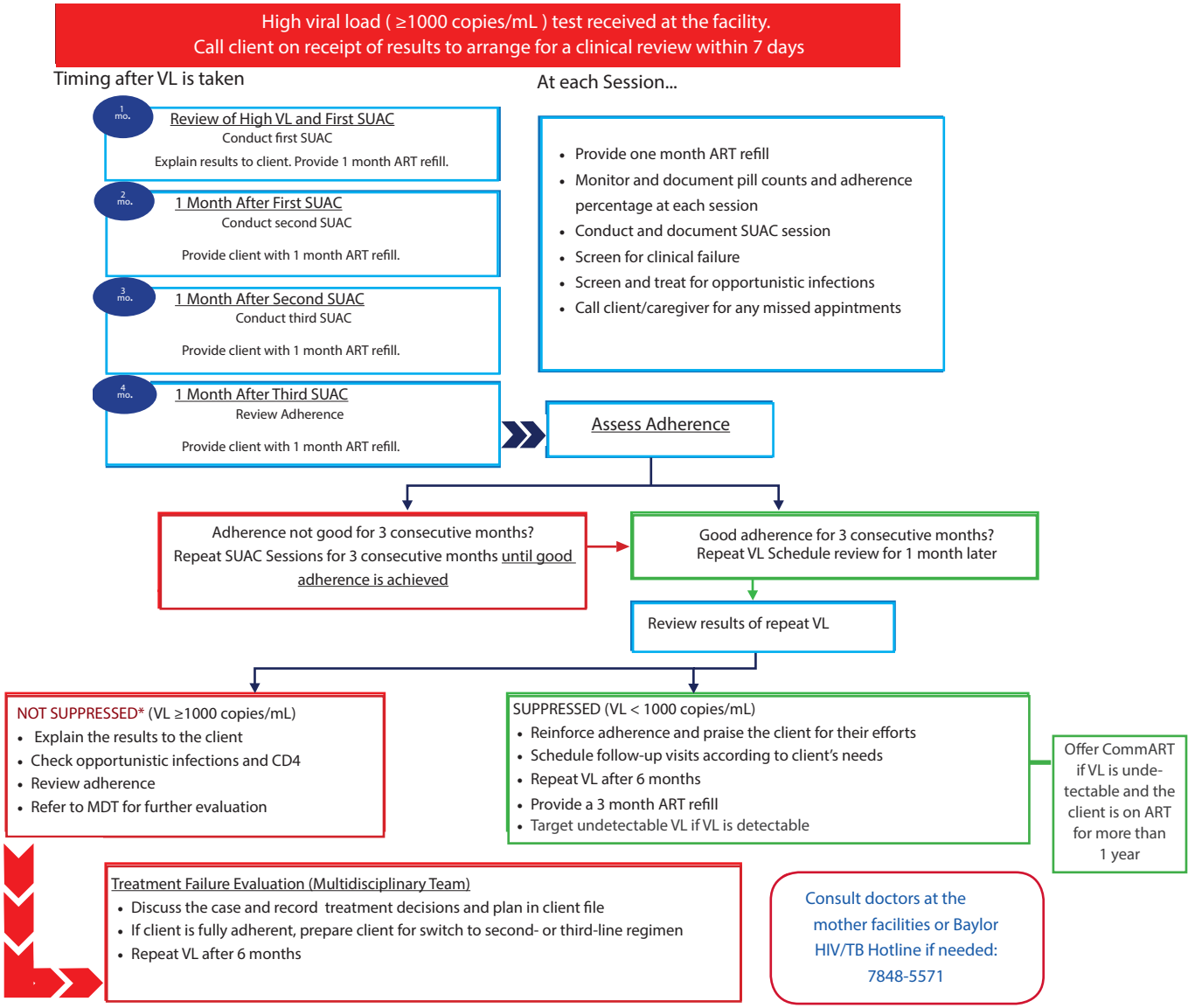
Table 5.10: Interpreting Repeat Viral Load Tests

Repeat VL Test Result	Most Likely Reason	Action
< 20 copies/mL (or undetectable VL result)	Client was poorly adhering to treatment and has improved adherence.	• VL should be rechecked every 6 months until 2 consecutive undetectable VL results are achieved, then annual monitoring can begin. • If VL is undetectable and client is on ART for more than 1 year, provide CommART models.
20 -1000 copies/mL (detectable and < 1000 copies/mL)		• Emphasize ongoing adherence (especially for clients who have VL > 400 copies/mL) • VL should be rechecked every 6 months until 2 consecutive undetectable VL results are achieved, then annual monitoring can begin. • Children and adolescents with VL > 400 copies/mL should be referred for SUAC
≥1000 copies/mL	Diagnosis is virological treatment failure, most likely due to resistant virus or continued non-adherence.	• Call client to come to the facility within the next 7 days to begin SUAC • Client should be referred to the doctor/multidisciplinary team for consideration of switching to second-line or third-line therapy. • See Figure 5.3 for the management of clients with ≥1000 copies/mL.

Management of a high viral load (>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 5.3 for the management protocol.

Figure 5.3: Management of Clients with VL >1000 copies/mL



*For clients with VL≥ 1000 copies/mL provide index HIV testing to their partners with negative or unknown HIV status.

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 5.4 below.

Figure 5.4: Structure of the Stepped-Up Adherence Counselling Session

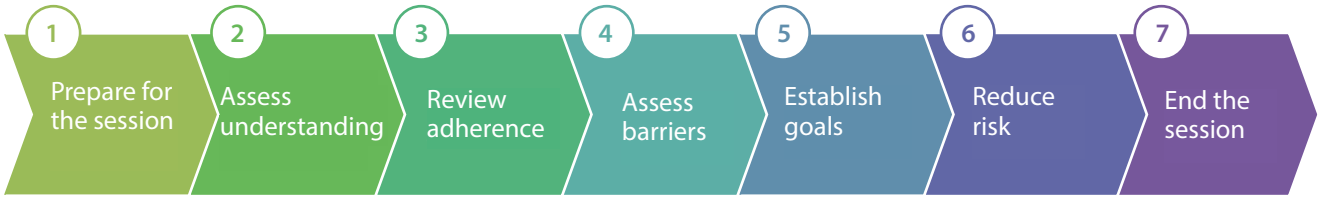
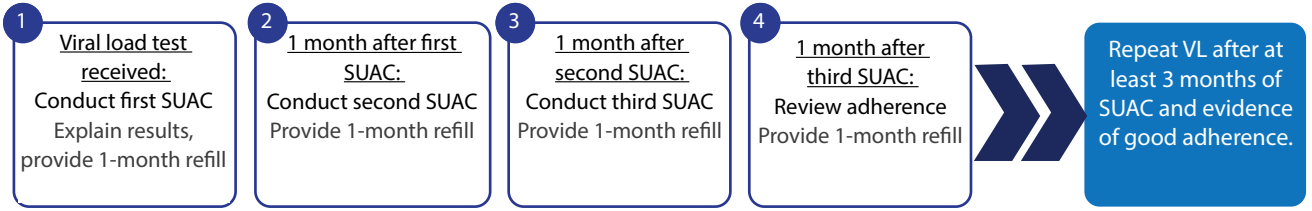


Figure 5.5: Timing of Stepped-Up Adherence Counselling Sessions



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

Table 5.11: 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 living 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.
Psychosocial—Other aspects of care	• On a regular basis, 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 contact details for clients (phone numbers and addresses). If possible, confirm the details. • Actively rule out opportunistic infections or other medical conditions. • Provide adherence counselling and follow up on issues at every visit. Encourage use of an alarm, cell phone or watch for reminders for medication doses. Encourage use of a pillbox and monitor use and maintenance if client benefits 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 client to take medications even if late or on an empty stomach, rather than skipping pills. Have client repeat doses that were spit 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.

5.9 Managing Treatment Failure

Definition of Treatment Failure

Treatment failure is defined as 2 consecutive VLs ≥1000 copies/mL, at least 3 months apart, irrespective of clinical and immunological findings, and with SUAC and good adherence between measurements. 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.
Although plasma is preferred for VL testing, dried blood spot specimen is an alternative.

A viral load threshold of ≥1000 copies/mL should be used to determine virological failure when using plasma or dried blood spot specimens.

WHO Definitions of Clinical, Immunological, and Virological Failure

Table 5.12: WHO Definitions of Types of Treatment Failure

Failure	Failure	Comments
Clinical failure	New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 condition) after 6 months of effective treatment.	• The condition must be differentiated from IRIS, which can occur after initiating ART, as well as from an adverse drug reaction. • For adults, certain WHO clinical stage 3 conditions (pulmonary TB and severe bacterial infections) may also indicate treatment failure.
Immunological failure	CD4 count falls to the baseline (or below). OR Persistent CD4 counts below 100 cells/mm^3.	• These clients are at risk of severe opportunistic infections. • Clients should receive intensified clinical follow-up and opportunistic infection prophylaxis. • If CD4 ≤100 cells/mm^3, treat client as having advanced immunodeficiency and complete the LF TB-LAM and CrAg LFA test appropriately. See Chapter 4, Section 5.
Virological failure	VL ≥ 1000 copies/mL based on 2 consecutive VL measurements at least 3 months apart, with SUAC support and good adherence in between measurements.	• A client must have taken ART for at least 6 months before it can be determined that a regimen has failed.

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.
Potential causes of treatment failure should be assessed. These include the following:

- Client factors
  - » Poor adherence
  - » Inter-current illnesses
  - » Comorbidities
  - » Substance abuse
  - » Advanced immunodeficiency (advanced disease)
  - » Transmitted resistance
  - » Social and economic factors
  - » Toxicity
  - » Drug-drug interactions
  - » Malabsorption
- Health system factors
  - » Drug stockouts
  - » Incorrect regimen and drug doses
  - » Service accessibility
  - » Drug-drug interactions

Clients should be switched soon after diagnosis of virological failure.

5.10 Second-Line ART for Adults and Adolescents

Before Switching 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.
- Treat and control all inter-current opportunistic infections.

What to Switch To

The recommended second-line ART for adults and adolescents should consist of 2 nucleoside reverse-transcriptase inhibitors (NRTIs) plus a ritonavir-boosted protease inhibitor.

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.

Table 5.13: Recommended Sequence of Second-Line NRTI Options

First-Line ART	Second-Line ART	
	Preferred	Alternative
TDF + 3TC + DTG	AZT + 3TC + ATV/r	AZT + 3TC + LPV/r
TDF + 3TC + EFV		
TDF + 3TC + NVP		
AZT + 3TC + EFV	TDF + 3TC + ATV/r	TDF + 3TC + LPV/r
AZT + 3TC + NVP		
AZT + 3TC + DTG		
ABC-based first-line regimen	AZT + 3TC + ATV/r	AZT + 3TC + ATV/r

Clients currently on a second-line antiretroviral therapy regimen that contains lopinavir/ritonavir (LPV/r) can be actively substituted to atazanavir/ritonavir (ATV/r) if they have the following characteristics:

- Age less than 20 years old
- Weigh more than 35 kgs
- Experiencing adherence issues
- Experiencing side effects

Considerations for Second-Line ART and TB Infection

- Table 5.14 provides options for managing clients in this likely scenario.

Table 5.14 Options for Managing Clients

TB Client on Treatment	Action
LPV/r	• Super boost LPV/r to 400 mg/400 mg by adding 300 mg ritonavir • Double-dose of LPV/r to 800 mg/200 mg twice daily
ATV/r and DRV/r	• Do not combine with RIF • Change to LPV/r with adjustments as stated above

Considerations for 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

Zidovudine (AZT) + Tenofovir (TDF) + Lamivudine (3TC) + a boosted Protease Inhibitor

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 1 member of each of the 3 drug classes (NRTI, non-nucleoside reverse-transcriptase inhibitor [NNRTI], and protease inhibitor).

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. Clients who were previously treated with regimens other than the standard first-line regimen must be individually evaluated before switching to a second-line regimen. Sequencing of treatment in treatment-experienced clients and use of a third-line regimen should be supported by HIV drug resistance testing.

Before Switching to Third-Line ART

- 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).
- 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:
  - » Advanced immunodeficiency (advanced disease) package
  - » Prophylaxis therapy

5.11 Third-Line ART 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.

HIV drug resistance testing (genotyping) is accessible through the HIV drug resistance committee at Swaziland National AIDS Program (SNAP), which reviews requests for genotyping.

The National Molecular Reference Laboratory provides the necessary logistics to facilitate outsourced sample testing while the program facilitates requisitions from health facilities for such services.

Contact email for HIVDR support: *snapthirdline@gmail.com*

Recommended Third-Line ART

- Initiate third-line regimen treatment after reviewing results of resistance tests and after satisfactory SUAC.
- Arrange for repeat VLs and follow-up metabolic tests (fasting blood sugar, cholesterol and triglycerides) at 3 and 6 months.

Recommended third-line ART regimen should include the following combinations*:

Darunavir/ritonavir (DRV/r) 600 mg/100 mg 12 hourly

+

**Dolutegravir (DTG) 50 mg once daily

+

Selected NRTI or 2nd generation NNRTI as guided by genotype test results

*Construction of third line ART regimens should be guided by HIV genotyping results.
**Raltegravir (RAL) 400 mg 12 hourly may be used as an alternative in INSTI-naive clients unable to use DTG.
***Caution: high level NNRTI resistance limits the use of Etravirine (ETR) 200 mg 12 hourly.

5.12 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. Differentiated ART Service Delivery (or CommART) and ongoing adherence and psychosocial support are key.

Adherence

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.

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.)

Importance of adherence

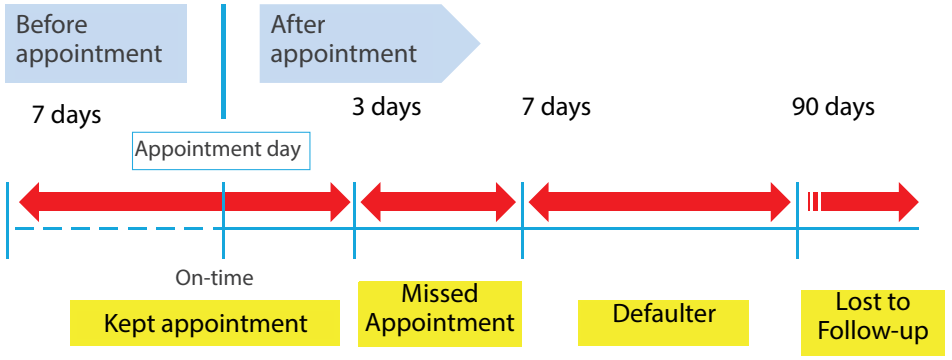
Adherence is a concern to clinicians, health care systems and other stakeholders (e.g., taxpayers) because of evidence that non-adherence is associated with adverse outcomes and higher costs of care.

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.

Figure 5.6: Adherence to Appointments



Source: Delamater AM. Improving client adherence. Clinical diabetes. 2006

Differentiated Service Delivery

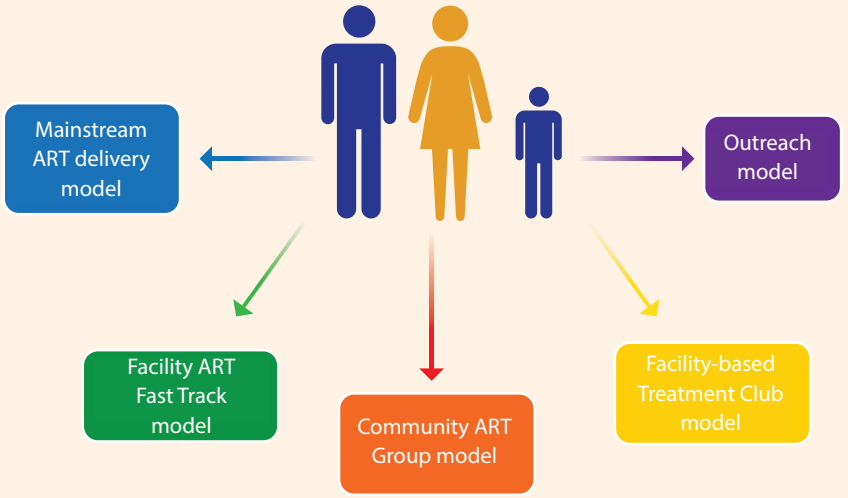
After 1 year on ART, stable clients should be offered an opportunity to choose one of the different ART service delivery models (or CommART) to enhance their adherence. (See Chapter 4, Section 1 for evaluating clients on ART.)

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. CommART or Differentiated ART Service Delivery 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
- Keep clients motivated to remain in care by ensuring clients have undetectable viral load
- Refer to Chapter 4, Section 1 for the basic care package.

Further guidance is provided through the CommART delivery guidelines (2016) and SOPs (2016). Figure 5.7 provides an outline of the available care models for clients on ART.

Figure 5.7: Available Care Models for Clients on ART



Models of ART delivery: PLHIV on treatment may choose any model of ART delivery and are free to switch from model to model for as long as they are eligible for the model of delivery chosen.

Defaulter Tracing

Facilities should set up defaulter tracing committees, and allocate time, with representation from the entire multidisciplinary team. The objective of the committee is to oversee and ensure timely follow-up of clients who have not kept their appointments and to develop a client tracking plan.

Defaulter tracing methodology

Short Message Service (SMS) reminders, telephone calls and home visits can be used to improve clients' appointment compliance. The Linkage and Retention to HIV Care and Treatment SOP should be referenced for implementation steps. Index testing opportunities should be utilised.

The following should be done to ensure effective defaulter tracing:

- Update physical/ residential address annually
- Update cellphone and/or telephone numbers annually

Chapter 6:

Prevention of Mother-to-Child Transmission of HIV

Prevention of Mother-to Child Transmission of HIV Strategy

Strategically, prevention of mother-to-child transmission (PMTCT) is implemented through a 4-pronged approach as shown in Table 6.1. Details of services under each prong are outlined in the subsequent sections.

Table 6.1 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 6.1
Prong 2	Prevention of unintended pregnancies among HIV-positive women	Non-pregnant HIV-positive women of childbearing age including adolescents and their partners	Section 6.2
Prong 3	PMTCT among HIV-positive pregnant and lactating women	Pregnant and lactating women	Section 6.3
Prong 4	Care, support and treatment for HIV-positive women and their families	HIV-infected women, their children, partners and families	Section 6.4 Section 6.5 Section 6.6

6.1 Primary Prevention of HIV Infection among Women of Childbearing Age

Table 6.2 summarizes the HIV primary prevention services that should be offered to non-pregnant women within maternal, newborn and child health (MNCH) settings and their partners.

Table 6.2: 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. • As much as feasible, women should be tested as a couple. • Promote family testing • 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 6.2: HIV Prevention Services for Non-Pregnant Women (continued from 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. • 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. » 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, on 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 and psychosocial support to victims of gender-based violence. • Provide information on services and organizations specialized on 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. Swaziland Action Group Against Abuse (SWAGAA) centres or One-Stop-Centres). • For further information, see the national gender-based violence guidelines.
Provide men's minimum health care package to partners of the women visiting the health facility	• Emphasing the role of the partner 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 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 measure: » Offer HTS – couple testing and appropriate linkage to prevention or care and treatment services. » Demonstrate correct use of male and female condoms. » Screen and treat for STIs, TB, NCDs, and other conditions as needed. » 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 newborns and male siblings.

6.2 Prevention of Unintended Pregnancies in Women Living with HIV

Table 6.3 describes services to be provided to HIV-positive non-pregnant women to prevent unintended pregnancies. See also National Family Planning Guidelines.

Table 6.3: Services to Prevent Unintended Pregnancies

Service	Description
Provide information and services to support family planning and reproductive rights	• Support women and couples to identify reproductive goals—whether pregnancy is desired and when. Review annually. • Counsel on the safety of and eligibility on 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 (see Chapter 7). • Family Planning (FP) services should be integrated with other HIV services (e.g., ART refill) • All PLHIV should be offered family planning services according to the National Guidelines on Integration of Family Planning in HIV Services.

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 6.4: 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 viral load is undetectable, advise on fertility days and timed ovulatory intercourse (condom use at all other times). • Prevent/treat STIs. • The final decision to conceive depends on the couple. HCWs should provide accurate and unbiased information necessary to support their decision-making.
Discordant 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 positive partner is already on ART, ensure he or she has an undetectable viral load. • If viral load is undetectable, advise on fertility days and timed ovulatory intercourse (use of condom 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 where available. • The final decision to conceive depends on the couple. HCWs should provide accurate and unbiased information necessary to support their decision-making.

6.3 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 take place as soon as the woman realizes she is pregnant, preferably within the first trimester (0-12 weeks of gestation).

HIV-Negative Women	• All HIV-negative pregnant women should be re-tested every 2 months (aligned with the ANC scheduled visits). • Emphasize primary prevention of HIV (see Table 6.2)
HIV-Positive Women	• All women testing HIV-positive should be re-tested (to verify HIV-positive status) before initiation on ART. • All pregnant HIV-positive women, 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. • Viral load testing should be done for all HIV-positive pregnant women already on ART if it was not done in the last 3 months. • Any detectable viral load in pregnant women should be treated with urgency

Summary of Key Services for Pregnant Women in Antenatal Care

Table 6.5: Key Services for Pregnant Women in Antenatal Care

Service	Description
Comprehensive history-taking and examination	• Take medical history including obotetric, family and psychosocial history. • Routine screening for GBV is not recommended. However, in the event of reported or suspicious cases refer to the National GBV Guidelines for management. • See Chapter 4, Section 2 for further information.
Tuberculosis screening	• Screen all women regardless of HIV status for TB using the National TB Screening Tool. • Refer or provide diagnostic and follow-up services according to National TB Management Guidelines.
Nutritional assessment, counselling and support	• Assessment: Assess nutritional status using mid-upper arm circumference. • Counselling: Counsel on proper diet based on locally available foods. • Nutritional support and supplements: Provide ferrous sulfate, folic acid and multivitamins. For women with a mid-upper arm circumference of less than 23 cm, enroll on or refer to food by prescription support.

Table 6.5: Key Services for Pregnant Women in Antenatal Care (continued from previous page)

Service	Description
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 date should be aligned to the woman's scheduled ANC visits. • 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 4, Section 6 for routine tests. • Routine laboratory tests: Haemoglobin, blood group and Rh factor, urinalysis, HepB, 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 6.1. 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.
Counselling and education	• Provide HTS for HIV-negative women as outlined in Section 6.1. • Educate appropriately on: » Family Planning- emphasise dual protection » Pregnancy and Delivery (including danger signs) » Birth preparedness planning » Infant and young child feeding, see Section 6.6. » Early Infant Male Circumcision, see Chapter 2, Section 1. » Harmful habits • 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, and heart disease, or any other pre-existing medical condition should be referred for care.

PMTCT Package for HIV-Positive Women in Antenatal Care

Table 6.6: Key Considerations for HIV-Positive Women in Antenatal Care

Service	Description
ALL HIV-Positive Women	• All HIV-positive women should be on ART with an undetectable viral load. • Initiate Co-trimoxazole 960 mg, INH 300mg, and Vitamin B6 25mg PO daily for women who are eligible and not already taking it. See Chapter 4, Section 6. • Give enhanced infant prophylaxis (eIP): 25-mL bottle of NVP and a 100 mL bottle of AZT 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.
Newly positive OR known positive not on ART	• First-line regimen for women is TDF + 3TC + DTG. See Chapter 6, Section 4. • Initiate ART as soon as possible at any gestational age, preferably on the same day and in the ANC (without waiting for the CD4 results and/or other baseline test results). • Ensure mother understands the significance of ART adherence once initiated. • Schedule a follow-up visit for the woman in 2 weeks to review baseline tests and make any necessary ARV changes if needed
Already on ART	• Check viral load (VL) if not done in the last 3 months. • Continue current ART regimen, if there is no evidence of treatment failure. • If VL is detectable, initiate SUAC and refer to doctor, mother facility and/or Baylor
Not ready for ART	• Counsel woman on the benefits of early initiation on ART for her own health, for the child and partner. • Address any fear and/or barriers for woman not being ready to initiate ART, including partner support. • Follow up with woman in 2 weeks and initiate ART if she is ready. • If woman is still not ready for ART, continue counselling at every visit.

6.4 Treatment for HIV-Positive Pregnant and Lactating Women

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

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

All pregnant women initiated on ART should present for clinical review after 2 weeks and every month thereafter for provision of routine ANC services and ART refills.

Table 6.7: Special Considerations for ART Regimens in Pregnant and Lactating Women

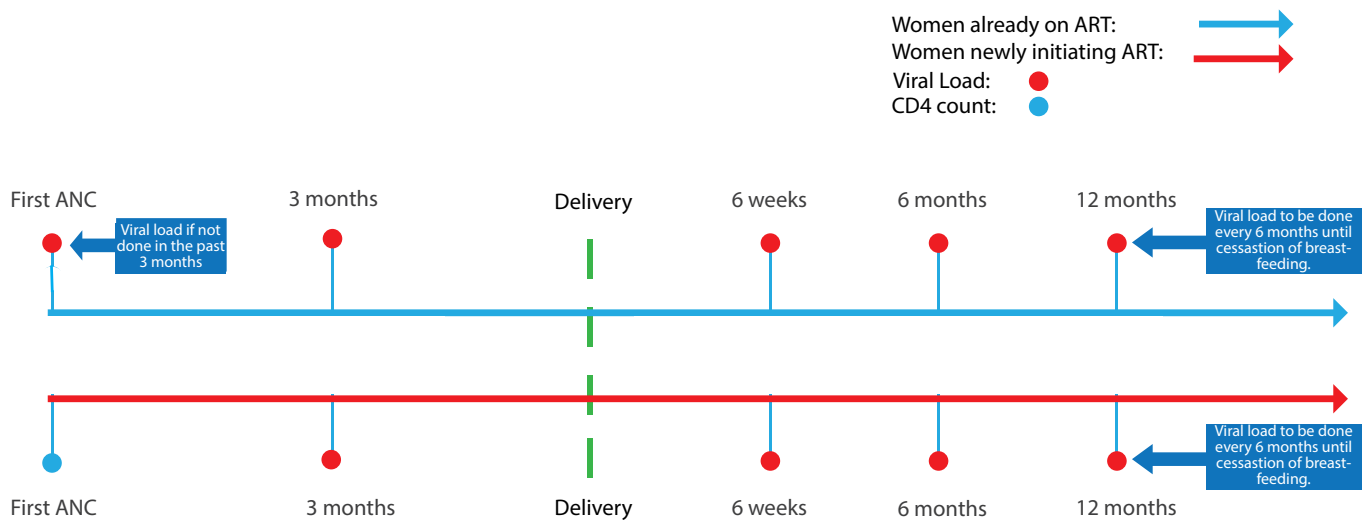
Condition	Recommended Regimen	Comments
TB	TDF (300 mg) + 3TC (300 mg) + DTG (50 mg twice daily) OR TDF (300 mg) + 3TC (300 mg) + EFV (600mg)	• HIV-positive pregnant women with TB co-fection should begin TB treatment as soon as possible and keep a close follow-up schedule. Refer if necessary. • Refer to Chapter 5, Section 4 for further detail.
Moderate to severe anaemia	TDF + 3TC + DTG	• Treat anaemia according to the guidelines, screen for active TB disease and refer if necessary. Prioritize management of severe anaemia before ART initiation.
Poor renal function (creatinine clearance <50 mL/min)	ABC + 3TC + DTG	• Monitor accordingly and refer for further investigation and management of renal insufficiency. Please note that the dose of 3TC needs to be adjusted when creatinine clearance is <50 mL/min. • See Chapter 5, Section 3 for creatinine adjustment table.
See Chapter 5, Section 1 for further detail.		

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.

Adverse drug reaction reporting to the CMS pharmaco-vigilance unit should extend to adverse drug reactions and toxicities noticed in pregnant women or their babies upon delivery.

Figure 6.1: Timing of Viral Load and CD4 Monitoring for Pregnant and Lactating Women



*Any detectable viral load in pregnant and lactating women should be treated with urgency

ANC services should be linked with ART care appointments for the mother.
PNC services should be linked to childwelfare visits and ART visits as per mother baby pair schedule.

Table 6.8: Follow-up and Monitoring of HIV-positive Pregnant Women Summary

Time	Services to be provided	
	Pregnant women already on ART at entry in 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 if not done in the past 3 months • Provide enhanced infant prophylaxis (eIP) package (AZT/NVP syrups) • TB Screening • Syphillis and 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
2 weeks after 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	• Routine ANC • Check and reinforce adherence to ART • Check for any side-effects and manage accordingly
3 months after first ANC	• Routine ANC • Check and reinforce adherence to ART • Check for any side-effects and manage accordingly • VL testing and manage appropriately if not undetectable	• Routine ANC • Check and reinforce adherence to ART • Check for any side-effects and manage accordingly • VL testing and manage appropriately if not undetectable
6 months after first ANC	• Routine ANC • Check and reinforce adherence to ART • Check for any side-effects and manage accordingly • VL testing and manage appropriately if not undetectable • Check creatinine if on TDF	• Routine ANC • Check and reinforce adherence to ART • Check for side-effects and manage accordingly • VL testing and manage appropriately if not undetectable • Check creatinine if on TDF
6 weeks after delivery	• VL testing and manage appropriately if detectable. Refer to Figure 6.1. • Offer mother family planning services	• VL testing and manage appropriately if detectable. Refer to Figure 6.1. • Offer mother family planning services

6.5 Services for Women 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 provided with enhanced infant prophylaxis (eIP):

- Dispense AZT and NVP from birth for 6 weeks in maternity (if not given during ANC).
- Continue NVP only from 6 weeks to 14 weeks. This should be dispensed during the 6 week postpartum care visit.
- Educate appropriately on family planning with emphasis on dual protection.

See Labor and Delivery Guidelines for more information.

Table 6.9: Infant Dosing Regimens of NVP and AZT

Infant Weight	Dosing of NVP	Dosing of AZT
Birth to 6 weeks		
Birth weight 2000–2499 g	10 mg once daily (1 mL of syrup once daily)	10 mg twice daily (1 mL of syrup twice daily)
Birth weight ≥ 2500 g	15 mg once daily (1.5 mL of syrup once daily)	15 mg twice daily (1.5 mL of syrup twice daily)
> 6 weeks to 14 weeks		
Any weight	20 mg once daily (2 mL of syrup once daily) or (½ a 50 mg tablet once daily)	STOP

Caesarean Section

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)

6.6 Services for Lactating Women and their Children

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 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 6.2. ART care appointments for the mother and their babies should also be linked to the mother-baby pair visit schedules.

Figure 6.2: 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 end of breastfeeding.

Services for HIV Exposed Infants

Initiate ART at any point along the continuum of care from pregnancy through breastfeeding for women not yet on ART or HIV-positive women.

Infant Diagnosis

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

Table 6.10: Infant Diagnostic Tests for Mothers of Varying HIV Statuses

Mother Status	Infant Diagnostic Tests
Mother Known HIV-Positive	• DNA PCR for child at 6 weeks, 9 months, and 12 months. Rapid test should be done at 18 months.
Mother HIV Status Unknown	• Conduct HIV rapid test for mother. • If mother is positive DNA PCR for child at 6 weeks, 9 months, and 12 months. Rapid test should be done at 18 months. • If mother is negative, the child is not HIV exposed. Repeat HIV rapid test for mother every 8 weeks until end of breastfeeding.
Mother is not Available	• DNA PCR for child at 6 weeks, 9 months, and 12 months. Rapid test should be done at 18 months.

Table 6.11: HIV Testing in Infants and Young Children

Age of infant	Infant and young child eligible for testing	Which test to use	Management
6–8 weeks	HIV-exposed infants (If exposure status is not known, test the mother. If the mother is not available, test the child using DNA antigen test.)	DNA PCR	*If child is HIV-negative and never breastfed*: inform mother that child is HIV-negative, contine eIP untill 14 weeks, and check and enforce ART adherence for the mother.
			If child is HIV-negative and still breastfeeding: continue eIP, start Co-trimoxazole preventive therapy (CPT), check and enforce ART adherence for the mother, and re-test child at 9 months or 2 months after stopping breastfeeding or if they present with symptoms suggestive of HIV (whichever comes first).
			If child is HIV-positive: stop eIP, take blood for second DNA PCR testing, initiate child on ART (do not wait for results of second DNA PCR test), start child on CPT, check and enforce ART adherence for mother. Continue breastfeeding.
9 months	HIV-exposed infants (If exposure status is not known, test the mother. If the mother is not available, test the child using DNA antigen test.)	DNA PCR	*If child is HIV-negative and never breastfed or stopped breastfeeding 2 months before current test:* inform the mother that the child is HIV-negative; check and enforce ART adherence for mother.
			If child is HIV-negative and stopped breastfeeding within 2 months of current test: check and enforce ART adherence for mother, re-test the child 8 weeks after cessation of breastfeeding (if negative—inform mother that child is HIV-negative; if positive—take blood for second DNA PCR testing and initiate ART).
			If child is HIV-negative and still breastfeeding: check and enforce ART adherence for mother; 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 child is HIV-positive: take blood for second DNA PCR testing; initiate child on ART (do not await results of second DNA PCR test), start child on CPT, and check and enforce ART adherence for mother or caregiver.

Table 6.11: HIV Testing in Infants and Young Children (continued from previous page)

Age of infant	Infant and young child eligible for testing	Which test to use	Management
12 months	HIV-exposed infants (If exposure status is not known, test the mother. If mother is not available, test child using DNA antigen test.)	DNA PCR	*Manage as above, however;* • If child tests HIV-negative and is still breast-feeding: re-testing should be done at 18 months or 2 months after stopping breast-feeding or if they present with symptoms suggestive of HIV (whichever comes first).
18 months	HIV-exposed infants (If exposure status is not known, test the mother. If mother is not available, test child using antibody test.)	HIV antibody test (follow national algo-rithm)	*Manage as above, however;* • If child tests HIV-positive: re-testing before ART initiation should be done using anti-body test instead of DNA PCR. • If child tests HIV-negative and is still breast-feeding: re-testing should be done 2 months after stopping breastfeeding or if they present with symptoms suggestive of HIV (whichever comes first).

Whenever discordant DNA PCR results (initial and confirmatory DNA PCR) are received, repeat DNA PCR and VL and consult a doctor.

Table 6.12: Package of care for HIV-Exposed Infants

Service	Description
Early infant diagnosis and treatment	• See Chapter 3, Section 8 for early infant diagnosis algorithm. • 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. • Immediately initiate all HIV-positive infants for ART: » A second HIV test should be conducted for all infected children before ART initiation (do not await results of the second test before initiating ART). » Refer to Chapter 7 for details on ART for children. • Refer to Table 6.10 for HIV testing in infants and young children.
Growth and developmental assessment and Immunization	• Follow EPI schedule for assessment and immunization.
Enhanced infant prophylaxis (eIP)	• See Section 6.5, Table 6.9

Table 6.12: Package of care for HIV-Exposed Infants (continued from previous page)

Service	Description
Co-trimoxazole 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 4, Section 6). • 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 sulfa 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.
INH prophylaxis 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 4, Section 6 for more information. • Investigate for TB and if TB is excluded, give isoniazid preventive therapy (IPT) 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 IPT and dosing. • Children receiving IPT 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).
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 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.
Infant feeding and nutrition counselling	• See Section 6.6 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, initiation of ART will be done urgently to keep the child alive and healthy.
5. Ensure that counselling and support are available to the family.

Enhaced Infant Prophylaxis (eIP)

All HIV-exposed infants should be given eIP (NVP and AZT syrup) from time of birth.

Table 6.13: Special Considerations for Enhanced Infant Prophylaxis in Exposed Infants

Special Considerations for Enhanced Infant Prophylaxis (eIP) in Exposed Infants *Provide dosing clips and syringe	
Mother diagnosed as HIV-positive during breastfeeding and is initiated on ART	• *If mother diagnosed as HIV-positive before 6 weeks post-delivery*: Initiate infant on eIP from point of diagnosis of mother and continue until 14 weeks. • *Mother diagnosed as HIV postive after 6 weeks post-delivery:* Give child NVP only for at least 6 weeks and the mother has an undetectable viral load.
Mother diagnosed as HIV-positive during breastfeeding and refuses to be initiated on ART	• *If mother diagnosed as HIV-positive before 14 weeks post-delivery*: Initiate infant on eIP from point of diagnosis of mother • Continue conselling the mother on benefits of ART for her own health, for the baby's and partner's health • If she continues to refuse initiating ART, continue eIP until 2 weeks after cessation of breastfeeding. • *If mother diagnosed as HIV-positive after 14 weeks post-delivery*: Give child NVP only for at least 6 weeks until the mother has an undetectable VL or 2 weeks after cessation of breastfeeding
Child defaulted from eIP before they are 14 weeks old	• Counsel on importance of ongoing prophylaxis and restart eIP per schedule until 14 weeks.

Infant and Young Child Feeding Recommendations

All mothers, including those living with HIV:

- Should 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 and consistent condom use.
- Replacement feeding can be advised if the woman fulfils certain criteria. (See Table 6.14 on replacement feeding)

Table 6.14: Reccomendation for Infant and Young Child Feeding Based on HIV Status of Mother

Situation	Reccomendation
Mothers known to be HIV-negative or whose HIV status is unknown	• Exclusive breastfeeding for the first 6 months with 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 cessation of breastfeeding
Mothers known to be HIV-positive and on lifelong ART whose infants are HIV-negative or of unknown HIV status	• Exclusive breast feeding for the first 6 months with 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 14 weeks. This should be dispensed during the 6 week PNC visit • The mother should continue with her ART for life
Mothers known to be HIV-positive and whose infants are HIV-positive	• Mothers should be encouraged to exclusively breastfeed for the first 6 months of life and continue breastfeeding up to two years or beyond • Complementary feeding should be introduced from six months while breastfeeding continues • HIV infected infant 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 to breastfeed	• Health care workers should conduct a one-on-one discussion/counselling session with each woman on how to feed their infants and consider her individual circumstances • Replacement feeding can be advised if the woman fulfils certain criteria. See replacement feeding section below • All HIV-exposed infants on replacement feeding should receive AZT and NVP prophylaxis from birth up to 6 weeks and then continue NVP only up to 14 weeks or beyond as guided in Table 6.12. • 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 to replacement feed 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 in Table 6.14.
- 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 6.12.
- 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 above 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 she cannot breastfeed on demand. In these instances, the HCWs must support the mothers.

Assessment for Replacement Feeding

Table 6.15: 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 in the community?		
2	Can the mother afford and reliably provide sufficient infant formula milk to support 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 is not enough but still contributes to about 50% of nutritional requirements between the age of 6 and 12 months. See infant and young child feeding guidelines.

Chapter 7:

ART for Children and Adolescents

7.1 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 have to be made aware of duties 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 primarily responsible for:

- Observe and give medications as prescribed.
- Bringing the child or accompanying the adolescent for scheduled medical visits.
- Providing ongoing care of the child and psychosocial support (e.g., nutrition, immunizations, disclosure).
- Ensure that the child is fully disclosed by age 10.

Healthcare workers should inform parents or primary caregivers to alert the facility with every change of caregiver and the new caregiver must receive counselling support and education to ensure continued quality care and support.

Adherence Counselling for Children and Adolescents

Counselling on benefits of ART, adherence, disclosure, and maintaining an undetectable viral load (VL) should be provided during all client encounters.

Children and adolescents should be initiated on ART as soon as possible, preferably on the same day of HIV diagnosis while adherence-counselling process is ongoing.

It is recommended that all caregivers and mature adolescent clients who are aware of their status should receive counselling—group counselling or individual counselling—before 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 effects and toxicity).

Developing an adherence plan is essential (see guidence below).

General Guidance on Paediatric Adherence Counselling and Developing an Adherence Plan

- Adopt a "no-blame" approach to facilitate open and honest discussion.
- Actively involve the client/parent (caregiver) in the decision-making of their child's or their own care and treatment.
- The benefits of ART and long-term optimal adherence should be emphasized:
  - » Improved quality of life (improved/normal growth and development, reduced illness)
  - » Sustained undetectable viral load
  - » Decreased risk of HIV transmission (particularly for adolescents)
  - » Decreased chance of HIV developing resistance to ARVs
- Interventions to support adherence should be individualized to address specific barriers:
  - » Identify and address any concerns about the need for and administering ART.
  - » Identify and address practical barriers to adherence (limitations in capacity and resources):
    - * Identifying an informed primary and secondary caregiver to be involved in providing care
    - * Fitting ART into the child's (or caregiver's) daily schedule(s)
    - * Use of calendars or other visual aids to illustrate dosing
    - * Directly observed therapy
    - * Use of pillboxes, reminders, alarms and timers
  - » Peer support groups (teen clubs) for children, adolescents, and caregivers
  - » Age-appropriate and family disclosure
  - » Clients' experience of taking ART and their needs for adherence support may change over time.
- Children, Adolescent, and caregivers' knowledge, understanding and concerns about medicines and the benefits they perceive should be reviewed regularly.
- Provide an outlook of client's care in terms of availability of diverse care models to choose from:
  - » Strategies in place for client-centred care models at least 1 year after starting ART when the virus is fully under control.

7.2 Assessment of Children Prior to ART Initiation

Table 7.1: Assessment of Children Prior to ART Initiation

Assessment Component	Key Questions and Evaluations
Medical History	• At the initial visit » Age of the child » Birth history, including maternal and infant PMTCT » Past medical history, including TB history » Any previous ART regimens and adherence history • At the initial visit and each subsequent visit » Presenting complaint, if any » Review of symptoms » Growth and developmental history » Nutritional history » Family/household history » Allergies » Current medications and traditional remedies
TB Screening	• Known TB contacts • Cough for >2 weeks • Any cough with fever and/or poor weight gain/weight loss • Poor weight gain or failure to thrive
Psychosocial assessment	• Identify the child's caregivers • Consider disclosure to the child and family members • Discuss child and caregiver fears and concerns regarding ART • Where appropriate, explore the child's understanding of HIV • Assess the child's education and socialization • Evaluate potential barriers to adherence • Assess the economic situation of the child's household
Complete physical examination	• Weight and height plotted on child's growth curve • Head circumference measured (in children under 2 years of age, it may be indicative of cognitive or developmental delay) • Head-to-toe examination of all systems, looking for signs of HIV disease and opportunistic infections • Review of developmental milestones and reflexes • Cognitive development assessment is important in adolescents (Tanner stages)

Table 7.1: Assessment of Children Prior to ART Initiation (continued from previous page)

Assessment Component	Key Questions and Evaluations
Laboratory testing	• CD4 count • Creatinine (if initiating on TDF or for very sick children [please refer to Chapter5, Section 3, Table 5.5]) • Hepatitis B surface antigen • Full blood count or haemoglobin • Repeat confirmatory DNA PCR for infants and re-testing for verification in children (> 24 months) and adolescents (aged 10 – 19) • LF TB-LAM testing for children and adolescents with presumptive TB and with advanced disease (please refer to Chapter 4, Section 5, Figure 4.2) • CrAG screening for children and adolescents with advanced disease (please refer to Chapter 4, Section 5, Figure 4.3) • Do NOT delay treatment initiation for baseline laboratory assessments or while confirmatory DNA PCR is pending
Assessment of client	• See Chapter 4, Section 4 • Establish chid/adolescent stage of disease

7.3 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.

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).

It is imperative to confirm all presumptively diagnosed children with DNA PCR.
(A presumptive HIV diagnosis is established based on a defined set of clinical symptoms in infants with antibodies against HIV.)

Prioritize assessment (clinical and social) and rapid ART initiation in children and adolescents with advanced immunodeficiency (advanced disease) as soon as possible (within 7 days) from the day of HIV diagnosis.

Children and adolescents with advanced immunodeficiency are:
- All children less than 5 years of age
  Children younger than 5 years have a much greater risk of disease progression and mortality regardless of their clinical and immune condition
- Children aged 5 years and older (please refer to Table 7.2)

Table 7.2: Definitions of Advanced Immunodeficiency and High-Risk Groups

	Advanced Immunodeficiency (Severe Immunodeficiency)	High-Risk Group (Very Severe Immunodeficiency)
Adolescents	• CD4 count ≤200 cells/mm^3 or WHO clinical stage 3 and 4	• CD4 count ≤100 cells/mm^3
Children	*Children 5 years and older:* • CD4 count ≤200 cells/mm^3 or CD4 less than 25% • WHO clinical stage 3 or 4 *Children under 5 years:* • All children less than 5 years old are managed as clients with advanced immunodeficiency (advanced disease)	*Children 5 years and older:* • CD4 count ≤100 cells/mm^3 or CD4 less than 25% *Children under 5 years:* • CD4 count ≤100 cells/mm^3 or CD4 less than 25%

Identify and treat opportunistic infections BEFORE initiating ART

Client with Active TB:
Initiate ART as soon as possible (within 2 weeks) following the initiation of anti-tuberculosis treatment.

Client with Cryptococcal Meningitis:
ART initiation should be delayed for at least 6 weeks after starting treatment for meningitis.

ART should be deferred in a seriously ill child presenting with any of the following danger signs:

- Temperature ≥39°C
- Unable to drink or breastfeed
- Lethargy or unconsciousness
- Convulsions
- Repeated vomiting
- Tachycardia and/or tachypnea

Children and adolescents with these danger signs require acute medical management +/- referral for admission and should not be initiated on ART until stable.

7.4 What to Start: ART for Children and Adolescents

Children and adolescents are a priority population. In the absence of severe opportunistic infections, initiate ART as soon as the parent/caregiver or child/adolescent is ready to start ART (preferably within 2 weeks, 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 7.3.

Table 7.3: Recommended First-Line ART Regimens for Children and Adolescents

Recommended Regimens for Children and Adolescents			
< 3 years	3 to ≤ 10 years	> 10 to 19 years	
ALL	ALL	<40 kg	≥40 kg
ABC + 3TC + LPV/r	ABC + 3TC + EFV	ABC + 3TC + EFV	TDF + 3TC + DTG

See Chapter 5 for additional information on antiretroviral (ARV) drugs. See Annex 9.17 for information on paediatric dosing.

Alternative First-Line ART Regimens for Children and Adolescents

Table 7.4 provides additional alternatives for special situations for ART initiation and substitutions in children. These situations include cases of children with side-effects due to non-nucleoside reverse-transcriptase inhibitors (NNRTIs) and lopinavir/ritonavir (LPV/r), or where caregivers are unable to correctly dose LPV/r syrup.

Table 7.4: Alternative First-Line ART Regimens for Children and Adolescents

Alternative Regimens for Children and Adolescents			
< 3 years	3 to ≤ 10 years	> 10 to 19 years	
ALL	ALL	<40 kg	≥40 kg
AZT + 3TC + LPV/r	ABC + 3TC + NVP AZT + 3TC + EFV (or NVP)	AZT + 3TC + EFV (or NVP)	ABC + 3TC + DTG AZT + 3TC + DTG TDF (or ABC) + 3TC + EFV TDF (or ABC) + 3TC + NVP

Use of nevirapine

Initiation of an NVP-based ART regimen for children requires a lead-in period of 2 weeks for hepatic enzyme induction.

Table 7.5: Example of lead-in dosing for routine NVP initiation using AZT-based FDCs

Exampe of lead-in dosing for routine NVP initiation using AZT-based FDCs		
	AM	PM
First 2 weeks	AZT + 3TC	AZT + 3TC + NVP
After 2 weeks (if no adverse reactions)	AZT + 3TC + NVP	AZT + 3TC + NVP

In clients on TB treatment or in clients switching to NVP from EFV start NVP with full dose (NVP BD)

For initiations of infants less than 4 weeks of age on LPV/r, see Annex 9.15.

Special Considerations for Substitutions

Conduct a viral load test if the most recent test result is older than 3 months:

- When substituting NRTIs (for example ABC/TDF to AZT or vice versa)
- Urgently consult a Baylor or facility doctor
  - » When substituting between drug classes (from an NNRTI to a PI; for example, NVP/EVF to LPV/r or ATV/r)
  - » For all clients with detectable VL requiring ARV substitutions

Table 7.6: Special Situations for Children and Adolescent Clients

Special Situation	Age/Weight	ARV Recommended or Substitution	Comments
Anemia on AZT (Hb<10 g/dL)	< 10 years OR < 40 kg	ABC	
	> 10 years OR > 40 kg	TDF	Do not use TDF if: • Confirmed and/or suspected renal dysfunction (CrCl <50 mL/min) • In the presence of nephrotoxic drugs
Severe NVP rash (WHO clinical grade 3,4)	<3 years OR <10 kg	LPV/r (syrup/pellets/tablets)	In cases where the child cannot tolerate tablets, pellets can be used as an option. Tablets can NOT be crushed, chewed or broken. Pellets are recommended in children > 3 months to 5 years of age.
	> 3 years OR >10 kg	EFV	EFV can also cause severe rash, if child using EFV, monitor as clinically appropriate
LPV/r (gastrointestinal side-effects)	< 3 years	NVP	Case-by-case basis, consult with a doctor or call the Baylor HIV/TB Hotline (see Annex 9.14)
	> 3 years OR > 10 kg	EFV	
	> 10 years OR > 40 kg	ATV/r	
Unable to tolerate EFV (severe central nervous system side-effets or moderate to severe rash); psychiatric history of EFV side-effects	> 3 years OR > 10 kg	NVP	Case-by-case basis, consult with a doctor or call the Baylor HIV/TB Hotline (see Annex 9.14)
		LPV/r (syrup/pellets/tablets)	
	> 10 years OR > 40 kg	DTG (preferred)	
		ATV/r (alternate)	

Table 7.6: Special Situations for Children and Adolescent Clients (continued from previous page)

Special Situation	Age/Weight	ARV Recommended or Substitution	Comments
Caregiver inability to correctly dose LPV/r syrup	< 3 years	NVP	
	> 3 years OR < 5 years	LPV/r pellets/tablets	Tablets can NOT be crushed, chewed or broken.
ABC hypersensitivity reaction (rare)	< 3 years or < 10 kg	AZT	Hb > 10 g/dL
	> 10 years OR > 40 kg	TDF	Do not use TDF if: • Confirmed and/or suspected renal dysfunction (CrCl <50 mL/min) • In the resence of nephrotoxic drugs
Provide close monitoring for clinical, immunologic, and viral failure after all drug substitutions			

Use of lopinavir/ritonavir

- Formulation and dosing: when using syrup formulation, provide appropriately sized syringes with dosing clips and detailed instructions on administration in a format appropriate to the audience (verbal, written and pictures).
- If LPV/r is being used as first-line therapy and there are adherence issues beyond solution, such as poor tolerability or side-effects, consider using the LPV/r pellets. In worst-case scenarios only, consider the fixed-dose combination with nevirapine (NVP).
- Storage: once syrup formulation is dispensed, keep refrigerated or in a cool-dry place (clay pot, under the bed, not near a window in direct sunlight).

If no refrigerator is available at home, refills should be supplied for a maximum of 8 weeks for children on LPV/r syrup, recommending storage in a cool place.

7.5 Prophylaxis Therapy for HIV-Exposed or -Infected Infants and Children

Co-trimoxazole Preventive Therapy

Table 7.7: Co-trimxazole Preventive Therapy for Children and Adolescent Clients

Group	When to start Co-trimoxazole preventive therapy?	When to discontinue Co-trimxazole preventive therapy?*
All HIV-exposed infants/ children	From 6 weeks of age (or at 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 %	At 5 years of age and after 1 year on ART if: • WHO clinical T-stage 1 or 2 • CD4 count ≥350 cells/mm^3 and • Viral load is undetectable
All HIV-infected children ≥ 5 years of age	WHO clinical stage 3 and 4 irrespective of CD4 OR CD4 ≤350 cells/mm^3 irrespective of WHO clinical stage	At 5 years of age and after 1 year on ART if: • WHO clinical T-stage stage 1 or 2 • CD4 count ≥350 cells/mm^3 and • Viral load is undetectable
As secondary prophylaxis	After completion of treatment for Pneumocystis jiroveci pneumonia (PJP)	<5 years old: • Do not stop ≥5 years old if: • CD4 count ≥350 cells/mm^3 and • Viral load is undetectable

*Can also be stopped due to adverse drug reactions (See Chapter 4, Section 6)

Isoniazid Preventive Therapy

Infants, children and adolescents living with HIV should routinely be screened for tuberculosis (TB) as part of standard clinical care, whether they are receiving TB prophylaxis or ART.

- IPT (10 mg/kg/day) should be given as part of a comprehensive package of HIV prevention and care services as below:
- In children living with HIV who are less than 12 months of age, only those who have contact with a TB case and who are evaluated and found unlikely to have TB disease (have no signs or symptoms of TB) should receive 6 months of IPT.
- Children living with HIV who are more than 12 months of age, who are unlikely to have active TB on symptom-based screening, and have no contact with a TB case should receive 6 months of IPT regardless of TB contact.

IPT can be started 1 month after ART intitiaton and should be repeated every 2 years from the date of completion.

7.6 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 screening questionnaire. Provide IPT if TB screening is negative.

In children with TB/HIV coinfection, initiate TB treatment before ART to avoid severe immune reconstitution inflammatory syndrome (IRIS). All HIV-infected children diagnosed with TB should be initiated on ART within 2 weeks after starting anti-TB treatment.

Recommended ART for Drug-Sensitive TB/HIV Coinfection

Table 7.8: Recommended ART for Drug-Sensitive TB/HIV Coinfection

Initiating ART on TB Rx		
Age/Weight	Regimen	Comments
< 3 years or < 10 kg	LPV/r with 1:1 ritonavir boosting (recommended) Or ABC+3TC+AZT (recommended if ritonavir not available) Or ABC or AZT+3TC+NVP	• Avoid NVP if prior exposure • Start NVP at full dose and adjust to 200 mg/m2/dose if formulation allows • NVP: Check VL at end of TB Rx. If < 1000 copies/mL continue NVP/If >1000 copies/mL change to LPV/r + change NRTI • NEVER continue ABC+3TC+AZT after TB Rx
3-10 years and >10 kg	ABC+3TC+EFV (recommended) Or ABC+3TC+AZT	• NVP can be substituted for EFV if intolerance or cannot swallow (see above box) • NEVER continue ABC+3TC+AZT after TB Rx
> 10 years	ABC+3TC+EFV	• TDF vs. ABC selection based on weight/age • If VL undetectable at end of TB Rx can switch to TDF+3TC+DTG (40 Kg or more) 2 weeks after completion of RIF
• Refer to job aid for 1:1 LPV/r dosing • General Principles • Attempt to provide the most potent ART regimen possible while on ATT • Attempt to avoid ONE drug changes between drug classes if VL is detectable • Consider ART and PMTCT history when changing ART regimens • Consult with Baylor TB/HIV hotline with any questions		

Table 7.8: Recommended ART for Drug-Sensitive TB/HIV Coinfection (continued from previous page)

Initiating ART on TB Rx			
Suggested modifications to ART when initiating TB Rx			
Age/Weight	Current ART	Suggested	Comments
< 3 years or < 10 kg	NVP	Continue NVP	• Increase dose to 200 mg/m2/dose if formulation allows
	LPV/r	LPV/r with 1:1 ritonavir boosting (recommended) or ABC+3TC+AZT (recommended if ritonavir not available) or NVP	• Avoid NVP if prior exposure • Increase NVP to 200 mg/m2/dose if formulation allows • NVP: Check VL at end of TB Rx. If < 1000 copies/mL continue NVP/If >1000 copies/mL change to LPV/r + change NRTI • NEVER continue ABC+3TC+AZT after TB Rx
3 – 10 years and >10 kg	NVP or EFV	EFV	• NVP can be continued instead of EFV if intolerance or cannot swallow (see above box)
	LPV/r as 1st Line Treatment	LPV/r based with 1:1 ritonavir boosting (recommended) or EFV (recommended if VL undetectable) or ABC+3TC+AZT	• Check VL at end of TB Rx to guide treatment (particularly if changed to EFV with prior NNRTI exposure) • NEVER continue ABC+3TC+AZT after TB Rx • Use ritonavir capsules when possible • Consider ABC+3TC+AZT if intolerant to LPV/r
	LPV/r as 2nd Line Treatment	LPV/r with 1:1 ritonavir boosting (recommended) or ABC+3TC+AZT	• Consider ABC+3TC+AZT if intolerant to LPV/r

Table 7.8: Recommended ART for Drug-Sensitive TB/HIV Coinfection (continued from previous page)

Initiating ART on TB Rx			
Suggested modifications to ART when initiating TB Rx			
Age/Weight	Current ART	Suggested	Comments
> 10 years	NVP Or EFV	EFV	• NVP can be substituted for EFV if intolerance
	ATV/r Or LPV/r	LPV/r Double dose (recommended) Or Twice daily DTG (40 Kg or more)	• Double dose LPV/r is appropriate in children over 10 years and adults • DTG must be given twice daily while on TB Rx • Consult with Baylor TB/HIV Hotline before starting DTG (must optimize NRTI backbone if detectable)
	DTG	Twice daily DTG (40 kg or more)	• DTG must be given twice daily while on TB Rx and continued twice daily for two weeks after TB Rx completion
• Refer to job aid for 1:1 LPV/r dosing • General Principles • Attempt to provide the most potent ART regimen possible while on ATT • Attempt to avoid ONE drug changes between drug classes if VL is detectable • Consider ART and PMTCT history when changing ART regimens • Consult with Baylor TB/HIV hotline with any questions			

See Annex 9.16 for Alternative ART for Paediatric Clients on TB Treatment.

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 (see Annex 9.14).

For more information on the diagnosis and management of tuberculosis, see National Tuberculosis Guidelines.

TB Treatment Drug Interactions

See Chapter 5, Section 4 and Annex 9.8.

7.7 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.

During the first 6 months after ART initiation, frequent visits are crucial to monitor for immune reconstitution inflammatory syndrome and for acute ART toxicities and adherence issues.

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 on monthly.

Immune Reconstitution Inflammatory Syndrome (IRIS)

Any opportunistic infection occurring during the first 6 months after ART initiation might have 2 causes:

1. The immune system is not yet fully functional (the least likely scenario).
2. 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 to the hospital.

Dolutegravir (DTG) has been associated with a higher risk of IRIS due the rapid viral suppression. Clients initiating on DTG should be closely monitored for the first 6 months.

Clients with advanced immunodeficiency (advanced disease) are at greater risk for IRIS when initiating on ART and should be closely monitored.

Components of the Clinical Assessment

Table 7.9: Components of the Clinical Assessment for Children and Adolescents on ART

Assessment Component	Key Questions and Evaluations
Medical History	• Presenting complaint, if any • Review of symptoms • Nutritional history (see Chapter 6) • Current medications and traditional remedies • Clinical review of symptoms, signs, medication use and side-effects
TB Screening	• Known TB contacts • Cough for >2 weeks • Any cough with fever and/or poor weight gain/ weight loss • Poor weight gain or failure to thrive
Adherence Counselling and Support	• Attending scheduled clinic appointments • Prescription refills (weight-based) • Modified lifestyle and avoiding risky behaviours (i.e., making a commitment to positive living and preventing new HIV infections) • 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
Psychosocial Assessment	• Identify the child's current caregivers • Consider disclosure to the child and family members • Discuss child and caregiver fears and concerns regarding ART • Where appropriate, explore the child's understanding of HIV • Assess the child's education and socialization • Evaluate potential barriers to adherence • Assess the economic situation of the child's household
Complete Physical Examination	• Weight and height plotted on child's growth curve/weight for age • Head circumference measured (in children under 2 years of age, it may be indicative of cognitive or developmental delay) • Head-to-toe examination of all systems, looking for signs of HIV disease or immune reconstitution inflammatory syndrome

Table 7.9: Components of the Clinical Assessment for Children and Adolescents on ART (continued from previous page)

Assessment Component	Key Questions and Evaluations
Laboratory Testing	• Viral load • CD4 count • HB (clients on zidovudine [AZT]) • Creatinine (adolescents on TDF) • Lipid profile (annually for clients on protease inhibitor-based regimens) • Urine human chorionic gonadotropin test for sexually active adolescent girls
WHO T- Staging	• Clinical evaluation
Management and clinical care	• Provide acute care, if necessary • Management of symptoms and underlying clinical conditions • ART refill (monthly/multiple refills) • Initiate or refill prophylactic drugs as indicated (e.g., Co-trimoxazole, isoniazid, fluconazole) • For all sexually active adolescents, screen for STIs and offer family planning services

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.

7.8 Laboratory Monitoring of Children and Adolescents on ART

CD4 Count

CD4 count testing at baseline for all children living with HIV remains important in order to avoid 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 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 6 months after initiation of ART and the second VL test repeated 12 months after ART initiation. After 2 consecutive undetectable VL results 6 months apart, VL monitoring should be done annually for children 0–10 years of age and every 6 months for adolescents (10-19 years old), see the schedule for VL monitoring in children and adolescents as shown in Figure 7.1.

Table 7.10: Repeat VL Test After Initial Non-suppression

Repeat VL Test Result	Most Likely Reasoning	What To Do
< 20 copies/mL (or undetectable VL result)	• Client was poorly adhering to treatment and has improved adherence	• VL should be rechecked every 6 months until 2 consecutive undetectable VL results are achieved, then annual monitoring can begin. • If VL is undetectable and client is on ART for more than 1 year, provide CommART models.
20 - 1000 copies/mL (detectable <1000 copies/mL)		• Adherence should be reinforced, and the VL should be rechecked after 6 months and annually thereafter if VL is undetectable
≥1000 copies/mL	• Diagnosis is virological treatment failure most likely due to resistant virus	• These clients should be referred to the doctor/ multidisciplinary team for consideration of 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.

A viral load threshold of ≥1000 copies/mL should be used to determine virological failure when using plasma or dried blood spot specimens.

Figure 7.1: VL Timeline for Children and Adolescents

For clients less than 10 years old

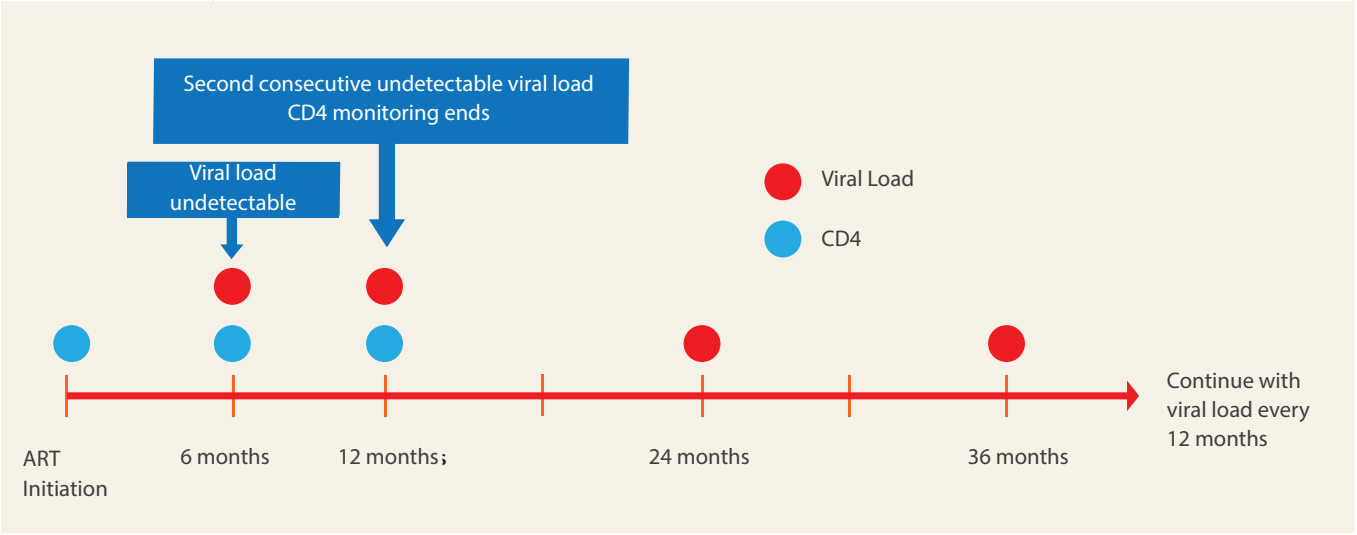
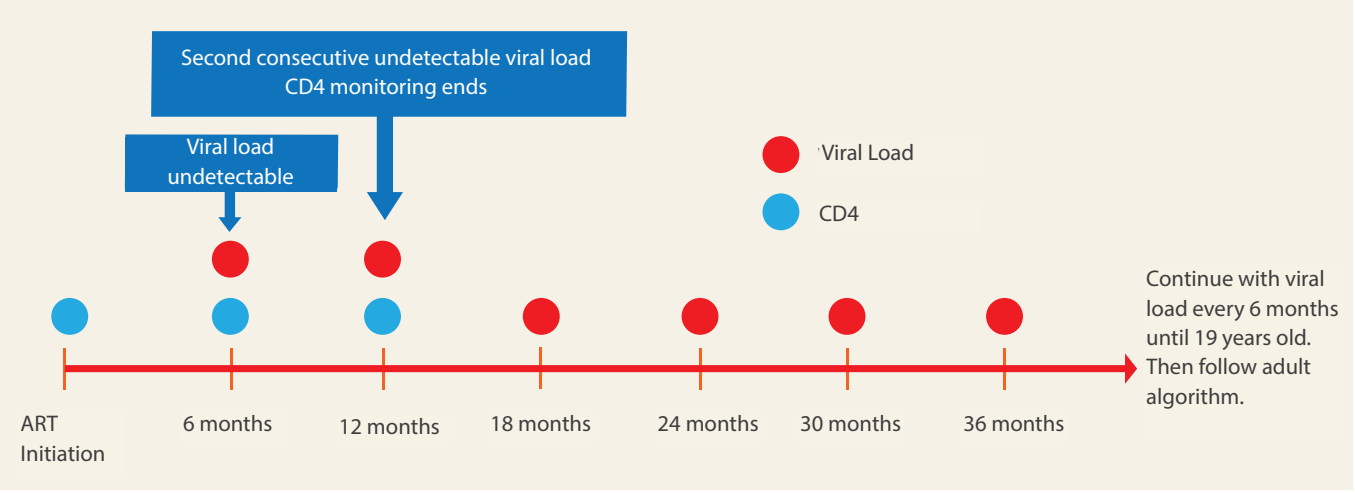


Figure 7.1: VL Timeline for Children and Adolescents (continued from previous page)

For clients 10-19 years old



Viral Load Test Results

See Chapter 5, Section 8 (Table 5.9) for VL test results and how to interpret the results of the tests.

Management of Clients with Detectable Viral Load and Stepped-Up Adherence Counselling (SUAC)

See Chapter 5, Section 8 (Table 5.9) for the appropriate steps once a detectable VL test result is received. Children and adolescents with VL > 400 copies/mL should be referred for SUAC.

7.9 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.

Note: Identification and management of treatment failure in children and adolescents should not be delayed.

Table 7.11: WHO Definitions of Types of Treatment Failure in Children and Adolescents

Failure	Definition	Comments
Virological Failure	• 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 should be carried out by a multidisciplinary team to give this final diagnosis
Immunological Failure	<u>Younger than 5 years</u> • Persistent CD4 counts below 200 cells/mm^3 or <10% <u>5–10 years</u> • Persistent CD4 counts below 100 cells/mm^3 <u>10–19 years</u> • CD4 count falls to the baseline (or below), or CD4 count at or below 200 cells/mm^3 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
Clinical Failure	<u>Children (less than 10 years)</u> • New or recurrent clinical event indicating advanced or severe immunodeficiency (WHO clinical stage 3 and 4 clinical condition with exception of TB) after 6 months of effective treatment <u>Adolescents (10–19 years)</u> • New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 condition) 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 with the goal of preserving the efficacy of first-line therapy in children.

Table 7.12: Prevention and Management of Treatment Failure in Children and Adolescents

Component	Interventions
Clinical Component	• Assure correct 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 • Monitor drug interactions • Identify previous ARV exposure (NVP for PMTCT and past treatments) • Identify suboptimal adherence • Ensure optimal storage conditions of the drug formulations • Routine monitoring of VL
Psychosocial Component in Children, Adolescents and Caregivers	• Identify psychological/mental conditions: depression, drug fatigue, self-stigma in the child and caregiver, and refer appropriately • Identify other structural barriers (e.g., long travel times, school, parental refusal of consent, home conflicts) • Address disclosure with age-appropriate messages • Refer to teen clubs or children support groups where available • Establish a close and transparent relationship with the child/adolescent • Empower and educate the child/adolescent to be part of their treatment plan

Steps for Management of Treatment Failure in Children

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
- Treat and control all comorbidities when possible

All providers should consider the steps in Figure 7.2 when managing treatment failure in children/adolescents.

Figure 7.2: Steps for Management of Treatment Failure

Identify cause of treatment failure	• Poor adherence: disclosure, recent changes in caregivers, drug fatigue, depression, timing of taking ARVs • Sub-optimal ARV levels from underdosing or drug-drug interactions • Previous exposure ARV from PMTCT prophylaxis or ARV treatments resulting in drug resistance
Provide appropriate intervention	• Intensify adherence interventions - SUAC • Correct medication doses or minimize drug-drug interactions • Screen and treat OIs • Preform laboratory tests: CD4 and viral load per recommendations
Assessment by MDT meeting	• Involve different members of your team in the management of the child; counsellor, nurse, or doctor • Involve relevant members of the child's family • Involve the child in his/her own care with age-adapted messages
Retain on first line or switch to second line	• Within the MDT decide if there is a need to extend the use of first-line ARV or switch to a second-line regimen

7.10 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 3 stepped-up adherence counselling 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.

See Chapter 5, Section 8 for details on stepped-up adherence counselling.

What to Switch To

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

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

Switch to a second-line regimen only when issues of adherence and treatment support have been fully addressed by a multidisciplinary team. Disclosure should not be a prerequisite for starting second-line unless it is a primary barrier to adherence.

Table 7.13: Recommended Second-Line Regimens for Children and Adolescents

First-Line Regimen	Recommended Second-Line Regimens	
	Children < 10 years*	Children ≥10 years (if >40 kg)
ABC+3TC+EFV ABC+3TC+NVP TDF+3TC+EFV TDF+3TC+NVP TDF+3TC+DTG ABC+3TC+DTG	AZT+3TC+LPV/r	AZT+3TC+ATV/r* (Alternate: AZT-3TC- LPV/r)
AZT+3TC+NVP AZT+3TC+EFV	ABC+3TC+LPV/r	TDF+3TC+ATV/r ABC+3TC+ATV/r (Alternate: ABC/ TDF+3TC+ LPV/r)
AZT+3TC+LPV/r ABC+3TC+LPV/r	Consult multidisciplinary team or call the Baylor HIV/TB Hotline (Annex 9.14) for second-line failure assessment for drug resistance test based on second-line regimen (See potential third-line regimens in Table 7.14)	
TDF+3TC+NVP TDF+3TC+EFV ABC+3TC+EFV	AZT+3TC+LPV/r	AZT+3TC+ATV/r (or LPV/r)
TDF+3TC+DTG		2 NRTIs + ATV/r (or LPV/r) or 2 NRTI + DRV/r

*See Annex 9.15 for use of LPV/r syrup and pellets in children less than 3 years.

Use of ATV/r 300/100 mg

Clinicians can substitute clients currently on a LPV/r-containing second-line regimen to an ATV/r containing regimen for all;

- Adolescents 10–19 years old
- Children or adolescents >40 kg.

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)

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 a number of 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 9.7 for information on drugs that should not be used with selected ARV regimens.)

7.11 Third-Line ART for Children and Adolescents

Evaluation for third-line ART is currently centralized and done by paediatric specialists. The recommendation is to contact the Baylor clinicians in Mbabane, Manzini or Hlatikhulu. It is highly recommended to refer or to call the Baylor HIV/TB Hotline to consult on each individual case.

Clients who fail second-line ART have limited options. Agents used to construct a third-line regimen are often more expensive, 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, then a resistance test (genotypic/phenotypic) should be performed. 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.

The decisions regarding treatment choices in third-line therapy are complex and need to be guided by resistance patterns found on 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 third-line regimen for the specific client. Each client on third-line regimen will require individualized treatment based on HIV genotype result.

Potential Options for Third-Line Regimens

Table 7.14: Potential Third-Line Regimens for Children and Adolescents

Age	Potential Third-Line Regimens
Children (0-10 years)	RAL (or DTG*) + 2 NRTIs
	DRV/r + 2 NRTIs
	DRV/r + RAL (or DTG*) ± 1-2 NRTIs
Adolescents (10-19 years)	DRV/r + DTG (or RAL) ± 1-2 NRTIs
	DRV/r + 2 NRTIs ± NNRTI
	Optimize regimen using genotype profile

*DTG is currently approved for children ≥12 years old or 40kg

7.12 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 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:

- Denial and fear related to their HIV diagnosis
- Misunderstandings related to their status and health needs
- Self-stigma
- Lack of belief in the efficacy of ARV
- Treatment fatigue
- Distrust of family, practitioners and the health care system
- Low self-esteem and chaotic, unstructured lifestyles
- Limited family and social support

Long travel times to the clinic
Conflicts with school schedules and work
Substance use and abuse
Peer pressure

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), 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).

Though 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, Section 2.

Disclosure

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, 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 assuring protection and support.

Children must be fully disclosed by age of 10.

In general, all adolescents should be linked to a regular ART support group (e.g., 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.

Transitioning Adolescents to Adult Care

There are parallels between the maturation of adolescents into adults and the transition from paediatric to adult HIV programs. This transition should involve adolescents 17 to 19 years of age. Adolescents living with HIV may face challenges in their transition to adult care and learning to independently manage their own 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
- 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 transition is to ensure the provision of uninterrupted, co-ordinated, 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 clear understanding of VL results
- Identification of developmental changes.
- 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.
- Child must know that transition is inevitable.

The role of the health care worker

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 are outlined in Table 7.14 and a list of skills an adolescent should have before transitioning to adult care and a checklist for successful transition are outlined in Table 7.15.

Table 7.15: General Principles for Effective Transitions to Adult Care

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 prior to and during 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. Plans should be flexible to meet the adolescent's needs: • Use a multidisciplinary transition team, which may include peers who are in the process of transitioning or who have transitioned successfully. • Address comprehensive care needs as part of transition, including medical, psychosocial and financial aspects of transitioning. • Allow adolescents to express their opinions. • Educate HIV care teams and staff about transitioning.

Table 7.16: Checklist for Successful Transitions to Adult Care

Skills an 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 to appointments on time. • Call ahead for urgent visits. • Request prescription refills correctly and allow enough time for refills to be processed before medications run out. • Establish a good working relationship with healthcare workers at the paediatric/adolescent site, which will enable the adolescent to work effectively with the health care worker at the adult site. • Negotiate multiple providers and subspecialty visits (for other services). • Condom use skills • Family planning • Transition to adult support groups	• The client has accepted their chronic illness and is oriented towards 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 is able to 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 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 • Consistentand correct condom use

7.13 Promoting Long-term 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 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 to the medical regimen includes the client taking the correct number of pills (correct dosing) at the correct frequency. 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.

Differentiated Service Delivery

Differentiated ARV service delivery (including teen clubs, family-centred care models, 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.

7.14 Elements of a Well-Functioning Paediatric HIV Program

Table 7.17: 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 medication formulations • NVP clips and syringes • Pill cutters/pill boxes • Dosing charts • Adolescent services—family planning, cervical cancer screening
Client education	• Paediatric medication formulations • Information, education and communication materials on paediatric ART • Disclosure counselling materials • U-report • Skills development
Job aids	• WHO clinical stages posters • Neurological developmental stages • Dried blood spot posters • ART guidelines • Stepped-up adherence counselling
Phlebotomy	• 1 mL tubes for laboratory tests • Butterfly needles for phlebotomy • VL required materials
Differentiated Service Delivery	• Teen Clubs • Paediatric specific days
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
Post-exposure prophylaxis paediatric materials	• Counselling tools • Post-exposure prophylaxis drugs package • PrEP as per need
Marketing materials on our telemedicine options	• DBS hotline, Baylor HIV/TB Hotline (see Annex 9.14), U-Report, Paediatric specific days

All facilities must have Teen Clubs.
Facilities should have dedicated days for children especially those that are failing treatment.

7.15 Summary of Monitoring and Clinical Service Timelines for Paediatrics and Adolescents

Table 7.18: 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
Viral load	None				X		X	Every year if <10 years Every 6 months for ages 10–19 years
Haemoglobin	X		X	X	X		X	Every 6 months
AST/ALT	As clinically indicated							As clinically indicated
Creatinine	TDF only				TDF only		TDF only	Every 6 months in on TDF
TB-LAM (TB symptoms present)	Adolescents and children with 100 cells/mm^3 and children who have a CD4 count less than 25% OR if seriously ill							Adolescents and children with 100 cells/mm^3 and children who have a CD4 count less than 25% OR if seriously ill
CrAg screening	Adolescents and children with 100 cells/mm^3 and children who have a CD4 count less than 25% OR if seriously ill							Adolescents and children with 100 cells/mm^3 and children who have a CD4 count less than 25% OR if seriously ill

Table 7.18: Summary of Monitoring and Clinical Service Timelines for Children and Adolescents (continued from previous page)

	Baseline	2 weeks	1 month	3 months	6 months	9 months	12 months	Thereafter
Hepatitis B screening	Adolescents with history of exposure or at risk of hepatitis B virus (HBV) infection Children and adolescents with clinical signs and symptoms, or laboratory markers indicating possible HBV Infants and children of close household contacts of clients with HBV infection							Same indications as baseline
Growth and development educational achievement and behaviour	X		X	X	X	X	X	All visits
Adherence and correct dosing, side-effects/toxicity	X	X	X	X	X	X	X	All visits
Opportunistic infections including TB	X	X	X	X	X	X	X	All visits
Social history/ psychosocial factors	X	X	X	X	X	X	X	All visits

Chapter 8:

Management of HIV and Non-communicable Diseases

8.1 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 has been increasing as people living with HIV (PLHIV) are getting older. Despite the lifesaving role of antiretroviral therapy (ART), some antiretroviral (ARVs) are associated with metabolic complications that can increase the long-term risk of cardiovascular diseases. Consequently, all clients infected with HIV and/or tuberculosis (TB) should be screened for concomitant non-communicable diseases.

8.2 Care and Management of Hypertension and HIV

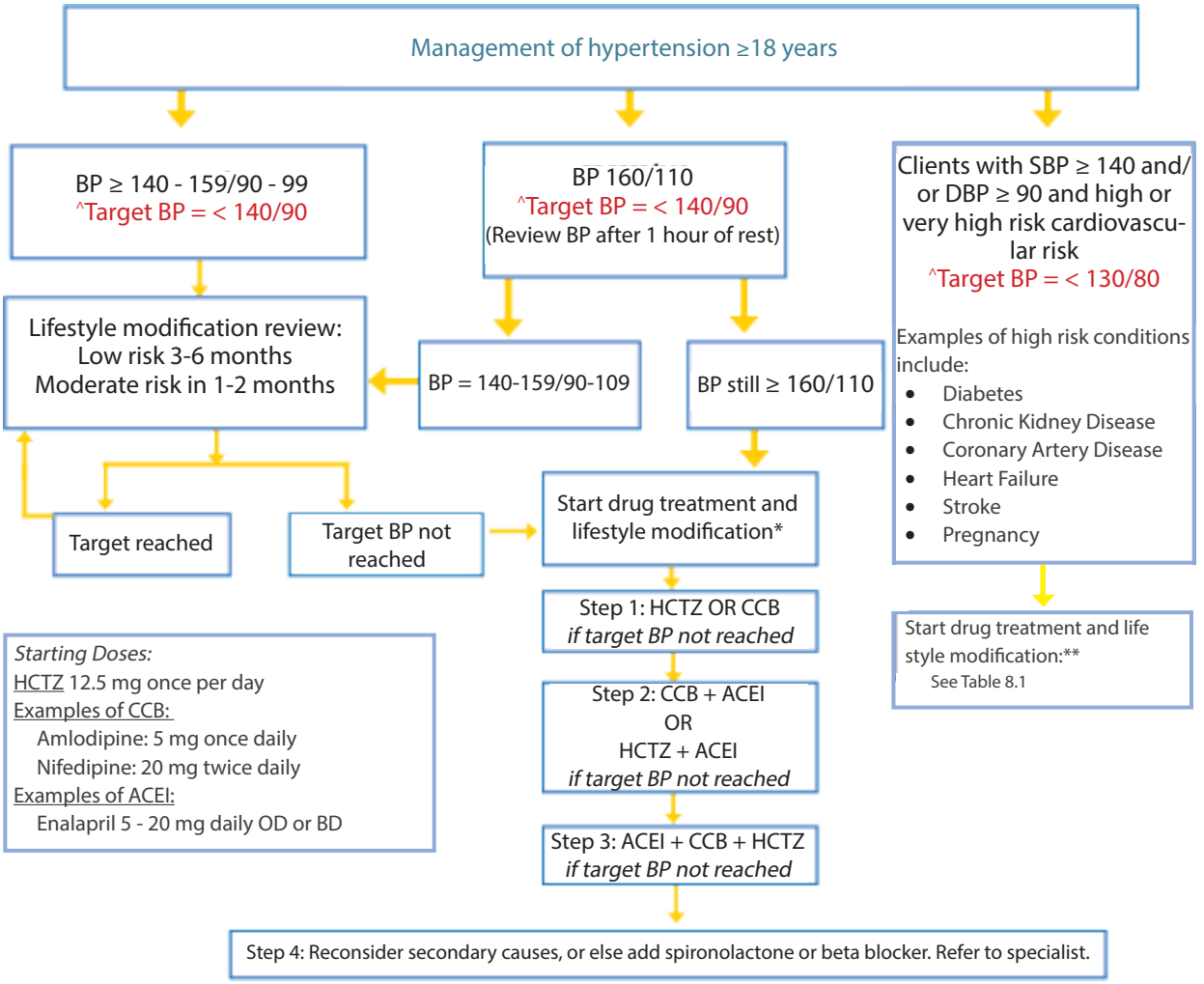
Management of Hypertension

Non-pharmacological management

- Lifestyle modication is required
  - » Dietary change
  - » Low-salt diet
  - » Low-fat diet
  - » High-fibre diet
  - » No alcohol abuse
- Behavioural change
  - » Regular aerobic exercise (i.e., 30 minutes of exercise 3 times a week to the point of sweating)
  - » No smoking
  - » Stress management
  - » Weight management to maintain an ideal BMI (18.5-25)

Pharmacological management

Figure 8.1: Hypertension Management Algorithm



*Review the client within one month when initiating Step 1, Step 2, Step 3 or Step 4.
** Review list of conditions within one to two weeks
^Aim to reach target BP within 3 months. For more details on management, refer to the Swaziland Hypertension Guidelines.

Recommended Drugs to Initiate in Special Cases

Table 8.1 Recommended Drugs to Initiate in Special Cases

Client type	Recommended First drugs	If second drug is needed to achieve blood pressure <130/80 add	If third drug is needed to achieve blood pressure 130/80 add
Hypertension and Diabetes	ACE inhibitor or ARB if ACEI cough or angioedema	Calcium channel blocker/thiazide	Calcium channel blocker or thiazide (the one not used as first drug)
Hypertension and Chronic kidney disease	ACE inhibitor or ARB if ACEI cough or angioedema (monitor K+ and creatinine closely)	Calcium channel blocker or thiazide*	
Hypertension and Coronary artery disease	Beta blocker and ACE inhibitor (initiate these 2 drugs regardless of blood pressure.)	Calcium channel blocker or thiazide	
Hypertension and stroke history	Calcium channel blocker	ACE inhibitor or thiazide	
Hypertension and Heart failure	Clients with symptomatic heart failure should receive an ACE inhibitor + diuretic + spironolactone regardless of blood pressure. Add a beta blocker if there is evidence of coronary artery disease.		
Pregnancy	Methyldopa	Beta blocker	Refer to specialist

* If the estimated glomerular filtration rate (eGFR) is <45 mL/min loop, diuretics are preferred over thiazides.
See Annex 9.13 for clinical evaluation of a client with high blood pressure and HIV infection

Aspirin
- Do not prescribe aspirin to hypertensive clients unless:
  - » clients aged > 40 years
  - » clients with cardiovascular risk factors
  - » clients with 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

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.

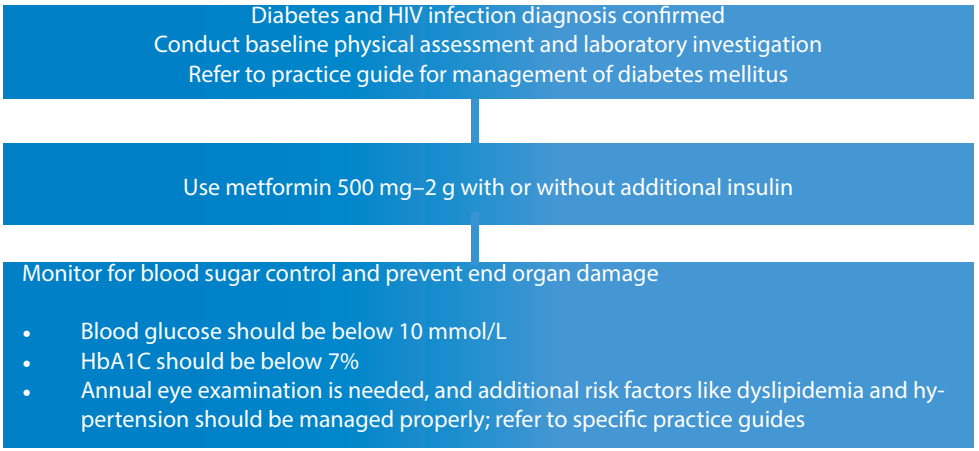
Interactions of HIV and Hypertension

- See Figure 8.1 for the screening and management of hypertension.
- HIV clients 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 disoproxilfumarate (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.
- Calcium channel blockers like nifedipine and amlodipine may interact with protease inhibitors, producing increased serum levels of the former; 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.

8.3 Care and Management of Diabetes and HIV

- Insulin resistance (glucose intolerance) is common with protease inhibitor-based regimen, but frank diabetes is uncommon and rarely requires insulin treatment unless the clients are prone to develop diabetes (e.g., first-degree relative).
- Diabetics have a potentially high risk of developing active TB because of the potential synergy of diabetes mellitus and HIV infection to suppress the cell-mediated immunity.
- Dolutegravir (DTG) can interact with metformin and metformin dose adjustment can be necessary (avoid high dose).
- Annual symptom screening for overt diabetes mellitus and random blood sugar test is recommended for early diagnosis of diabetes among PLHIV

Figure 8.2: Evaluation of a Client with Diabetes and HIV Infection



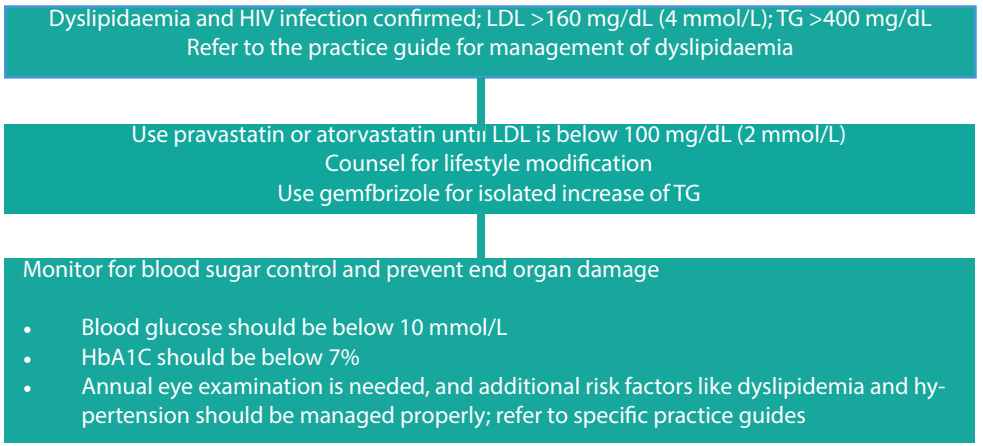
Management of diabetes in a client with HIV follows a similar protocol for non- diabetics but with the following special considerations:

- 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 potential protracted hypoglycaemia.
- Metformin is safe and effective in controlling blood sugar. It also has the additional advantage of reducing weight.
- Dolutegravir can increase the blood levels of metformin. It is not clear whether this is clinically significant, but it is recommended that when starting either of these drugs for a client already taking the other, one should start with the lowest dose of metformin and titrate according to blood sugar to avoid hypoglycaemia.
- Insulin is often required for tight control of blood sugar.

Care and Management of Dyslipidaemia and HIV

- HIV infection, indirectly through the effect of ART, causes an increase of 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 8.3: Evaluation of a Client with Dyslipidaemia and HIV Infection



Simvastatin and lovastatin should not be used with protease inhibitors because of the risk for rhabdomyolysis. However, atorvastatin or pravastatin are safe to use concurrently with protease inhibitors.

Table 8.2 Pharmacotherapy and Drug Information for Treatment of Hyperlipidaemia

Drug Name and Class	Indications	Starting Dose	Maximal Dose	Mechanism of Action	Common Side-Effects
HMG-COA reductase inhibitors (statins)	Elevated low-density lipoprotein-C			Reduce cholesterol synthesis, and very low density lipoprotein production Inhibit hepatic low-density lipoprotein receptors	Joint and muscle pain with elevated transaminases
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 Swaziland National Essential Medicines List as lipid-lowering agents in Swaziland					

8.4 Care and Management of Depression and HIV

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 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 9.20 for the depression assessment in both English and Siswati)

Pharmacological Management of Depression

Table 8.3: Clinical Diagnosis and Recommendations for Management of Depression

Clinical Diagnosis	Recommendation
Depression only	Use antidepressants (see Table 8.4)
Depression with psychotic features	Use antidepressants + antipsychotic drugs
Bipolar affective disorder, depressive phase	Use mood stabilizer + antidepressants (add an antipsychotic drug if 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 in the morning to avoid sleep deprivation.	

Table 8.4: Drugs Used to Treat Depression

Antidepressant Tablets	Initial Dosage	Max Dose/Day	Indication
Tricyclic Antidepressants			
Amitriptyline	25 mg for 3/7, then 50 mg every night	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.
- Nevirapine may decrease levels of fluoxetine.
- 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.
- Use of 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 8.5: 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 500 mg–600 mg twice daily (mostly preferred in PLHIV):
- Maximum therapeutic dose 2500 mg/day in divided dose.
- Increase dose by 200–500mg.
- Check valproate levels yearly or every 6 months if the client is on maximum dose.
- Lamotrigine 25 mg for the first 14 days then increase by 25-50 mg, maximum 500 mg/day in divided doses.
- Carbamazepine is contraindicated as it increases levels of PIs and NNRTIs.

8.5 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 life-threatening illness. The aim of palliative care is to prevent and relieve suffering by means of 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

8.6 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 8.6: 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. • Latrogenic (AZT) • Peripheral neuropathy • Herpes neuritis • Neuropathies associated with didanosine and stavudine toxicities • 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 2 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 symptom 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 8.4 Numeric Pain Rating Scale

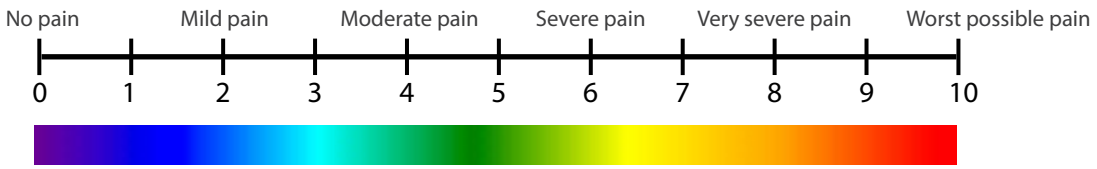
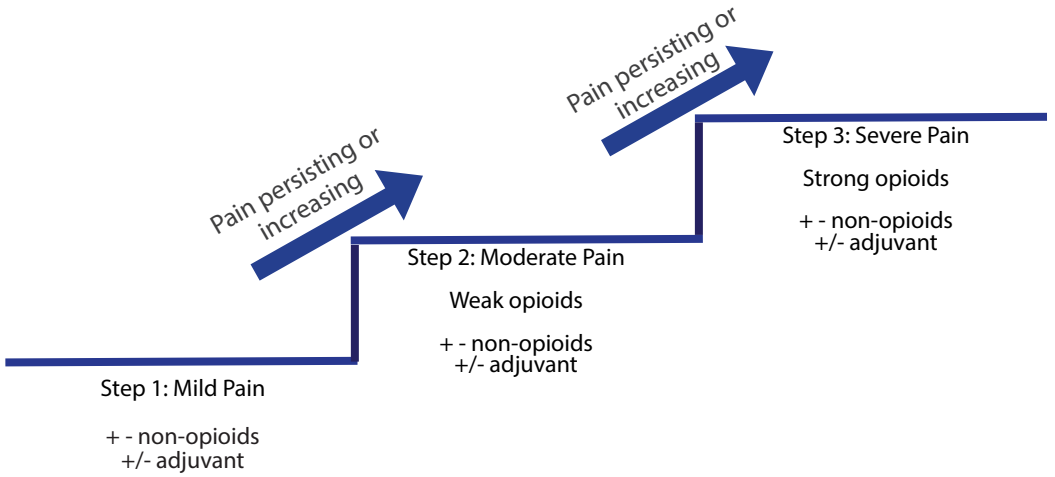


Table 8.7 Pain Intensity

Pain Intensity	Score
No Pain	0
Mild Pain	1-3
Moderate Pain	4-6
Severe Pain	7-10

World Health Organization Analgesic Step Ladder

Figure 8.5 World Health Organization Analgesic Step Ladder



Step 1: Non-opioids (e.g., paracetamol, ibuprofen, diclofenac) ± adjuvant (e.g., antidepressant, anticonvulsant, antispasmodic, muscle relaxant, bisphosphonate, or corticosteriod). If pain is not controlled by Step 1 analgesics, move to Step 2 by adding a weak opioid.

Step 2: Weak opioids for moderate pain (e.g., codeine, tramadol, or low dose of morphine) ± non-opioid ± adjuvant. If a weak opioid has been used to a maximum dose for moderate pain and the client still has pain, then move to Step 3 by changing to a strong opioid.

Step 3: Strong opioid (e.g., morphine, fentanyl, methadone) ± non-opioid ± adjuvant.

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 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 9.5.

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, and so caution needs to be shown when giving analgesics to clients on ART. In particular:

- The main interactions occur with the adjuvant analgesics such as phenytoin, carbamazepine, dexamethasone and amitriptyline.
- Potential interactions between ARVs and other drugs are set out in Annex 9.4.

Specific Considerations for Pain in Children

Table 8.8: 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 under-diagnosed. 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 spasm.
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 mycostatine 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 8.9: Specific Pain-Related Syndromes in HIV

Pain Type	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 stauvine 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 8.9: Specific Pain-Related Syndromes in HIV (continued from previous page)

Pain Type	Clinical Presentation	Causes	Treatment
Abdominal pain in HIV	Abdominal pain in HIV	• TB abdomen • Mycobacterium avium complex • 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 underlying cause if possible • Start ARVs if indicated • Treat pain according to WHO analgesic ladder • Beware of ileus/constipation caused by opioids: can make 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 in HIV	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 for musculoskeletal pain • Baclofen (for muscle spasm, can cause seizures) • Adjuvants, especially Clonazepam
Raised Intracranial pressure	Headache with focal neurological deficits	• Cryptococcal meningitis • Toxoplasmosis	• Treat pain according to 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

- By the mouth
- By the clock
- By the ladder

8.7 Control of Additional Symptoms

Dosing for Nausea

Prescribe an anti-emetic for 7–10 days, after which the 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 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 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.

8.8 Psychosocial and Spiritual Support

Caring for clients with chronic illness involves responding to their total needs, including:

- Social needs: 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.

Chapter 9:
Annex

Chapter 9: Annex Overview

9.1 Pharmacovigilance in ART

Pharmacovigilance, also known as drug safety, is the pharmacological science relating to the collection, detection, assessment, monitoring and prevention of adverse effects with pharmaceutical products. Pharmacovigilance promotes the systematic rational use of drugs and assures confidence in the safety of drugs. It improves client care and safety, and public health and safety. The ultimate purpose of pharmacovigilance is in clinical practice to minimize the potential harm that is associated with all active medicines.

Healthcare workers prescribing antiretroviral drugs (ARVs) 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.

Monitoring and reporting of 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 to their medication and advise clients on when to report to their healthcare providers.

All health care providers—doctors, pharmacists, nurses, counsellors and more, at various service delivery points—should assess clients for adverse drug reactions at every encounter. All suspected adverse events should be documented and recorded on the prescribed adverse drug reaction reporting form and forwarded to the Pharmacovigilance Unit of the Ministry of Health at the Central Medical Stores for analysis.

There are 2 methods of pharmacovigilance:

- Active pharmacovigilance:
  - » The active method involves the routine screening of all clients on treatment at every visit for signs and symptoms indicating possible adverse reactions, and follow-up and documentation of all suspected adverse reactions observed after commencement of treatment.
- Passive pharmacovigilance:
  - » The passive method involves an unplanned voluntary communication of adverse reactions or events in a client on therapy with 1 or more drug products; this method depends on the discretion of the healthcare provider.

What Should Be Reported About Adverse Drug Reactions?

- All serious or unexpected (unusual) reactions that one supects for established or well-known drugs
- All suspected reactions, including minor ones for new drugs
- An observed increased frequency of a given reaction
- All suspected adverse reactions associated with drug-drug, drug-food or drug-food-supplement interactions
- Adverse drug reactions during pregnancy and lactation
- Adverse drug reactions occurring from overdose or medication error
- Lack of efficacy of a medication, or suspicion of pharmaceutical defects based on observation
- Adverse drug reactions suspected of causing death, danger to life, admission to hospital, prolongation of hospitalization, or birth defects
- When in doubt, report: whether the suspected adverse event or reaction is an adverse drug reaction or not, it should be reported.

9.2 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 fetus
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	—

9.2 Overview of ARV Drugs (continued from previous page)

Generic Name	Standard Adult Dose	Adult Formulation	Paediatric Formulation	Food Restrictions / Special Considerations	Contraindications	Information on Use in Pregnancy
Non-nucleoside reverse-transcriptase inhibitors (NNRTIs)						
Efavirenz (EFV)	600 mg at night	200 mg caps/tabs, 600 mg caps/tabs	50 mg caps/tabs, 30 mg/mL susp	Without food, at bedtime on an empty stomach	Psychosis	Potential fetal 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 syr	With or without food	Severe liver disease, history of Stevens-Johnson syndrome	Potential risk of life-threatening hepatotoxicity in women with ≥250 cells/mm^3 CD4 counts
Rilpivirine (RIL)	25 mg every 24 hours	25 mg	—	With food	Previous history of depression	—
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	

9.2 Overview of ARV Drugs (continued from previous page)

Generic Name	Standard Adult Dose	Adult Formulation	Paediatric Formulation	Food Restrictions / Special Considerations	Contraindications
NRTI/NtRTI Fixed-Dose Combinations					
Tenofovir + Lamivudine	1 tablet every 24 hours	300 mg + 300 mg tabs	—	See tenofovir, lamivudine	
NNRTI/NRTI Fixed-Dose Combinations					
Stavudine + Lamivudine + Nevirapine	1 tablet every 12 hours	30 mg + 150 mg + 200 mg tabs	12 mg + 60 mg + 100 mg tabs	See stavudine, lamivudine, nevirapine	
Zidovudine + Lamivudine + Nevirapine	1 tablet every 12 hours	300 mg + 150 mg + 200 mg tabs	60 mg + 30 mg + 50 mg tabs	See zidovudine, lamivudine, nevirapine	
NRTI/NRTI Fixed-Dose Combinations					
Abacavir + Lamivudine	1 tablet every 24 hours		60 mg + 30 mg tab	See abacavir, lamivudine	
Stavudine + Lamivudine	1 tablet every 12 hours	30 mg + 150 mg tabs	12 mg + 60 mg tabs	See stavudine, lamivudine	
Zidovudine + Lamivudine	1 tablet every 12 hours	300 mg + 150 mg tabs	60 mg + 30 mg tabs	See zidovudine, lamivudine	

9.2 Overview of ARV Drugs (continued from previous page)

Generic Name	Standard Adult Dose	Adult Formulation	Paediatric Formulation	Food Restrictions / Special Considerations	Contraindications
NtRTI/NRTI/NNRTI Fixed-Dose Combinations					
Tenofovir + Lamivudine + Efavirenz	1 tablet every 24 hours	300 mg + 300 mg + 600 mg tabs	—	See tenofovir, lamivudine, efavirenz	
Tenofovir + Lamivudine + Nevirapine (co pack)	1 tablet every 24 hours (TDF+3TC) 1 tablet every 12 hours (NVP)	300 mg + 300 mg + 200 mg tabs	—	See tenofovir, lamivudine, nevirapine	
Tenofovir + Lamivudine + Nevirapine	1 tablet every 24 hours (TDF + 3TC) 1 tablet every 12 hours (NVP)	300 mg + 300 mg + 200 mg tabs	—	See tenofovir, emtricitabine, efavirenz	
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
Indinavir (IDV)	800 mg every 8 hours	400 mg caps	—	Without food—take 2 hours before or 1 hour after a meal Avoid taking within an hour of taking didanosine	Kidney or liver disease

9.2 Overview of ARV Drugs (continued from previous page)

Generic Name	Standard Adult Dose	Adult Formulation	Paediatric Formulation	Food Restrictions / Special Considerations	Contraindications
Protease Inhibitors					
Lopinavir (boosted 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 syr 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	
Saquinavir (boosted with ritonavir) (SQV/r)	1000 mg with 100 mg ritonavir every 12 hours	200 mg caps	—	With food	Kidney or liver disease
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

9.3 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.

9.4 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	• Stavudine (d4T)—Proven antagonism; overlapping toxicities • 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
Stavudine (d4T)	Amphotericin B, Co-trimoxazole, Isoniazid, Methadone, Hydroxyurea, Ethionamide, Ethambutol	• Zidovudine (AZT)—Proven antagonism; overlapping toxicities • Didanosine (ddI)
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)	Artemisin, Amiodarone, Buprenorphine, Carbamazepine, Clarithromycin, Codeine, Dexamethasone, Diazepam, Digoxin, Erythromycin, Estradiol, Ethinyl Estradiol, Fluconazole, Furosemide, Garlic, Gliclazide, Glipizide, Glitazones, Halofantrine, Haloperidol, Itraconazole, Ketamine, Ketoconazole, Levonorgestrel, Lorazepam, Medroxyprogesterone (intramuscular and oral), Methadone, Miconazole, Norethisterine, 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 estradiol/norethindrone acetate—Possible contraceptive failure due to the induction of CYP450 3A4 by nevirapine

9.4 Potential ARV Interactions with Other Drugs (continued from previous page)

ARV Drug	Potential Interaction With	Avoid Combination With
Nevirapine (NVP)	Artemisin, Amiodarone, Buprenorphine, Carbamazepine, Clarithromycin, Codeine, Dexamethasone, Diazepam, Digoxin, Erythromycin, Estradiol, Ethinyl Estradiol, Fluconazole, Furosemide, Garlic, Gliclazide, Glipizide, Glitazones, Halofantrine, Haloperidol, Itraconazole, Ketamine, Ketoconazole, Levonorgestrel, Lorazepam, Medroxyprogesterone (intramuscular and oral), Methadone, Miconazole, Norethisterine, 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 estradiol/norethindrone acetate—Possible contraceptive failure due to the induction of CYP450 3A4 by nevirapine
Efavirenz (EFV)	Artemisin, Codeine, Buprenorphine, Cimetidine, Clarithromycin, Diazepam, Ergometrine, Estradiol, Ethinyl Estradiol, 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 Estradiol, 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)

9.4 Potential ARV Interactions with Other Drugs (continued from previous page)

ARV Drug	Potential Interaction With	Avoid Combination With
Darunavir/ritonavir (DRV/r)	Amiodarone, clarithromycin colchicine, diltiazem, ethinyl estradiol, norethindrone, phenobarbital, simvastatin, rifampicin, midazolam, sertraline, 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) • Lopinavir/ritonavir—Decreased darunavir/ritonavir effects; increased lopinavir/ritonavir effects • Phenobarbital and phenytoin—Decreased darunavir/ritonavir effects
Etravirine (ETV)	Rifampicin, St John's Wort, Artemether/Lumefantrine	• Unboosted protease inhibitors ATV/r, FPV/r, or TPV/r, or other NNRTIs • Atazanavir—Possibly increased etravirine effects; decreased atazanavir effects • Clarithromycin—Increased etravirine effects; decreased clarithromycin effects • Clopidogrel—Possibly decreased clopidogrel effects • Dolutegravir—Potentially reduced dolutegravir effectiveness. • Efavirenz—Decreased etravirine and efavirenz effects
Raltegravir (RAL)	Antacids, Carbamazepine, H2 Antagonists, Hydroxyurea, Phenobarbital, Phenytoin, Proton-pump inhibitors, Rifampicin	• Fosamprenavir (fAVP) • Rifapentine—Potential for increased raltegravir adverse effects if given with rifapentine once weekly; potential for decreased raltegravir effectiveness if rifapentine co-administered daily
Dolutegravir (DTG)	Carbamazepine, Phenobarbital, Phenytoin Rifampicin - double dose of DTG	• Use alternative anticonvulsant agent

9.5 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 anticonvulsant as an adjuvant analgesic
Efavirenz (EFV)	Phenytoin and carbamazepine	May decrease serum levels of EFV and anticonvulsants	Delayed	Moderate	Consider alternative anticonvulsant as an adjuvant analgesic
Indinavir (IDV)	Phenytoin and carbamazepine	May decrease serum levels of IDV; IDV may increase serum levels of anticonvulsants	Delayed	Moderate	Consider alternative anticonvulsant as an adjuvant analgesic
Saquinavir (SQV)	Dexamethasone	May decrease serum levels of SQV	Delayed	Moderate	Clinical significance unknown
	Phenytoin and carbamazepine	May decrease serum levels of SQV	Delayed	Moderate	Consider alternative anticonvulsant as an adjuvant analgesic
	Amitriptyline	May increase serum levels of tricyclics	Immediate	Minor	Monitor closely and adjust medication as needed
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 anticonvulsant as an adjuvant analgesic
	Antidepressants	Increased serum levels of antidepressants	Immediate	Major	Monitor closely and adjust dose or change medication as needed

9.5 Possible Interactions between ARVs and Pain Management Medicines (continued from previous page)

ARV	Analgesic	Effect	Time Course	Severity	Comments
Nelfinavir (NFV)	Benzodiazepine	Prolonged sedation due to accumulation of benzodiazepines	Delayed	Major	Monitor closely and adjust medication as needed
	Phenytoin and carbamazepine	May decrease serum levels of NFV; NFV may increase serum levels of anticonvulsants	Delayed	Moderate	Consider alternative anticonvulsant as an adjuvant analgesic
Amprenavir (APV)	Midazolam	Prolonged sedation	Immediate	Major	Monitor closely and adjust medication as needed
	Dexamethasone	May decrease APV	Delayed	Moderate	Use with caution
	Amitriptyline	May increase serum levels of tricyclics	Immediate	Moderate	Monitor closely and adjust medication as needed
	Phenytoin and carbamazepine	May decrease serum levels of APV	May decrease serum levels of APV	Delayed	Consider alternative anticonvulsant as an adjuvant analgesic
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 antidepressants	Immediate	Moderate	May increase toxicities
	Phenytoin (also carbamazepine)	May significantly decrease serum levels of LPV/r	Delayed	Major	Consider alternative anticonvulsant 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 anticonvulsant as an adjuvant analgesic

9.6 ARV Interactions with Contraceptives

Family Planning Options		Antiretroviral Therapy					Rifampicin	HIV Stage III/IV (Severe/ advanced clinical disease, CD4<200)		Untreated STI (Gonorrhea and/or Chlamydia)	
		NNRTI		NRTIs (AZT, d4T, 3TC, ABC, TDF)	PIs (ATV/r, LPV/r, DRV/r)	Integrase Inhibitors (RAL, DTG)					
		NVP	EFV								
Male/Female Condoms											
Oral Contraceptive Pills (COCs/ POP)											
Impants (Jadelle or Implanon)*											
IUD (copper or hormonal IUD)								Initiation	Continuation	Initiation	Continuation
Progestin-only Injectables	Depo										
	NST										
Emergency Contraception (ECP)											
Tubal Ligation/ Vasectomy								Case by Case basis		Delay	

Key	
	No Restrictions for 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

9.7 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; Midazolame; Pimozide; Triazolam
Darunavir/cobicistat (DRV/c) or DRV/r	Rifampin Rifapentine	DRV/c only: Carbamazepine Phenobarbital; Phenytoin	Lurasidone; Midazolame; Pimozide; Triazolam
FPV +/– RTV	Rifampin Rifapentine	None	Lurasidone; Midazolame; Pimozide; Triazolam
LPV/r	Rifampin Rifapentine	None	Lurasidone; Midazolame; Pimozide; Triazolam
SQV/r	Clarithromycin; Dapsone Erythromycin; Pentamidine (parenteral);Rifampin; Rifapentine; Quinine	None	Clozapine; Haloperidol; Lurasidone;Midazolame; Phenothiazines; Pimozide; Trazodone; Triazolam; Ziprasidone
TPV/r	Rifampin Rifapentine	None	Lurasidone; Midazolame; Pimozide; Triazolam
EFV	None	None	None
ETV	Rifampin Rifapentine	Carbamazepine; Phenobarbital; Phenytoin	None
NVP	Rifapentine	None	None
RPV	Rifampin Rifapentine	Carbamazepine; Oxcarbazepine; Phenobarbital; Phenytoin	None
MVC	Rifapentine	None	None
DTG	Rifapentine	Carbamazepine; Phenobarbital; Phenytoin	None

9.8 Most Common Adverse Drug Reactions to ARV Drugs

Adverse drug reaction (ADR) is defined by World Health Organization as "a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function"

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 clearly 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 discoloration	Medium	Black lines perpendicular to nail growth line (fingers, toes)	None	None
	Bone marrow* suppression	Medium	Anaemia, bicytopoenia or pancytopoenia	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
	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

9.8 Most Common Adverse Drug Reactions to ARV Drugs (continued from previous page)

Generic Name	Adverse Reactions	Frequency	Signs and Symptoms	Management	Prevention
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
	Paresthesia/ 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 symptoms	None
	Minor symptoms	Medium	Loss of appetite, headache, malaise, nausea, vomiting, diarrhea	Continue medication, symptoms improve within a few weeks of starting ART	None
Didanosine (ddI)	Lactic acidosis	Medium	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	Avoid alcohol
	Pancreatitis	Low	Nausea, vomiting, abdominal pain	Stop all ART, treat symptoms	None
	Peripheral neuropathy	Medium	Pain, tingling, numbness, burning sensation in hands and or feet	Stop ddI and substitute with another NRTI that does not cause neuropathy, e.g. AZT	None
	Minor symptoms	High	Nausea, headache, dry mouth, CNS symptoms (anxiety, insomnia, irritability, restlessness)	Continue treatment, symptoms subside within weeks of starting ART	None
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

9.8 Most Common Adverse Drug Reactions to ARV Drugs (continued from previous page)

Generic Name	Adverse Reactions	Frequency	Signs and Symptoms	Management	Prevention
Stavudine (d4T)	Peripheral neuropathy	High	Numbness, pins and needles, burning sensation of the limbs	Pyridoxine, amitriptyline. If high grade, switch regimen to one without D4T or DDI	Avoid alcohol and other neurotoxic drugs
	Lipodystrophy	High	Shrinking of lower limbs and buttocks, accumulation of fat around the abdomen, gynaecomastia, buffalo hump	If clearly marked, switch to TDF	Regular exercise
	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
	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
	Liver failure*	Low	Jaundice, fatigue, pruritus, drowsiness, restlessness, confusion, coma.	Emergency hospitalisation	Avoid alcohol and other hepatotoxic drugs
Tenofovir (TDF)	Reduction in bone mineral density				Avoid concomitant corticosteroids
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.	
	Gynacomystia		Enlargement of breast	Substitute with NVP or another therapeutic class (integrase inhibitors or boosted PIs).	
Nevirapine (NVP)	Rash	Females have greater risk than males		If rash occurs in the first 14 days do not increase dose until it resolves (up to 28 days). If rash persists after 28 days choose alternate ARV. Stop treatment if rash is severe or Stevens-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.

9.8 Most Common Adverse Drug Reactions to ARV Drugs (continued from previous page)

Generic Name	Adverse Reactions	Frequency	Signs and Symptoms	Management
Lopinavir (LPV/r)	Rash, diarrhoea			
Atazanavir (ATV/r)	Unconjugated Hyperbilirubinaemia		Jaundice - yellowing of the eyes and skin	
	Cholelithiasis		Abdominal pain. History of kidney stones increases risk and clients may present with cholelithiasis and Kiidney stones concurrently	Substitute with LPV/r or DRV/r. If boosted PIs are contrain-dicated 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, Head-ache, Transaminase elevation, Fat maldistribution, Hyperglycaemia	
Ritonavir*	GI intolerance, Paraesthesia, Hyperlipi-daemia, Hepatitis		Nausea, vomiting, diarrhoea, Fat maldistribution, Taste perversion, Hyperglycaemia	
Raltegra-vir (RAL)	Pyrexia, CPK elevation, muscle weak-ness, and rhabdomyolysis		Headache, Rash, diarrhoea and nausea	
Etravirine (ETV)	Hypersensitivity reactions have been reported , characterized by rash, constitutional findings , and sometimes organ dysfunction, including hepatic failure	Rash: 2% discon-tinuation because of rash during clinical trials	Rash, Nausea	
Dolutegra-vir (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)

9.9 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 inability to perform usual social and functional acticities; requires medical care and possible hospitalization	Symptoms causing 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 acticities, learning tasks). [c] Activities appropriate for age and culture (e.g., feeding self with cultually 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 - 0.749 x 10^9/L	250-500/mm^3 0.25 x 109-0.5 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	100,000 - < 125,000/mm^3 100 x 109 - 125 x 10^9/L	50,000- < 100,000/mm^3 50 x 109 - < 100 x 10^9/L	25,000 - < 50,000/ mm^3 25 x 109 - <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
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

9.9 Grading of Severity of ARV Toxicities (continued from previous page)

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Severe and potentially life-threatening (Grade 4)
Lipase	1.1 - 1.5 x ULN	1.6 - 3.0 x ULN	3.1 - 5.0 x ULN	> 5.0 x ULN
Pancreatic amylase	1.1 - 1.5 x ULN	1.6 - 2.0 x ULN	2.1 - 5.0 x ULN	> 5.0 x ULN
Clinical				
Diarrhea > 1 year of age	Transient or intermittent episodes of unformed stools OR incrase of < 3 stools over baseline per day	Persistent episodes of unformed to watery stools OR increase of 4-6 stools over baseline per day	Grossly bloody diarrhea OR increase of > 7 stools per day OR intravenous fluid replacement indicated.	Life-threatening consequences (e.g. hypotensive shock) < 1 year of age
Diarrhea < 1 year of age	Liquid stools (more unformed than usual) but usual number of stools	Liquid stools with increased number of stools OR mild dehydration	Liquid stools with moderate dehydration	Liquid stools resulting in severe dehydration with aggressive rehydration indicated OR hypotensive shock
Nausea	Not applicable	Symptomatic AND hospitalization not indicated (other than emergency treatment)	Symptomatic AND hospitalization not indicated (other than emergency treatment)	Life-threatening consequences (i.e. circulatory failure, haemorrhage, sepsis).
Vomitting	Transient or intermittent vomitting with no or minimal interference with oral intake	Frequant episodes of vomitting with no or mild dehydration	Persistent vomitting	Life-threatening consequences (e.g. hypotensive shock)
Allergic / Dermatological				
Acute systemic allergic reaction	Localized urticaria (weals) lasting a few hours	Localized urticaria with medical intervention indicated OR mild angioedema	Generalized urticaria OR angioedema with medical intervention indicated OR symptomatic mild brochospasm	Acute anaphylaxis OR life-threatening brochospasm or laryngeal oedema
Cutaneous reaction-rash	Localized macular rash	Diffuse macular, maculopapular or morbiliform rash, OR target lesions	Diffuse macular maculopapular or morbiliform rash with vesicles or limited number of bullae OR supervicial ulcerations of mucous membrance 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).

9.9 Grading of Severity of ARV Toxicities (continued from previous page)

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Severe and potentially life-threatening (Grade 4)
Neurological				
Alteration in personality behavior 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 inability to perform usual social and functional activities [b] AND intervetnion indicated	Behavioral potential harmful to self or others OR life - threatening consequences
Altered mental status	Changes cuasing 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]	Onset of confusion, memory impairment lethary or somnolence causing inability to perform usual social and functional activities [b]	Onset of delirium obtundation or coma
Neuromuscular weakness (including myopathy and neuropathy)	Asymptomatic with decreased strengthen 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 paraestesia causing greater than minimal interference with suual social and functional activities	Disabiing muscle weakness causing inabiliyt to perform basic self-care functions OR respiatory muscle weakness impairing ventilation.
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 paraesthesia causing greater than minimal interference with usual social and functional acticities	Sensory alteration or paraesthesia causing inability to performan usual social and functional acticvities	Disabling sensory alteration or paraesthesia causing inabilty to perform basic self-care functions [c]
[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

9.9 Grading of Severity of ARV Toxicities (continued from previous page)

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Severe and potentially life-threatening (Grade 4)
Other Laboratory Functions - continued				
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 condition 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

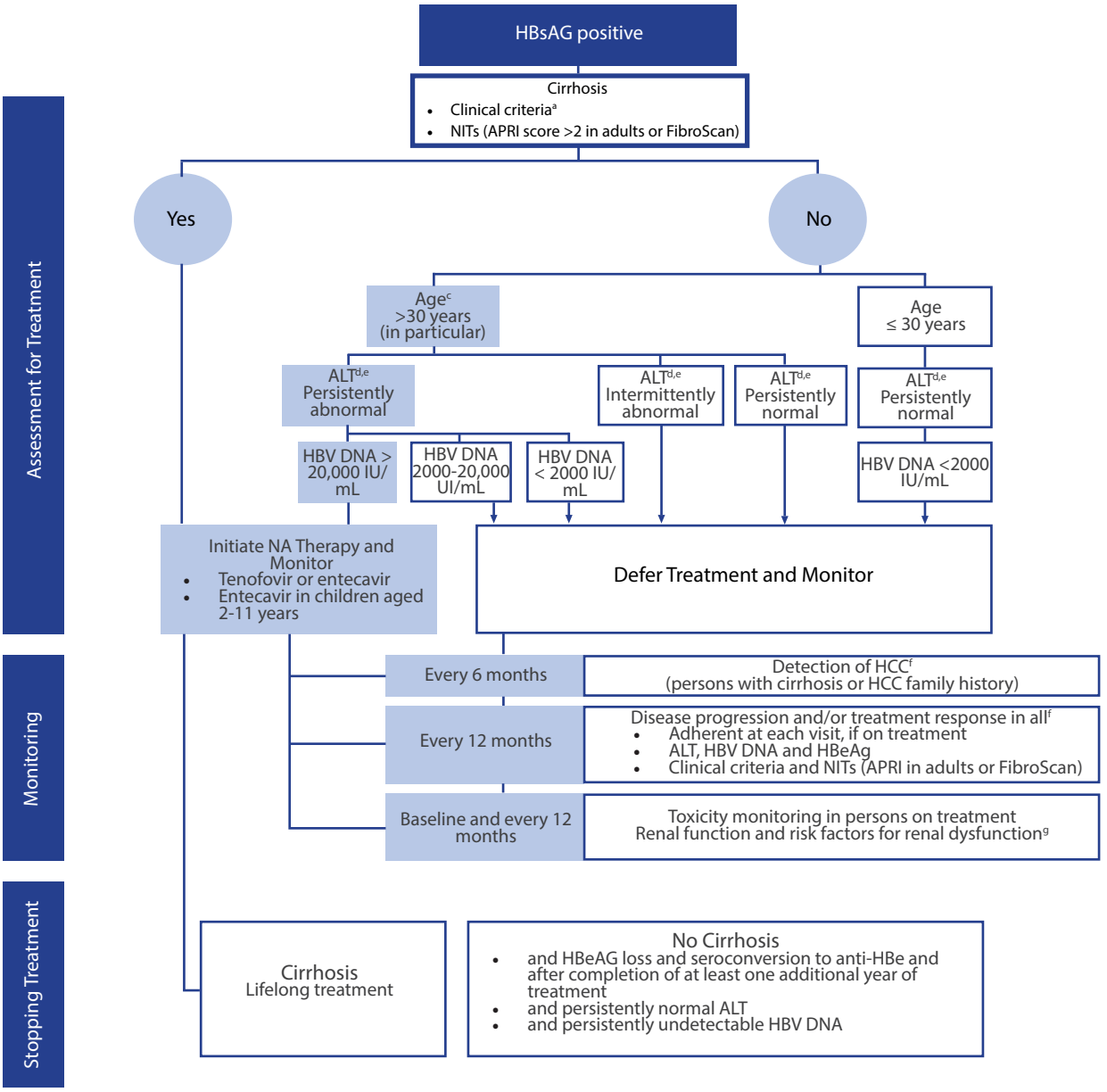
9.10 Supplementary Information on Dolutegravir

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.

Additional information regarding DTG:

- DTG may be taken without food.
- The most commonly reported adverse drug reactions include insomnia (3%), fatigue (2%) and headache (2%).
- 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 previous history of hypersensitivity. Discontinue DTG immediately if signs of hypersensitivity develop.
- DTG inhibits OCT2 and MATE1, which are responsible for tubular secretion of creatinine resulting in mild increase in creatinine after initiation, which remains stable. No DTG dose adjustment is necessary in 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 prior to any adjustments.
- Clients with underlying hepatitis B or hepatitis C may be at increased risk for worsening or development of transaminase elevations with use of DTG. Appropriate laboratory testing prior to initiating therapy, and monitoring for hepatotoxicity during therapy with DTG, is recommended in clients with underlying hepatic disease 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 fetus observed. Studies in animals have also not shown evidence of an increased occurrence of fetal damage.

9.11 Hepatitis B Virus Treatment Algorithm[a]



9.11 Hepatitis B Virus Treatment Algorithm[a] (continued from previous page)

NITs non-invasive tests, ALT alanine aminotransferase, APRI aspartase 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 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 6–12–month period or predefined intervals during 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 maybe 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, 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/m^2 (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.

9.12 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 rapid development of HBV resistance
• Provide pretreatment counselling about indications for treatment, likely benefits and side-effects, need for follow-up both on and off therapy, and 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 risk of reactivation
• Relapse may occur after discontinuation, and re-treatment is recommended</td></tr>
</table>

9.13 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 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 with caution.
- Monitor closely for occurrence of Ischemic heart disease.

9.14 Baylor HIV/TB Hotline and Email Information

Paediatric HIV and TB hotlines available to clinicians (nurses and doctors)

Baylor HIV/TB Hotline: 7848-5571

- Toll-free number, 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

TB/HIV email: swazihivtb@gmail.com. To address clinical questions to Baylor physicians

9.15 Initiation of Infants Less Than 4 Weeks 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

9.16 Alternative ART for Paediatric 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 completion of TB treatment.
		Alternative 1: ABC(AZT)+3TC+LPV/r Super boosting with 1:1 ritonavir for duration of TB treatment	Check VL at the end of ATT. Change back to LPV/r standard dosing at completion of 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 at completion of TB treatment.
		Alternative 1: Continue ABC (AZT)+3TC+LPV/r. Superboosting with 1:1 ritonavir for 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 efficacy of 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

9.16 Alternative ART for Paediatric Clients on TB Treatment (continued from previous page)

Alternative ART for Paediatric Clients on TB Treatment			
Consideration		Regimen	Comments
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	TDF+3TC+EFV	Check VL at the end of TB treatment. If VL is undetectable, substitute EFV to DTG
		Alternative ABC+3TC+AZT while on ATT	Check VL at the end of ATT. Change back to LPV/r at completion of 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 NNRTI-based regimen if VL 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 superboosting (see below) Check VL at the end of ATT. Change back to LPV/r at completion of TB treatment.
		Alternative 2: Continue ABC(AZT)+3TC+LPV/r Superboosting with 1:1 ritonavir for 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: Cotinue 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 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 NNRTI-based regimen if VL is undetectable.

9.16 Alternative ART for Paediatric Clients on TB Treatment (continued from previous page)

Alternative ART for Paediatric Clients on TB Treatment			
Consideration		Regimen	Comments
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 Superboosting with 1:1 ritonavir for 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 • Consult doctor and Baylor HIV/TB Hotline for 3rd line evaluation (see Annex 9.14)
		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 duration of ATTs	Change back to ATV/r at completion of 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 (see Annex 9.14)

9.17 Paediatric ARV Dosing Card

ART Regimen	3-5.9 kg	6-9.9 kg	10-13.9 kg	14-19.9 kg	20-24.9 kg	25-39.9 kg	30-39 kg	≥ 40 kg
AZT/3TC/NVP 60/30/50 mg	1 BD	1.5 BD	2 BD	2.5 BD	3 BD	Adult BD 300/150/200 mg	Adult BD 300/150/200 mg	Adult BD 300/150/200 mg
AZT/3TC 60/30 mg	1 BD	1.5 BD	2 BD	2.5 BD	3 BD	Adult BD 300/150 mg	Adult BD 300/150 mg	Adult BD 300/150 mg
ABC/3TC 120/60 mg	0.5 BD	0.5 AM 1 PM	1 BD	1 AM 1.5 PM	1.5 BD	Adult OD 600/300 mg	Adult OD 600/300 mg	Adult OD 600/300 mg
ABC/3TC 60/30 mg	1 BD	1.5 BD	2 BD	2.5 BD	3 BD	Adult OD 600/300 mg	Adult OD 600/300 mg	Adult OD 600/300 mg
RAL 25 mg	Not recommended		3BD	4 BD	6 BD	Adult BD 400 mg	Adult BD 400 mg	Adult BD 400 mg
RAL 100 mg	Not recommended			1.5 BD	1.5 BD	Adult BD 400 mg	Adult BD 400 mg	Adult BD 400 mg
LPV/r 200/50 mg	Not recommended			1 BD	1 BD	2 AM 1 PM	Adult BD 400/100 mg	Adult BD 400/100 mg
LPV/r 40/10 mg (pellets)	2 BD	3 BD	4BD	5 BD	6BD	2AM/1PM 200/50mg	Adult BD 400/100 mg	Adult BD 400/100 mg
LPV/r 80/20 mg/mL	1 BD	1.5 BD	2 BD	2.5 BD	3 BD	Not recommended		
NVP 50mg	1 BD	1.5 BD	2 BD	2.5 BD	3 BD	Adult 200mg BD	Adult 200mg BD	Adult 200mg BD
EFV 200 mg	Not recommended		1 OD	1.5 OD	1.5 OD	2 OD	Adult 600 mg	Adult 600 mg
ABC 60 mg	1 BD	1.5 BD	2 BD	2.5 BD	3 BD	Adult BD 300mg	Adult BD 300mg	Adult BD 300mg
AZT 60 mg	1 BD	1.5 BD	2 BD	2.5 BD	3 BD	Adult BD 300mg	Adult BD 300mg	Adult BD 300mg
TDF/3TC/DTG 300/300/50 mg	Not recommended							Adult FDC OD

9.18 HIV Testing Screening Tool

HIV Testing Screening Tool for Adults and Adolescents
Have you ever tested for HIV?

Yes	No
Record date of last HIV test and status in HTS client record and continue with HIV testing screening tool to identify the need for re-testing	Offer routine HIV testing

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.		

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?	[___] Yes	[___] No
2. Has the child been admitted to the hospital before?	[___] Yes	[___] No
3. Does the child have reocurring skill problems?	[___] Yes	[___] No
4. Has the child had poor health in the last 3 months?	[___] Yes	[___] No

9.19 ART Readiness and Psychosocial Assessment Form

The ART readiness and psychosocial assessment can be used in screening ART clients who may be at risk of disengaging from care or defaulting on ART.

Categories	Key Variables Identified	Questions
ART readiness/ overview of psychosocial wellbeing	Basic HIV and ART knowledge	What do you know about ARVs?
		What are opportunistic infections?
		Can you tell me the names of the ARVs you will be taking and what time you will take each?
		Can you tell me some of the side effects of your medicines and what you will do if you have side effects?
		Do you know what can happen if you do not take all of your ARVs every day, at the same time for life?
		How and where will you store your medication?
		Do you feel confident that you can take ARVs every day at the same time for the rest of your life? **(Yes/No)**
		What is the goal of viral load monitoring? (Viral load tests should be conducted at 6, 12, 24 and 36 months)
	Motivation	Can you explain why you think you need to take ARVs?
		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 every day at the same time for the rest of your life? **(Yes/No)**
		Do you forsee / are there any potential barriers with taking treatment? **(Yes/No)** *If yes how can these be addressed?*
Assessment of Potential adherence Barriers	**Theme**	**Specific Questions**
Individual	Alcohol/ Substance Use	Do you sometimes forget to take your medicines/ARVs because you used alcohol or other drugs? **(Yes/No)**
	Side Effects of Treatment	Do you sometimes experience side effects from your medication/ARVs that make you want to stop treatment? **(Yes/No)**
	Pill Burden	Do you sometimes feel that taking your medication is tiresome because you have to take them every day at the same time for the rest of your life? **(Yes/No)**
	Missed Clinic Appointment in Past 6 Months	Have you missed your HIV clinic appointment(s) by more than 1 week since you started taking your HIV medications? **(Yes/No)**

9.19 ART Readiness and Psychosocial Assessment Form

Assessment of Potential adherence Barriers	Theme	Specific Questions
Economic	Poverty/Economic Struggles	Is it sometimes difficult for you to keep your HIV clinic appointments because you do not have money for transport? **(Yes/No)**
	Food Insecurity	Do you sometimes forget, skip or are unable to take your HIV medications because you are hungry/lack food? **(Yes/No)**
Psycho-Social	HIV Disclosure	Have you told your partner or family members about your HIV status? **(Yes/No)**
	Experienced Violence at Home	In the past 24 months, have you experiences emotional, physical or sexual violence from a sexual partner that prevented you taking your HIV medications or coming to the HIV clinic for follow-up? **(Yes/No)**
	Family/Partner Relationship/ Inadequate Psychosocial Support	Do you have someone at home who can remind you about or make sure you are taking your HIV medications? **(Yes/No)** Has this person been trained on HIV treatment and care? **(Yes/No)**
	Stigma and Discrimination	Do you feel stigmatized because of your HIV positive status? **(Yes/No)**
	Emotional Issues/ Depression/Mental Health	Over the last two week, how much have you been bothered by: 1. Feeling sad, down, or uninterested in life? 2. Feeling anxious or nervous? 3. Feeling stressed? 4. Feeling angry? 5. Not having the social support you feel you need? Scale: 0 to 9, with 0 = not at all, 3 = a little, 6 = moderately, 9 = severely
Structural	Distance from the Health Facility	Do you find it difficult to get to the clinic because of the distance from home or availability of transport? **(Yes/No)**
Disease/ Treatment Consequences	Co-Morbid Health Conditions	Do you have any other chronic conditions (hypertension, diabetes) that require you to come to the clinic frequently? **(Yes/No)**
	Poor Functional Status	Do you have energy to carry out your usual day-to-day activities? **(Yes/No)**
	Low Self-Efficacy regarding treatment	How sure are you that you can take your HIV medications as recommended by your health care provider? **(Yes/No)**

9.20 Depression Assessment (Siswati)

Sebentisa nalu luphawu √ kuphendvula				
	Akukake kwenteka	Emalanga lambalwa	Lokungetulu kweliviki (7 days)	Cishe onkhe emalanga
1. Kuncishelwa ngumdlandla/inshisekelo ekwenteni tintfo letikuchazako/letikujabulisako	0	1	2	3
2. Kutiva uphansi emoyeni, ukhatsatekile noma ute litsemba	0	1	2	3
3. Bulukhuni bekwehlelwa butfongo noma kuphelelwa butfongo noma kuba nebutfongo lobuningi	0	1	2	3
4. Kutiva udziniwe noma uphelelwa ngemandla	0	1	2	3
5. Kungakhanuki kudla (inhlitiyo imnyama) noma kudla kakhulu	0	1	2	3
6. Kuva utisola/utenyanya noma usehluleki noma utentele phansi noma wentele phansi umndeni wakho	0	1	2	3
7. Kuba nebulukhuni kubeka umcondvo/kulandzelela etintfweni lotentako, letinjengekufundza liphephandzaba noma kubukela mabonakudze (TV)	0	1	2	3
8. Kuhamba kancane noma kunamula lokunakekako kulabanye bantfu. Noma kungahlaliseki kangangekutsi uhlala uphitsitela lokungetulu kwalokutayelekile	0	1	2	3
9. 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 nebantfu

Akukabi nebulukhuni
Kube lukhunyana
Kube lukhuni kakhulu
Kube lukhuni ngalokwecile

9.20 Depression Assessment (English) (continued from previous page)

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 of 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 . . .
Somewhat difficult . . .
Very 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.

9.21 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

9.22 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 oonducted	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

9.23 Adverse Drug Reaction Report Form

Report can be returned to Central Medical Stores by:
Fax: 2518 6279
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 terapies/ vaccines prior to ADR (please use trade names and circle the suspected drug)	Batch number	Daily Dosage	Route	Date Be-gun	Date Stopped	Indication for Use

Allergies or other relevant history (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 _____

9.23 Adverse Drug Reaction Report Form (continued from previous page)

Section D: Treatment and Outcomes

Treatment of ADR: ____ No ____ Yes
Details (including dosage, frequency, route, duration): _____
_____

Outcome:
___ Recovered on (dd/mm/yyyy) / /
___ Not yet recovered
___ Unknown
___ Died on (dd/mm/yyyy) / /
___ Persistent disability
___ Birth defect
___ Medically significatn events
Details: _____
_____

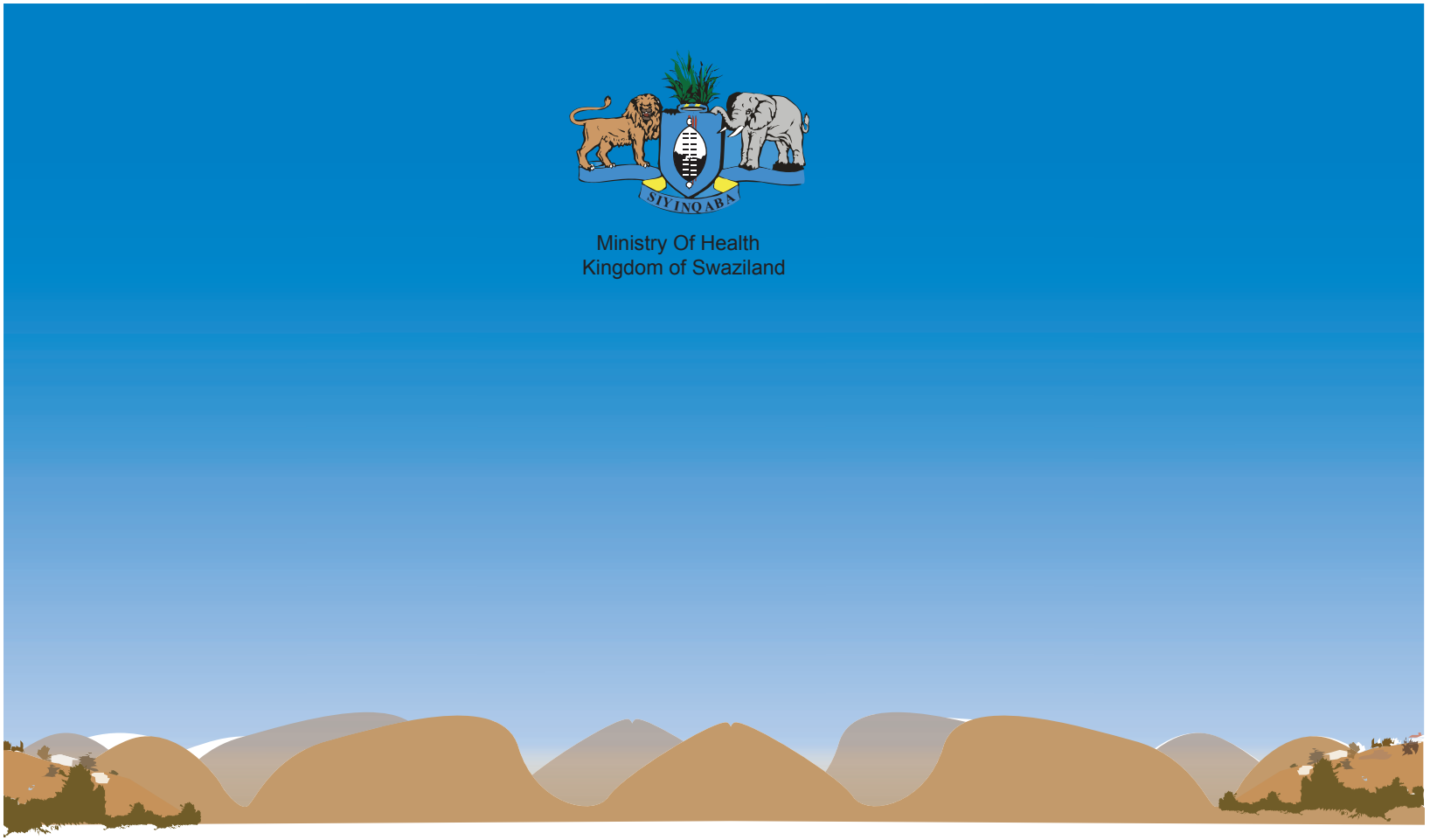
Section E: Reporter Details

Name: _____ Dector of 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



Ministry Of Health
Kingdom of Swaziland

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HIV /AIDS
SNAP
SWAZILAND NATIONAL AIDS PROGRAM

CDC
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