Republic of Zambia
Ministry of Health

Zambia Consolidated Guidelines

for Treatment & Prevention of HIV Infection

Directorate of Clinical Care and Diagnostic Services
2016

Zambia Consolidated Guidelines

for Treatment and Prevention of HIV Infection

Contents

Acronyms

3TC	lamivudine
ABC	abacavir
AIDS	acquired immunodeficiency syndrome
ALT	alanine aminotransferase
ANC	antenatal care
ART	antiretroviral therapy
ARV	antiretroviral
AST	aspartate aminotransferase
ATC	advanced treatment centre
ATT	anti-tuberculosis treatment
ATV	atazanavir
AZT	azidothymidine (also known as zidovudine, or ZDV)
BID	twice daily
BMI	body mass index
cART	combination antiretroviral therapy
CD4	T-lymphocyte bearing CD4 receptor
CD4 %	CD4 percentage
CDC	Centers for Disease Control and Prevention
CNS	central nervous system
CPT	co-trimoxazole preventive therapy
CrCl	creatinine clearance
CTX	co-trimoxazole
d4T	stavudine
DBS	dried blood spot
ddI	didanosine
DMPA	depot medroxyprogesterone acetate
DNA	deoxyribonucleic acid
DOTS	directly observed therapy, short course
EFV	efavirenz
EMTCT	elimination of mother-to-child transmission (of HIV)
EPI	expanded program for immunisation
FANC	focused antenatal care
FBC	full blood count
FDC	fixed-dose combination
FP	family planning
FTC	emtricitabine
GRZ	Government of Republic of Zambia
Hb	haemoglobin
HBeAg	hepatitis B e-antigen
HBsAg	hepatitis B virus surface antigen
HBV	hepatitis B virus
HCW	health care worker
HEI	HIV-exposed infant
HIV	human immunodeficiency virus
HPV	human papilloma virus
HTS	HIV testing services
INH	isoniazid
INSTIs	Integrase strand transfer inhibitors
IPT	isoniazid preventive therapy
IRIS	immune reconstitution inflammatory syndrome
L&D	labour and delivery
LPV	lopinavir
MNCH	maternal, newborn, and child health
MOH	Ministry of Health
MCDMCH	Ministry of Community Development, Mother and Child Health
MTCT	mother-to-child transmission (of HIV)
NAT	Nucleic Acid Test
NNRTI	non-nucleoside reverse transcriptase Inhibitor
NRTI	nucleoside reverse transcriptase inhibitor
NUPN	national unique patient number
NVP	nevirapine
OD	once daily
OI	opportunistic infection
PCP	pneumocystis pneumonia
PCR	polymerase chain reaction
PEP	Post-exposure prophylaxis
PHDP	positive health dignity and prevention
PI	protease inhibitor
PMTCT	prevention of mother-to-child transmission (of HIV)
PNC	postnatal care
PO	per os (orally)
PrEP	Pre-exposure prophylaxis
RAL	raltegravir
-r	ritonavir (low-dose)
RNA	ribonucleic acid
sd-NVP	single-dose nevirapine
TasP	treatment as prevention
TB	tuberculosis
TDF	tenofovir disoproxil fumarate
UNAIDS	Joint United Nations Programme on HIV/ AIDS
UNICEF	United Nations Children's Fund
VIA	visual inspection with acetic acid
WHO	World Health Organization
XTC	3TC or FTC

Foreword

Zambia continues to face the HIV epidemic with the latest HIV prevalence estimated at 13.3% among adults. The government of Zambia has responded positively to this challenge by using the “prevention-to-care continuum” in the fight against HIV. The government recognizes that HIV prevention efforts must be complemented by care and support initiatives and thus has taken steps to provide antiretroviral therapy to all people living with HIV in Zambia. This is in line with the UNAIDS targets of “90-90-90,” which are expected to bring the country closer to achieving universal access to HIV treatment and care and ending AIDS as a public threat. These new guidelines will be used to prepare health care providers and support staff to diagnose and treat all people living with HIV/AIDS in Zambia. The 2016 World Health Organization consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection have been used to update the content of the new guidelines. These new guidelines reflect the latest evidence supporting the “Test and Start” approach, incorporating findings from studies such as the Strategic Timing of Antiretroviral Therapy (START) study and TEMPRANO trials. This approach also requires use of viral load for monitoring treatment to ensure viral suppression among patients on treatment.

The Zambian government expects these guidelines to improve the quality of HIV treatment and care and bring the nation closer to universal health coverage. Integrated services, community-centered, and community-led health care approaches will be used to help achieve this goal and allow people living with HIV to live healthy and productive lives.

Finally, I wish to thank all partners for their contributions in developing these guidelines. I therefore wish to encourage all health care workers to take advantage of these new guidelines to scale up HIV treatment and care services to all people living with HIV.

Dr. Peter Mwaba
Permanent Secretary
Ministry of Health (MOH)

Acknowledgements

The Government of Zambia would like to extend their appreciation and thanks in particular to the following organization and individuals:

Ministry of Health
University Teaching Hospital
University of Zambia School of Medicine
Centers for Disease Control and Prevention
Centre for Infectious Diseases Research in Zambia
University of Maryland
Clinton Health Access Initiative
Churches Association of Zambia
Elizabeth Glaser Paediatric AIDS Foundation
EQUIP Zambia
Konkola Copper Mines Medical Services
Family Health International 360
AIDS Relief-Transition
Procurement & Supply Management (USAID | GHSC)
Treatment Advocacy & Literacy Campaign
United Nations Children's Fund
World Health Organization
Zambia Centre for Applied Health Research and Development IIB
Jhpiego
USAID Systems for Better Health

Special Thanks to the Editorial Committee:

Ministry of Health
Dr. Gloria Munthali
Dr. Crispin Moyo
Dr. Kebby Musokotwane
Dr. Wezi Kaonga

University Teaching Hospital/University of Zambia, School of Medicine
Dr. Lloyd Mulenga
Dr. Aggrey Mweemba
Dr. Mwiya Mwiya
Dr. Chipepo Kankasa
Dr. Paul M. Zulu
Dr. Rachael Thomas
Mr. Lameck Chirwa

World Health Organization
Dr. Lastone Chitembo

University of Maryland

Dr. Cassidy Claassen

Centers for Disease Control and Prevention

Dr. Annie Mwila

Dr. Bridget Mugisa

Clinton Health Access Initiative

Nakululombe Kwendeni

Centre for Infectious Diseases Center in Zambia

Dr. Mwangelwa Mubiana

Dr. Izukanji Sikazwe

Jhpiego

Dr. Joseph Nikisi

USAID Systems for Better Health

Dr Kenny Kapembwa

Introduction

In September 2015, the World Health Organization released the guidelines on when to start antiretroviral therapy, including pre-exposure prophylaxis for HIV. This 2016 version of the Zambia Consolidated Guidelines for Treatment and Prevention of HIV Infection provides simplified guidance on a continued approach that positively affects the continuum of HIV care, while adding to innovative methods that will reduce transmission rates and increase life span for those on treatment. This is all to further accelerate efforts to meet the ambitious Fast-Track target for 2020, including achieving major reductions in the number of people dying from HIV-related causes and the 90–90–90 treatment target: ensuring that 90% of the people living with HIV know their HIV status; 90% of the people living with HIV who know their HIV status are accessing treatment; and 90% of people living with HIV who are receiving treatment have suppressed viral load.

These guidelines present several new recommendations, including the recommendation to provide lifelong ART to all children, adolescents, and adults, including all pregnant and breastfeeding women living with HIV, regardless of CD4 cell count. The aim is to place more children on treatment by expanding eligibility criteria: all HIV-infected individuals regardless of WHO clinical stage and CD4 count should be started on cART. By doing so, we promote early treatment of HIV-infected children and reduce missed opportunities to prevent severe morbidity and mortality. In addition, a family-based approach to HIV testing services (HTS) encourages testing of all children and adolescents of unknown HIV status in the community and at the health facility irrespective of individual risk factors. Finally, these guidelines emphasize the vulnerable transition of adolescence from childhood to adulthood.

Our 2016 guidelines have also adopted the recommendations to offer PrEP to selected people at substantial risk of acquiring HIV. Alternative treatment regimens are recommended, including an integrase inhibitor as an option in resource-limited settings and reduced dosage of a key recommended first-line drug. Importantly, there has been introduction of raltegravir, an integrase inhibitor, as a part of the second-line regimen for children failing lopinavir/ritonavir-based first-line therapy. These guidelines also highlight the management of patients failing second-line ART with third-line ART, who should be managed at higher-level health facilities called Advanced Treatment Centres (ATCs). All of the recommendations have been adopted because of their anticipated public health effect.

Several significant recommendations from the previous guidelines remain a priority, namely providing lifelong ART regardless of CD4 cell count to all pregnant and breastfeeding women and moving toward viral load testing as the preferred means of monitoring people on ART. Newer developments aim to complement and improve the service delivery of HIV services to our population. Importantly, in this guidance WHO emphasizes the need for differentiated approaches to care for people who are stable on ART, such as reducing the frequency of clinic visits and community ART distribution. Such efficiencies are essential if countries with a high burden of HIV infection are to manage their growing numbers of people receiving ART and reduce the burden on people receiving treatment and on health facilities.

There will be continued concerted efforts required toward implementing these guidelines at district and health facility levels; the 2016 Consolidated Guidelines represent an important step toward achieving the goal of universal access to ARV drugs, treating and preventing HIV, and ultimately ending the HIV epidemic by 2030.

HIV Testing Services (HTS)

2016 Recommendations

- Introduction of HTS to emphasize testing and linking to services
- Addition of Nucleic Acid Testing (NAT) at birth
- POC Technologies for early diagnosis of HIV-infected infants and children to complement conventional testing

HIV testing services (HTS) refers to the full range of services that should be provided with HIV testing, including counseling (pre-test information and post-test counseling); linkage to appropriate HIV prevention, treatment, and care, and other clinical services; and coordination with laboratory services to support quality assurance (QA) and the delivery of accurate results.

HIV testing is the gateway to HIV prevention, treatment, care, and other support and clinical services, primarily conducted by health care workers. Lay providers who are trained, certified by MOH, and supervised can independently conduct safe and effective HIV testing using rapid diagnostic tests (RDTs) (strong recommendation, moderate-quality evidence).

The five essential C's of HTS:

1. Individuals must give informed **Consent** for HTS and should be told of their right to decline testing. Mandatory or coerced testing is never appropriate, whether that coercion comes from a health care worker (HCW), partner, or family member.

2. HTS are **Confidential**.

3. HTS includes appropriate, high quality pre-testing formation and post-test **Counseling,** and HTS services should be offered to all without discrimination.

4. HTS includes provision of **Correct** test results.

5. HTS should provide linkages to **Care**, prevention, and treatment services by issuance of a National Unique Patient Number (NUPN), regardless of test result.

HTS should be done at all service delivery points (see Table 1) within the facility, as well as in the community, as an efficient and effective way to identify people with HIV. Community-based testing embraces a family-centred approach based on the index-patient model and leads to early diagnosis of HIV infection and prompt linkage to care and treatment. Every individual in the index-patient's home, regardless of age and risk factors, should be tested with a serologic test, also known as antibody test or rapid test (see Figure 1). All individuals testing negative should re-test after 3 months (to account for the window period).

Provider Initiated Testing and Counseling (PITC)

PITC should be offered to all clients and in all service points [including services for sexually transmitted infections (STI), viral hepatitis, tuberculosis (TB), children under the age of 5 years, immunization, malnutrition, antenatal care, and all services for key populations] as an efficient and effective way to identify people with HIV.

HTS should be offered to all prisoners as per general population guidelines. In addition, there should be HTS at entry to and exit from prisons. All HIV positive prisoners must be enrolled into Care and Treatment programs.

For children <12 months old who are breastfeeding, the mother should be tested first. If she is HIV-positive, perform a nucleic acid testing (NAT) on the HIV-exposed infant (HEI), regardless of age. If NAT cannot be done at a facility closer to the HEI, refer the HEI to the nearest health facility for NAT. The advantage of new NAT technologies is that they are done at the point-of-care and offer same-day results. Infants who have HIV detectable by NAT at birth are likely infected in utero, will progress to disease rapidly, and, in the absence of treatment, will experience high mortality in the first few months of life. Infants infected at or around delivery may not have virus detectable by NAT for several days to weeks. The ability of NAT to detect virus in the blood may be affected by ARV drugs taken by the mother or infant for postnatal prophylaxis, resulting in false-negative results. This includes drugs present in breast milk as a result of maternal ART during breastfeeding.

However, the rationale behind this recommendation is that infants who are first identified as HIV-exposed postpartum have a high cumulative risk of already having acquired HIV by the time prophylaxis is initiated; thus NAT should be performed around the time of initiating prophylaxis, which would be at birth. This will help to minimize the risk of development of resistance because of extended prophylaxis in infected infants and help to promote linkage to timely initiation of ART.

Quality Assurance/Improvement

All testing sites should participate in HIV proficiency testing at least twice per year. If testing is performed in the community by community health workers, every 10th sample (10%) should be retested at the nearest health facility.

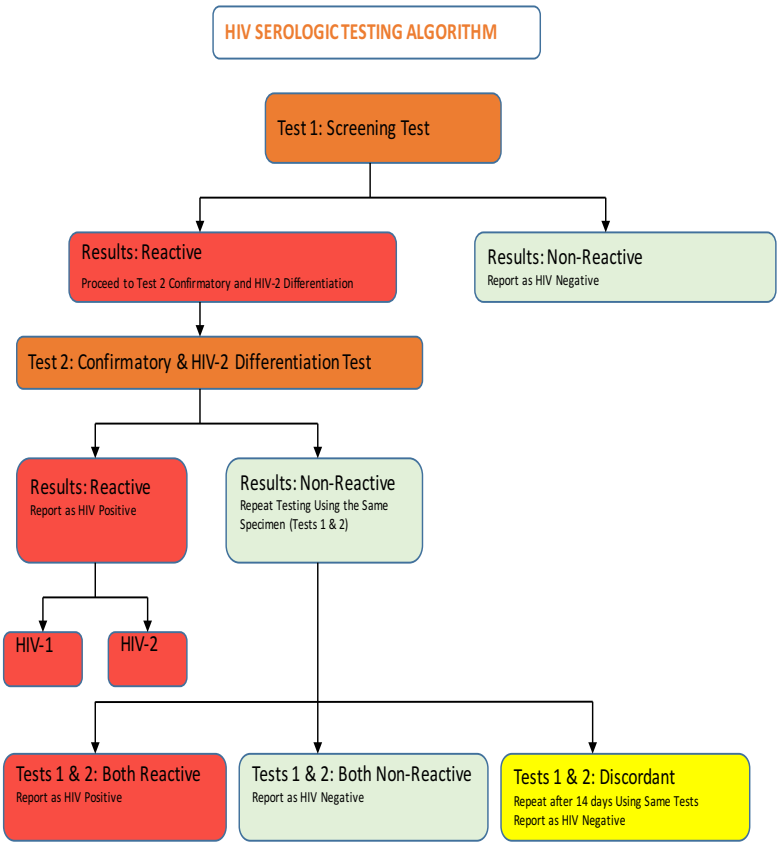
Table 1: Timing of HIV testing services for specific populations

Specific populations	Whom to test	When to test	HIV testing
Pregnant women, breastfeeding women (and their sexual partners)	All	During antenatal care (ANC): at first ANC visit and repeat test every 3 months if negative In labour and delivery (L&D): test if last test >6 weeks ago During postnatal care (PNC): test at first contact if unknown status. Serologic test at 6 weeks if negative. If breastfeeding: repeat test every 3 months if negative until cessation of breastfeeding Partner testing: same time points Partner testing: same time points	Serologic test
(0 to <10 years old)	Well, non-breastfed HIV Exposed Infant (HEI)	At birth or at first contact	
		At birth/first week of life	NAT*
		6 weeks old	
		6 months old	
		9 months old	Serologic test, if positive, follow with NAT. If negative, follow up with serologic test at 18 months
	Well, breastfed HEI	At birth/first week of life	NAT*
		6–8 weeks old	
		6 months old	
		9 months old	Serologic test. If positive, follow with NAT. If negative, follow up with serologic test at 18 months
		18 months old	Serologic test
		24 months old	Serologic test
	Infant or child who has completely stopped breastfeeding	≥6 weeks after breastfeeding cessation	Serologic test; NAT for positive serologic child <18 months old
		≥18 months old	Serologic test
	Asymptomatic infant with unknown HIV exposure	At first contact	Maternal serologic test and/or infant serologic test; follow with NAT for positive serologic child <18 months old
	Infant or child symptomatic for HIV infection	Immediately regardless of age	Serologic test; follow with NAT for positive serologic child <18 months old
	Positive serologic child <18 months old	At first contact	NAT

Specific populations	Whom to test	When to test	HIV testing
	All infants and children with unknown HIV status admitted for inpatient care, attending malnutrition clinic, outpatient care or immunization clinics	Routine HIV testing	Age-appropriate tests
Adolescents (10 – 19 years) and adults	All sexually active persons with their partners and any person of unknown HIV status	At first contact, 3 months if negative and every 6 months	Serologic test

*Where NAT is positive, a repeat test should be done to rule out false-positive results. cART should be initiated without waiting for the receipt of the second test result because of the high risk of mortality with in utero infection; if the second specimen tests negative, a third NAT should be performed before interrupting cART.

Figure1: HIV serologic testing algorithm[1]



Summary/Key Points

[1]HIV testing for those <18 months, NAT is gold standard. Although plasma remains the gold standard sample for NAT, DBS will be the preferred mode of sample transportation for both DNA and RNA testing.

- HIV testing services (HTS) include HIV testing, pre-test information, post-test counseling, linkage to appropriate HIV prevention, treatment, care, other clinical services, and coordination with laboratory services to support quality assurance (QA) and delivery of accurate results.
- The five essential C's of HTS include informed Consent, Confidential, high quality pre-test information and post-test Counseling, provision of Correct test results, and linkage to Care, prevention, and treatment services.
- HTS should be done at all service delivery points within the facility, as well as in the community, as an efficient and effective way to identify people with HIV.
- HIV testing is the gateway to HIV prevention, treatment, care, and other support and clinical services, and Provider Initiated Testing and Counseling (PITC) should be offered to all clients and in all services points.
- HIV testing is primarily conducted by health care workers. Lay providers who are trained, certified by MOH, and supervised can independently conduct safe and effective HIV testing using rapid diagnostic tests (RDTs).
- All mothers of breastfeeding children <12 months old should be tested. If she tests HIV positive, a nucleic acid testing (NAT) is performed on the HIV-exposed infant (HEI), regardless of age.
- Where NAT is positive, a repeat test should be done to rule out false-positive results. cART should be initiated without waiting for the receipt of the second test result because of the high risk of mortality with in utero infection; if the second specimen tests negative, a third NAT should be performed before interrupting cART.
- Community-based testing embraces a family-centered approach based on the index-patient model and leads to early diagnosis of HIV infection and prompt linkage to care and treatment.

Management of HIV-Exposed Infants

2016 Recommendations

Infant ARV prophylaxis in high-risk infants = AZT + NVP for 12 weeks

HIV virologic testing concurrent with Expanded Program for Immunization (EPI visits)

Table 2: HEIs ARV prophylaxis for routine cases

Case scenario	Management of the mother at delivery and in Postnatal Care (PNC)	Infant ARV prophylaxis and Nucleic acid testing (NAT)
High-Risk HIV-Exposed Infants		
1. Born to women with established HIV infection not on ART; or: 2. Born to women with established HIV infection and having received less than 12 weeks of ART at the time of delivery; or: 3. Born to women with established HIV infection with viral load >1000 copies/mL within the four weeks before delivery, if viral load measurement available.*	Start or continue cART immediately	All exposed infants to be put on AZT/NVP for 12 weeks
Known HIV positive woman who refuses ART	Continue counseling for need to start therapy. Suggest to start ART with possibility of stopping after delivery (Option B) while counseling continues toward the mother accepting lifelong cART (Option B+).	Prophylactic ART (AZT/NVP) until confirmed final outcome HIV negative after complete cessation of breastfeeding
Low-Risk HIV-Exposed Infants		
Known HIV-positive women on ART for more than 12 weeks	Continue ART	All exposed infants to be put on (AZT/NVP) for 6 weeks
HIV-negative women with known positive partner	Pre-Exposure Prophylaxis and provide HTS every 3 months	NAT on the mother, and if positive NAT on the baby

- **ALL HIV POSITIVE PREGNANT WOMEN ON cART SHOULD HAVE A VIRAL LOAD DONE 1 TO 4 WEEKS BEFORE DELIVERY**

Table 3: HEI ARV prophylaxis in complicated cases

Case scenario	Management of the mother at delivery and in Postnatal Care (PNC)	Infant ARV prophylaxis and Nucleic acid testing (NAT)
Woman with an HIV positive test in ANC who starts cART in ANC and has been on ART for >12 weeks. She has a home delivery. Infant does not receive AZT/NVP at birth, but presents >72 hours after birth.	Continue cART	Do NAT: If positive, start cART. If negative, start AZT/NVP for 6 weeks and repeat NAT at 6 weeks of age. *If NAT results are delayed, start AZT/NVP immediately.
Woman with unknown antenatal HIV status who has a home delivery and has an HIV positive test in postnatal clinic >72 hours after delivery Born to woman with established HIV infection who has received less than 12 weeks of ART at the time of delivery; or Born to woman with established HIV infection with viral load >1000 copies/mL in the four weeks before delivery, if viral load measurement available	Start (or switch to) cART	AZT/NVP for 24 weeks NAT testing
Woman with an HIV negative test in ANC and has an HIV positive test in L&D or during breastfeeding period*		

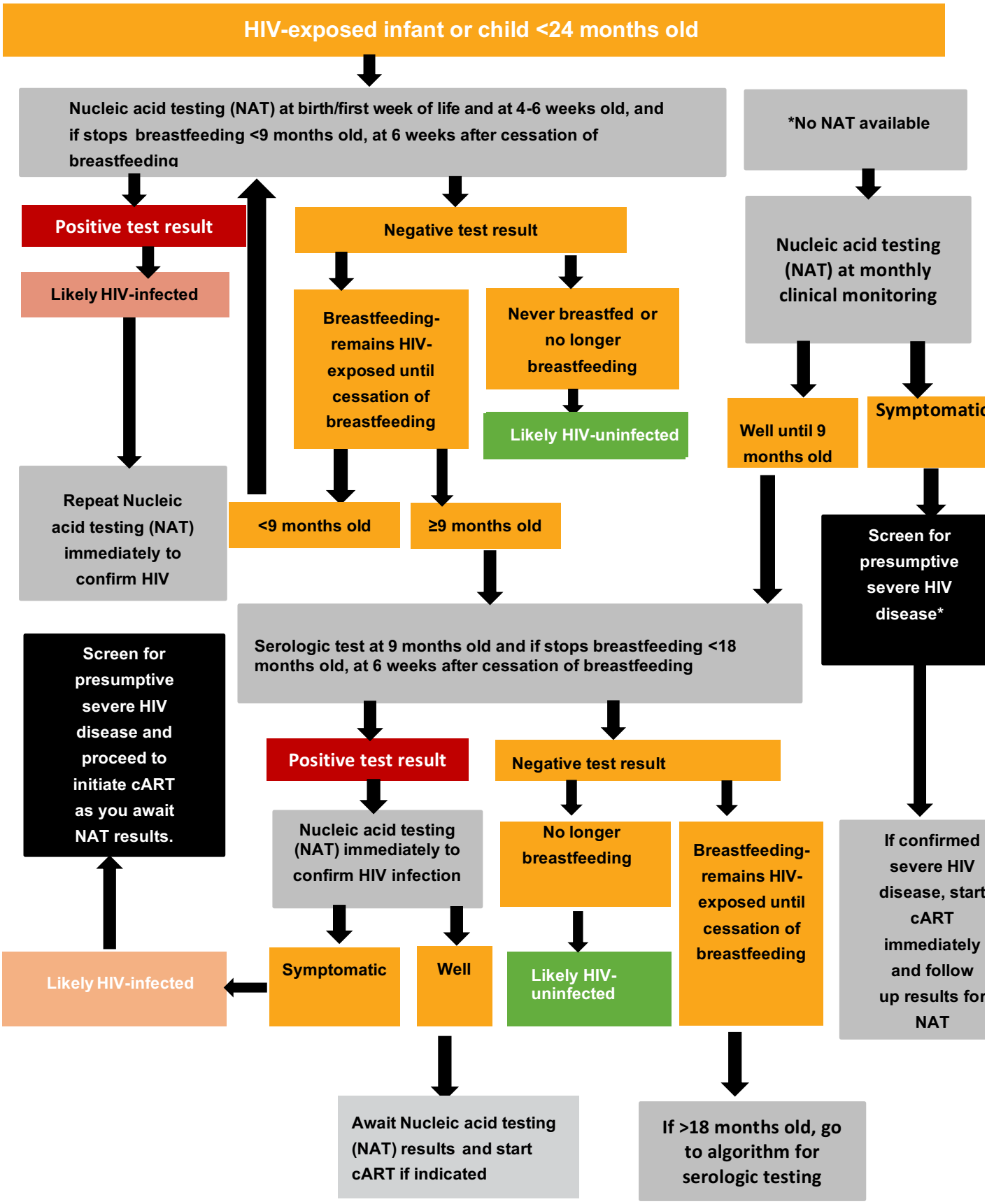
For scenarios not found in Tables 2 and 3 above, consult the Advanced Treatment Centres or call the toll-free line 7040, which is the University Teaching Hospital HIV Expert Hotline.

Table 4: Simplified infant prophylaxis dosing

Infant age	Dosing of NVP	Dosing of AZT
Birth to <6 weeks old		
Birth weight 2000g – 2499g**	10mg once daily (1ml of syrup once daily)	10mg twice daily (1ml of syrup twice daily)
Birth weight ≥ 2500g	15mg once daily (1.5ml of syrup once daily)	15mg twice daily (1.5ml of syrup twice daily)
> 6 weeks to 12 weeks		
	20mg once daily (2ml of syrup once daily or half a 50mg tablet once daily)	Use treatment dose 60mg twice daily (6ml syrup twice daily or a 60mg tablet twice daily

**For infants weighing <2000g and older than 35 weeks of gestational age, the suggested doses are: NVP 2mg/kg per dose once daily and AZT 4mg/kg per dose twice daily. Premature infants younger than 35 weeks of gestation age should be dosed using expert guidance.

Figure 2: Algorithm for HIV Nucleic acid testing (NAT) testing in children <24 months old



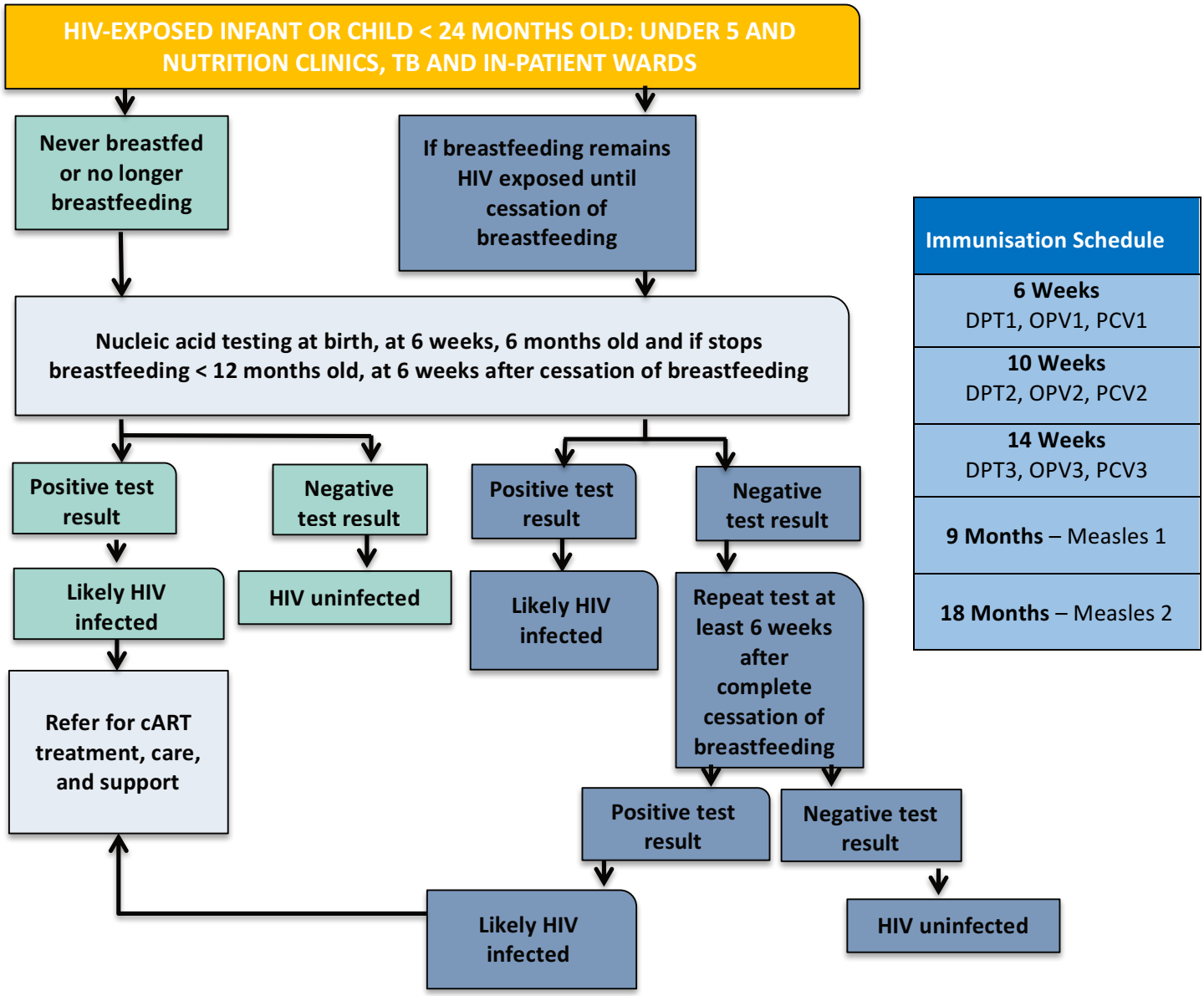
*Presumptive clinical diagnosis of HIV infection is done in infants and children <18 months old where there is no access to Nucleic acid testing (NAT) or reporting of results is delayed, but the child has symptoms suggestive of HIV infection. The criteria for making a presumptive diagnosis of HIV infection are:

- HIV serologic test positive in infant or child **AND**

- Symptomatic with two or more of the following: oral thrush, severe pneumonia, severe sepsis, or has any Stage 4 condition

*No NAT available means unable to collect sample because of various logistical issues or the test cannot be run at the testing lab because of logistical problems.

Figure 3: Testing algorithm of HIV-exposed infants or child integrated into EPI visits



Post-Exposure Prophylaxis

Post-exposure prophylaxis is the use of cART to prevent HIV transmission. Non-occupational exposure to HIV in children is mostly because of sexual abuse. In adults, exposure to HIV is mostly associated with occupational injuries. The risk of acquiring HIV infection after occupational exposure to HIV-infected blood is low (1:300 after percutaneous exposure to <1:1000 after mucocutaneous exposure).

There is no risk of transmission when the skin is intact. Factors associated with an increased risk include: deep injury, visible blood on the device that caused the injury, injury with a large bore needle from artery or vein, and terminal HIV illness in source patient. Body fluids and materials that pose a risk of HIV transmission are amniotic fluid, cerebrospinal fluid, human breast milk, pericardial fluid, peritoneal fluid, pleural fluid, saliva in association with dentistry, synovial fluid, unfixed human tissues and organs, vaginal secretions, semen, any other visibly blood-stained fluid, and fluid from burns or skin lesions. Other blood-borne infections are hepatitis B and hepatitis C viruses. Thus all HCWs should receive HBV vaccination.

Management of occupational exposure to infectious substances includes the following steps:

Immediately after exposure

- Clean the site: wash skin wounds with soap and running water. If the exposed area is an eye or mucous membrane, flush with copious amounts of clean water. DO NOT USE BLEACH or other caustic agents/disinfectants to clean the skin.
- Contact your In-Charge or supervisor.
- Consult the clinical officer or medical officer, who does the following:
    - Determine the need for post-exposure prophylaxis (PEP) based on the risk of transmission and risks and benefits of taking (or not taking) cART.
    - Counsel regarding PEP's risks and benefits. Start PEP (Table 5) preferably within 2 hours of the exposure. If 72 hours have passed since exposure, do not provide PEP because of lack of effectiveness.
- For high-risk exposure, arrange immediate HIV testing services. If HTS will likely last ≥1 hour, give first dose of PEP before HTS.
- Do not give PEP to exposed employees who refuse HIV testing or are HIV positive at the initial test. Instead, refer to cART clinic for assessment of cART eligibility. Maintain confidentiality.
- Send baseline creatinine (FBC if starting AZT).
- Complete the appropriate government PEP Register.

Follow up

- HIV testing on the day of the exposure.
- If negative, retest at 6 weeks, 3 months, and 6 months after exposure.
- Retest for HIV whenever acute illness includes fever, rash, myalgia, fatigue, malaise, and lymphadenopathy.
- See clinical officer or medical officer within 72 hours after starting PEP and monitor for side effects for at least 2 weeks.

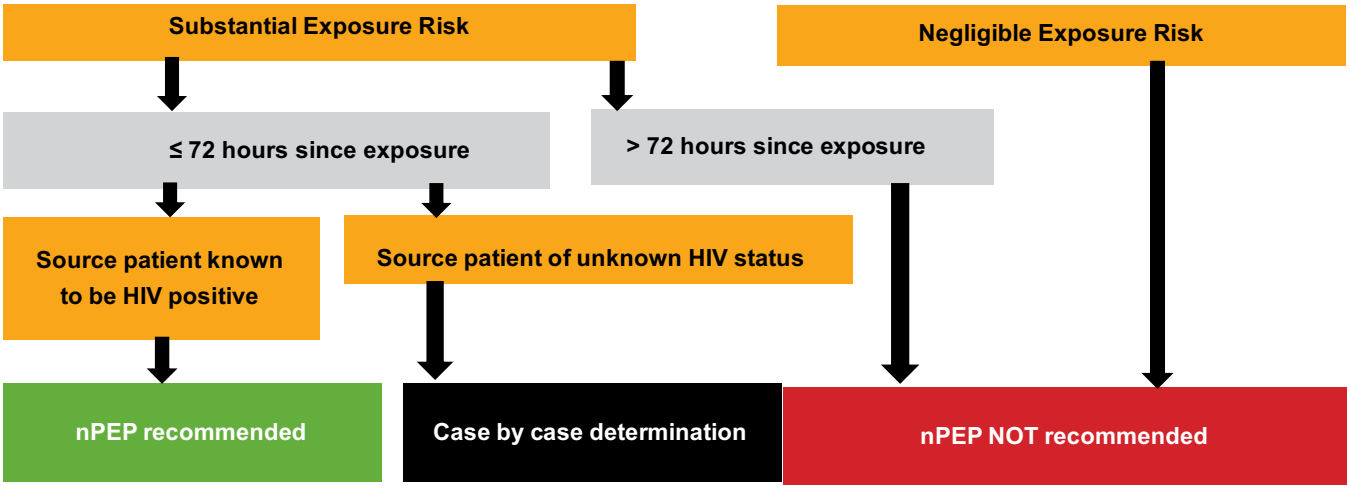
Table 5: Post-exposure prophylaxis recommendations by risk category

Risk category	cART	Duration
No risk: intact skin	Not recommended	
Medium risk: invasive injury, no blood visible on needle	TDF + XTC + ATV-r* AZT + 3TC + LPV-r (children <10 years)	28 days
High risk: large volume of blood/fluid, known HIV-infected patient, large bore needle, deep extensive injury		
Penetrative sexual abuse		

*For intolerance to ATV-r use LPV-r,
PIs are preferred ARVs for PEP because of concerns for transmitted resistance to NNRTIs
For patients with CrCl <50ml/min, replace TDF with AZT

Management of non-occupational exposure to infectious substances should be managed as shown in Figure 4 below.

Figure 4: Algorithm for evaluation and treatment of possible non-occupational HIV exposures (nPEP)



Substantial risk for HIV exposure of:
Vagina, rectum, eye, mouth, or other mucous membrane, non-intact skin, or percutaneous contact;
With:
Blood, semen, vaginal secretions, rectal secretions, breast milk, or any body fluid that is visibly contaminated with blood;
When:
The source is known to be HIV–infected or source's status is unknown

Negligible risk for HIV exposure of:
Vagina, rectum, eye, mouth, or other mucous membrane, non-intact skin, or percutaneous contact;
With:
Urine, nasal secretions, saliva, sweat, or tears if NOT visibly contaminated with blood; Regardless:
Of the known or suspected HIV status of the source

Managing HIV Infected Populations

2016 Recommendations

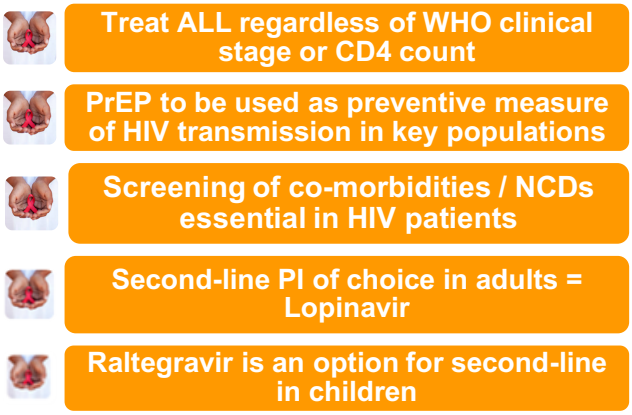


Table 6: ARV prescribers and corresponding regimens for cART initiation

Cadre with specific training	Initiation of cART
Nurse/Midwife (registered, enrolled) certified with Integrated HIV Care Training*	1st line
Nurse Prescribers with Integrated HIV Care Training*	1st line, 2nd line**
Clinical Officers with Integrated HIV Care Training*	1st line, 2nd line**
Medical Licentiates with Integrated HIV Care Training*	1st line, 2nd line
Medical Officers with Integrated HIV Care Training*	1st line, 2nd line
Medical Specialists with relevant training and experience†	1st line, 2nd line, 3rd line

*Providers with Integrated HIV Care Training should satisfy requirements of competency-based training in the use of cART for treatment and prevention of HIV

**Initiation on second line should only be done in consultation with a medical officer with appropriate training

†Relevant training and experience refers to management of advanced and complicated HIV, including second line treatment failure

To improve cART initiation and adherence, counseling must be done so that the individual (or caregiver) understands its benefits. The benefits of starting cART earlier include:

- Reduced rates of HIV-related morbidity and mortality
- Reduced MTCT (in pregnant and breastfeeding women)
- Potential reductions in the incidence and severity of chronic conditions (e.g., renal disease, liver disease, certain cancers, and neurocognitive disorders)
- Reduction in infectious complications (e.g., TB)
- Reduced sexual transmission

High levels of adherence to cART are needed to attain these objectives.

Table 7: Eligibility criteria for cART initiation in children, adolescents, pregnant and breastfeeding women, and adults

Specific populations	Description
Pregnant & Breastfeeding Women	Treat irrespective of WHO clinical stage or CD4 count
Children (0 to <10 years old)	
Adolescents (10 to ≤19 years old)	
Adults	

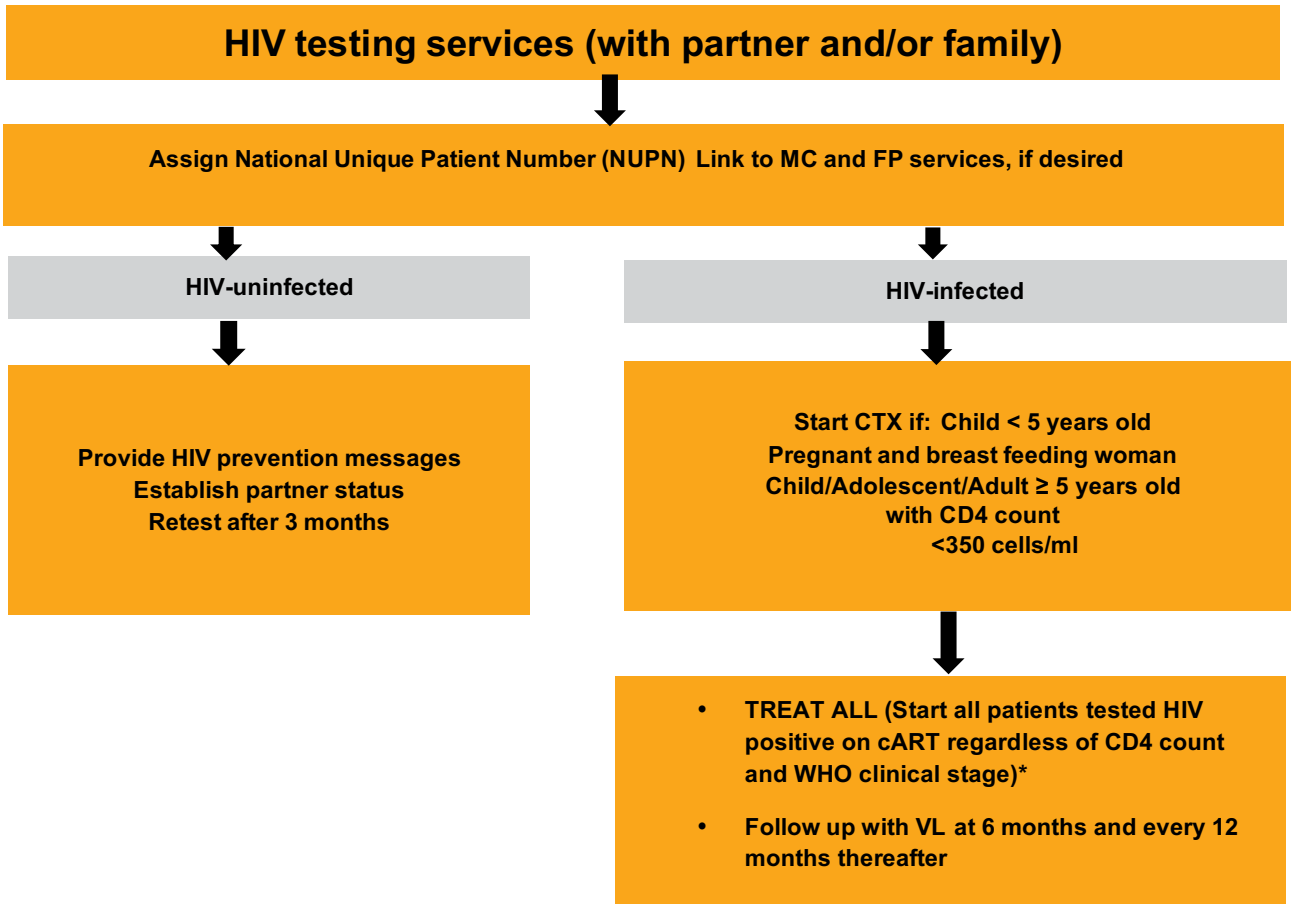
Under these new guidelines: **Treat ALL**. The assessment through WHO Staging (Table 7) guides the evaluation and management of HIV; however initiating on ART does not require a CD4 count.

Table 8: Pre-initiation tasks

Timeline/Specific populations		Clinical tasks	Laboratory tests*
Visit 1 Enrollment/ Initiate cART **based on patient readiness**	Children	Complete history & examination Screen for TB and other opportunistic infections (OIs) › Adherence counseling and PHDP† messages, including the caregiver: sessions 1 & 2 › Initiate CTX for child >6 weeks old › HPV vaccine for girl <10 years old	› Creatinine (calculate CrCl) ** › ALT › Hb/FBC** › CD4 ** › HBsAg (if not vaccinated) › Pregnancy test (Adolescent or woman of reproductive age) › Syphilis test (adolescent or adult) › If starting PI: cholesterol, glucose, and triglycerides › HPV test or visual inspection with acetic acid (VIA) in sexually active adolescent or woman
	Adolescents Adults	› Complete history & examination › Screen for TB and other OIs › Initiate CTX for ALL adolescents › Initiate CTX for adults if eligible (CD4 <350, Pregnancy and breastfeeding) › Adherence counseling and PHDP† messages › Urinalysis	
Visit 2 1-2 weeks later	Children	› Targeted history and examination › Screen for TB, Cryptococcus, and PCP › Review CTX adherence (if already started) › Initiate CTX (if eligible and not initiated at enrollment) › Review laboratory test results › Initiate cART if not initiated at enrollment and if patient/caregiver is ready and motivated › Adherence counseling and PHDP† messages, including the caregiver	
	Adolescents Adults		
Visit 3 2-4 weeks from enrollment	Children Adolescents Adults	› Targeted history and examination › Screen for TB and other OIs › And review CTX adherence › Initiate cART if not yet started in the last two visits › Adherence counseling and PHDP† messages	

† Positive Health Dignity and Prevention (PHDP) includes: risk reduction, ART adherence, correct condom use, family planning, STI screening, and partner HIV testing.
*If health facility is unable to perform a required laboratory test, refer sample or patient to higher level facility.
** Creatinine should be done in all patients initiating TDF based cART and Hb for all children initiating AZT based cART, according to the guidelines. CD4 should be done in all patients, but should not be used to determine eligibility.

Figure 5: Flow diagram for HIV care and treatment from HIV testing to cART initiation



*Linking HIV testing to services is key to ensuring all patients receive follow up care. This, particularly, should be accelerated in the pregnant or breastfeeding woman, all adults and adolescents with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with CD4 count ≤350 cells/mL, all children ≤2 years of age or children younger than 5 years of age with WHO clinical stage 3 or 4 or CD4 count ≤750 cells/mm³ or CD4 percentage <25%, and children 5 years of age and older with WHO HIV clinical stage 3 or 4 disease or CD4 count ≤350 cells/mL. Severe opportunistic infections should be treated or controlled before initiation of cART.

Table 9: WHO clinical staging of HIV disease by specific populations

Children (0 to <10 years old) Adolescents (10 to 15 years old)	Adolescents (15 to 19 years old) Pregnant & Breastfeeding Women Adults
Clinical Stage 1	
• Asymptomatic • Persistent generalized lymphadenopathy	• Asymptomatic • Persistent generalized lymphadenopathy
Clinical Stage 2	
• Unexplained persistent hepatosplenomegaly • Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis) • Herpes zoster • Lineal gingival erythema • Recurrent oral ulceration • Papular pruritic eruption • Fungal nail infections • Extensive wart virus infection • Extensive molluscum contagiosum • Unexplained persistent parotid enlargement	• Moderate unexplained weight loss (<10% of presumed or measured body weight) • Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis) • Herpes zoster, Angular cheilitis • Recurrent oral ulceration • Papular pruritic eruption • Fungal nail infections • Seborrhoeic dermatitis
Clinical Stage 3	
• Unexplained moderate malnutrition not adequately responding to standard therapy • Unexplained persistent diarrhoea (14 days or more) Unexplained persistent fever (above 37.5°C, intermittent or constant, for >1 month) • Persistent oral candidiasis (after 6 weeks old) • Oral hairy leukoplakia • Lymph node tuberculosis • Pulmonary tuberculosis • Severe recurrent bacterial pneumonia • Acute necrotizing ulcerative gingivitis or periodontitis, Unexplained anaemia (<8g/dl), neutropaenia (<0.5 x 109/l) or chronic thrombocytopaenia (<50 x 109/l) • Symptomatic lymphoid interstitial pneumonitis • Chronic HIV-associated lung disease, including bronchiectasis	• Unexplained severe weight loss (>10% of presumed or measured body weight) • Unexplained chronic diarrhoea for longer than 1 month Unexplained persistent fever (intermittent or constant for >1 month) • Persistent oral candidiasis • Oral hairy leukoplakia • Pulmonary tuberculosis • Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia) • Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis • Unexplained anaemia (<8g/dl), neutropaenia (<0.5 x 109/l) and/or chronic thrombocytopaenia (<50 x 109/l)

Children (0 to <10 years old)	Adolescents (15 to <20 years old)
	Pregnant & Breastfeeding Women
Adolescents (10 to <15 years old)	Adults
Clinical Stage 4	
• Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy • Pneumocystis jirovecii pneumonia • Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia) • Chronic herpes simplex infection (or labial or cutaneous of more than 1 month's duration or visceral at any site) Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) • Extrapulmonary tuberculosis • Kaposi sarcoma • Cytomegalovirus infection (retinitis or infection of other organs with onset at > 1 month old) • Central nervous system toxoplasmosis (after the neonatal period) • HIV encephalopathy • Extrapulmonary cryptococcosis, including meningitis • Disseminated non-tuberculous mycobacterial infection • Progressive multifocal leukoencephalopathy • Chronic cryptosporidiosis (with diarrhoea) • Chronic isosporiasis • Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidioidomycosis, penicilliosis) • Cerebral or B-cell non-Hodgkin lymphoma • HIV-associated nephropathy or cardiomyopathy	• HIV wasting syndrome • Pneumocystis (jirovecii) pneumonia • Recurrent severe bacterial pneumonia • Chronic herpes simplex infection (or labial, genital or anorectal of more than 1 month's duration or visceral at any site) • Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) • Extrapulmonary tuberculosis • Kaposi sarcoma • Cytomegalovirus infection (retinitis or infection of other organs) • Central nervous system toxoplasmosis HIV encephalopathy • Extrapulmonary cryptococcosis, including meningitis • Disseminated non-tuberculous mycobacterial infection • Progressive multifocal leukoencephalopathy • Chronic cryptosporidiosis • Chronic isosporiasis • Disseminated mycosis (extrapulmonary histoplasmosis, coccidioidomycosis) • Lymphoma (cerebral or B-cell non-Hodgkin) • Symptomatic HIV-associated nephropathy or cardiomyopathy • Recurrent septicaemia (including non-typhoidal Salmonella) • Invasive cervical carcinoma • Atypical disseminated leishmaniasis

Immune Reconstitution Inflammatory Syndrome and HIV

Immune reconstitution inflammatory syndrome (IRIS) is an exaggerated inflammatory reaction from a re-invigorated immune system presenting as unmasking of previously sub-clinical opportunistic infections OR clinical deterioration of pre-existing opportunistic infections OR development of autoimmune disease.

- Onset: usually within 2-12 weeks after starting ART
- Frequency: 10% among all patients on ART, up to 25% when ART initiated with CD4 <50 cells/mm^3
- Risk factors:
  - Initiating ART close to diagnosis of an opportunistic infection
  - Initiating ART when CD4 is less than 50 cells/mm^3
  - Rapid initial fall in HIV-1 RNA level in response to ART in patients with low CD4 counts
  - Commonly seen with TB, cryptococcal disease, Kaposi's Sarcoma, and Mycobacterium avium complex infection

Management of IRIS

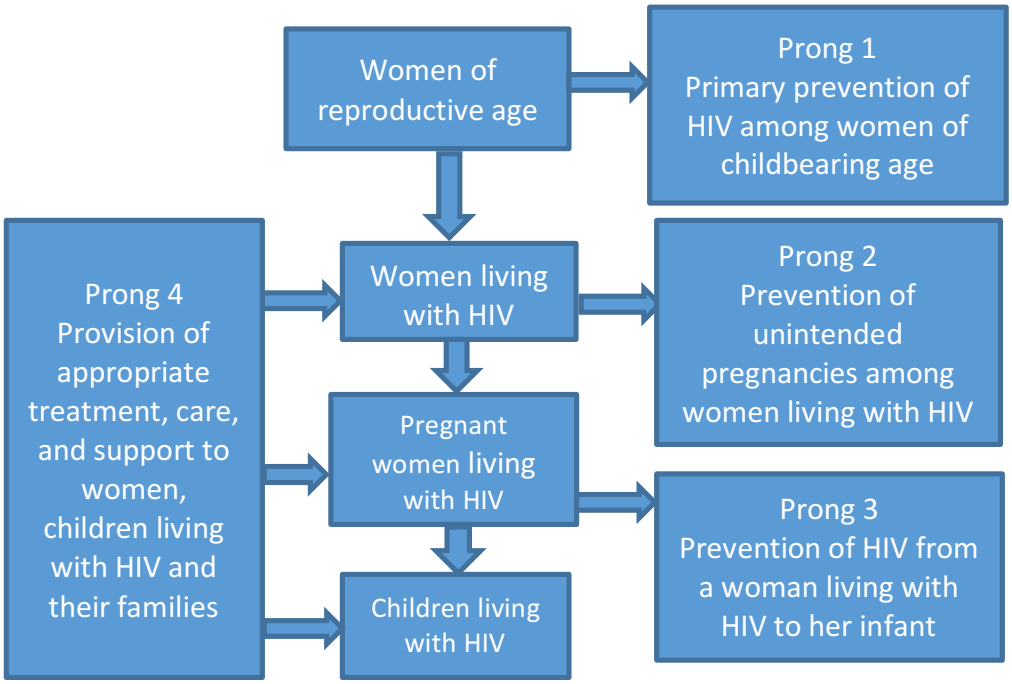
- Have high index of suspicion with early complications
- ART should be continued
- If ART continuation is impossible, temporarily interrupt ART and restart same regimen after OI or inflammatory condition is treated

- Diagnose and treat OI or inflammatory condition
- Corticosteroid treatment in moderate to severe cases: Prednisolone 0.5-1.0mg/kg/day for 5-10 days

Treatment as Prevention

In prevention of HIV transmission, PMTCT or EMTCT will remain a key strategy with a four-pronged approach. Clinical trial results have strongly confirmed the efficacy of the ARV drug tenofovir disoproxil fumarate alone or in combination with emtricitabine for use as pre-exposure prophylaxis (PrEP) to prevent HIV acquisition in a wide variety of settings and populations.

Prevention of Transmission: PMTCT



Primary HIV Prevention	
The drivers of the HIV epidemic include low rates of HIV testing, multiple concurrent sexual partners, low rates of male circumcision, MTCT, commercial sex workers, and migrant workers. Adolescents, especially young female adolescents, are vulnerable to HIV infection. The following interventions should be done in the health facilities and community: • Counsel regarding STIs and HIV prevention, including post-test information on how to remain HIV negative or to live positively based on the outcome of the HIV test result	• Provide condoms or information on where to access condoms, including female condoms • Refer to youth friendly services for more comprehensive sexual information, including HIV prevention • Treatment of discordant couples • Provide adherence support for adolescents on cART (prevention with positives)
Prevention of Unintended Pregnancies	
Prevention of unintended pregnancies in HIV-infected women contributes to elimination of mother-to-child transmission. It includes counseling and provision of a variety of family planning (FP) methods. With timely initiation of cART and adherence to cART in HIV-infected non-pregnant women, planning for pregnancy is encouraged. • Refer patients to Family Planning clinics, if needed, for further counseling and alternative methods • Promote mixed methods, also known as dual protection, because condoms alone or hormonal methods alone when the woman is on cART have been associated with unintended pregnancies	• Offer condoms to all men and women ≥15 years old • Offer long-term FP methods to all women ≥15 years old • Depot medroxyprogesterone acetate (DMPA) 150mg (1 vial) IM injection in deltoid muscle every 3 months • Noristerat 200mg IM injection in deltoid or gluteal muscle, every 2 months • Hormonal implant • Intrauterine contraceptive device (IUCD) • Sterilization (male or female) if child-bearing is complete • Patients have the right to choose their FP method, including declining all methods

Prevention of mother-to-child transmission of HIV using ARVs	

• In pregnant and breastfeeding women of unknown HIV status should be offered: HIV test & counseling (and depending on the result follow the guidelines) and routine antepartum, intrapartum, and postpartum obstetric care
• For mothers testing positive, immediately initiate cART among all pregnant or breastfeeding women diagnosed with HIV within MNCH under the key steps of:
  • Treatment preparation and adherence counseling should be accelerated so that it is completed on the same day where feasible
  • Initiation may be done by ART trained HNPs, nurses/midwives within MNCH
  • Where there is NO adequate capacity within MNCH to initiate the pregnant woman on cART, she should be fast-tracked through the ART clinic
	• Start CTX among all HIV-infected pregnant and breastfeeding women, regardless of CD4 count or WHO stage or gestational age
	• Viral load should be performed 1 to 4 weeks before delivery to estimate risk of transmission for all mothers who are pregnant and on cART
	• At 6 weeks postnatally, check CD4 count and if >350 cells/mL CTX may be discontinued.
	• Continuous counseling
	• Positive health, dignity, and prevention
	• Promoting safer sex practices

Care and Support to HIV infected women and their infants/families	
Continued treatment and adherence support for HIV infected women on treatment. Both high and low risk infants should be provided with prophylaxis. Encourage counseling and provision of a variety of family planning (FP) methods. For HIV-positive partners, transfer the sexual partner after cART initiation to ART clinic for further management. Refer all HIV-uninfected male partners in serodiscordant relationships to medical male circumcision and encourage routine retesting every 3-6 months.	

Prevention of Transmission: Pre-Exposure Prophylaxis (PrEP)

Oral PrEP is the use of antiretroviral (ARV) drugs before HIV exposure by people who are not infected with HIV to block the acquisition of HIV. Twelve trials on the effectiveness of oral PrEP have been conducted among serodiscordant couples, heterosexual men, women, men who have sex with men, people who inject drugs, and transgender women. Where adherence has been high, significant levels of efficacy have been achieved, showing the value of this intervention as part of combination prevention approaches. WHO recommends oral PrEP containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches.

Recommendations:

- Oral PrEP should be initiated to negative partner in a serodiscordant relationship whose HIV positive partner has refused to initiate cART.
- Persons engaged in high-risk activities may also be considered for PrEP.
- HIV testing is required before PrEP is offered.
- Repeat HIV testing is recommended while PrEP is taken every three months.
- The frequent HIV testing during PrEP use should also ideally become an opportunity for STI screening and management.
- Those diagnosed HIV positive should be maintained on the same regimen.
- PrEP should be provided as part of the combination prevention package (with condom use, HTS, family planning, STI testing etc.).

Lab Tests before PrEP

- HIV test (only HIV-negative partners should be on PrEP)
- Creatinine
- ALT
- Hb

- RPR/RST
- Repeat HIV testing is recommended while PrEP is taken every three months
- Hepatitis B (those with positive results should be on lifelong TDF/XTC to treat HBV)
- ARV regimen to be used for oral PrEP
- TDF/XTC should be used for those on PrEP

Lab Monitoring while on PrEP

- Creatinine at 1 month, 2 months, every 3 months for first 12 months then annually thereafter
- ALT every 3 months for first 12 months then annually thereafter

Adherence Support on PrEP

- Support for adherence should include information that PrEP is highly effective when used with strict adherence.
- PrEP users should be advised that PrEP reaches protection after 7 doses.
- Brief client-centred counseling that links daily medication use with a daily habit (such as waking up, going to sleep, or a regular meal) may be helpful.
- Special programmes to facilitate adherence among particular groups—such as young people and women—may be needed.
- Support groups for PrEP users, including social media groups (for example, https://www.facebook.com/groups/PrEP Facts) may be helpful for peer-to-peer sharing of experience and challenges.
- People who start PrEP may report side effects in the first few weeks of use. These side effects include nausea, abdominal cramping, or headache, are typically mild and self-limited, and do not require discontinuation of PrEP. People starting PrEP who are advised of this start-up syndrome may be more adherent.

When to stop PrEP

- PrEP can be discontinued if a person taking PrEP is no longer at risk and when this situation is likely to be sustained (i.e., partner starts ART and is virally suppressed and there are no other sexual partners).
- For safety concerns if the creatinine clearance decreases to <60ml/min.
- When the positive partner initiated treatment and has achieved viral load suppression, the negative partner on PrEP may discontinue therapy.
- PrEP safety during pregnancy and breastfeeding has yet to be fully determined. PrEP can be used with caution in these settings if the prescribing clinician believes that the risk of HIV seroconversion is significant, and the risks and benefits have been clearly described to the patient.

cART Regimens

First Line cART

Providing optimized, fixed-dose cART regimens in all populations have consistently demonstrated that there are better clinical and laboratory outcomes if HIV treatment is initiated early. Reduce the time between HIV diagnosis and ART initiation based on an assessment of person's readiness must be initiated within 2 weeks.

Table 10: Preferred first-line cART and alternative regimens by specific populations

Specific Populations	Description	Preferred 1st line cART	Alternative regimen
Pregnant & Breastfeeding Women [b]	First-line	TDF + XTC + EFV (Note: 400mg)	TDF + XTC + NVP [c] or ABC + 3TC + EFV
	Previous sd-NVP exposure; or NVP monotherapy exposure (NVP without 7 days of AZT + 3TC cover); or: Unsure of tail coverage	TDF + XTC + LPV-r	TDF + XTC + LPV-r or ATV-r
Children (0-2 weeks)		AZT + 3TC + NVP	AZT + 3TC + LPV-r
Children (2 weeks to < 5 years old)	First-line	ABC + 3TC + LPV-r	After completion of ATT, substitute to preferred 1st line with LPV-r
	HIV and TB co-infection	ABC + 3TC + EFV	
Children (5 to <10 years old)	First-line	ABC + 3TC + EFV	AZT + 3TC + EFV or ABC + 3TC + NVP
Adolescents (10 to <19 years old) weighing <35kg	First-line (NO history of maternal sd-NVP; maternal NVP monotherapy; mother unsure of tail coverage)	TDF + XTC + EFV (weight-based dosing)	TDF + XTC* + NVP† ABC + 3TC + EFV (weight-based dosing)
Adults	First-line	TDF + XTC + EFV 400 [a]	TDF + XTC + NVP or ABC + 3TC + EFV

a. EFV 400 is lower dose EFV of 400mg/day
b. Safety and efficacy data on the use of EFV 400 in pregnant women, people with HIV/TB co-infection and adolescents younger than 12 years of age are not yet available.
c. For NVP initiation, refer to section below: Practical Hints for EFV or NVP

Practical Hints for EFV or NVP initiation

- EFV is the preferred NNRTI for first line cART initiation
  - Consider using EFV at all times unless there are contraindications to its use, see Figure 6
  - EFV 400 mg/day as preferred options in fixed dose TDF/FTC/EFV first-line regimens
- EFV 600mg/day is associated with central nervous system (CNS) side effects (e.g. dizziness, drowsiness, insomnia, abnormal dreams, and impaired concentration).
  - In systematic reviews, there is evidence showing that EFV 400mg/day is comparable to EFV 600 mg/day in terms of viral suppression, but better in terms of CD4 cell count recovery and protective in terms of treatment discontinuation because of adverse events. When compared with the standard dose of EFV, EFV 400mg/day is also associated with lower toxicity, lower cost, and smaller pill size. It is also comparable to other treatment regimens with respect to mortality or AIDS-defining illnesses and emergent serious adverse events. There is, however, no safety and efficacy data on the use of EFV400 in pregnant women, people with HIV/TB co-infection and adolescents younger than 12 years of age.

EFV 400mg/day is thus recommended as part of the preferred first line regimen to EFV 600mg/day in the following populations:

- Adult patients who are NOT pregnant or on TB treatment
- Adolescents aged 12 to 19 years who are NOT pregnant or on TB treatment
- Adult patients and adolescents who are pregnant or on TB treatment should be on EFV 600mg/day

If CNS effects persist beyond 6-8 weeks on EFV 400mg/day substitute to NVP-based cART

Avoid fatty meals 4 hours before or after taking EFV. Recommend taking EFV before bedtime.

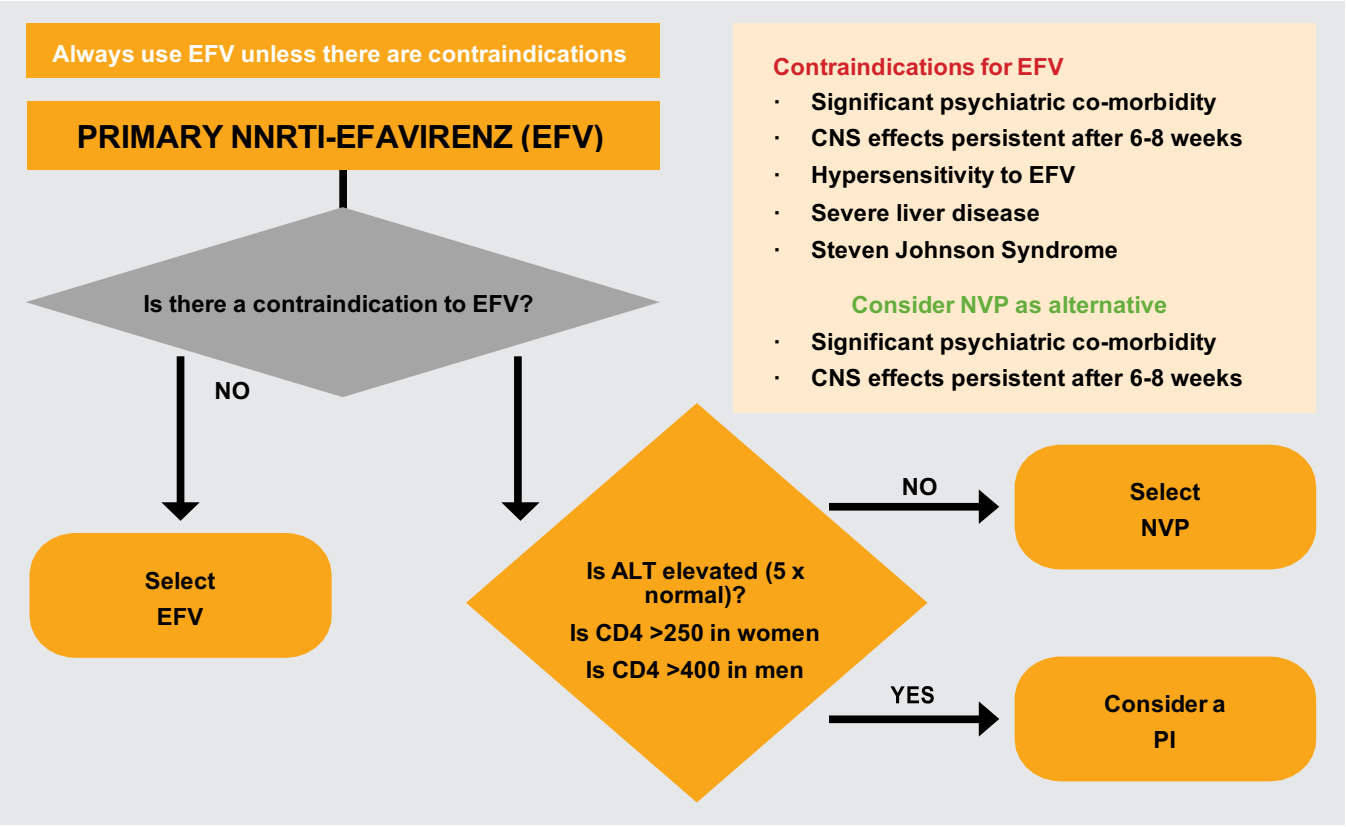
Non-pregnant women with CD4 count >250 cells/mm3 (men with CD4 count >400 cells/mm3) have a higher incidence (11%) of symptomatic hepatotoxicity when treated with NVP. Initiate NVP-based cART with caution in women with CD4 count >250 cells/mm3 (monitor ALT/AST during first 12 weeks) and avoid in women who are pregnant or at risk for pregnancy with CD4 count >250 cells/mm3 (men with CD4 count >400 cells/mm3).

If CD4 count >250 cells/mm3 in women or CD4 count >400 cells/mm3 in men, consider PI in consultation with next level of care or refer.

When initiating NVP-based cART, start with NVP 200mg once daily for 2 weeks and then increase to 200mg twice daily (BD) to reduce risk of rash and hepatotoxicity.

- **EFV or NVP should not be used to treat patients with HIV-1/HIV-2 co-infections or HIV-2 mono-infection. See section on HIV-2 Treatment**

Figure 6: Algorithm for choosing NNRTI



HIV-2 Treatment

- Clinicians should
  - include two NRTIs and a PI lopinavir/ritonavir when prescribing ART for HIV-2 mono-infected or HIV-1/HIV-2 co-infected individuals
  - not prescribe NNRTIs or the PI Atazanavir as part of an ART regimen against HIV-2 mono-infection
  - consult with a provider with the ATCs in the management of HIV-2 where there doubts before initiating ART in HIV-2-infected patients
  - educate patients with confirmed HIV-2 infection about the types of drugs that can be used to treat HIV-2
- No randomized clinical trials have been conducted to determine when to initiate ART in the setting of HIV-2 infection, and the best choices of therapy for HIV-2 infection remain under study. Because the optimal treatment strategy for HIV-2 infection has not been defined, the recommendations provided in this section are based on this committee's expert opinion with supporting evidence highlighted in Table 11 below.
- Although HIV-2 is generally less aggressive, and progression to AIDS is less frequent, HIV-2 responds less predictably to ART when progression occurs, and response is more difficult to monitor. The standard methods and interpretation protocols that are used to monitor ART for HIV-1-infected patients may not apply for HIV-2-infected patients. Some ART regimens that are appropriate for HIV-1 infection may not be as effective for HIV-2. The following factors should be considered:
  - The majority of HIV-2-infected patients are long-term nonprogressors
  - HIV-2 may confer more rapid resistance to ART agents because of wild-type genetic sequence that results in a significant increase in resistance to ART agents compared with HIV-1
  - Pathways for the development of drug mutations may differ between HIV-1 and HIV-2

Table 11: Efficacy of Antiretroviral Therapy Against HIV-2 Infection

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

- Although most in vitro studies have shown that similar concentrations of NRTIs are needed to block both HIV-1 and HIV-2 replication, data suggest that some NRTIs may not be as effective against HIV-2.[1]
  - For example, HIV-1 more readily incorporates zidovudine and is more susceptible to zidovudine than HIV-2, and there is a lower barrier to resistance with HIV-2 than with HIV-1.[2,3]
- Genotypic analysis of HIV-2-infected patients on ART has shown that many of the same amino acid substitutions that are associated with NRTI resistance in HIV-1 may be implicated in HIV-2. Some resistance mutations (K65R, Q151M, and M184V) in combination can confer class-wide NRTI resistance and cause rapid virologic failure.[2]

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

- NNRTIs block HIV-1 reverse transcription through a specific binding site that is not present in HIV-2; this class of drugs will not be effective against HIV-2.[4,5]
- HIV-2 appears to be intrinsically resistant to NNRTIs[4]; the *Y188L* polymorphism appears naturally in all HIV-2 isolates. Reversion to *Y188* restores the reverse transcriptase sensitivity to some NNRTIs, including efavirenz.[6]
- In general, NNRTIs inhibit HIV-2 at effective concentrations that are at least 50-fold higher than those that inhibit HIV-1,[7] making the use of these drugs for HIV-2 infection problematic.
- **Etravirine appears to have limited activity against HIV-2, but this may not be clinically relevant because the mean 50% effective concentration in MT4 cells is 2500-fold higher than that observed for HIV-1.**[8]

Protease Inhibitors (PIs)

- HIV-2 expresses natural polymorphisms in the protease that may be implicated in emergent drug resistance and accelerate time to development of PI resistance.[9]
- One study noted that the pathways for HIV-2 protease drug resistance may differ from those for HIV-1.[1]
- Saquinavir, lopinavir, and darunavir have shown comparable activity against HIV-1 and HIV-2.[10-12]
- Atazanavir has lower and variable activity against HIV-2 in comparison with HIV-1.[11]

Integrase Strand Transfer Inhibitors (INSTIs)

- Little is known about the use of integrase inhibitors in HIV-2 infection.
- The integrase inhibitors raltegravir and elvitegravir have demonstrated activity in vitro.[13] Clinical response to raltegravir was reported in a patient with highly treatment-experienced HIV-2 infection,[14] but the emergence of mutations was reported in another patient.[15]

CCR5 co-receptor antagonists

- The activity of maraviroc has been limited to patients with CCR5-tropic viruses.
- Primary HIV-2 isolates can utilize a broad range of co-receptors, including CXCR4, CCR5, CCT-5, GPR15, and CXCR6. This limits the therapeutic utility of maraviroc in HIV-2 infection.

Fusion inhibitors

- HIV-2 is intrinsically resistant to the fusion inhibitor enfuvirtide.[8,16]

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Table 12: Preferred first-line cART and alternative regimens for HIV-2

Specific Populations	Description	Preferred 1st line cART	Alternative regimen
HIV-1 / HIV-2 Co-infected	First-line	TDF + XTC + LPV-r	TDF + XTC + ETR or ABC + 3TC + LPV-r or ABC + 3TC + ETR
HIV-2 mono-infected			

Switching cART Regimens

When patients are switched to second-line cART regimens, the goals are to achieve HIV viral suppression resulting in reconstitution of the clinical and immunologic status, avoid adverse events, and optimize adherence. ATV-r is the primary recommended second-line PI (see Figure 6).

Table 13: Recommended second-line cART regimens by specific populations and failing first-line cART regimen

Specific populations	Initial 1st line category	Failing 1st line cART	2nd line cART
Children <5 years old	LPV-r-based first-line regimen	ABC + 3TC + LPV-r	AZT + 3TC + RAL
		AZT + 3TC + LPV-r	ABC + 3TC + RAL
Children 5-10 years old		ABC + 3TC + LPV-r	AZT + 3TC + RAL
		AZT + 3TC + LPV-r	ABC + 3TC + RAL
Children 5-10 years old	NNRTI-based first-line regimen	ABC + 3TC + EFV (or NVP) →→ TDF + 3TC + EFV (or NVP) →→	AZT + 3TC + LPV-r or ATV-r
Adolescents 10-19 years old All ages		AZT + 3TC + EFV (or NVP) →→	
Pregnant & Breastfeeding Women			TDF + 3TC + LPV-r or ATV-r
Adults			

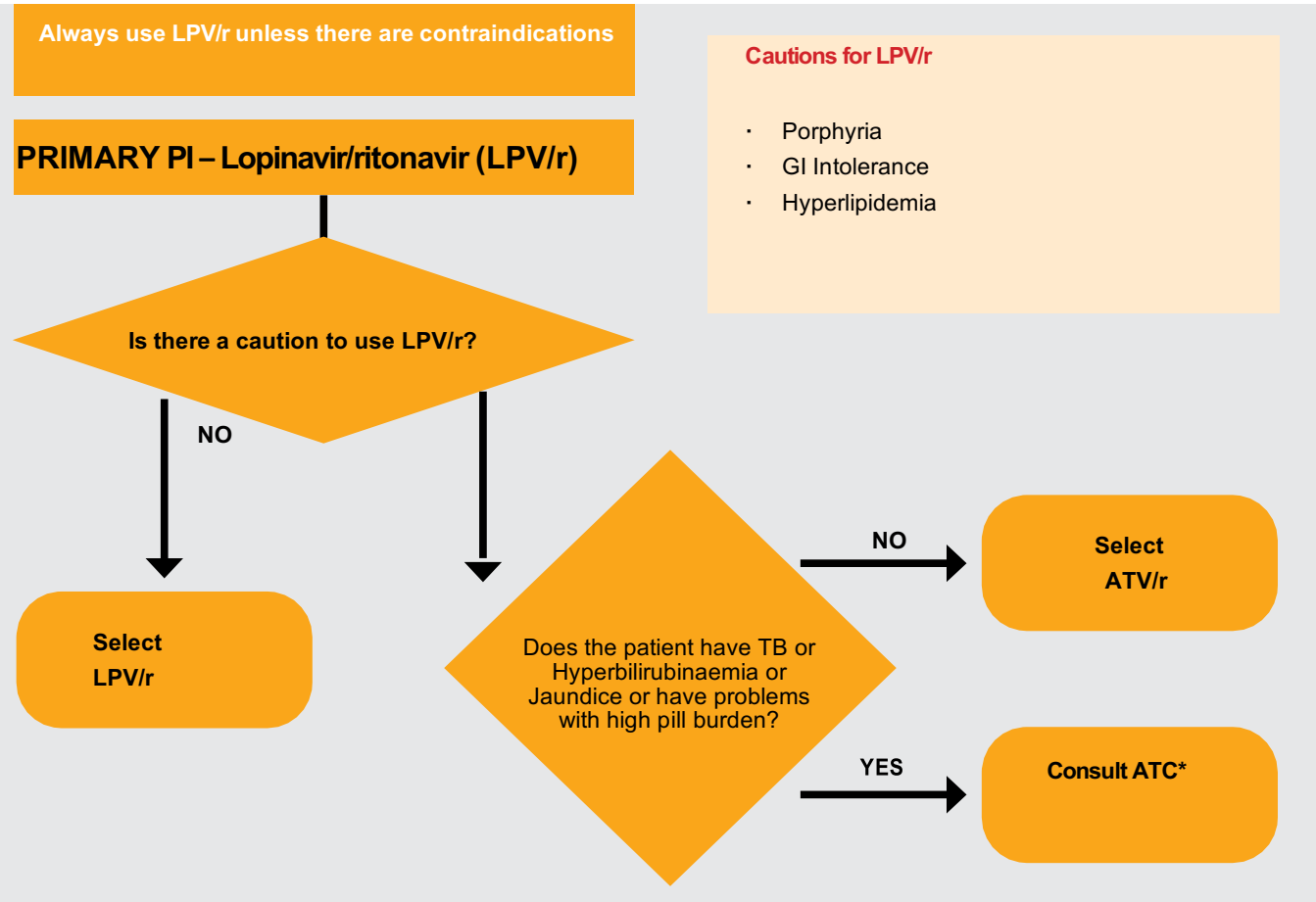
Table 14: Summary of preferred second-line ART regimens for adults and adolescents

Specific populations	Preferred 2nd line cART	
Adults and adolescents	If AZT was used in first-line ART	TDF + XTC + ATV-r or LPV-r
	Or if TDF was used in first-line ART	AZT + XTC + ATV-r or LPV-r
Pregnant or breastfeeding women	Same regimens as recommended for adults and adolescents	
HIV and TB co-infection	If rifabutin is available	Same PI regimens as recommended for adults and adolescents
	Or if rifabutin is not available	Double dose LPV-r (LPV-r 800mg/200mg twice daily)
HIV and HBV co-infection	AZT + TDF/ XTC* + (LPV-r or ATV-r) * TDF/XTC should always be part of the combination in HBV/HIV co-infections	

Table 15: Recommended second-line cART regimens for HIV-2

Specific populations	Initial 1st line category	Failing 1st line cART	2nd line cART
HIV-1 / HIV-2 Co-infected	LPV-r-based first-line regimen	TDF + 3TC + LPV-r	AZT + 3TC + DRV-r
HIV-2 mono-infected		ABC + 3TC + LPV-r	AZT + 3TC + DRV-r
HIV-1 / HIV-2 Co-infected	ETR -based first-line regimen	TDF + 3TC + ETR	AZT + 3TC + LPV-r
HIV-2 mono-infected		ABC + 3TC + ETR	AZT + 3TC + LPV-r

Figure 7: Algorithm for choosing a PI in second line



*ATC–Advanced Treatment Centre

Clinical guidance on use of ATV/r

Administration

- ATV/r is given once a day (300/100mg)
- Do not split or crush ATV/r tablets
- ATV/r should be used for children above 6 years and 35kg or more and adults

Patient Sensitization

- ATV/r is safe for use in pregnancy
- Ensure patients on ATV/r drink plenty of fluids to reduce the risk of kidney stones
- A common side effect associated with ATV/r is jaundice, which is benign and in most cases, should resolve in a few weeks.
  - Jaundice from unconjugated hyperbilirubinaemia is largely a cosmetic issue and not related to hepatitis or liver damage
  - A liver function test, if available, should be conducted to help rule out other causes of jaundice
  - If patient has symptomatic or profound jaundice, consult the UTH Advanced Treatment Centre

Contraindications

- **Do not use ATV**/r with rifampicin-containing TB treatment. Preferably, patients on rifampicin for TB treatment should be switched from ATV/r to "super-boosted" LPV/r (400mg/400mg twice daily) for the course of TB treatment; if not possible, a double dose of LPV/r (800mg/200mg twice daily) should be used
- Do not use ATV/r with proton pump inhibitors (omeprazole, pantoprazole, lansoprazole)
- Do not start patients with pre-existing jaundice or suspected hepatitis on ATV/r

Co-morbidities

2016 Recommendations
ART should be started in all TB patients living with HIV regardless of CD4 count
Xpert MTB/RIF is the gold standard for HIV associated TB infection diagnosis
Assessment and management of Cardiovascular Diseases (CVDs) in all HIV patients

Tuberculosis and HIV

There is a high incidence of TB among HIV-infected persons. All HIV-infected individuals should be screened for TB and placed on TB treatment if found with TB. HIV-infected individuals with TB should begin anti-tuberculosis therapy (ATT) via directly observed therapy, short course (DOTS) as per National TB Guidelines. Persons who screen negative for TB should be given TB INH Preventive Therapy (TB-IPT).

Screening for Active Tuberculosis

Figure 8: TB screening algorithm

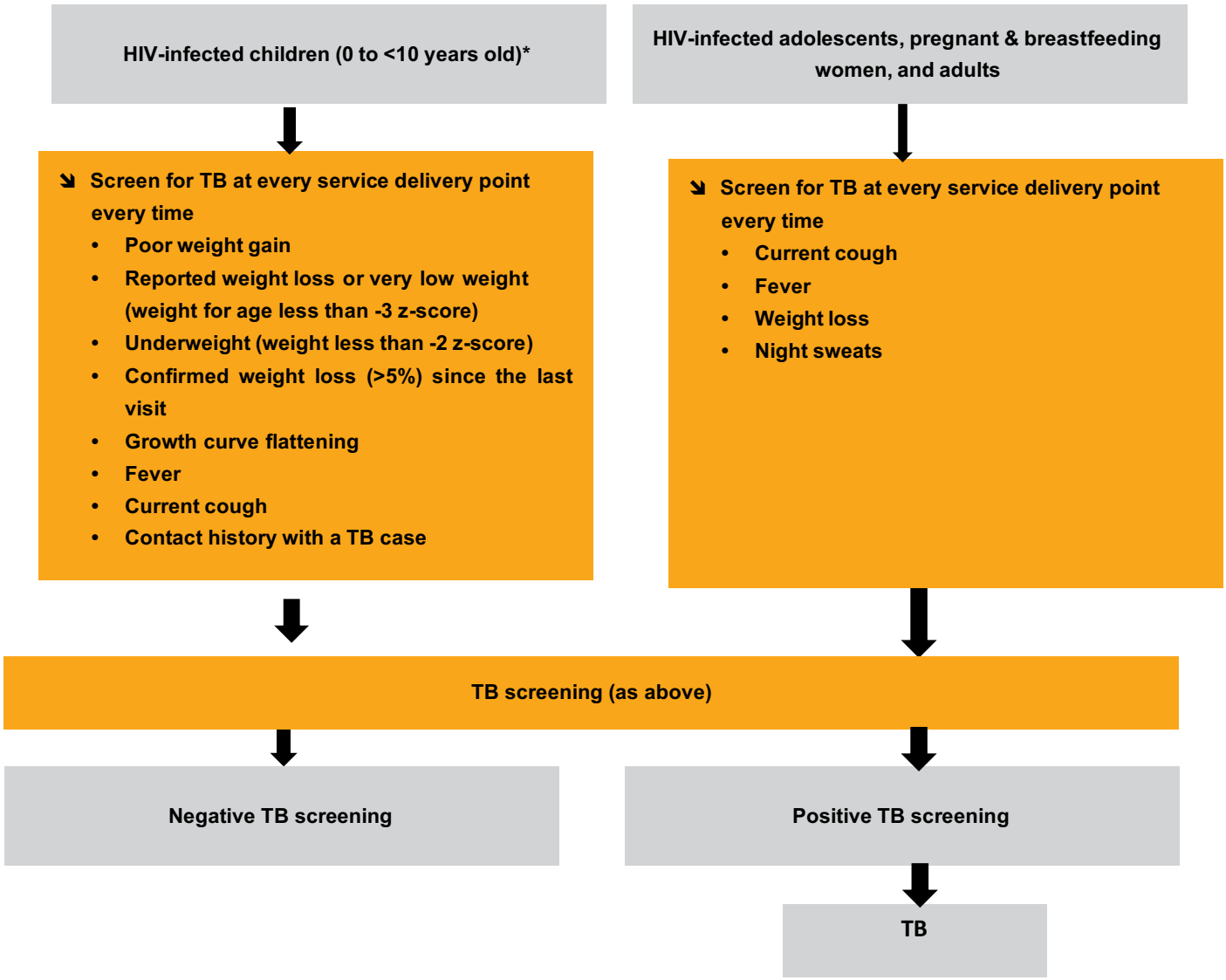


Table 16: Criteria for ATT with categories and recommended medications

Cases	ATT Category	TB Medications
All new cases (MTB RIF+*, MTB RIF-, smear positive, smear negative, EPTB)	Category I (CAT I)	Intensive phase: EZRH (2 months) Continuation phase: RH (4 months)
All re-treatment cases including treatment failure, treatment after default	Category II (CAT II)	Intensive phase: EZRHS (2 months) Second intensive phase: EZRH (1 month) Continuation: ERH (5 months)
*Needs to be confirmed with culture/DST or Line Probe Assay. Change regimen based on DST results.		

Table 17: HIV-TB co-infection case scenarios and recommended management

Scenario	TB management	Recommended cART
Pregnant, on cART and develops TB	Start ATT immediately	Continue EFV-based cART Evaluate for failure and consider switching to 2nd line cART in consultation with next level
Pregnant, on ATT, and diagnosed with HIV	Continue ATT	Start cART immediately TDF/XTC/EFV (600mg) If renal insufficiency, ABC + 3TC + EFV (600mg)
Children 3 months to <3 years old with TB-HIV co-infection	Start ATT (RHZ) immediately	ABC + 3TC + EFV
Newly diagnosed TB (category I) and HIV co-infection	Start CAT I ATT immediately	Start cART as soon as ATT is tolerated (usually within 2-3 weeks) regardless of CD4 count or WHO Clinical Stage TDF/XTC + EFV (600mg) If renal insufficiency, ABC + 3TC + EFV (600mg)
TB retreatment case (category II) and HIV co-infection	Start CAT II ATT immediately	
On cART and develops TB	Start ATT immediately	If NVP-based regimen, switch NVP to EFV (600mg) and continue cART. If on ATV/r, switch to LPV/r and double the dose If on LPV/r, double dose of LPV/r Evaluate for failure and consider switching to 2nd line cART in consultation with next level
On ATT and diagnosed with HIV	Continue ATT	Start cART as soon as ATT is tolerated (usually within 2-3 weeks*), regardless of CD4 count or WHO clinical stage TDF/XTC + EFV (600mg) If renal insufficiency, ABC + 3TC + EFV (600mg)
On 2nd line cART with LPV/r and develops TB	Start CAT I or CAT II ATT per guidelines immediately	Increase LPV/r from 2 tabs BD to 3 tabs BD for 2 weeks and then to 4 tabs BD for the remainder of TB treatment. If rifabutin available (in place of rifampicin), start at 150mg Monday/Wednesday/Friday.
Patients on TB treatment should be initiated on EFV 600mg/day **Patients on cART who develop TB and on EFV 400mg/day should be switched to EFV 600mg/day** HIV-positive TB patients with profound immunosuppression (e.g., CD4 counts less than 50 cells/mm^{3}) should receive ART within the first two weeks of initiating TB treatment.		

Tuberculosis Isoniazid Preventive Therapy (TB-IPT)

These guidelines focus on key interventions branded as the three I's (intensive case finding, isoniazid prophylaxis therapy, infection contrc for TB) for HIV-TB activities that reduce TB-related morbidity and mortality in HIV-infected individuals. Another key intervention is the provision of cART.

Daily TB-IPT can prevent TB in people who are at a high risk for developing TB, including HIV-infected individuals.

- Screen all patients for TB at any opportunity that presents (see Figure 8)
- Screen all pregnant and breastfeeding women, regardless of HIV status, for TB at every contact as it is part of Focused ANC
- Screen all children for TB at every contact
- Give TB-IPT for 6 months to the following:
  - HIV-infected children <12 months old with TB contact and after ruling out active TB
  - HIV-infected pregnant and breastfeeding women, children ≥12 months old, adolescents, and adults after ruling out active TB
  - After completing a full course of ATT, HIV-infected children should be given an additional IPT x 6 months
- Do not give IPT to a patient who has any signs suggestive of active TB. This patient needs full investigation for TB and combination TB treatment if confirmed to avoid TB drug resistance.

Standard TB screening questions include:

- Current cough: any duration, productive or non-productive
- Unexplained weight loss (adults)
- Failure to thrive and/or malnutrition (children)
- Fever or night sweats
- Stop IPT if any of the following:
  - Suspected or confirmed active TB (start ATT)
  - Jaundice and/or icterus (yellow eyes) or active hepatitis
  - Severe skin rash
  - Confusion/convulsions
  - Dizziness
  - Severe numbness/burning pain and muscular weakness of legs and/or arms
- How to give IPT
  - Give IPT during pre-cART period
  - Review and assess for side effects at months 1, 3, and 6 after starting IPT
  - IPT initiation: Give INH and pyridoxine for 1 month
  - Month 1: Give INH and pyridoxine for 2 months
  - Month 3: Give INH and pyridoxine for 3 months
  - Give concomitant pyridoxine (vitamin B6) 1 tablet 25mg once daily to prevent side effects of isoniazid in pregnant and breastfeeding women, adolescents, and adults.

Table 18: Dosage for isoniazid preventative therapy, co-trimoxazole prophylaxis, and combinatio INH/CTX/B6 drugs

Drug	Child Tablet or Oral Suspension	Number of Scoops or Tablets by Weight Band					Adult tablet
		3 to <6 kg	to <10 kg	10 to <14 kg	14 to <20 kg	20 to <25 kg	≥25 kg
INH	100mg	0.5	1	1.5	2	2.5	300mg 1 tablet
CTX	Suspension 200/40 per 5ml	2.5ml	5ml	5ml	10ml	10ml	
	Tablet 100/80mg	1	2	2	4	4	
	Tablet 400/80mg	NA*	1/2	1/2	1	1	400/80mg 2 tablets
	Tablet 800/160mg	NA	NA	NA	1/2	1/2	800/160mg 1 tablet
INH/CTX/B6	Tablet 960/300/25mg	NA	NA	NA	1/2	1/2	960/300/25mg 1 tablet

*NA = Not applicable

Co-trimoxazole Preventative Therapy (CPT)

CPT prevents Pneumocystis pneumonia (PCP), toxoplasmosis, isosporiasis, malaria, and other HIV- and non-HIV related diseases and prolongs survival. CPT can be safely taken with cART and/or ATT and in pregnancy (table 18 and 19). HIV-infected pregnant women on CPT should not be given sulfadoxine-pyrimethamine (SP; malaria prophylaxis in pregnancy).

Table 19: Criteria for initiating, discontinuing, and monitoring co-trimoxazole preventive therapy

Specific populations	Whom to Start	When to Start	When to Stop*
Pregnant & Breastfeeding Women	Pregnant women	Start as early as possible. Do not give SP. If SP taken, start CTX after 14 days.	(Continue throughout pregnancy)
	Breastfeeding women	Continue if CD4 count <350 cells/mm^3 or WCS 2, 3 or 4	CD4 count ≥350 cells/mm^3 for two consecutive values at least 6 months apart while on cART
Children (0 to <5 years old)	HIV-exposed (e.g. breastfed) child	At 6 weeks old or first contact	Confirmed HIV-uninfected after full cessation of breastfeeding
	HIV-infected child <24 months old	Start regardless of WCS or CD4%	At 5 years old and CD4 ≥25% and Stage I
	HIV-infected child ≥24 months to <5 years old	WCS 2, 3 and 4 or CD4 level <25%	
	Presumptive HIV diagnosis <18 months old	Start (or continue) regardless of WCS or CD4%	Stop if confirmed HIV negative; if infected, stop at 5 years old and CD4 level ≥25% and Stage I
Children (5 to <10 years old)	Child with a history of PCP	Start regardless of CD4 count or CD4%	At 5 years old and CD4 level ≥25% and Stage I If 5 to <10 years old, stop based on adult criteria
Adolescents Adults	HIV-infected children ≥5 years old, adolescents, and adults	CD4 count <350 cells/mm^3 or WCS 2, 3 or 4	CD4 count ≥350 cells/mm^3 for two consecutive values at least 6 months apart while on cART

Stop CTX if the person has Stevens-Johnson syndrome, severe liver disease, severe anaemia, severe pancytopaenia, or HIV negative status.

CPT contraindications: severe allergy to sulfa drugs; severe liver disease, severe renal disease, and glucose-6-phosphate dehydrogenase (G6PD) deficiency and in these conditions DO NOT re-challenge.

Hepatitis B and HIV

Screening and Management of Hepatitis B Virus (HBV) and HIV Co-Infection

- Hepatitis B surface antigen (HBsAg) should be done at baseline and in patients with unknown HBV status.
  - For children who have been fully vaccinated, do not screen for HBV
  - Start TDF-containing cART regardless of CD4 count

- Discontinuation of combination HBV therapy can be associated with a fatal flare-up of hepatitis.
- For HBsAg positive patients with renal insufficiency (CrCl <50), consult or refer to next level.
- For HBV-HIV co-infection in child <36 months

• Patients failing 1st-line TDF + XTC treatment should continue the TDF in their 2nd-line therapy (i.e. TDF + AZT + 3TC + LPV-r or ATV-r) to control their HBV infection	old, consult or refer to next level

Hepatitis B mono-infected

Screening and Management of Hepatitis B Virus (HBV) and HIV Co-Infection

- Hepatitis B surface antigen (HBsAg) should be used for screening and diagnosis of HBV infection
- Assessment for cirrhosis at baseline and follow up
- APRI (AST-to-platelet ratio index) is the preferred non-invasive test (NIT) to assess for the presence of cirrhosis
- APRI score >2 in adults is highly suggestive of cirrhosis

Eligibility criteria for treatment

- All adults, adolescents, and children with chronic HBV infection and clinical evidence of compensated or decompensated cirrhosis should be treated, regardless of ALT levels, HBeAg status, or HBV DNA levels.
- Diagnosis of cirrhosis is based on APRI score >2 in adults
- Treatment is recommended for adults with who do not have clinical evidence of cirrhosis (or based on APRI score >2 in adults) and:
  - Aged more than 30 years and have persistently abnormal ALT levels **and** evidence of high-level HBV replication (HBV DNA >20 000 IU/mL), regardless of HBeAg status
  - Treat when ALT is persistently abnormal regardless of HBeAg status in the absence of HBV DNA testing.

Non-Eligible patients.

Antiviral therapy is **not** recommended or deferred in the following situations:

- No clinical evidence of cirrhosis
- APRI score ≤2 in adults
- Persistently normal ALT levels
- Low levels of HBV DNA replication (HBV DNA <2000 IU/mL), regardless of HBeAg status or age
- May defer treatment in HBeAg-positive persons aged 30 years or less **and** persistently normal ALT levels where HBV DNA is unavailable

Continue monitoring in all persons with chronic HBV infection especially those who do not meet the above eligibility and non-eligibility criteria to determine if antiviral therapy may be indicated in the future to prevent progressive liver disease.

These include:

- persons without cirrhosis aged 30 years or less, with HBV DNA levels >20 000 IU/mL, **but** persistently normal ALT levels;
- HBeAg-negative persons without cirrhosis aged 30 years or less, with HBV DNA levels that fluctuate between 2000 and 20 000 IU/mL, or who have intermittently abnormal ALT levels;
- *Where HBV DNA testing is not available:* Persons without cirrhosis aged 30 years or less, with persistently normal ALT levels, regardless of HBeAg status in HBV/HIV-co-infected individuals, TDF based cART should be initiated regardless of CD4 count.

First-line Regimen

- In all adults, adolescents and children aged 12 years or older the preferred drug is TDF/3TC.
- In children aged 2–11 years Entacavir is the preferred drug

When to discontinue therapy

Discontinuation of NA therapy may be considered exceptionally in:

- persons without clinical evidence of cirrhosis (or based on APRI score ≤2 in adults);
- **and should be** followed carefully long term for reactivation;
- **and** if there is evidence of HBeAg loss and seroconversion to anti-HBe (in persons initially HBeAg positive) and after completion of at least one additional year of treatment;
- **and** in association with persistently normal ALT levels and persistently undetectable HBV DNA level;
- *Where HBV DNA testing is not available:* Discontinuation of NA therapy may be considered in persons who have evidence of persistent HBsAg loss and after completion of at least one additional year of treatment, regardless of prior HBeAg status.

Relapse may occur after stopping therapy with NAs. Restart therapy if there are consistent signs of reactivation (HBsAg or HBeAg) becomes positive, ALT levels increase, or HBV DNA becomes detectable again.

General measures to reduce HBV transmission

- HBsAg-positive persons should adopt correct and consistent condom use during sexual intercourse; not share razors, toothbrushes, or other personal care items; not donate blood, organs, or sperm; and follow standard universal precautions with open cuts or bleeding.
- HBV vaccination of household and sexual contacts. Household members and sexual partners of persons with CHB should be vaccinated if they are negative for HBsAg.
- Alcohol reduction to reduce disease progression

Measures to reduce HBV transmission in hospital settings

- hand hygiene: including surgical hand preparation, hand washing, and use of gloves
- safe handling and disposal of sharps and waste
- safe cleaning of equipment
- testing of donated blood
- improved access to safe blood
- training of health personnel

Eligibility CRITERIA FOR TREATMENT

- To all adults, adolescents, and children with CHB and clinical evidence of compensated or decompensated cirrhosis should be treated, regardless of ALT levels, HBeAg status, or HBV DNA levels.
- cirrhosis based on APRI score >2 in adults
- Treatment is recommended for adults with CHB who do not have clinical evidence of cirrhosis (or based on APRI score ≤2 in adults)
    - aged more than 30 years and have persistently abnormal ALT levels and evidence of high-level HBV replication (HBV DNA >20 000 IU/mL), regardless of HBeAg status
    - Treat when ALT is persistently abnormal regardless of HBeAg status in the absence of HBV DNA testing:
- In HBV/HIV-co-infected individuals, TDF based cART should be initiated regardless of CD4 count.

Non-Eligible patients

Antiviral therapy is **not** recommended or deferred in the following situations:

- No clinical evidence of cirrhosis
- APRI score ≤2 in adults
- persistently normal ALT levels
- low levels of HBV DNA replication (HBV DNA <2000 IU/mL), regardless of HBeAg status or age
- May defer treatment in HBeAg-positive persons aged 30 years or less and persistently normal ALT levels where HBV DNA is unavailable
- Continue monitoring in all persons with CHB especially those who do not meet the above eligibility and non-eligibility criteria to determine if antiviral therapy may be indicated in the future to prevent progressive liver disease. These include:
    - persons without cirrhosis aged 30 years or less, with HBV DNA levels >20 000 IU/mL, but persistently normal ALT levels;
    - HBeAg-negative persons without cirrhosis aged 30 years or less, with HBV DNA levels that fluctuate between 2000 and 20 000 IU/mL, or who have intermittently abnormal ALT levels;
    - *Where HBV DNA testing is not available:* Persons without cirrhosis aged 30 years or less, with persistently normal ALT levels, regardless of HBeAg status.

First line Regimen

- In all adults, adolescents and children aged 12 years or older, tenofovir is the preferred drug (TDF/3TC) and entecavir for children aged 2–11 years.
    - Tenofovir 300mg once daily
    - Tenofovir 300mg plus Lamivudine 300mg
    - Entecavir 0.5mg once daily (adult with compensated liver disease and lamivudine naive)
    - Entecavir 1mg once daily (adult with decompensated liver disease)

When to discontinue therapy

Discontinuation of NA therapy may be considered exceptionally in:

- persons without clinical evidence of cirrhosis (or based on APRI score ≤2 in adults);
- **and should** be followed carefully long term for reactivation;
- **and** if there is evidence of HBeAg loss and seroconversion to anti-HBe (in persons initially HBeAg positive) and after completion of at least one additional year of treatment;
- **and** in association with persistently normal ALT levels **and** persistently undetectable HBV DNA level
- *Where HBV DNA testing is not available*: Discontinuation of NA therapy may be considered in persons who have evidence of persistent HBsAg loss and after completion of at least one additional year of treatment, regardless of prior HBeAg status.
- Relapse may occur after stopping therapy with NAs. Restart therapy if there are consistent signs of reactivation (HBsAg or HBeAg becomes positive, ALT levels increase, or HBV DNA becomes detectable again.

Prevention of transmission of hepatitis B and measures to reduce disease progression in persons with chronic hepatitis B

Diagnosis of Cryptococcal disease

- Prompt lumbar puncture with measurement of Cerebrospinal fluid (CSF) opening pressure and rapid CSF Cryptococcal antigen (CrAg) assay or rapid serum CrAg (either LA or LFA) is the preferred diagnostic approach

Prevention of Cryptococcal disease

- The routine use of antifungal primary prophylaxis for Cryptococcal disease in HIV-infected adults, adolescents, and children with a CD4 count less than 100 cells/mm3 and who are CrAg negative or where CrAg status is unknown is not recommended before ART initiation, unless a prolonged delay in ART initiation is likely.

Treatment Options

- Induction phase of treatment in HIV-infected adults, adolescents, and children with cryptococcal disease (meningeal and disseminated non-meningeal),
- The following two-week antifungal regimens are recommended in order of preference.
  - Amphotericin B + fluconazole
  - Amphotericin B + flucytosine
- For the consolidation phase treatment of HIV-infected adults, adolescents, and children with cryptococcal meningitis or disseminated non-meningeal disease, the following eight-week antifungal regimen is recommended:
  - Fluconazole 400–800mg/day after a two-week induction with amphotericin B regimen (6–12mg/kg/day up to 400–800mg/day, if below 19 years).
  - Fluconazole 800mg/day after induction treatment with short-course amphotericin B or fluconazole-based induction regimen (fluconazole 12mg/kg/day up to 800mg/day, if below 19 years).
- For maintenance treatment of cryptococcal disease in HIV-infected adults, adolescents, and children, oral fluconazole 200mg daily (6mg/kg/day up to 200mg/day, if below 19 years) is recommended.

Mental Illness and HIV Infection

All HIV patients should be assessed and managed for neuropsychiatric conditions (e.g., depression, anxiety, mania, alcohol and substance use, HIV-associated neurocognitive disorder, and delirium disorders) may have a substantial impact on HIV disease progression and cART adherence. For individuals with mental illness, refer to a mental health provider. If an individual with mental illness appears to worsen after EFV 400 initiation, consider switching EFV 400 to NVP or LPV-r

Non–Communicable Diseases and HIV

Cardiovascular Disease (CVD) assessment and Management of Non-Communicable Diseases (NCDs)

HIV-infected persons are at increased risk of cardiovascular disease and other non-communicable diseases, including cancers. This is in part because of the chronic immune activation that persists even in HIV infection, even if on treatment. Assessment and management of cardiovascular risk should be provided for all individuals living with HIV according to standard protocols recommended for the general population using risk factors: older than 40 years, obesity, diabetes mellitus, known hypertension, waist circumference of >90cm (women) and 110cm (men), family history of premature CVDs.

Up to two thirds of premature deaths from the major NCDs are linked to four shared modifiable risk factors—tobacco use, harmful use of alcohol, unhealthy diet, and physical inactivity. These risk factors result in a series of metabolic and physiological changes that eventually lead to NCDs. Broader social, economic, and environmental determinants of health and inequities associated with globalization and urbanization, alongside population ageing, are the underlying drivers of the behavioural risk factors, and thus the NCD epidemic.

Figure 9: Causal links between underlying drivers for NCDs, behavioral risk factors, metabolic/physiologic risk factors and NCDs

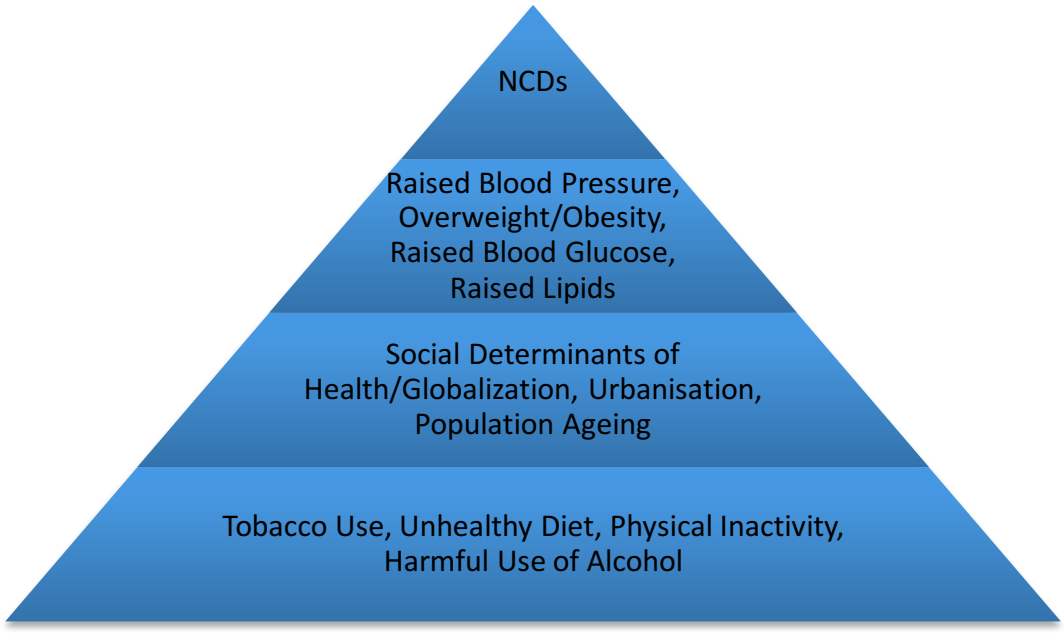


Table 20: Lifestyle modifications to prevent and manage CVDs among HIV-infected individuals

Smoking Cessation
• Smoking cessation has multiple short-term and long-term benefits, including: ✓ Skin does not age/wrinkle as quickly ✓ Improved fitness and quicker recovery from common infections ✓ Reduced risk of respiratory infections and chronic lung disease ✓ Reduced risk of high blood pressure, diabetes, kidney disease, heart disease, and stroke ✓ Improved infant outcomes (for pregnant women who smoke) ✓ Reduced risk of cancers: lung, bladder, breast, mouth, throat, esophagus ✓ Evidence of better response to ART (better viral suppression)
Dietary Changes and Weight Loss
✓ Weight loss to maintain a healthy BMI (nutritionists to be engaged in patient care) ✓ Reduce/abstain from alcohol ✓ Cut down sugar intake ✓ Cut down red meat intake ✓ Cut down consumption of fatty foods, fat for flavouring, and of fried foods ✓ Increase intake of whole grains, vegetables, fruit, and beans (eating at least five servings of fruit and vegetables a day) ✓ Increase intake of fish ✓ Cut down salt intake to less than one teaspoon a day
Physical Activity
• Active lifestyle with moderate-intensity physical activity • 30 minutes of aerobic activity such as brisk walking, at least 5 days per week

Table 21: Hypertension screening, diagnosis, and initial management for HIV-infected individuals

Screening
• BP should be measured and recorded at every visit
Diagnosis
• Hypertension requiring intervention is defined as BP ≥140/90mmHg on at least two different occasions ✓ It can also be diagnosed at the same visit if the BP is 180/110 or any BP associated with target organ damage
Management
If baseline BP is 140-159/90-99: • Lifestyle modifications for at least 6 months, along with monthly BP monitoring • If does not meet treatment target with lifestyle modifications, then add drugs: ✓ Introduce 1 drug at a time, and allow 2-3 weeks to achieve maximal effect before titrating up dosage; titrate to maximum dosage before adding an additional drug ✓ In PLHIV without kidney disease or diabetes, first-line antihypertensive therapy is a **thiazide diuretic** such as hydrochlorothiazide starting at 12.5mg OD (maximum dose 25mg OD) **OR** a **calcium channel antagonist** such as amlodipine starting at 2.5mg OD (maximum 10mg OD) ✓ In PLHIV **with** kidney disease or diabetes the first antihypertensive should be an ACE-I or ARB such as Enalapril 2.5-10mg OD (maximum dose is 20mg BD); Losartan 50mg OD (maximum dose is 100mg OD) ✓ If inadequate response once dose has been titrated, an additional agent may be required (e.g., hydrochlorothiazide starting at 12.5mg OD [maximum dose 25mg OD]) ✓ If inadequate response to two agents, consider consultation with or referral to a clinician experienced in the management of refractory hypertension. Note: Calcium-channel blockers have known drug interactions with PIs and NNRTIs and should be used with caution • If baseline BP ≥160/100mmHg: initiate lifestyle modifications and introduce anti-hypertensive medications concurrently • Target BP measurements ✓ Diabetic patients: <140/90 ✓ None Diabetic & Chronic Kidney Disease (CKD) patients: 140/90 ✓ None Diabetics & None CKD patients: <140/90 (<60 years); 150/90 (>60 years old)

Table 22: Type 2 Diabetes mellitus screening, diagnosis, and initial management for HIV-infected individuals

Screening
• Blood glucose (fasting or random) should be evaluated at baseline for all PLHIV, then annually if baseline screening is normal; urine dipstick for protein and glucose can be used if blood glucose testing is not available
Diagnosis
• Diabetes Mellitus is defined as fasting blood sugar ≥7.0mmol/L, or random blood sugar ≥11.1mmol/L, or HbA1C >6.5% • Abnormal results should be repeated to confirm the diagnosis
Management (treatment target is HbA1C ≤7.0% or FBS 4-7mmol/L)
• Monitor HbA1c (or FBS if HbA1c not available) every 3 months for patients with confirmed diagnosis of diabetes mellitus • Lifestyle modifications (weight loss, nutritional support to manage portion sizes and calculate glycaemic index of various foods to help with control of blood sugar) for 3-6 months • If does not meet treatment target with lifestyle modifications, then add drugs: ✓ Metformin ✓ Obtain baseline Creatinine; do NOT use metformin if creatinine clearance <45mL/min ✓ Start with low dose (500mg OD or BD) and titrate up every 1-2 weeks until reaches 1g BD (or maximum tolerated dose if less than 1g BD) ✓ If does not meet treatment targets with metformin for 3-6 months at maximum tolerated dose, then consider adding oral drugs from another class (such as glyberide) and/or specialist consultation. Some patients may require insulin • At every visit: A thorough history (to elicit features of hypoglycaemia, other cardiovascular disease risk factors, neuropathy, diabetic foot ulcers) and a physical exam (for BP, neuropathy, foot ulcers) • Additional routine screening for patients with diabetes: ✓ Annual ophthalmology examination for diabetic retinopathy ✓ Annual urinalysis: start on an ACE-I/ARB if proteinuria develops (even if BP normal)

Table 23: Dyslipidaemia screening, diagnosis, and initial management for HIV-infected individuals

Screening
• Fasting lipid profile should be evaluated at baseline for all PLHIV, then annually if baseline screening is normal
Diagnosis
• Dyslipidaemia is defined as high fasting total cholesterol (>5.2mmol/L), LDL (>3.4mmol/L) or triglycerides (>2.2mmol/L)
Management
• Lifestyle modifications for 3-6 months • If the patient is on an ARV known to cause or exacerbate dyslipidaemia (primarily LPV/r) then consider a single-drug substitution to a more lipid-friendly drug (such as from LPV/r to ATV/r) as the treatment of choice before adding a lipid-lowering drug. • If does not meet treatment target with lifestyle modifications, then add drugs: ✓ Atorvastatin: starting dose of 10mg OD (maximum dose 20mg if patient is on a PI/r and a maximum dose of 80mg once daily if not on a PI/r) ✓ Allow at least 3 months before repeating fasting lipids and titrating dose • Once targets achieved can monitor lipids every 6-12 months

Table 24: Chronic kidney disease screening, diagnosis, and initial management for HIV-infected individuals

Screening
• Urinalysis (for protein) and serum creatinine should be evaluated at baseline for all PLHIV
Diagnosis
• Impaired renal function is defined as creatinine clearance < 60ml/min, or dipstick proteinuria ≥ 1 • Abnormal results should be repeated to confirm diagnosis
Management
• Management depends on the cause of the renal impairment; additional investigations and/or specialist consultation may be required • Treat dehydration promptly and aggressively • If on TDF-containing regimen, substitute with another ARV, with the exception of patients with HBV/HIV co-infection who need TDF to be maintained on adjusted doses or switch to Entacavir (see section on Hep B/HIV co-infected) • Avoid nephrotoxic drugs • Evaluate for and treat hypertension • All NRTIs except ABC require dose adjustments for renal impairment, depending on the severity. NNRTIs, PIs, and Integrase Strand Transfer Inhibitors (INSTIs) do not require dose adjustments for impaired renal function

Cervical Cancer and HIV

Cervical cancer is preventable and is curable if diagnosed and treated early. All women regardless of age should be assessed for cervical cancer; women living with HIV have a higher risk of pre-cancer and invasive cancer. Cervical cancer screening leads to early detection with HPV test or visual inspection with acetic acid (VIA).

Figure 10: Recommended screening for cervical cancer among HIV infected women

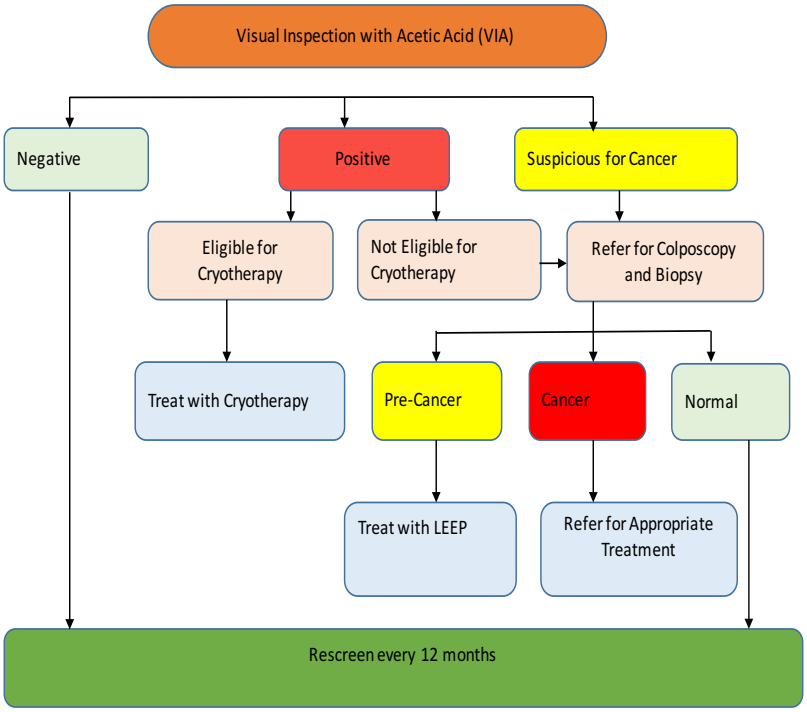


Table 25: Recommended tests for HIV screening and monitoring for co-infections and NCDs

Phase of HIV Management	Recommended	Desirable (*if feasible)
HIV Diagnosis	• HIV testing (serology for adults and children 18 months or older: NAT or children younger than 18 months • Screen for TB • CD4 cell count (assess CTX)	• HBV or HCV serology • Screening for STIs • Hb or FBC • Pregnancy test (woman of reproductive age) • HPV test or visual inspection with acetic acid (VIA) in sexually active adolescent or woman) • Syphilis test (adolescent or adult) • NCDs risk factors: cholesterol, glucose, and triglycerides
ART Initiation		• Hb • Pregnancy test (woman of reproductive age) • BP measurement • Serum creatinine (for starting TDF) • Baseline CD4
Receiving ART	• Viral load (at 6 months, 12 months after initiating ART and every 12 months thereafter)	• Pregnancy test, especially for women of childbearing age not receiving family planning or on treatment with TLE 400mg • Serum creatinine for TDF
Suspected Treatment Failure	• Serum creatinine for TDF • Pregnancy test, especially for women of childbearing age not receiving family planning or on treatment with TLE 400mg • And review CTX adherence • Initiate cART if eligible • Adherence counseling and positive health dignity and prevention (PHDP) messages	• HBV (HBsAg) serology (for HIV/HBV co-infected already using TDF and develop ART failure, TDF should be maintained regardless of selected second line regimen)

* Reference 2016 WHO Guidelines

Terminal Illness/Cancer and HIV

- Palliative care aims to relieve suffering in all stages of disease and is not limited to end-of-life care. The goals of palliative care include:
  - To improve the quality of life
  - To increase comfort
  - To promote open communication for effective decision making
  - To promote dignity
  - To provide a support system to the person who is ill and those close to them

In HIV-infected individuals, palliative care focuses on symptom management and end-of-life care. Throughout all stages of HIV disease, including when on cART, individuals may experience various forms of pain and other discomfort. HCWs should identify and treat the underlying cause when possible, while controlling the pain. Effective management of side effects and possible overlapping cART-associated toxicities is important to support adherence.

The care of the terminally ill child is a particular challenge in Zambia because there are few replicable models of planned terminal care, both institutional and community-based. At the end of life, there are typically more symptoms that must be addressed, and the child may need to take multiple drugs to control and treat a variety of symptoms and conditions.

Terminal care preparation for children and their families is a long-term process and requires continuity of care through providers and services. Families must be involved in decisions about the best place for care and the preferred place of death in the child with end-stage HIV disease.

Monitoring cART

2016 Recommendations

- Viral load is the gold standard for monitoring for HIV-infected patients on treatment
- The role of CD4 now lies in identifying patients who need CTX prophylaxis

Clinical and Laboratory Monitoring

Monitoring consists of two components: clinical and laboratory. Clinical monitoring includes history and examination, as well as evaluation of adherence, side effects, and relevant drug toxicities. Laboratory tests need to be conducted routinely and as needed (Table 22). It includes CD4 count, viral load, and toxicity monitoring. Viral load is the preferred monitoring approach to determine the performance of cART in an individual and is more sensitive than CD4 count. If viral load is not available, CD4 count and clinical monitoring should be used.

The purpose of monitoring includes:

- Evaluation of treatment response and diagnose treatment failure early
- Evaluation of adherence
- Screening for Pulmonary tuberculosis
- Detection of toxicity to ARV drugs

Viral load is recommended as the preferred monitoring approach to determine the performance of cART in an individual. If viral load is not routinely available, CD4 count and clinical monitoring should be used.

Monitoring and managing a chronic condition while on cART

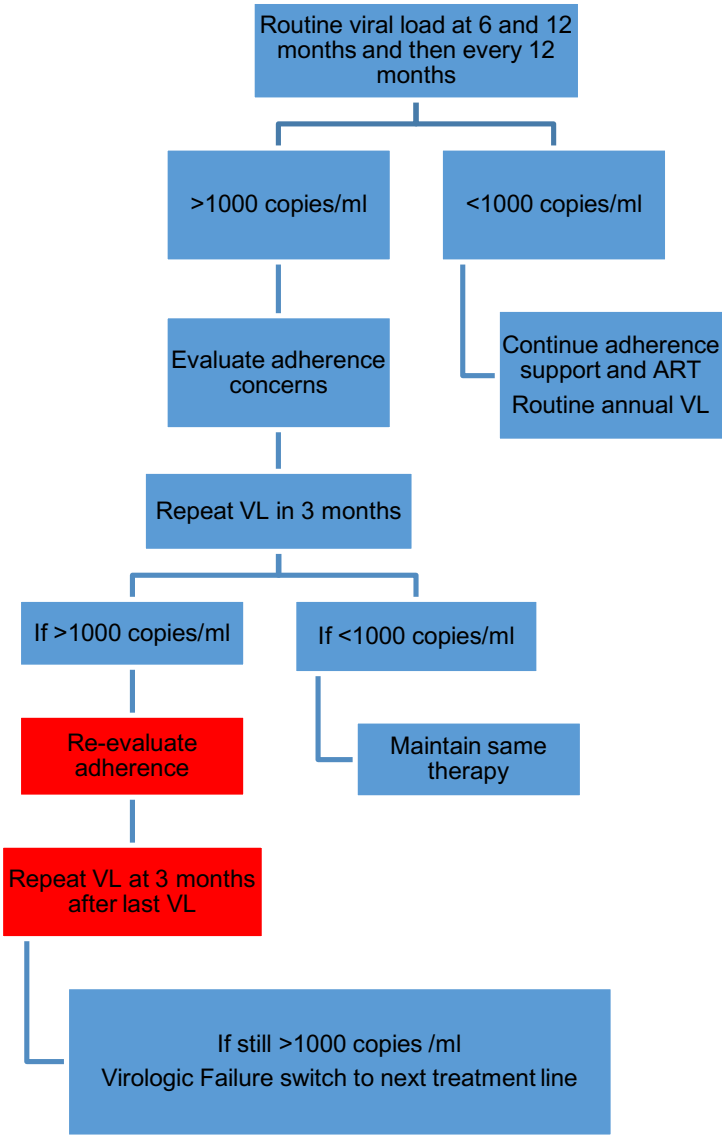


Table 26: Clinical and laboratory monitoring for HIV-infected pregnant and breastfeeding women

Timeline	Clinical tasks	Laboratory tests
Day 0: Enrollment & cART initiation	› History and examination	› Serum creatinine
	› If pregnant, focused ANC (FANC)	› ALT
	› Screen for TB, cryptococcus, and PCP	› Hb or FBC Blood glucose
	› Adherence counseling and	› CD4 count
	› PHDP† messages	› HBsAg
	› Initiate cART after accelerated	› Syphilis test
	› If no signs and symptoms of active TB disease, initiate IPT	› Viral load testing at baseline for known HIV positives
		› Urinalysis for protein and glucose, RBCs
		› If starting PI: cholesterol, and triglycerides
Week 2 post-initiation	› Targeted history & examination	› Serum creatinine
		› Urinalysis
Week 4 post-initiation	› Screen for TB, cryptococcus, and PCP	
Subsequent visits to occur per: › FANC if pregnant › HEI schedule if postnatal and breastfeeding › Adult cART schedule if postnatal and not breastfeeding		HIV viral load to be done every 6 months during pregnancy and breastfeeding period › Serum creatinine and urinalysis at every FANC visit Laboratory testing to occur per: FANC while pregnant except for viral load Adult cART schedule when postnatal except for viral load
	› If pregnant, FANC	
	› Review adherence, side effects, toxicity*	
	› Adherence counseling and	
	› PHDP† messages	
	Review laboratory tests	
	› Refill cART with enough supply to next visit (maximum: 3 months of	
First postnatal visit	› CD4 cell count to determine need for continuation of co-trimoxazole; if more than 350 cells/ul, repeat CD4 after 6 months	
24 months after delivery	› cART dispensed in MNCH until transferred	
	› Transfer to ART clinic for continuum of HIV care and treatment	
	› Earlier transfer or referral may be done for logistical reasons or complicated cases	

† Positive Health Dignity and Prevention (PHDP) includes: risk reduction, ART adherence, correct condom use, family planning, STI screening, and partner HIV testing

* See Appendix 3 regarding WHO toxicity estimates

Table 27: Common co-morbidities and recommended ART regimens

Special Cases of Adolescents, Adults, and Pregnant & Breastfeeding Women	Preferred 1st line cART	Alternative Regimen
HIV and TB co-infection	TDF + XTC + EFV	ABC + 3TC + EFV + DTG
	TDF + XTC + LPV-r (double the dose of LPV-r if on rifampicin regimen) or switch rifampicin to rifabutin (avoid in pregnancy or breastfeeding mothers)	ABC + 3TC + LPV-r
Severe untreated mental illness	TDF + XTC + NVP	TDF + XTC + LPV-r or ABC + 3TC + NVP
HIV-2 infection or HIV-1/HIV-2 co-infection	TDF + XTC + LPV-r	TDF + XTC + ATV-r or ABC + 3TC + LPV-r or ABC + 3TC + ATV-r
Renal insufficiency (CrCl <50ml/min)	ABC-based cART	
Renal insufficiency in pregnant women (Serum Cr >125µmol/l)	ABC-based cART	
Renal insufficiency and ABC hypersensitivity	Adjust dose of TDF, 3TC, FTC, and AZT	
Renal insufficiency** and on dialysis	Adjust dose of TDF, 3TC, FTC, and AZT	
1st line regimen (TDF + XTC + EFV) Defaulters (no treatment failure suspected)	TDF + XTC + EFV 400	

Monitoring Drug Side Effects and Toxicities

Changing an ARV drug should be done only after careful review of adherence. The indication for changing needs to be addressed. A specific ARV drug may be changed (substitution) because of:

- Toxicity, such as anaemia, peripheral neuropathy, lipodystrophy, liver or renal abnormalities
- Intolerance or unresolved and prolonged side effects
- Poor adherence: change indicated only to simplify dosing schedule and to improve adherence
- Occurrence of active TB (refer to section on TB-HIV co-infection)
- Failure (clinical, immunologic, or virologic)

When patients are substituted to alternative regimen (see Table 24), the goals are to achieve HIV viral suppression, avoid adverse events, and optimize adherence.

Table 28: Common cART toxicities and recommended substitutes (for all populations)

ARV drug	Common associated toxicity	Recommended ARV substitute
ABC	Hypersensitivity reaction	TDF (if normal creatinine clearance) AZT (if child <5 years old)
ATV-r	Hyperbilirubinaemia, icterus*	LPV-r
AZT**	Severe anaemia or neutropenia, severe gastrointestinal intolerance, lactic acidosis	TDF or ABC (if on 1st line cART regimen; rule out failure before substitution) d4T (if on 2nd line cART regimen for anaemia)
EFV	Severe or persistent CNS side effects	Consider using lower dose 400mg or substitute to NVP, if not effective in reducing symptoms
LPV-r	Persistent diarrhoea, hyperlipidaemia	ATV-r
NVP (or EFV)	Rash, Steven Johnson Syndrome, hepatitis	ATV-r or LPV-r
RAL	Rash and hypersensitivity reaction	ATV-r or LPV-r
TDF	Renal toxicity (renal tubular dysfunction)	ABC

Hyperbilirubinaemia and icterus do not reflect hepatic disease and are not contraindications to continued therapy. Only substitute ATV-r if the condition is intolerable to the patient.
AZT should no longer be used in 1st line cART. Patients on AZT-based 1st line cART and are not failing treatment should be substituted to TDF- or ABC-based 1st line cART.

ART Adherence

2016 Recommendations

Strengthening adherence support interventions at the community level

Good adherence means:

- Taking ARV drugs at the same time of the day all the time
- Taking all the medications at the right time and in correct doses
- Not skipping doses
- Not stopping and restarting therapy without medical advice
- Adopting appropriate health seeking behaviour
- Keeping appointments
- Not sharing medications with others

Ensure patients identify treatment supporters with whom they are comfortable (e.g., family members, buddies) and encourage treatment supporters to attend counseling sessions and clinic visits.

Key Populations to target reinforced adherence

- **Late -** classified as late up to 60 days of missing scheduled appointment
- **Lost to follow up (LTFU) -** more than 60 days after last scheduled pharmacy pick up (all tracking efforts have been exhausted) and patient cannot be traced
- **Defaulter -** when a person who has been located as late or lost to follow up chooses not to return to care
- **Unknown status -** tracking measures not exhausted to determine enrollment status

Structured treatment preparation before cART initiation (Table 8 and Figure 5) should be conducted for all patients for successful HIV treatment and care. All children, adolescents, and adults should undergo 3 sessions before cART initiation (pregnant and breastfeeding women should be fast-tracked, and education regarding adherence should be integrated into ANC):

- Session 1 (Enrollment and Assessment): HIV education
- Session 2 (cART Eligibility): cART support, cART preparation
- Session 3 (cART Initiation): cART education, cART preparation, cART dispensation

Adherence assessment should be done by all members of the health care team using:

- Clinical and laboratory parameters
- Patient reports
- Pill counts
- Pharmacy pick-ups
- Other tools of adherence

Provider-related Strategies to Improve Adherence

- **Establish trust** and make sure the patient feels you are there to help manage and solve problems
- **Involve the patient in developing a plan** for taking the drugs that is simple and works with the patient's daily activities
- **Educate about goals of therapy, side effects**, what will happen if the patient does not take all the drugs
- **Treat depression** or substance abuse issues
- Treat and **manage side-effects**
- **Monitor adherence** at each visit
- **Reinforce importance of adherence** at each follow-up visit

HIV Treatment Failure

2016 Recommendations

Patients failing on second-line regimen with no new ARV options should continue on the same regimen

Third-Line cART: Second-Line Treatment Failure

Treatment failure is defined by a persistently detectable viral load >1,000 copies/ml. For adolescents and adults, failure is two consecutive viral load measurements within a three-month interval, with adherence support between measurements after at least six months of using triple combination ARV drugs. For children, viral load may still be detectable at 6-9 months after initiation and does not necessarily mean treatment failure. Viral blips or intermittent low-level viremia (50–1,000 copies/ml) can occur during effective treatment, but have not been associated with an increased risk of treatment failure unless low-level viremia is sustained. A repeat blip should be assessed further at the ATC. Additionally, clinical and epidemiological studies show that the risk of HIV transmission and disease progression is very low when the viral load is lower than 1,000 copies/ml.

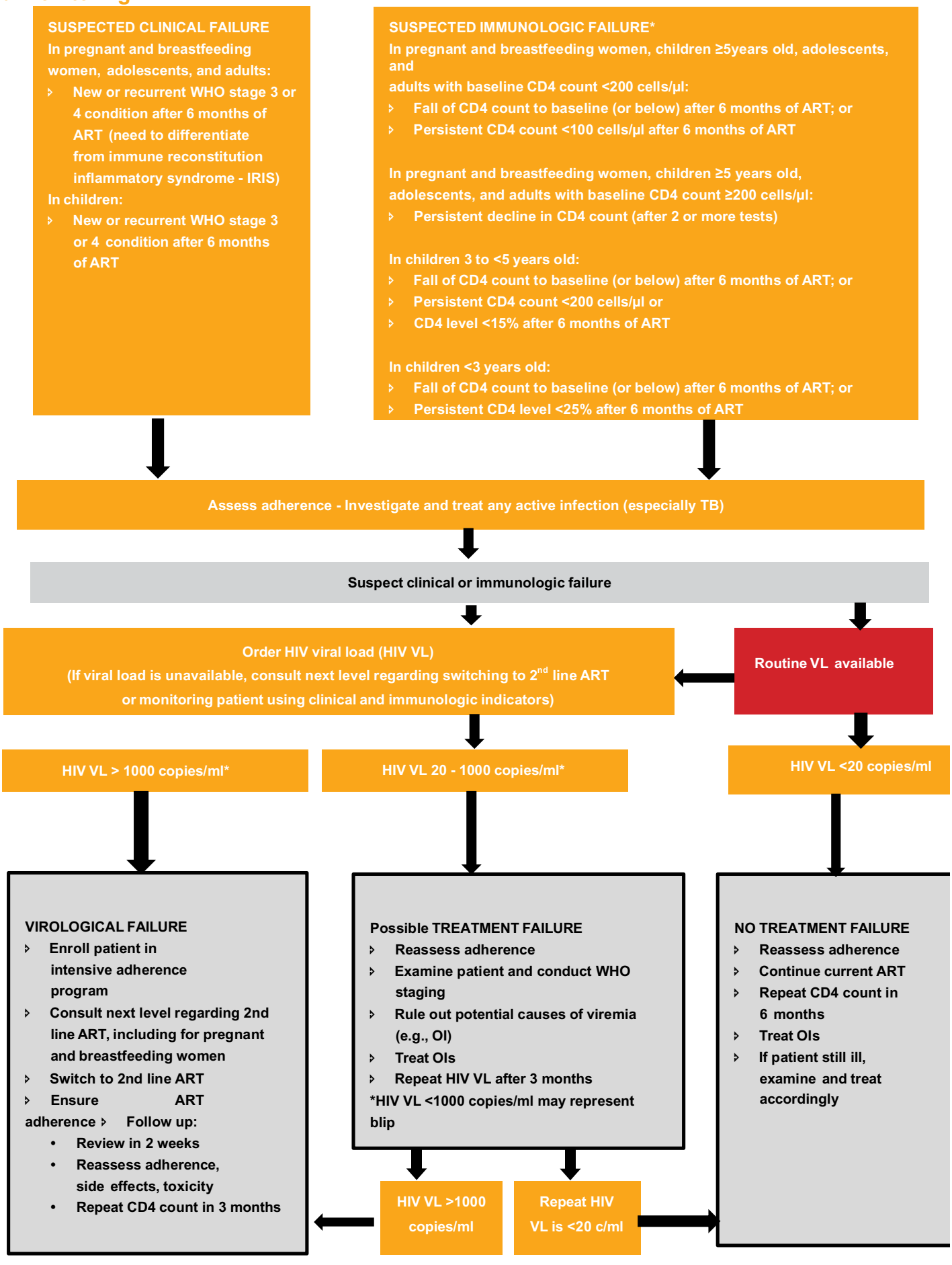
Provision of third-line cART occurs in very rare circumstances and is beyond the scope of most cART providers. All patients being considered for third-line cART should have:

- Confirmed second-line cART failure (defined by a persistently detectable viral load exceeding 1,000 copies/ml [i.e., two consecutive viral load measurements within a three-month interval with enhanced adherence support between measurements] after at least six months of using second-line cART)
- Genotype (resistance) testing
  - Refer (see Figure 12) to an HIV Specialist at an Advanced Treatment Centre (ATC) with a complete cART treatment history (i.e., all previous ARV drugs that the patient has taken with duration of use).
  - Before starting third line, establish the reason for treatment failure (e.g., poor adherence, suboptimal dosing, drug-drug interactions) and conduct intensive adherence counseling sessions until there is agreement between the patient, provider, and adherence counselor that the patient is ready to commence third-line cART.
- Use of treatment supporters for such patients is STRONGLY recommended.
- The most likely ARVs to be successful in patients who have followed National Guidelines are Raltegravir (integrase inhibitor) or darunavir with ritonavir (protease inhibitor) plus optimal nucleoside background (e.g. TDF + XTC or AZT + 3TC).
- Other considerations with major constraints:
  - Etravirine: especially if genotype is available at time of 1st line NNRTI failure, although in some patients NNRTI mutations persist even after non-exposure to NNRTIs in second line
  - Maraviroc: needs special tropism test before initiation, which is currently not available in Zambia

Before switching therapy in suspected treatment failure, HCWs need to rule out:

- Poor adherence: change therapy only after enhanced adherence counseling has been conducted
- Immune Reconstitution Inflammatory Syndrome (IRIS): treat underlying condition and continue cART if tolerated
- Untreated OIs: treat underlying condition and continue cART if tolerated
- Pharmacokinetics (e.g. rifampicin reduces NVP or LPV-r blood levels): switch NVP to EFV or double the dose of LPV-r or switch rifampicin to rifabutin
  - Current infections causing transient decrease in CD4 count: treat infection, and if possible, repeat CD4 one month after resolution of illness to confirm immunologic failure

Figure 11: Algorithm for diagnosing treatment failure with targeted and routine viral load monitoring



Management of Patients Previously on cART (Includes but not limited to Defaulters)

Individuals who interrupt cART for any reason are at increased risk of resistance and treatment failure. Management in cART re-initiation is based on several factors, and a complete history to establish why the treatment was stopped is critical. For HIV-infected children, the caregivers must be questioned.

- If treatment failure or toxicity is not suspected as the reason for stopping cART, and previous good adherence is reported, reinitiate original cART in consultation with next level.
- If previous adherence is poor and there is treatment failure, these individuals (and caregivers of children) MUST be enrolled in intensive adherence counseling sessions until there is agreement among the patient, provider, and adherence counselor that the patient is ready to commence second line cART. Use of treatment supporters for such patients is strongly recommended.
- If severe toxicity is the reason for stopping cART, refer to the next level and initiate cART using the appropriate drug substitution and counsel regarding adherence.
- Viral load testing should be done 6 months after re-initiation of the original regimen to document HIV viral suppression.

When to Stop cART

Patients may choose to postpone or stop therapy, and providers, on a case-by-case basis, may elect to defer or stop therapy on the basis of clinical and/or psychosocial factors.

The following are indications for stopping cART:

- Patient's inability to tolerate all available ARV medications
- Patient's request to stop after appropriate counseling
- Non-adherence despite repeated counseling: treatment should be stopped to avoid continued toxicity, continued evolution of drug resistance, and transmitting drug resistant HIV
- Unreliable caregiver
  - For children, the caregiver is instrumental in cART adherence. Any factors that affect the capability for the caregiver to give medications consistently may be an indication to stop cART in an HIV-infected child.
- Serious drug toxicity or interactions
- Intervening illness or surgery that precludes oral intake
- ARV non-availability

How to Stop cART

- Stop ALL the drugs when discontinuing therapy.
- Discontinue EFV or NVP; continue the NRTI components (backbone) for 1-2 additional weeks.
- Preventive measures, such as condom use and safer sex practices, should be strongly emphasized for all patients, especially those discontinuing treatment.

Treatment Failure with No Further Treatment Options

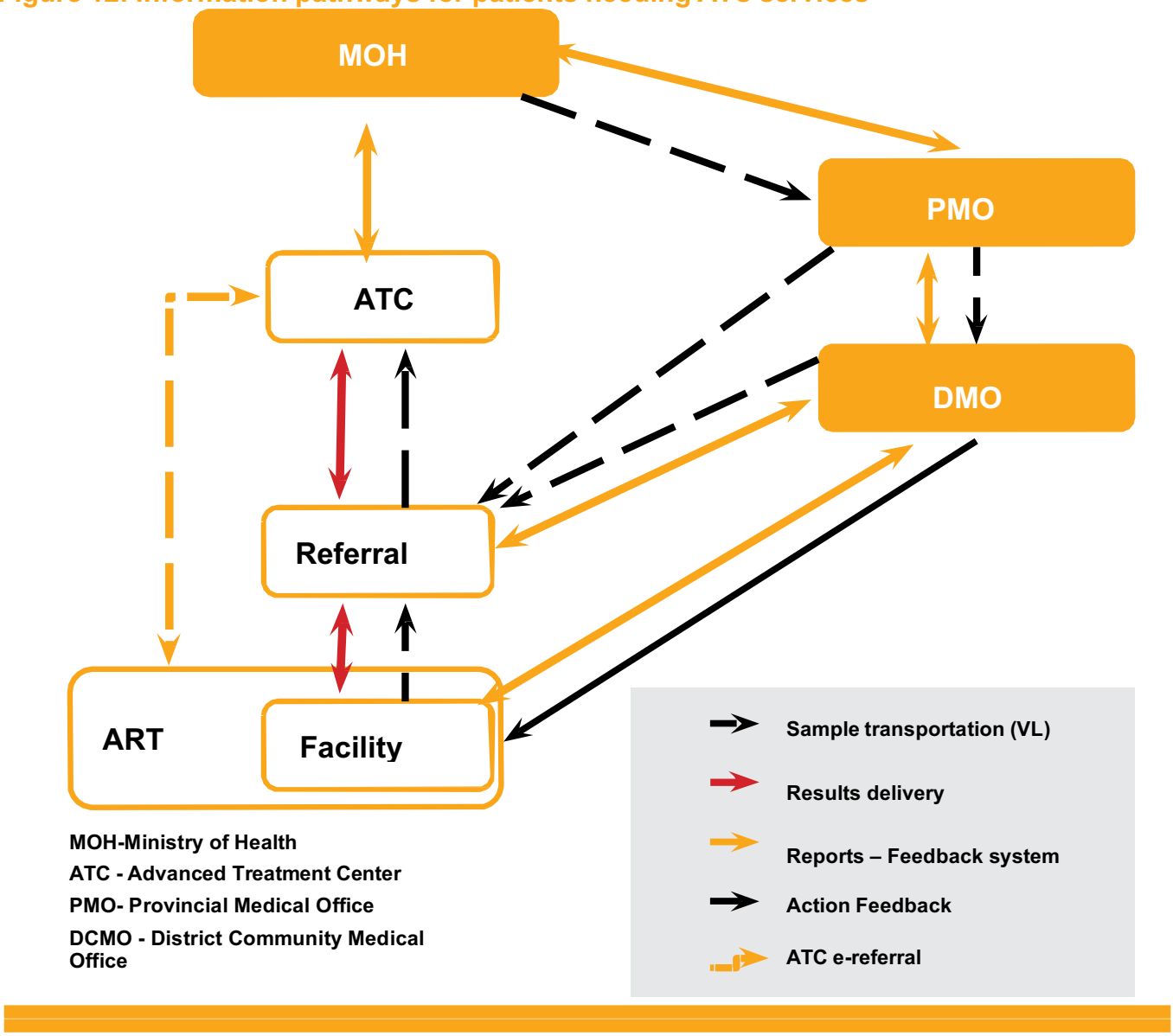
Continue the failing cART regimen unless there are intolerable toxicities or drug interactions. Even with treatment failure, the regimen is likely to have some residual antiviral activity. Stopping therapy in the setting of virologic failure can be associated with rapid falls in CD4 counts and development of OIs.

When to Consult or Refer the Next Level

The following criteria are indications to consult or refer to the next level:

- Suspected hepatotoxicity not responding to standard management (e.g. TB/HIV co-infection treatment, ALT/AST >5-fold of upper limit of normal)
- Second line treatment failure or inability to tolerate second-line therapy
- Complications on PI-based regimen
- Severe or life-threatening adverse reactions
- Inability to tolerate therapy despite change in regimen
- HIV-HBV co-infection with renal insufficiency

Figure 12: Information pathways for patients needing ATC services



Service Delivery

2016 Recommendations

- Diversify interventions to ensure timely linkage to HIV services
- Less frequent medication pick-ups [3-6 months) for stable patients
- Task-shifting of distribution of ART to stable patients

Following diagnosis and throughout the spectrum of care, HIV services must be tailored to accommodate the event-changing needs of patients. A package of support interventions should be offered to ensure timely linkage to care and follow up for all people living with HIV.

The differentiated care framework (Figure 13) is characterized by four delivery components: location of service delivery, infrastructure available, trained human resource to task shift services, logistic management of commodities and the need for monitoring and evaluation.

Figure 13: Framework for differentiated care

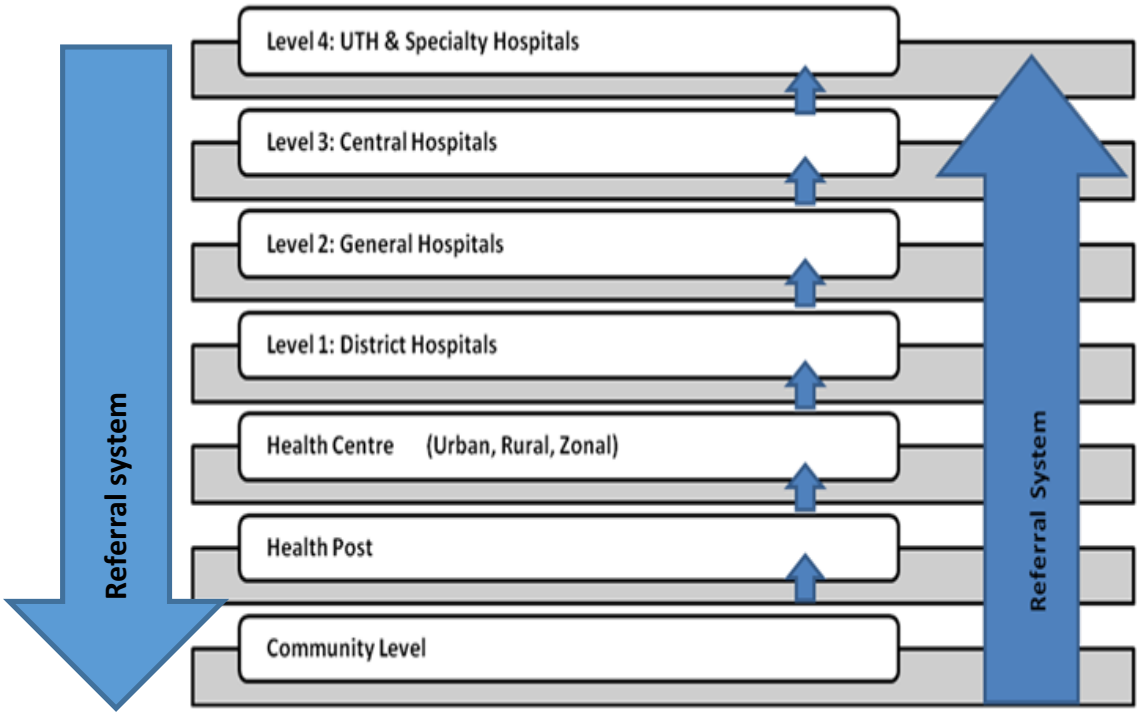


Table 29: Categorization of service offer at delivery points

<table>
<tr><td colspan="2">HIV/AIDs Management
• At facility level are “high risk,” i.e., Pregnant and breastfeeding women, HEI, discordant couples, newly diagnosed/initiated patients
• Community services to focus on “stable” patients</td></tr>
<tr><td>Community structures such as: Community Adherence Groups (CAGs), Treatment Clubs, Private sector, Faith based groups, Health shops, etc.</td><td>Facility: Health Centre, Level 1, Level 2, Level 3, and Level 4</td></tr>
<tr><td>Decentralization of Services</td><td>Diagnostic and Clinical Services</td></tr>
<tr><td>Retention in Care:
• PMTCT sites should have functional community structure/groups affiliated with timely support and connection between health facility and community
• Interventions of mother-baby follow up through reminders for appointments, adherence support
• Community workers and message on identifying sick infants and sending to facilities
• Use of current interventions to follow up patients and infants (e.g., nutritional assessment and DBS sample collection)

Task Shifting and Sharing:
• Less frequent clinical visits (3-6 months) being recommended for people stable on ART.
• The use of Community ART models for pick-up of ART, while initiation and monitoring at peripheral health facilities with maintenance at community level
• Trained and supervised community health workers can dispense ART between regular clinical vests</td><td>Health Centre:
• HIV testing at birth, 6 weeks, 6 months, 9 months, 12 months, 18 months, 24 months
• Triple prophylaxis (AZT, NVP, 3TC) till cessation of breastfeeding
• Co-trimoxazole (CTX) at 6 weeks
• Growth monitoring
• Immunization as per EPI schedule
• Clinical review and follow up
• Infant feeding counseling
• Ongoing HIV/AIDS counseling and screening.
• Uptake of newly diagnosed cases and commence ARVs
• Treatment of OIs as per Standard Treatment Guidelines
• Palliative care (pain relief and management of common illnesses)

Level 1:
• HIV testing at birth, 6 weeks, 6 months, 9 months, 12 months, 18 months, 24 months
• Dual prophylaxis (AZT, NVP) for 12 weeks
• Co-trimoxazole (CTX) at 6 weeks
• Growth monitoring
• Immunization as per EPI schedule
• Clinical review/examination
• FBC, CXR, HIV +/-CD4 count, U+E, Creatinine, urinalysis, treatment, and follow up management of OIs
• Infant feeding counseling If referred for further management, acceptance of referral back and joint management

Level 2:
• Management of severe symptoms and investigations
• Urine protein creatinine ratio
• FBC, LFTs, CXR, U/E & creatinine
• HIV +/-CD4 count

Level 3:
• VL and genotype for treatment failures
• Metabolic complications management
• Research 3rd line management
• Follow-up arrangements & referral back to home base agreed with patient and district or HC level</td></tr>
</table>

	Level 4:
	• HIV testing at birth, 6 weeks, 6 months, 9 months, 12 months, 18 months, 24 months
	• Dual prophylaxis (AZT, NVP) for 12 weeks
	• Highly specialized research
	• Complicated cases:
	  ▪ HIV plus co-morbidities
	  ▪ Renal issues
	  ▪ ARVs resistance
	  ▪ Drugs for salvage care

Community Involvement

2016 Recommendations

From acute to chronic care to allow for service delivery at the community level

Introduction of community cART for stable patients

To accommodate the growing number of stable individuals on ART and improve retention in care and health outcomes, innovative models of community ARV delivery have been developed and currently are being piloted.

The key points are to:

- Decentralize ART services to be more patient focused
- Improve retention in HIV care
- Less frequent clinical visits (3–6 months) are recommended for people stable on ART
- Less frequent medication pickup (3–6 months) is recommended for people stable on ART

Table 30: Community cART Objectives

Health service driven → Patient driven

Key objective	Appointment spacing and fast-track ARV refill	At enrolment into care		Community ART distribution points	Community ART groups
		Facility-based clubs	Community-based clubs		
Patient perspective					
Reduce costs (time and transport)	Yes	Yes	Yes	Yes	Yes
Increase peer support	No	Yes	Yes	Yes	Yes
Enhance community participation	No	Potentially	Potentially	Potentially	Yes
Health-care perspective					
Reduce workload					
Nurse	Yes	Yes	Yes	Yes	Yes
Pharmacist	Yes	Yes	No	Yes	Yes
Counsellor/health-care worker/peer supporter	N/A	No	No	No	No
Maintain and improve health care					
Retention	Yes	Yes	Yes	Yes	Yes
Improve self-management of patients	Yes	Yes	Yes	Yes	Yes

Nutritional Care

Nutrition in HIV-Infected Children

Routine assessment is essential to identify malnutrition and growth faltering early. The following should be done for HIV-infected infants and children:

- Assess nutritional status, diet, and symptoms at every visit
- Laboratory monitoring includes: total cholesterol, triglycerides, glucose, and Hb
- Assess WHO clinical stage, ask about history of recent diseases such as persistent diarrhoea or OIs (associated with increased nutritional need), determine energy needs, and provide additional energy
- Measure weight and height at each visit and plot against national growth curves
  - Normal growth
  - Underweight (weight-for-age <3rd %)
  - Stunted (height-for-age <3rd %)
  - Wasted (weight-for-height <3rd %)
- If normal child growth, inform on healthy eating and avoidance of obesity
- If poor child growth
  - Full dietary assessment is needed
  - Assessment of drug adherence if the child is on cART
  - Mothers or caregivers should be asked about food availability and food types offered to the child, as well as who feeds the child, how much, and how often
  - Children should be examined for signs of OIs or wasting
  - Provide appropriate clinical interventions (e.g., food support programmes)
- If severe malnutrition
  - Stabilize the acute phase of malnutrition, similar to HIV-uninfected children with severe malnutrition, and initiate cART soon after
  - Immediately initiate cART if unexplained malnutrition (e.g., not associated with untreated opportunistic infection [OI]) and does not respond to standard nutritional therapy
  - If unknown HIV status, test for HIV and consider cART initiation as needed
- If on cART, reassess frequently to adjust dose as needed. Recurrence of growth failure and severe malnutrition may indicate treatment failure, poor cART adherence, or OIs.
- Nutrition supplementation
  - Give high-dose vitamin A supplementation every 6 months for children 6 to <60 months old
  - Give zinc supplementation for acute diarrhoea
  - Mothers should exclusively breastfeed HIV-infected infants and young children for 6 months minimum and may continue up to 2 years old

Infant and Young Child Feeding

As a public health approach, all mothers should be encouraged to practice exclusive breastfeeding (EBF) for 6 months (Table 26). EBF is defined as giving a baby only breast milk and no other liquids or solids, not even water unless medically indicated. Thereafter, mothers should introduce nutritionally adequate complementary feeding while continuing breastfeeding up to at least 24 months old. Replacement feeding should only be considered if acceptable, feasible, affordable, sustainable, and safe (AFASS).

Table 31: Infant and young child feeding options

Maternal HIV status	Infant HIV status	Recommended Feeding	Timing of Complementary feeding	Recommended Timing of Complete Cessation of Breastfeeding*
Positive on cART	Negative or unknown	Exclusive breastfeeding (EBF) for 6 months Replacement feeding	After 6 months	At 12 months if food security assured Up to 2 years if food security not assured
Positive	Positive	EBF for 6 months		Up to 2 years
Negative or unknown	N/A	EBF for 6 months		Up to 2 years

*HIV-infected women should stop breastfeeding (at any time) gradually within one month.

Nutrition in HIV-infected Adolescents, Breastfeeding Women, and Adults

- Calculate the body mass index (BMI) = weight/height^2 to determine if the individual is underweight (<18.5kg/m^2), normal (18.5 to 24.9kg/m^2), overweight (25 to 29.9kg/m^2), or obese (≥30kg/m^2).
- If BMI <16kg/m^2 or anaemia (Hb <10g/dl) or has TB, refer for nutrition support programmes. Observe closely for treatment complications, such as re-feeding syndrome, undiagnosed OIs, and IRIS.
- If BMI >25kg/m^2, provide nutrition counseling, including dietary advice and need for physical exercise.
- Table 27 lists some the specific BMI-related ARV drug risks

Table 32: Specific BMI-related ARV drug risks

BMI	ARV drug	Associated Risks	Recommended Actions
<1kg/m^2	TDF	Tubular renal dysfunction Fanconi syndrome	Manage these patients with caution. Consult next level if necessary.
>25kg/m^2	AZT	Lactic acidosis Severe hepatomegaly with steatosis	
	d4T	Lactic acidosis Severe hepatomegaly with steatosis Acute pancreatitis	

Managing the HIV Programme

Tracking and Keeping Patients in Care

Keeping patients in care is essential for achieving good outcomes and preventing resistance. Lost to follow up (LTFU), defaulting and late drug picks may lead to treatment failure, emergence of resistance, and the possibility of transmitting resistant virus. Health facilities should aim to do the following to minimize LTFU:

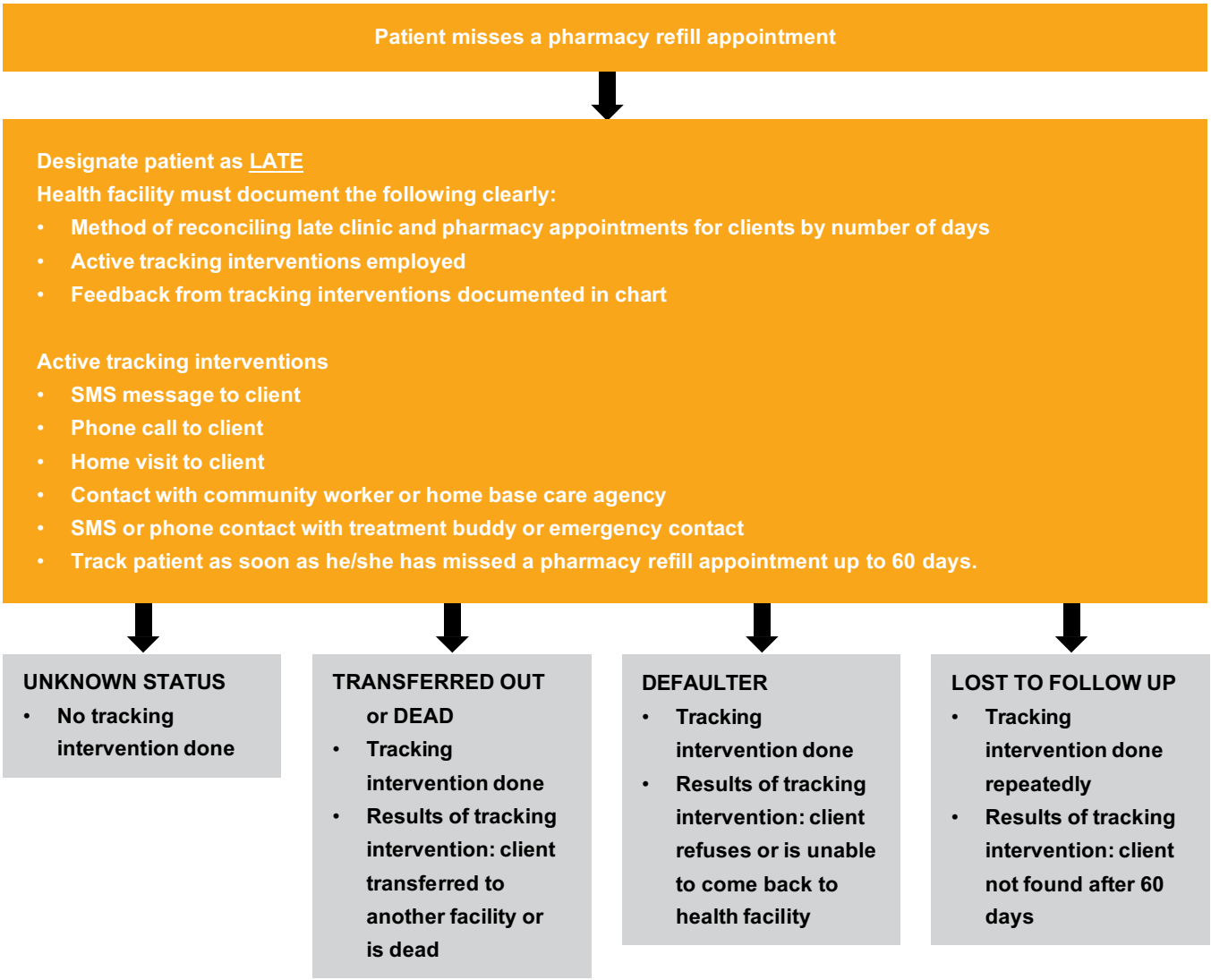
- Have a structured plan to track patients and prevent LTFU
- Monitor all missed clinic and pharmacy visits
- Create linkages with home-based care workers and volunteers
- Dedicate health facility staff to ensure patients who miss visits are contacted

Attrition

Attrition in an HIV programme can occur as the following: late, LTFU, defaulter, death, transferred out to another facility, or unknown status.

- Late: HIV-infected individual misses a pharmacy refill visit, from 1 to <60 days after the last scheduled pharmacy visit
    - For pregnant and breastfeeding women, late is defined as missing a scheduled pharmacy visit.
    - Take immediate action (e.g., CHW follow up, SMS or mobile health [mHealth] follow up) and document findings. Every effort must be made to re-engage these women in care.
- LTFU: HIV-infected individual is missing for ≥60 days after missed pharmacy refill visit after all active tracking interventions (e.g., documented physical follow up to home, phone calls to client and emergency contacts, SMS recall, treatment buddy) have been exhausted and HIV-infected individual cannot be traced.
    - For pregnant and breastfeeding women, LTFU is define as missing for ≥60 days after last scheduled pharmacy refill visit with inability to be traced after all active trackir mechanisms have been exhausted.
- Defaulter: HIV-infected individual has been located while la or LTFU, but chooses not to return to care.
- Unknown status: all active tracking interventions have not been exhaustively done to determine current status of HIV-infected individual (for ≥60 days), see Figure 14.

Figure 14: Algorithm for active interventions when HIV-infected clients are late and determining their attrition status



Structured Plan for Tracking Patients Supply Chain Management Systems (SCMS)

Ideally patients should be tracked as soon as possible after missed pharmacy pick up or clinic appointment. Each day that elapses after missed appointment could be a day without cART, and increasing the likelihood of resistance development and treatment failure. Scheduling patients for appointments and reviewing the list of patients expected on a given day is critical to tracking patients' missed appointments. If the facility does not schedule patients, then a clear log of pharmacy refills must be reviewed daily to identify patients that have missed pharmacy pickups and are potentially out of cART medications. Once a patient is identified as missing, a plan of action for tracking must be initiated.

Monitoring and Evaluation Tools

There are many government tools to assist sites in providing comprehensive, family-centred HIV care and treatment. The standard data collection and patient care tools include documents for children, adolescents, pregnant and breastfeeding women, and adults.

- Safe Motherhood Card (with SM number)
- cART file/clinical case record with cART number and SmartCard
- Antenatal Care register
- Safe Motherhood register
- L&D register
- Postnatal Care register
- Mother Baby Follow-up register
- Community Follow-up register
- Family Planning register
- Under five cards
- Under five registers
- Early Infant Diagnosis (EID) register/log book/EID lab requisition
- Laboratory register

Wherever feasible, data regarding the continuum of HIV care and treatment should be entered into electronic health record systems (e.g., SmartCare). In addition, all facilities should record birth defects using the forms obtainable from the Zambia Medication Regulatory Authority (ZMRA, formerly PRA) to feed into the national Birth Defects Registry.

Use of standard tools is required by all health facilities to ensure a functioning supply chain system to avoid stock outs. The recommended standard tools include:

- Report and Requisition (R&R) form
- Daily Activity Register
- Interval Monthly Summary Report
- Stock control cards
- Laboratory usage report
- Report for Essential Medicines and medical supplies

Quality Improvement

Quality improvement (QI) is a process that aims to strengthen the quality of services provided at health facilities. The QI Technical Working Group (TWG) at the MOH has identified five key QI indicators that will be tracked by all levels in the health sector. Of the five indicators, two are HIV-related:

- Percentage of exposed infants tested for HIV at 9 months old
- Percentage of all HIV positive clients retained on HIV care and treatment the last 12 months
    - Number of HIV testing sites scoring ≥80% in proficiency testing
    - Number of EID testing labs scoring ≥80% in proficiency testing
    - Number of viral load testing labs scoring ≥80% in proficiency testing

- Number of labs enrolled in the CD4 External Quality Assurance (EQA) program scoring ≥80% in proficiency testing

Lifelong cART in pregnant and breastfeeding women also enhances maternal and child survival. For this reason, the following two QI indicators are also pertinent:

- Number of maternal deaths at the facility recorded in the last 1 month, 3 months (quarter), and 12 months
- Number of under-five children who died in the last 1 month, 3 months (quarter), and 12 months. (If possible, differentiate between early neonatal death, neonatal death, infant death, and under-five death.)

Through structures that have been formed at all levels, the QI committees review these indicators regularly to identify performance gaps and root causes using the performance improvement approach (PIA). This should be followed by implementation of appropriate interventions coupled with regular monitoring and evaluation to track progress.

These indicators will be reported through the Health Management Information System (HMIS), as well as tracked through the QI reporting structures from the health facility to the national level QI TWG. QI committees at any level should not be restricted to implement QI projects only related to the key indicators. Other areas of underperformance in health service delivery should be covered at the local level as identified with stakeholders, including clients and the community.

Mentoring and Supervision

Mentorship is a QI strategy that provides motivation to HCWs while building their knowledge and skills base.
In collaboration with cooperating partners, the MOH developed national guidelines and a mentorship training package. The multi-disciplinary clinical care teams (CCT) at national, provincial, and district level spearhead mentorship and supervision of health facility staff. CCTs comprise clinicians, nurses, nutritionists, pharmacy staff, and laboratory staff and hold regular meetings to review HMIS reports, performance assessment reports, and any other source of information to identify performance gaps in health service delivery, including HIV care and treatment and PMTCT. Appropriate mentors are assigned from the CCT to conduct targeted, needs-based mentorship for QI. Request for specialized mentorship from higher level CCTs is encouraged. The multi-disciplinary approach achieves the following:

- Comprehensive coverage of clinical and support systems, including logistical and health information management
- Coordination, continuity, and availability of a pool of highly experienced mentors in the relevant fields
- Strengthened institutionalized, decentralized system of mentorship

Appendix 1

a) Dosages of Antiretrovirals for adults and adolescents

Drug	Normal Dose	Renal Dose
Abacavir (ABC)	Adult: 300mg BID PO Pediatrics: 8mg/kg 12 hourly PO	No adjustment
Atazanavir (ATV) + Ritonavir (RTV)	Adult: 300/100mg OD PO Pediatrics: see pediatric dosing by weight bands. No data for children <6 years old.	No adjustment
Darunavir + RTV	Adult: 600/100mg BID PO Pediatrics: see pediatric dosing by weight bands. Do not use in children <3 years old.	No adjustment
Efavirenz	Adults and adolescents 12-19 years: 400mg OD PO Adults/Adolescents 10-12 years on TB treatment, Pregnant and/or breastfeeding: 600mg OD PO Pediatrics: see pediatric dosing by weight bands.	No adjustment
Emtricitabine (FTC)	Adult: 200mg OD PO Pediatrics: 0-3 months old: 3 mg/kg/day (solution) 3 months-15years old (>33kg): 6mg/kg/day (solution; max 240mg daily) or capsule: 200mg OD (capsule)	Adult: CrCl 30-49: 200mg every 48 hours CrCl 15-29: 200mg every 72 hours CrCl <15: 200mg every 96 hours (give after hemodialysis if on dialysis) Pediatrics: reduce dose or increase dosing interval following adult recommendations in consultation with experienced clinician in renal dosing
Etravirine (ETR)	Adult: 200mg BID PO Pediatrics: see pediatric dosing by weight bands. Not approved for children <6 years old (approval under way for 2 months to 6 year old). • 16kg-<20kg: 100mg twice daily • 20kg-<25kg: 125mg twice daily • 25kg-<30kg: 150mg twice daily • ≥30kg: 200mg twice daily	No adjustment
Lamivudine (3TC)	Adult: 150mg BID or 300mg OD PO Pediatrics: 2-4mg/kg BID PO	Adults: CrCl 30-49: 150mg OD PO CrCl 15-29: 150mg x1 then 100mg OD PO CrCl 5-14: 150mg x 1 then 50mg OD PO CrCl <5: 50mg x1 then 25mg OD (50-75mg OD still acceptable) Pediatrics: reduce dose or increase dosing interval following adult recommendations in consultation with experienced clinician in renal dosing
Lopinavir-ritonavir	Adult: 400/100 BID PO Pediatrics: 10-13mg/kg BID PO for Lopinavir component	No dose adjustment, but use with caution in patients with CrCl <50
Nevirapine (NVP)	Adult: 200mg OD PO x 14 days then 200mg BID PO Pediatrics: 4-7mg/kg BID PO	No dose adjustment, but give dose after dialysis

Drug	Normal Dose	Renal Dose
Tenofovir (TDF)	Adult: 300mg OD PO Pediatrics: 8mg/kg OD PO	Same for adult & pediatrics: NOTE: Generally avoid when CrCl <50. Only adjust dose when sure that the CKD is independent of the drug in consultation with experienced clinician in renal dosing. CrCl 30-49: 300mg (8mg/kg) every 48 hours CrCl 10-29: 300mg (8mg/kg) twice weekly CrCl <10: consider 300mg (8mg/kg) OD PO (inadequate data) Hemodialysis: 300mg (8mg/kg) once weekly. To be given after dialysis. CAPD: no data
Raltegravir (RAL)	Adult: 400mg BID PO (with Rifampicin 800mg BID PO) Pediatrics: see pediatric dosing by weight bands.	No dose adjustment
Zidovudine (AZT)	Adult: 300mg BID PO Pediatrics: see pediatric dosing by weight bands.	CrCl 30-49: 300 BID PO CrCl 10-29: 300 BID PO CrCl <10: 300mg OD PO in consultation with experienced clinician in renal dosing

b) Simplified dosing of child-friendly fixed dose solid formulations for twice daily dosing for infants and children 4 weeks of age and older

Drug	Strength of Tablet (mg)	Number of Tablets by Weight Band morning and evening										Strength of Adult tablet (mg)	Number of Tablets by Weight Band	
		3.0-5.9 kg		6.0-9.9 kg		10.0-13.9 kg		14.0-19.9 kg		20.0-24.9 kg			25.0-34.9 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM
Zidovudine/Lamivudine AZT/3TC	Tablet (dispersible) 60mg/30mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300mg/150mg	1	1
Zidovudine/Lamivudine/Nevirapine AZT/3TC/NVP	Tablet (dispersible) 60mg/30mg/50mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300mg/150mg/200mg		
Abacavir/Lamivudine ABC/3TC	Tablet (dispersible) 60mg/30mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	600mg/300mg		
Abacavir/Lamivudine ABC/3TC	Tablet (dispersible) 120mg/60mg	0.5	0.5	0.5	1	1	1	1	1.5	1.5	1.5	600mg/300mg		

c) Simplified dosing of child-friendly fixed dose solid and oral liquid formulations for once daily dosing for infants and children 4 weeks of age and older

Drug	Strength of Tablet (mg)	Number of Tablets by Weight Band morning and evening					Strength of Adult tablet (mg)	Number of Tablets by Weight Band
		3.0-5.9 kg	6.0-9.9 kg	10.0-13.9 kg PM	14.0-19.9 kg PM	20.0-24.9 kg		25.0-34.9 kg
Efavirenz EFV	Tablet (scored) 200mg	-	-	1	1.5	1.5	200mg	2
Abacavir/Lamivudine ABC/3TC	Tablet (dispersible) 60mg/30mg/50mg	2	3	4	5	6	600mg/300mg	1
Abacavir/Lamivudine ABC/3TC	Tablet (dispersible) 120mg/60mg	1	1.5	2	2.5	3	600mg/300mg	1
Atazanavir ATV	Capsules 100mg	-	-	1	2	2	300mg	2 (100mg) or 1 (300mg)
Tenofovir TDF	Oral powder scoops 40mg/scoop	-	-	3	-	-	300mg	1 (200mg) or 1 (300mg)
	Tablet 150mg or 200mg	-	-	-	1 (150mg)	1 (200mg)		

d) Simplified dosing of child-friendly fixed dose solid and oral liquid formulations for twice daily dosing for infants and children 4 weeks of age and older

Drug	Strength of tablet (mg) or oral liquid (mg/ml)	Number of tablets or ml by weight band morning and evening										Strength of Adult tablet (mg)	Number of Tablets by Weight Band	
		3.0-5.9 kg		6.0-9.9 kg		10.0-13.9 kg		14.0-19.9 kg		20.0-24.9 kg			25.0-34.9 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM
Solid formulations														
Zidovudine AZT	Tablet (dispersible) 60mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300mg	1	1
Abacavir ABC	Tablet (dispersible) 60mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300mg	1	1
Nevirapine NVP	Tablet (dispersible) 50mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	200mg	1	1
Lopinavir/ritonavir LPV/r	Tablet 100mg/25mg	-	-	-	-	2	1	2	2	2	2	100mg/25mg	3	3
	Pellets 40mg/10mg	2	2	3	3	4	4	5	5	6	6	100mg/25mg	3	3
Darunavir DRV	Tablet 75mg	-	-	-	-	3	3	5	5	5	5			
Raltegravir RAL	Chewable tablets 25mg	-	-	-	-	3	3	4	4	6	6	400mg	1	1
	Chewable tablets 100mg	-	-	-	-	-	-	1	1	1.5	1.5	400mg	1	1
	Granules (100mg/sachet)	0.25	0.25	0.5	0.5	-	-	-	-	-	-			
Liquid formulations														
Zidovudine AZT	10mg/ml	6ml	6ml	9ml	9ml	12ml	12ml	-	-	-	-	-	-	-
Abacavir ABC	20mg/ml	3ml	3ml	4ml	4ml	6ml	6ml	-	-	-	-	-	-	-
Lamivudine 3TC	10mg/ml	3ml	3ml	4ml	4ml	6ml	6ml	-	-	-	-	-	-	-
Nevirapine NVP	10mg/ml	5ml	5ml	8ml	8ml	10ml	10ml	-	-	-	-	-	-	-
Lopinavir/ritonavir LPV/r	80/20mg/ml	1ml	1ml	1.5ml	1.5ml	2.0ml	2.0ml	2.5ml	2.5ml	3ml	3ml	-	-	-
Darunavir DRV	100mg/ml	-	-	-	-	2.5ml	2.5ml	3.5ml	3.5ml	-	-			

e) Drug dosing of liquid formulations for twice daily dosing for infants younger than 4 weeks of age

Drug	Strength of oral liquid (mg/ml)	2-3 kg	3-4 kg	4-5 kg
Zidovudine AZT	10mg/mL	1mL	1.5mL	2mL
Nevirapine NVP	10mg/mL	1.5mL	2mL	3mL
Lamivudine 3TC	10mg/mL	0.5mL	0.8mL	1mL
Lopinavir/ritonavir LPV/r	80/20mg/mL	0.6mL	0.8mL	1mL

f) Dosing of EFV for HIV-infected children (≥3 month old)

Body Weight	Daily Dose	Number of Capsules or Tablets and Strength
3.5 to <5kg	100mg	2 x 50mg capsules
5 to <7.5kg	150mg	3 x 50mg capsules
7.5 to <15kg	200mg	1 x 200mg capsule
15 to <20kg	250mg	1 x 200mg capsule + 1 x 50mg capsule
20 to <25kg	300mg	1 x 200mg capsule + 2 x 50mg capsules
25 to <32.5kg	350mg	1 x 200mg capsule + 3 x 50mg capsules
32.5 to <40kg	400mg	2 x 200mg capsules
≥40kg	600mg	1 x 600mg capsule OR 3 x 200mg capsules

Appendix 2

Key drug–drug interactions for antiretroviral drugs

	ABC	TDF	AZT	3TC	FTC	d4T	ATV	LPV	RTV	EFV	NVP	DTG	RAL
Antibiotics (incl. TB drugs)							1	2			3		
Rifampicin											4		
Rifabutin													
Antimalarial drugs													
Amodiaquine										5			
Artemisinin													
Halofantrine							6	7	8				
Antifungal													
Itraconazole											9		
Ketaconazole											10		
Antiretrovirals													
Efavirenz										11	12		
Etravirine							13						
Nevirapine													
Emtricitabine				14									
Zidovudine						15							
Lamivudine					16								
Stavudine			17										
Atazanavir											18		
Darunavir								19					
Lopinavir													
Abacavir													
Ritonavir													
Dolutegravir													
Gastrointestinal Agents													
Omeprazole							20						
Esomeprazole							21			22			
Lansoprazole							23						
Cardiovascular drugs													
Quinidine							24		25				
Statins							26	27	28				
Amlodipine													
Enalapril													
Hydrochlorothiazide													
Anticonvulsants													
Carbamazepine												29	
Phenytoin												30	

Appendix 3

WHO toxicity estimates

Grade (Severity)	Characteristics	Management
1 (mild)	Transient or mild discomfort, no limitation in activity, no medical intervention needed	Does not require change in therapy Symptomatic treatment may be given
2 (moderate)	Limitation in activity, some assistance may be needed, no or minimal medical intervention or therapy required	Consult Continue cART if possible If no improvement, consider substitution with a drug in the same ARV class, but with a different toxicity profile
3 (severe)	Marked limitation in activity, some assistance usually required, medical intervention required, possible hospitalization	Refer or consult Substitute the offending drug without stopping therapy
4 (life-threatening)	Extreme limitation in activity, significant assistance required, significant medical intervention or therapy required, hospitalization or hospice care	Discontinue all ARV drugs, manage the medical event until patient is stable and toxicity has resolved

Appendix 4

Co-trimoxazole desensitization protocol for adolescents and adults

Time Point	Dose for desensitization
Day 1	80mg SMX/16mg TMP (2ml of oral suspension)
Day 2	160mg SMX/32mg TMP (4ml of oral suspension)
Day 3	240mg SMX/48mg TMP (6ml of oral suspension)
Day 4	320mg SMX/64mg TMP (8ml of oral suspension)
Day 5	1 single-strength SMX/TMP tablet (400mg SMX/80mg TMP)
Day 6 onward	2 single-strength SMX/TMP tablets or one double strength tablet (800mg SMX + 160mg TMP)

Oral suspension is 40mg TMP/200mg SMX per 5ml of syrup

Appendix 5

Positive Health Dignity and Prevention (PHDP)

To have a significant effect on slowing the spread of the epidemic, prevention efforts must also be directed toward HIV-infected individuals who can transmit the virus.

Deliver consistent, targeted prevention messages and strategies during routine visits

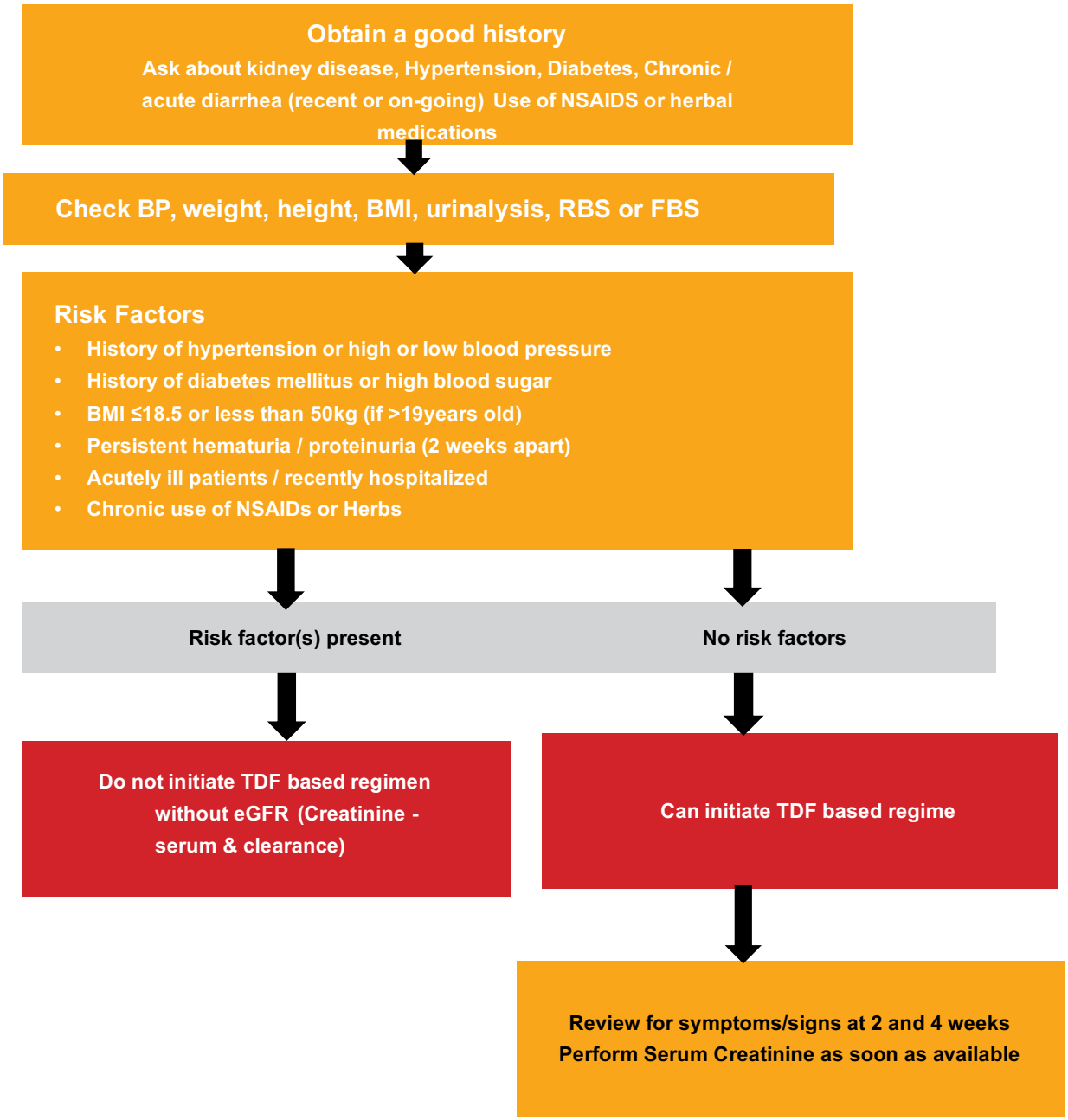
- At every visit, assess for and counsel regarding:
  - High risk sexual activity
  - Partner's and children's HIV status
  - Disclosure to partner/guardian/treatment supporter
  - Signs and symptoms of STIs and cervical cancer
  - Pregnancy status
  - Adherence to cART and other medications
  - Abuse of alcohol and other substances
  - Positive living (nutrition, alcohol and smoking cessation)

Six (6) key steps for PHDP

- Step 1: Give risk reduction messages to every patient at every visit
- Step 2: Assess adherence to ARVs
- Step 3: TB and STI screening and management
- Step 4: Family planning services and safer pregnancy counseling
- Step 5: Give patient condoms at every visit
- Step 6: Partner HIV testing

Appendix 6

Renal insufficiency screening algorithm (in the absence of Creatinine test)



Appendix 7

Formulae for calculating Creatinine Clearance in different patient populations

IN CHILDREN (5-19 years) GLOMERULAR FILTRATION RATE (SCHWARTZ)

- Clinical use: A simple estimate of glomerular filtration rate in children derived from body length and serum creatinine.
- Formula:

$$\text{Creatinine Clearance} = \frac{(k \times \text{height})}{\text{Creatinine}}$$

- Units:

Creatinine: [mg/dL]
mg/dl=88.4µmol/L
Height: [cm]

k, Constant as follows:
0.55 for children (<10 years) and adolescent girls
0.7 for adolescent boys

- **For Women**
  CrCl=(140-age) (weight in kg) (0.85) / 72 x serum Creatinine (mg/dl)

OR

CrCl=(140-age) (weight in kg) (0.85) / 0.815 x serum Creatinine (µmol/l)

ADULTS (>19 years)

- **For men**
  CrCl=(140-age) (weight in kg) / 72 x serum Creatinine (mg/dl)

OR

CrCl=(140-age) (weight in kg) / 0.815 x serum Creatinine (µmol/l)

Glossary

Combination antiretroviral therapy (cART)**:** Use of antiretroviral regimens consisting of a combination of at least three or more drugs from at least 2 classes

Body Mass Index: A measure of body fat based on one's weight in relation to height

Co-trimoxazole Preventive Therapy (CPT)**:** Use of co-trimoxazole to prevent opportunistic infections in susceptible Persons Living With HIV/AIDS (PLWHA)

Creatinine Clearance (CrCl): An estimation of mills of blood filtered by the kidneys per minute

Directly Observed Therapy Short Course (DOTs): refers to the WHO-recommended strategy for TB control and involves direct observation of patients taking TB medications. This is done to ensure that the patient takes the right medicines, in the right doses, at the right intervals.

Focused Antenatal Care (FANC)**:** A standard package of basic ANC services that all pregnant women should receive. FANC emphasizes the importance of developing a plan of care that meets each woman's individual needs.

HIV Testing Services (HTS): Refers to the full range of services provided with HIV testing, including counseling; linkage to appropriate HIV prevention, treatment, and care, and other clinical services; and coordination with laboratory services to ensure delivery of accurate results

Isoniazid Preventive Therapy (IPT): Use of Isoniazid for prophylaxis to susceptible patients to offer protection against Mycobacterium TB

Immune Reconstitution Inflammatory Syndrome (IRIS): An exaggerated inflammatory reaction from a re-invigorated immune system

National Unique Patient Number (NUPN): A unique client identification number used in SmartCare patient records system

Nucleic Acid Testing (NAT): Virological testing technology used for early infant HIV diagnosis developed and validated for use at the point of care

Polymerase Chain Reaction (PCR): A test done to detect HIV specific genetic material that indicates presence of HIV. In Zambia, through the use of Dry Blood Spot (DBS) specimen, this test diagnoses HIV infection in children below 18 months of age.

Positive Health Dignity and Prevention (PHDP): An HIV prevention strategy among PLWHA that focuses on: risk reduction, ART adherence, correct condom use, family planning, STI screening, and partner HIV testing

Pre-exposure Prophylaxis (PrEP): An HIV prevention strategy were those at high risk of acquiring HIV are covered on prophylactic ARVs before exposure to the HIV virus

Post-exposure Prophylaxis (PEP): Short term antiretroviral treatment to reduce the likelihood of HIV infection after potential exposure to the virus

Treatment as Prevention (TasP): Refers to use of antiretroviral therapy in PLWHA to decrease the risk of HIV transmission to others

Treat All: WHO recommendation that all clients testing HIV positive should be initiated on cART irrespective of their WHO Clinical staging, CD4 or Viral load levels

Visual Inspection with Acetic acid: A cervical cancer screening method done using acetic acid