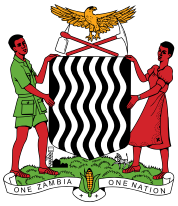
Zambia Consolidated Guidelines
for Treatment and Prevention of HIV Infection



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for Treatment and Prevention of HIV Infection

February 2014

Contents

Abbreviations & 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	azidovudine (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)
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
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
HTC	HIV testing and counselling
INH	isoniazid
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)
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
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)
-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

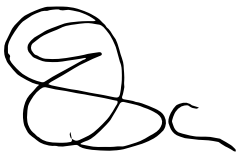
Foreword

Zambia has had an effective treatment and prevention HIV/AIDS response for over a decade now. During this time systems have been strengthened and access to care has been provided to many Zambians. The HIV epidemic is a significant challenge to many communities but strategies have been devised and implemented to curb and mitigate the effects of the disease. Zambia has made tremendous strides to begin to bring under control and start reversing the scourge of HIV. As a nation we are more resolute to reduce the number of new infections in adults and children. Since 2001, Zambia has recorded significant change in reducing risk behaviour such as reduction in early debut of sexual activity, reduction in multiple sexual partnership and increased consistent use of condoms during high risk sex. We have scored success in reducing the number of new infections in adults and children.

Interventions to scale up HIV prevention and treatment have resulted in improving the quality of care for HIV infected individuals. The 2013 Zambian Consolidated Guidelines recommend comprehensive approaches to reducing new HIV infections, preventing mother to child transmission, and provision of lifelong combination antiretroviral therapy. The 2013 Zambian Consolidated Guidelines are evidence based and bring all the key HIV prevention and treatment disciplines in one harmonious and simple document. The new guidelines have expanded eligibility criteria. This will bring us closer to providing treatment and care to nearly all individuals infected with HIV (the test & treat and the treatment as prevention models). The guidelines are simpler and more standardised than ever before to allow as many providers as possible to provide health care to many Zambians. The simplification and standardisation will make it possible to provide high quality care in the most efficient and cost effective manner. Prevention and treatment will be provided in a timely and non–discriminatory manner to all populations whilst respecting all the rights of patients.

The new guidelines set a high standard of care. They demand diligence from both the provider (professional and lay) and the patient. Community and health systems must be strengthened, patient management must improve. High levels of retention in care and adherence to treatment will be essential for us to triumph over HIV. The Government of the Republic of Zambia is fully committed to providing its citizenry equitable access to cost effective and quality health care, as close to the family as possible.

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



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Summary

The *Zambia 2013 HIV Consolidated Guidelines* provide guidance on the diagnosis of HIV infection, care of people living with HIV, and use of antiretroviral drugs for treating and preventing HIV infection. They are structured along the continuum of HIV prevention, testing, treatment, and care. Comprehensive guidance is now provided on using antiretroviral drugs among the different populations of pregnant and breastfeeding women, children, adolescents, and adults.

The *2013 HIV Consolidated Guidelines* are based on a public health approach to expand the use of antiretroviral drugs for HIV treatment and prevention. The clinical recommendations in these guidelines include:

- Starting lifelong triple combination ART (cART) in the following HIV-infected individuals:
  - All confirmed HIV-infected children and adolescents <15 years old regardless of CD4 count and/or World Health Organization Clinical Stage (WCS)
  - Adolescents ≥15 years old and adults with CD4 count ≤500 cells/mm^3 regardless of WCS

- Starting lifelong triple combination ART regardless of CD4 count and WCS in:
  - Pregnant & breastfeeding women
  - HIV-infected sexual partners of pregnant & breastfeeding women
  - HIV-infected partners in serodiscordant couples
  - Patients with active tuberculosis (TB) disease
  - Patients with hepatitis B virus (HBV) co-infection with severe liver disease

- New, preferred, simplified first-line cART regimen (TDF + XTC + EFV) harmonized for pregnant & breastfeeding women, children >5 years old, adolescents, and adults

- Accelerating the phasing out of stavudine (d4T) and zidovudine (AZT) in first-line cART regimens for all populations

- Viral load testing as the preferred approach to monitoring cART and diagnosing treatment failure, in addition to immunological and clinical monitoring

- Community-based HIV testing and counselling to diagnose early people infected with HIV and link them to care and treatment

- Use of lifelong ART as prevention
  - For all pregnant and breastfeeding women to prevent mother to child transmission
  - Reduce transmission of HIV to uninfected sexual partners

Introduction

In June 2013, the World Health Organisation released the 2013 Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection, from which these guidelines have been adapted. These guidelines reflect an integrated approach to HIV prevention and treatment, unlike the 2010 standalone Adult ART, Paediatric ART, and PMTCT guidelines. Furthermore, these guidelines combine evidence-based recommendations that apply to all aspects of HIV prevention and treatment.

With regard to PMTCT, life-long treatment for all HIV-infected pregnant and breastfeeding women and their HIV-infected sexual partners has been adopted for Optimal Survival and Prevention (OSAP). Whereas previous national guidelines focused on prophylactic options for preventing vertical transmission of HIV, these guidelines are based on the concept of treatment as prevention (TasP) with the goals of keeping the mother alive, protecting future pregnancies, reducing risk of transmission to partners, and achieving elimination of mother-to-child transmission of HIV (EMTCT). These guidelines embrace the four prongs of PMTCT: primary prevention of HIV, prevention of unintended pregnancies among HIV-infected women, prevention of HIV transmission from mothers to their babies, and care and support to HIV-infected families.

These guidelines aim to place more children on treatment by expanding eligibility criteria: all children under 15 years old 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 and counselling (HTC) 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.

In adult HIV management, there is expansion of the eligibility for cART from the threshold of 350 cells/mm^3 to 500 cells/mm^3. There has been introduction of an alternative protease inhibitor: atazanavir boosted with ritonavir. These guidelines also highlight the management of patients failing 2nd line ART with 3rd line ART, who should be managed at higher level health facilities called Advanced Treatment Centres (ATCs).

HIV Testing & Counselling

HIV testing and counselling (HTC), regardless of the model of service delivery, must adhere to the five Cs: consent, confidentiality, counselling, correct test results, and linkage to care.

- Individuals must give informed **consent** for HTC 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.
- HTC services are **confidential**.
- HTC includes appropriate, high quality pre-test information and post-test **counselling**.
- HTC includes provision of **correct** test results.
- HTC should provide linkages to **care**, prevention, and treatment services by issuance of a National Unique Patient Number (NUPN) regardless of test result.

HTC should be done at all service delivery points (see table 1) within the facility, as well as in the community. 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). For children <12 months old who are breastfeeding, the woman should be tested first. If she is HIV positive, perform a virologic (DNA PCR) test on the HIV-exposed infant (HEI), regardless of age. If this dried blood spot (DBS) test cannot be done in the community, refer the HEI to the nearest health facility for virologic testing. All individuals being tested for the first time should re-test after 3 months (to account for the window period). At health facilities, quality assurance should be conducted on 10% of all community referred patients.

Table 1: Timing of HIV testing and counselling 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. Test at 6 weeks if negative. If breastfeeding: repeat test every 3 months if negative Partner testing: same time points	Serologic test
Children (0 to <10 years old)	Well, non-breastfed HIV-exposed infant (HEI)	6–8 weeks old	Virologic (DNA PCR) test
		18 months old	Serologic test; follow with virologic (DNA PCR) test for positive serologic child <18 months old
	Well, breastfed HEI	6–8 weeks old	Virologic (DNA PCR) test
		6 months old	Virologic (DNA PCR) test
		12 months old	Serologic test; follow with virologic (DNA PCR) test for positive serologic child
	Infant or child who has completely stopped breastfeeding	18 months old and/or ≥6 weeks after breastfeeding cessation	Serologic test; follow with virologic (DNA PCR) test for positive serologic child <18 months old
	Asymptomatic infant with unknown HIV exposure	At first contact, as early as 6 weeks old	Maternal serologic test and/or infant serologic test; follow with virologic (DNA PCR) test for positive serologic child <18 months old
	Infant or child symptomatic for HIV infection	Immediately regardless of age	Serologic test; follow with virologic (DNA PCR) test for positive serologic child <18 months old
	Positive serologic child <18 months old	At first contact	Virologic (DNA PCR) test

Specific populations	Whom to test	When to test	HIV testing
Adolescents (10 to <15 years old)	All with their sexual partners	At first contact and every 6 months	Serologic test
Adolescents (15 to <20 years old)	Pre-marital, after separations, new partnerships		
Adults	Any person of unknown HIV status		

HIV-negative pregnant and breastfeeding women should be tested more often because women who have recently seroconverted have high levels of viremia, and frequent testing will identify those at highest risk for transmitting HIV to their children.

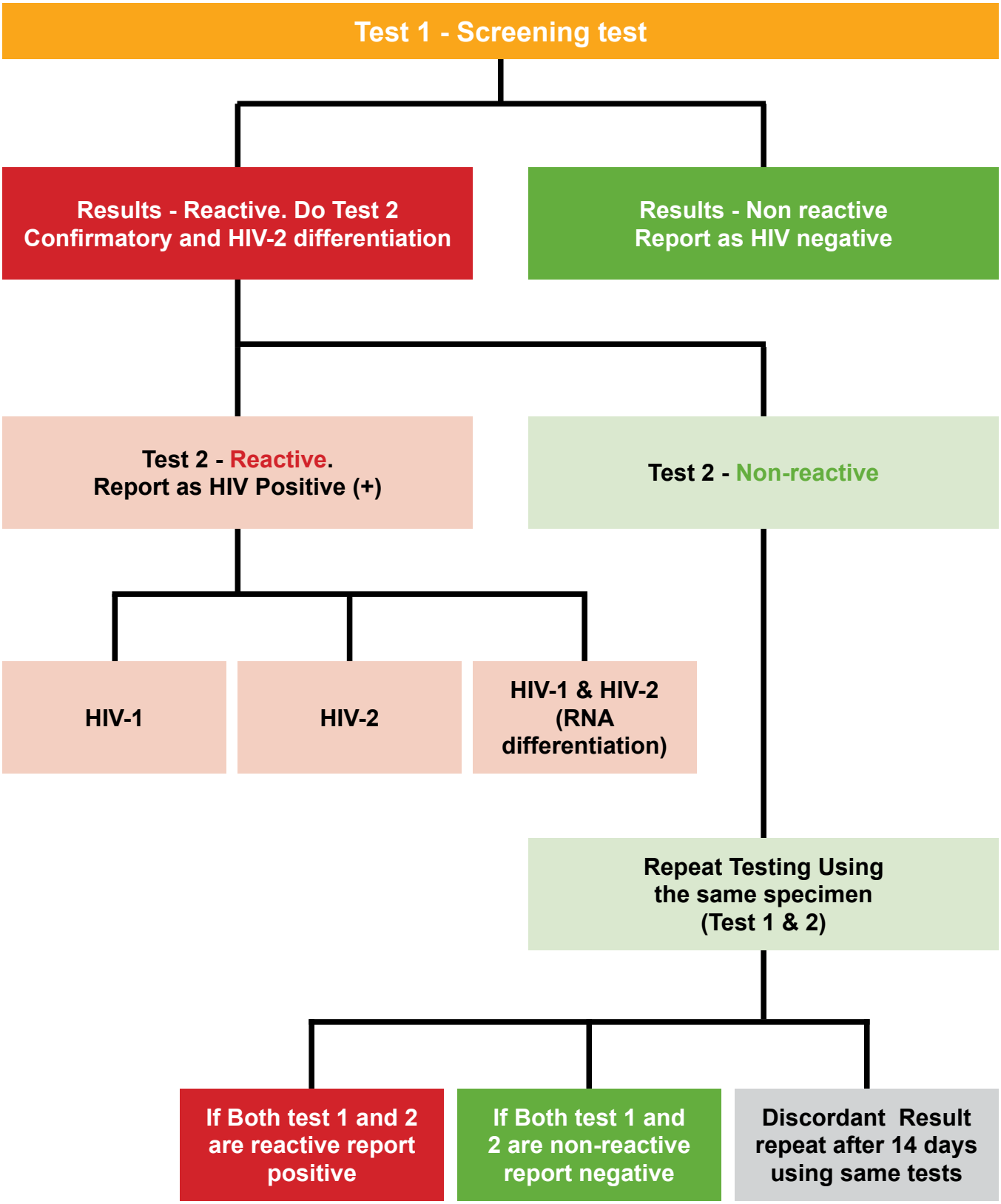
Infants born to HIV-infected women who are not breastfeeding need be tested for HIV at 6 weeks old and, if negative, again at 18 months old to confirm their status. Infants who stop breastfeeding before 12 months old should be tested at ≥6 weeks after breastfeeding cessation and, if HIV negative, again at 18 months old to confirm their status.

For an initial positive virologic test, start cART without delay and repeat virologic (DNA PCR) test immediately (on the same day) to confirm. Ideally, repeat blood samples should be labelled as such so that the laboratory can link the repeat blood sample with the first test.

For discrepancies in the repeat virologic test result, continue cART and collect a third virologic test (labelled as such); results of the third sample will be considered the final status.

Delaying cART in an HIV-infected child significantly increases morbidity and mortality, and the benefits of cART in an HIV-infected child outweigh its risks in an HIV-uninfected one. In all cases, except for presumptive diagnosis of HIV infection in HEIs, there should be clear documentation of HIV positive test results prior to cART initiation.

Figure 1: HIV serologic testing algorithm



Management of HIV Exposed Infants

Maternal cART coupled with infant ARV prophylaxis significantly reduces the risk of MTCT. HIV exposed infants (HEIs) whose mothers are on cART should receive NVP from birth until they are 6 weeks old (table 2 and 3). Dosages for NVP are listed below in table 4.

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 virologic testing
Known HIV positive woman on cART before ANC or starts cART in ANC	Continue cART	NVP until 6 weeks old Virologic testing per Figure 2
Woman with an HIV positive test in ANC and starts cART in ANC	Continue cART	
Woman with unknown antenatal HIV status who has an HIV positive test in L&D	Start cART	

Specific guidance is given for the following:

- HIV-infected women who deliver at home and present to health facilities after 72 hours;
- Maternal HIV seroconversion (documented negative status with subsequent HIV positive test); and
- Severe HIV disease

The latter two conditions are associated with very high risks of MTCT. Thus, provide NVP to the breastfed infant for **6 months** to allow time for cART to suppress high levels of maternal viremia to undetectable.

Table 3: HEI ARV prophylaxis in complicated cases

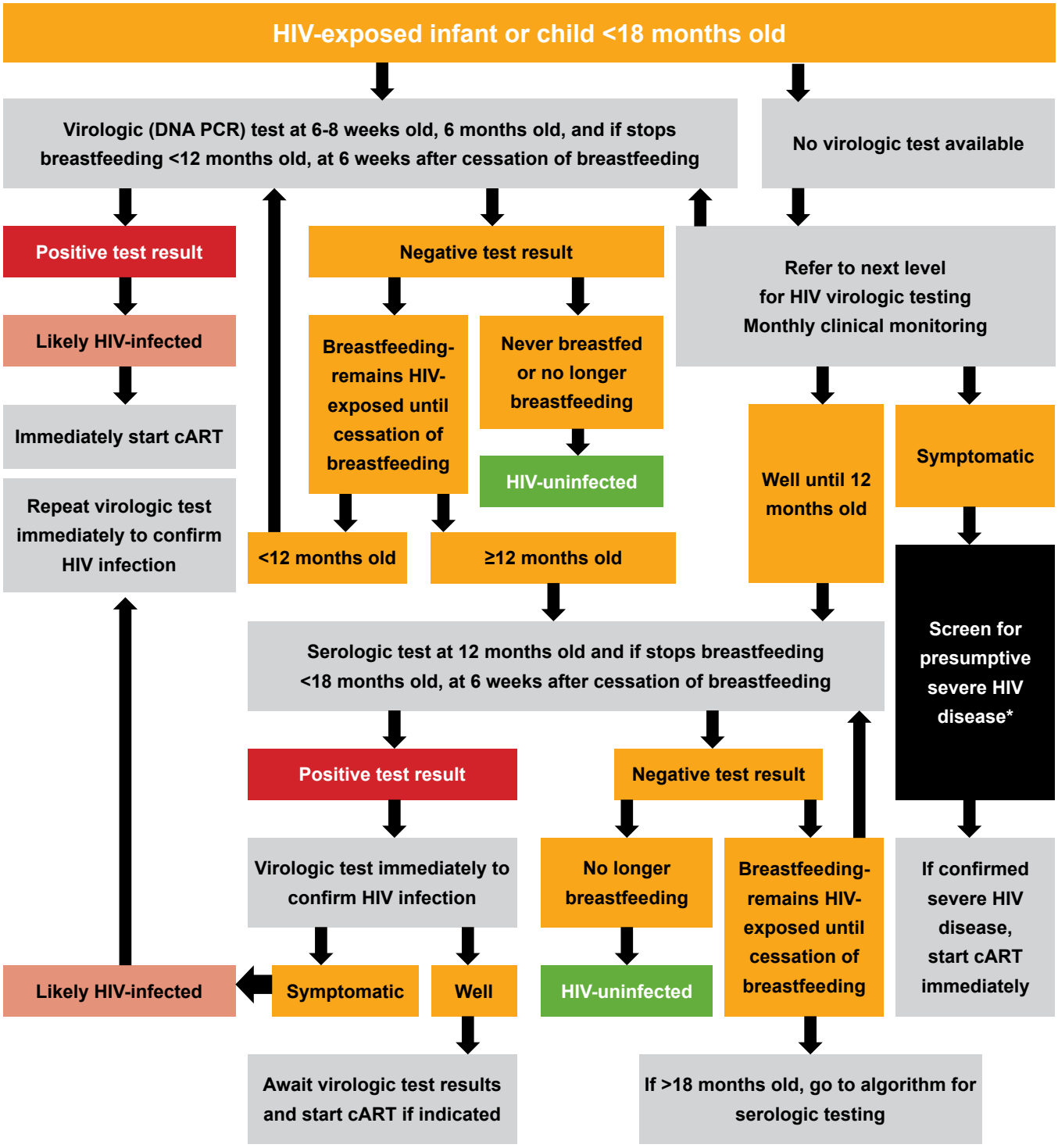
Case scenario	Management of the mother at delivery and in Postnatal Care (PNC)	Infant ARV prophylaxis and virologic testing
Woman with an HIV positive test in ANC who starts cART in ANC and has a home delivery. Infant does not receive NVP at birth but presents >72 hours after birth.	Continue cART	NVP until 6 weeks old Virologic (DNA PCR) testing immediately unless <6 weeks old
Woman with unknown antenatal HIV status who has a home delivery and has an HIV positive test in postnatal clinic >72 hours after delivery	Start (or switch to) cART	NVP for 6 months (if breastfeeding) Virologic (DNA PCR) testing immediately and repeat testing at 6 weeks old per schedule if negative
Woman with an HIV negative test in ANC and has an HIV positive test in L&D or during breastfeeding period*		
Woman not on cART with Stage III or IV disease*		
Woman with CD4 >350 cells/mm^3 on AZT in ANC		

For scenarios not found in Tables 2 and 3 above, consult the next level or refer.

Table 4: Extended simplified infant NVP dosing recommendations

Infant age	NVP dosing (mg)	NVP dosing (ml) (NVP concentration of 10 mg/ml)
Birth to <6 weeks old Birth weight <2,000 g Birth weight 2,000 - 2,499 g Birth weight ≥2,500 g	 8 mg once daily 10 mg once daily 15 mg once daily	 0.8 ml once daily 1.0 ml once daily 1.5 ml once daily
6 weeks old to <6 months old	20 mg once daily	2.0 ml once daily
6 to <9 months old	30 mg once daily	3.0 ml once daily
9 months old to 1 week after cessation of breastfeeding	40 mg once daily	4.0 ml once daily
Reference: Mirochnick Metal, 2006		

Figure 2: Algorithm for HIV virologic testing in children <18 months old



*Presumptive clinical diagnosis of HIV infection is done in infants and children <18 months old where there is no access to virologic testing, 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 2 or more of the following: oral thrush, severe pneumonia, severe sepsis, or has any Stage 4 condition

All HEIs should start CTX at ≥6 weeks old and stop after final HIV testing is negative (After cessation of breastfeeding)

Managing HIV Infected Populations

Management of HIV-infected individuals may start at different service delivery points within the facility and will promote a family-based approach. Nurses and midwives (table 5) with appropriate training will be able not only to perform HIV testing and counselling, but also to initiate 1st line cART when specific populations have positive test results in MNCH and other non-ART clinics. In addition, HIV Nurse Prescribers (HNPs) and clinical officers with appropriate training and in consultation are encouraged to initiate 2nd line as needed.

Table 5: 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 2nd 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 2nd line treatment failure

In order to improve cART initiation (see figure 3) and adherence, counselling 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

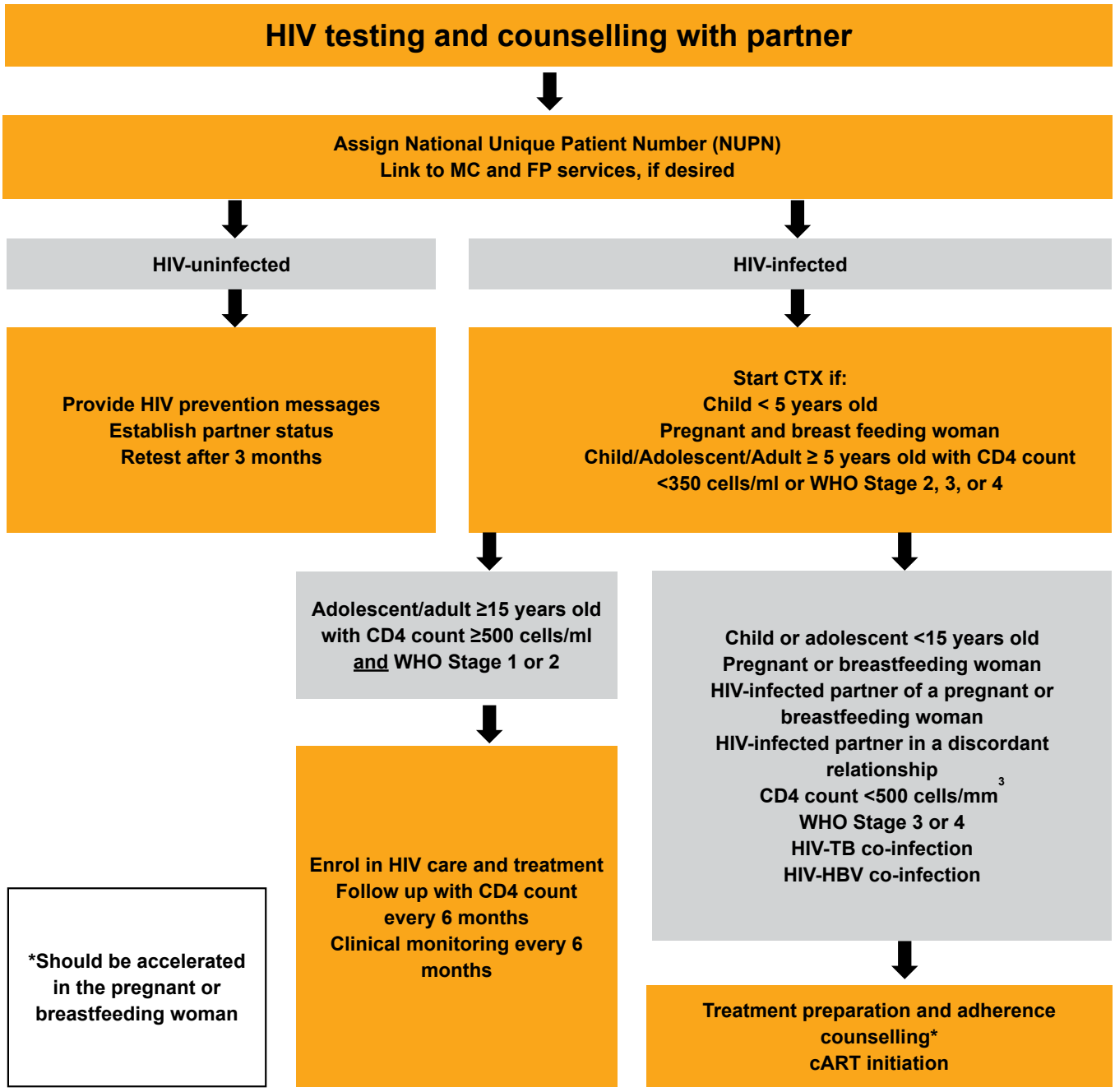
High levels of adherence to cART are needed to attain these objectives.

Table 6 lists the eligibility criteria for HIV infected patients.

Table 6: Eligibility criteria for cART initiation in children, adolescents, pregnant & breastfeeding women, and adults

Specific populations	Description
Pregnant & Breastfeeding Women	Regardless of WHO Clinical Stage or CD4 count
Children (0 to <10 years old)	
Adolescents (10 to <15 years old)	
Adolescents (15 to <20 years old)	CD4 count ≤500 cells/mm^3 WHO Clinical stage 3 or 4 HIV-infected sexual partners of pregnant & breastfeeding women HIV-infected sexual partners in serodiscordant couples Patients with active TB disease and HIV co-infection Patients with hepatitis B virus (HBV) and HIV co-infection with severe liver disease
Adults	

Figure 3: Flow diagram for HIV care and treatment from HIV testing to cART initiation



WHO Clinical Staging

Staging (table 7) is based on clinical findings that guide the diagnosis, evaluation, and management of HIV and does not require a CD4 count.

Table 7: WHO clinical staging of HIV disease by specific populations

Children (0 to <10 years old) Adolescents (10 to <15 years old)	Adolescents (15 to <20 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[b] not adequately responding to standard therapy *Unexplained persistent diarrhoea (14 days or more)* *Unexplained persistent fever (above 37.5°C, intermittent or constant, for > 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 (<8 g/dl), neutropaenia (<0.5 x 10^9/l) or chronic thrombocytopaenia (<50 x 10^9/l)* *Symptomatic lymphoid interstitial pneumonitis* *Chronic HIV-associated lung disease, including bronchiectasis*	*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 (<8 g/dl), neutropaenia (<0.5 x 10^9/l) and/or chronic thrombocytopaenia (<50 x 10^9/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 malnutritiond not responding to standard therapy *Pneumocystis (jirovecii) pneumonia* *Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)* *Chronic herpes simplex infection (orolabial or cutaneous of more than 1 month's duration or visceral at any site)* *Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)* *Extrapulmonary tuberculosis* *Kaposi sarcoma* *Cytomegalovirus infection (retinitis or infection of other organs with onset at > 1 month old)* *Central nervous system toxoplasmosis (after the neonatal period)* *HIV encephalopathy* *Extrapulmonary cryptococcosis, including meningitis* *Disseminated nontuberculous mycobacterial infection* *Progressive multifocal leukoencephalopathy* *Chronic cryptosporidiosis (with diarrhoea)* *Chronic isosporiasis* *Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidioidomycosis, penicilliosis)* *Cerebral or B-cell non-Hodgkin lymphoma* *HIV-associated nephropathy or cardiomyopathy*	*HIV wasting syndrome* *Pneumocystis (jirovecii) pneumonia* *Recurrent severe bacterial pneumonia* *Chronic herpes simplex infection (orolabial, genital or anorectal of more than 1 month's duration or visceral at any site)* *Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)* *Extrapulmonary tuberculosis* *Kaposi sarcoma* *Cytomegalovirus infection (retinitis or infection of other organs)* *Central nervous system toxoplasmosis* *HIV encephalopathy* *Extrapulmonary cryptococcosis, including meningitis* *Disseminated nontuberculous mycobacterial infection* *Progressive multifocal leukoencephalopathy* *Chronic cryptosporidiosis* *Chronic isosporiasis* *Disseminated mycosis (extrapulmonary histoplasmosis, coccidioidomycosis)* *Lymphoma (cerebral or B-cell non-Hodgkin)* *Symptomatic HIV-associated nephropathy or cardiomyopathy* *Recurrent septicaemia (including nontyphoidal Salmonella)* *Invasive cervical carcinoma* *Atypical disseminated leishmaniasis*

Reference: WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children, 2006

1st Line cART: Which cART Regimen to Initiate

Providing an optimized, fixed-dose cART regimen of TDF + XTC + EFV to children ≥5 years old, pregnant and breastfeeding women, and adults provides important programmatic and clinical benefits, including ease of implementation, harmonized regimens, patient and provider acceptability, increased coverage of cART, reduced vertical transmission, improved maternal health, and STIs prevention. Adherence to cART is essential to achieve these benefits. Table 8 and 9 give the preferred and alternative regimens for various populations.

Table 8: Preferred 1st line cART and alternative regimens by specific populations

Specific Populations	Description	Preferred 1st line cART	Alternative regimen
Pregnant & Breastfeeding Women	First-line	TDF + XTC + EFV	TDF + XTC + NVP† or ABC + 3TC + EFV
	Previous sd-NVP exposure; or NVP Mono-therapy exposure (NVP without 7 days of AZT + 3TC cover); or Unsure of tail coverage	TDF + XTC + LPV-r	TDF + XTC + ATV-r
Children (6 weeks to <3 months old)	First-line Maternal sd-NVP exposure; or Maternal NVP mono-therapy exposure (NVP without 7 days of AZT + 3TC cover); or Mother unsure of tail coverage	AZT + 3TC + LPV-r	After 3 months substitute to preferred 1st line with ABC + 3TC + LPV-r
Children (3 months to <5 years old)	First-line	ABC + 3TC + LPV-r	AZT + 3TC + LPV-r After 5 years substitute to preferred 1st line with TDF + XTC + LPV-r
	HIV and TB co-infection	ABC + 3TC + EFV	After completion of ATT, substitute to preferred 1st line with LPV-r
Children (5 to <10 years old)	First-line (NO history of maternal sdNVP; maternal NVP monotherapy; mother unsure of tail coverage)	TDF + XTC + EFV (weight-based dosing)	TDF + XTC + NVP† ABC + 3TC + EFV (weight-based dosing)
Adolescents (10 to <19 years old) weighing < 35 kg			
Adolescents (10 to <20 years old) weighing ≥ 35 kg	First-line A once-daily fixed-dose combination is recommended	TDF + XTC + EFV	TDF + XTC + NVP† or ABC + 3TC + EFV
Adults			

† For NVP initiation, refer to section below: Practical Hints for EFV or NVP Initiation.

Table 9: Special cases and their preferred 1st line cART and alternative regimens

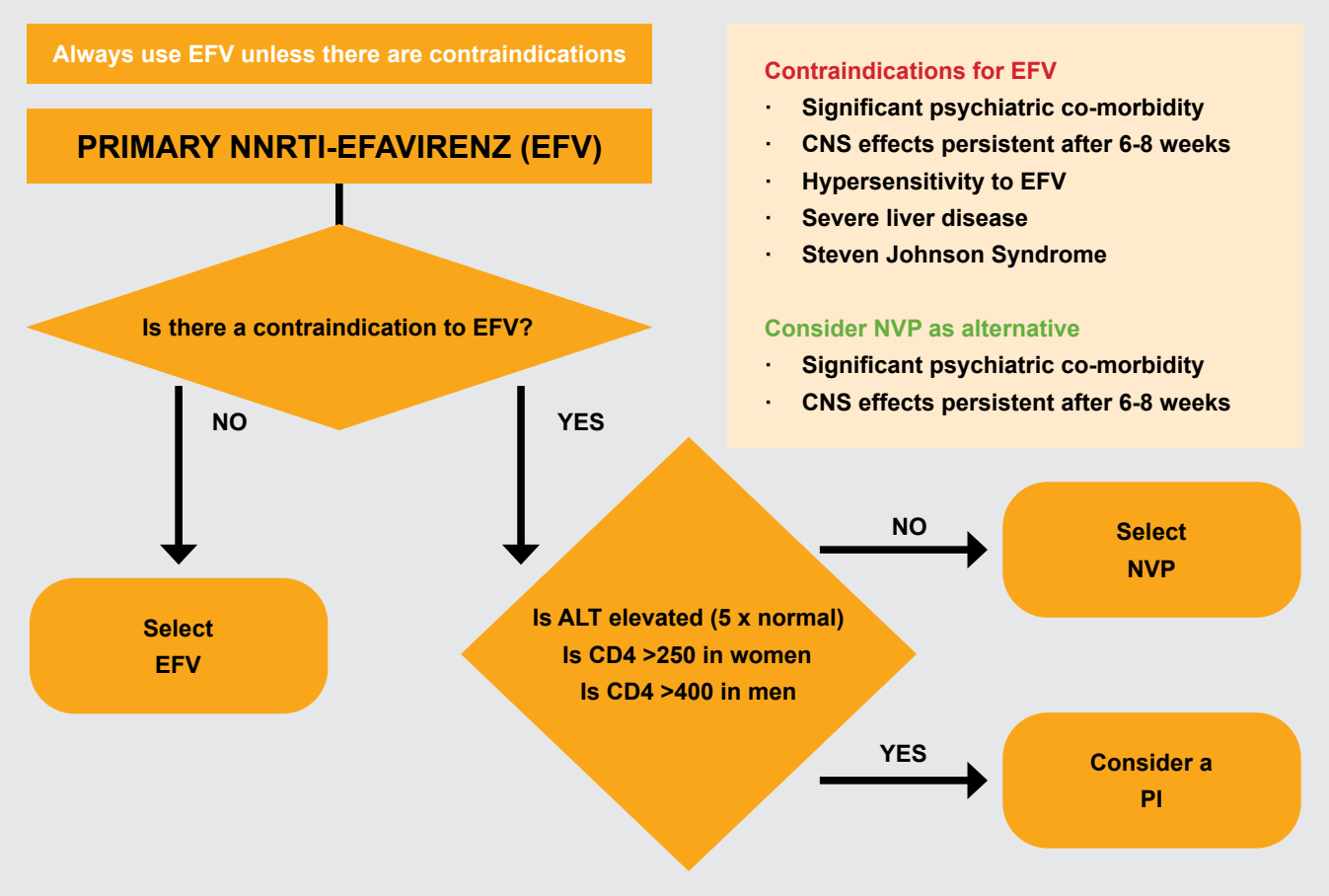
Special Cases of Adolescents, Adults, and Pregnant & Breastfeeding Women	Preferred 1st line cART	Alternative Regimen
HIV and TB co-infection	TDF + XTC + EFV	ABC + 3TC + EFV
	TDF + XTC + LPV-r (double the dose of LPV-r if on rifampicin regimen) or switch rifampicin to rifabutin (avoid in in pregnancy or breast-feeding 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
Renal insufficiency* (CrCl <50 ml/min)	ABC-based cART	
Renal insufficiency* in pregnant women (Serum Cr >125 µmol/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	

*In absence of serum creatinine screen for risk of renal insufficiency. See appendix 4 and appendix 5.

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 4.
- EFV is associated with central nervous system (CNS) side effects (e.g. dizziness, drowsiness, insomnia, abnormal dreams, and impaired concentration) that generally occur with the first few doses and usually diminish or disappear after 2-4 weeks.
- Avoid fatty meals 4 hours before or after taking EFV. Recommend taking EFV before bedtime.
- If CNS effects persist beyond 6-8 weeks, substitute to NVP-based cART.
- Non-pregnant women with CD4 count >250 cells/mm^3 (men with CD4 count >400 cells/mm^3) 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/mm^3 (monitor ALT/AST during first 12 weeks) and avoid in women who are pregnant or at risk for pregnancy with CD4 count >250 cells/mm^3 (men with CD4 count >400 cells/mm^3).
- 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 200 mg once daily for 2 weeks and then increase to 200 mg twice daily (BD) to reduce risk of rash and hepatotoxicity.

Figure 4: Algorithm for choosing NNRTI



Practical Hints for Starting Pregnant & Breastfeeding Women (and their Sexual Partners) on Lifelong cART

- It is a commonly held belief in Zambia that a pregnant woman must not attend ANC or announce her pregnancy until it is visible to everyone. This belief results in pregnant women presenting late for their first ANC visit and missing opportunities for early intervention. Instead, HCWs and community health workers should encourage pregnant women to attend ANC as early as the first trimester so that Focus Antenatal Care (FANC) can be provided, including HTC.
- Immediately initiate cART among all pregnant or breastfeeding women diagnosed with HIV within MNCH. Initiation may be done by HNPs, nurses/midwives within MNCH.
  - Where there is inadequate capacity within MNCH to initiate the pregnant woman on cART, she should be **fast-tracked** through the ART clinic.
  - Treatment preparation and adherence counselling should be accelerated so that it is completed on the **same day** where feasible.
  - Initiate CTX among all HIV-infected pregnant women, regardless of CD4 count or WHO stage or gestational age. Do not give intermittent presumptive therapy with sulfadoxine-pyrimethamine (e.g. Fansidar). For breastfeeding women, initiate CTX if eligible per adult guidelines, i.e. CD4 count <350 cells/mm^3 or WHO Clinical Stage 2, 3 or 4.
  - Initiate cART and CTX among all HIV-infected sexual partners of pregnant and breastfeeding women within MNCH.
  - Initiation may be done by HNPs, nurses/midwives within MNCH after treatment preparation and adherence counselling.
  - Transfer the sexual partner after cART initiation to ART clinic for further management.
  - If the HIV-infected partner, especially in serodiscordant couples, refuses to start cART, continue counselling, counsel on correct and consistent condom use, provide condoms, and refer to ART clinic for enrolment.
  - Refer all HIV-uninfected male partners in serodiscordant relationships to medical male circumcision and encourage routine retesting every 3-6 months.

Monitoring cART

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.

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 10). 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 (see figure 5).

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

Monitoring and managing a chronic condition whilst on cART

For HIV-infected patients including pregnant and breastfeeding women with co-morbidities (e.g. hypertension, diabetes, asthma, thyroid disorders, other chronic conditions), refer to a second level facility where a medical officer and/or obstetrician is available to manage the chronic condition

With regard to paediatric patients on AZT- or d4T-based cART who are transitioning to adolescent and adult care, follow the recommendations in Tables 8 and 12.

Table 10:
Clinical and laboratory monitoring for HIV-infected pregnant & breastfeeding women

Timeline	Clinical tasks	Laboratory tests
Day 0 Enrolment & cART initiation	▸ History and examination ▸ If pregnant, focused ANC (FANC) ▸ Screen for TB, cryptococcus, and PCP ▸ Adherence counselling and PHDP† messages ▸ Initiate cART after accelerated treatment preparation	▸ Serum creatinine ▸ ALT ▸ Hb or FBC ▸ CD4 count ▸ HBsAg ▸ Syphilis test ▸ Urinalysis ▸ If starting PI: glucose, cholesterol, and triglycerides
Week 2 post-initiation	▸ Targeted history & examination ▸ Screen for TB, cryptococcus, and PCP ▸ If pregnant, FANC ▸ Review adherence, side effects, toxicity* ▸ Adherence counselling and PHDP† messages ▸ Review laboratory tests ▸ Refill cART with enough supply to next visit (maximum: 3 months of cART)	▸ Serum creatinine ▸ Urinalysis
Week 4 post-initiation		
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
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 Table 13 regarding WHO toxicity estimates

ART Adherence

Adherence remains the single most important strategy for long term success and sustainability of patients on cART. Adherence to cART is important to control HIV infection and to prevent cART resistance. Treatment failure is generally a failure with adherence; therefore, efforts to ensure good adherence from the onset of cART initiation are mandatory.

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 counselling sessions and clinic visits.

Structured treatment preparation prior to cART initiation (table 11 and 12) should be conducted for all patients for successful HIV treatment and care. All children, adolescents and adults should undergo 3 sessions prior to cART initiation (pregnant and breastfeeding women should be fast-tracked and education regarding adherence should be integrated into ANC):

- Session 1 (Enrolment 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

Table 11: Pre-initiation tasks

Timeline/Specific populations		Clinical tasks	Laboratory tests*
Visit 1 Enrolment	Children	▸ Complete history & examination ▸ Screen for TB ▸ Adherence counselling 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 or FBC ▸ CD4 count ▸ Urinalysis ▸ HBsAg (if not vaccinated) ▸ 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) ▸ If starting PI: cholesterol, glucose, and triglycerides
	Adolescents Adults	▸ Complete history & examination ▸ Screen for TB ▸ Initiate CTX if eligible ▸ Adherence counselling and PHDP† messages: session 1	
Visit 2 1-2 weeks later Initiation	Children	▸ Targeted history and examination ▸ Screen for TB, cryptococcus, and PCP ▸ Review CTX adherence ▸ And review laboratory tests ▸ Initiate cART ▸ Adherence counselling and PHDP† messages, including the caregiver: session 3	
Visit 2 1-2 weeks later pre-initiation	Adolescents Adults	▸ Targeted history and examination ▸ Screen for TB, cryptococcus, and PCP ▸ And review laboratory tests ▸ Initiate CTX if eligible ▸ Determine cART eligibility ▸ Adherence counselling and PHDP† messages: session 2	
Visit 3 2-4 weeks later Initiation	Adolescents Adults	▸ Targeted history and examination ▸ Screen for TB, cryptococcus, and PCP ▸ And review CTX adherence ▸ Initiate cART if eligible ▸ Adherence counselling and PHDP† messages: session 3	

† 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.

Table 12: Clinical tasks for starting with cART initiation

Timeline	Clinical tasks	Laboratory tests*
Day 0 Initiation	› Targeted history and examination › Screen for TB, cryptococcus, and PCP › Review CTX adherence › And review laboratory tests › Initiate cART › Adherence counselling and PHDP† messages, including the caregiver	
Week 2	› Targeted history and examination › Screen for TB, cryptococcus, and PCP › Review adherence, side effects, and toxicity › Adherence counselling and PHDP† messages › Monitoring for new illnesses (including immune reconstitution inflammatory syndrome; IRIS) › If on NVP: dose escalation (at week 2)	› Creatinine › Urinalysis › If on NVP with rash, CD4 count >250 cells/mm3*, or pregnancy: ALT (AST if ALT is not available)
Week 4		› Creatinine** › If on NVP: ALT (AST if ALT is not available) › If on AZT: Hb
Week 8		› Creatinine**
Week 12		› Creatinine › Urinalysis › If on AZT: Hb
Week 16 and 20	› Review adherence, side effects, and toxicity › Adherence counselling and PHDP† messages	
Month 6 and every 3-6 months	› Targeted history & examination › Screen for TB, cryptococcus, and PCP › Review adherence, side effects, and toxicity › Adherence counselling and PHDP† messages	› Every 6 months: › Creatinine** › ALT › CD4 count › HIV viral load (Month 6 and then every 12 months) › Syphilis test (every 12 months; adolescent or adult) › HIV viral load in children and pregnant / breast feeding women (month 6,9,12 and then every 12 month) › If HPV test is positive or VIA, follow guidelines for treatment. If HPV test is negative or VIA, repeat screening within 3 years (sexually active adolescent or woman) › If on PI: glucose, cholesterol, and triglycerides

† 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.

** If serum creatinine is not available and patient is on TDF-containing cART, request urinalysis for protein.

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) due to:

- Toxicity (table 13), 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 14), the goals are to achieve HIV viral suppression, avoid adverse events, and optimize adherence.

Table 13: 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

Table 14: Common cART toxicities and recommended substitutes (for all populations)

ARV drug	Common associated toxicity	Recommended ARV substitute
TDF	Renal toxicity (renal tubular dysfunction)	ABC
ABC	Hypersensitivity reaction	TDF (if normal creatinine clearance) AZT (if child 3 months to <5 years old)
EFV	Severe or persistent CNS side effects	NVP
NVP (or EFV)	Rash, Steven Johnson Syndrome, hepatitis	LPV-r or ATV-r
LPV-r	Persistent diarrhoea, hyperlipidaemia	ATV-r
ATV-r	Hyperbilirubinaemia, icterus*	
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)
d4T**	Lactic acidosis, lipodystrophy, peripheral neuropathy	TDF or ABC (rule out failure before substitution; if failure suspected, switch to 2nd line)

* Hyperbilirubinemia 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 and d4T should no longer be used in 1st line cART. Patients on AZT- or d4T-based 1st line cART and are not failing treatment should be substituted to TDF- or ABC-based 1st line cART.

HIV 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 viraemia (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 viraemia 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.

If viral load testing is not routinely available, CD4 count (every 6 months) and clinical monitoring should be used to diagnose treatment failure, with targeted viral load testing to confirm virologic failure where possible.

Considerations for Pregnant & Breastfeeding Women

- Initiate cART in all pregnant & breastfeeding women regardless of patient's CD4 count
- Breastfeeding women should be assessed for treatment failure after 6 months of cART by virologic, immunologic, and clinical criteria.
- If treatment failure is suspected, consult HCW who can provide 2nd line cART as soon as possible.
    - Intensive adherence counselling should be conducted.
    - If breastfeeding, do age-appropriate HIV testing for HEI. If child is HIV-infected, inform ART clinic that child may be infected with resistant virus.

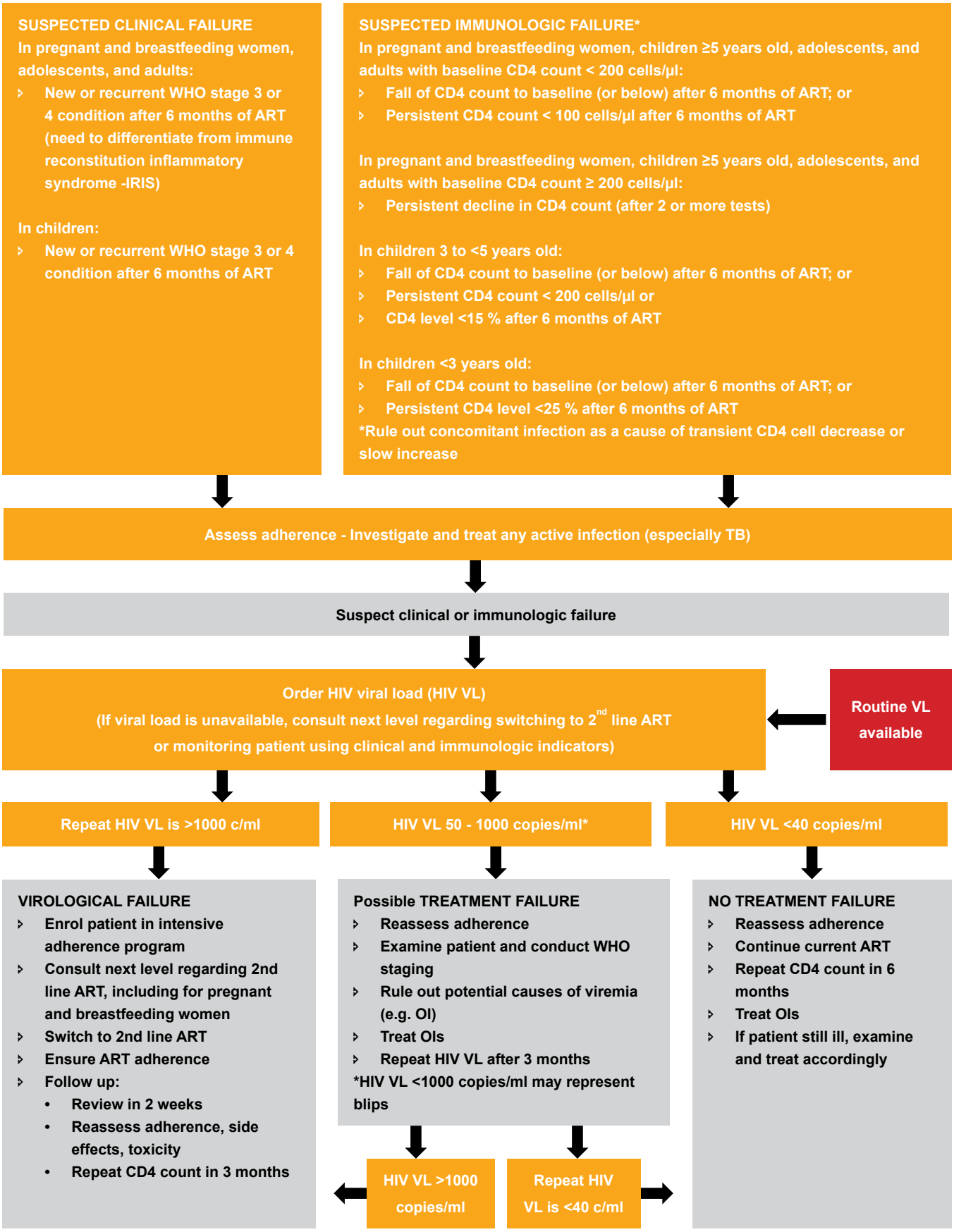
Considerations for Children and Adolescents <15 Years Old

- Initiate cART in all children and adolescents <15 years old regardless of CD4 count or WCS
- In children, viral load test at 6-9 months after initiating cART should be interpreted carefully, as virologic suppression may take longer to achieve because of high baseline viral load.
- For children <5 years old, viral load > 1,000 copies/ml may be detectable at 6 months but does not indicate treatment failure. Repeat the viral load 3 months later.

Targeted Viral Load Monitoring to Detect Treatment Failure

Where there is limited access to viral load testing, a targeted viral load strategy to confirm failure suspected based on immunologic or clinical criteria should be used to avoid unnecessary switching to second-line cART.

Figure 5: Algorithm for diagnosing treatment failure with targeted and routine viral load monitoring



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

- Poor adherence: change therapy only after adherence issues have been addressed
- Immune Reconstitution Inflammatory Syndrome (IRIS): treat underlying condition and continue cART if tolerated
- Untreated OIs: treat underlying condition and continue cART if tolerated
- Pharmocokinetics (e.g. rifamipicin 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

Switching cART Regimens

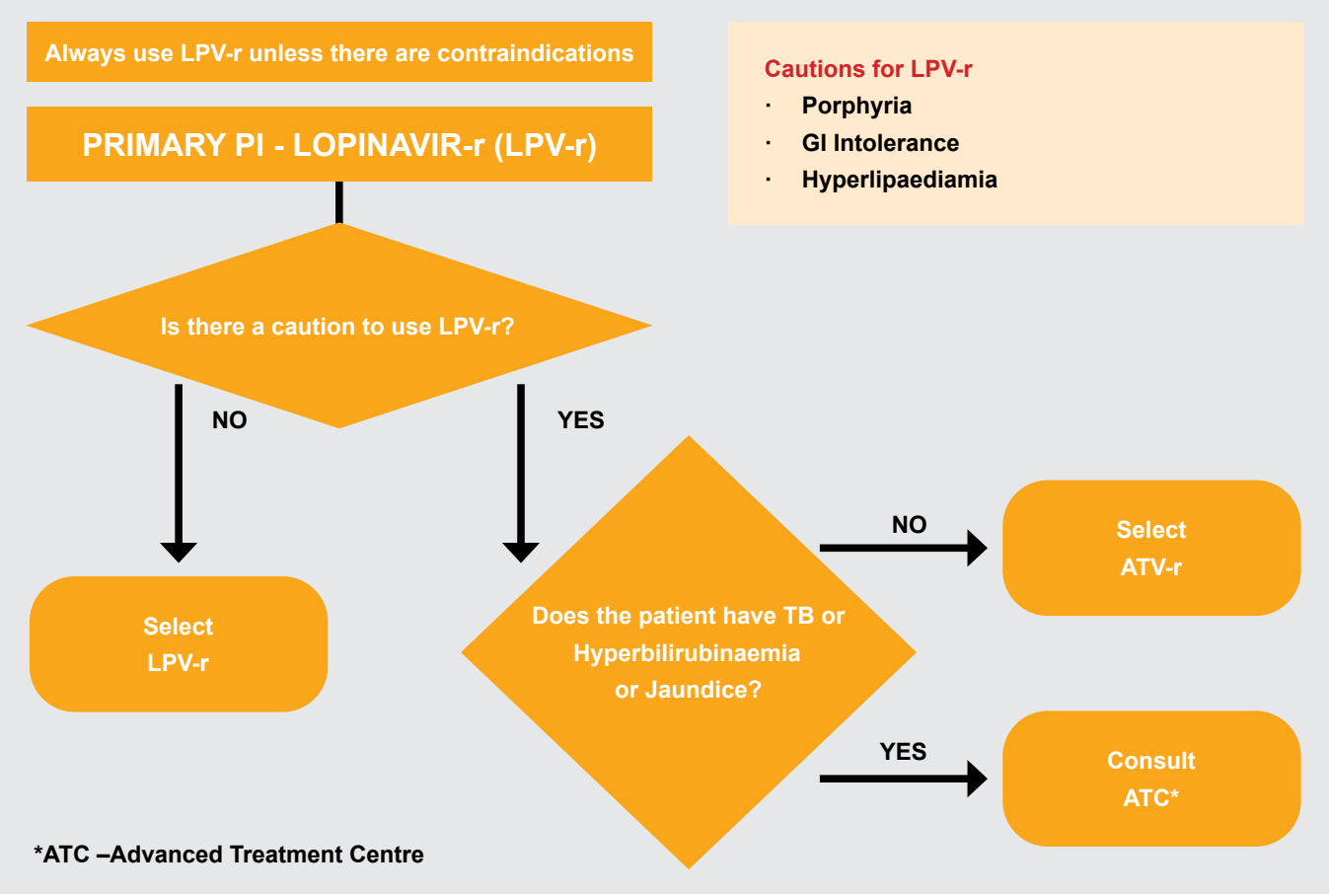
2nd Line cART

When patients are switched to 2nd line cART regimens (table 15), the goals are to achieve HIV viral suppression resulting in reconstitution of the clinical and immunologic status, avoid adverse events, and optimize adherence. LPV-r is the primary recommended second line PI (see figure 6)

Table 15: Recommended 2nd line cART regimens by specific populations and failing 1st line cART regimen

Specific populations	Comment	Failing 1st line cART	2nd line cART
Children (0 to <10 years old)		ABC or TDF + XTC	AZT + 3TC
		AZT or d4T + XTC	ABC or TDF + XTC
		NNRTI-based cART	LPV-r-based cART
Children <3 years old	Improve adherence and refer to next level	LPV-r	No switch
Children ≥3 years old	NNRTI non-exposed/naive	LPV-r-based cART	EFV-based cART
Adolescents (10 to <15 years old)	2nd line should consist of 2 NRTIs + LPV-r the alternative of 2 NRTIs + ATV-r	TDF + XTC + EFV	AZT + 3TC + LPV-r
		TDF + XTC + NVP	
Adolescents (15 to <20 years old)		ABC + 3TC + EFV	
		ABC + 3TC + NVP	
Adults		AZT + 3TC + EFV	TDF + XTC + LPV-r
		AZT + 3TC + NVP	
Pregnant & Breastfeeding Women		d4T + 3TC + NVP	
	HIV-HBV co-infection	TDF + XTC + EFV (or NVP)	TDF + XTC + AZT + LPV-r

Figure 6: Algorithm for choosing protease inhibitor (PI)

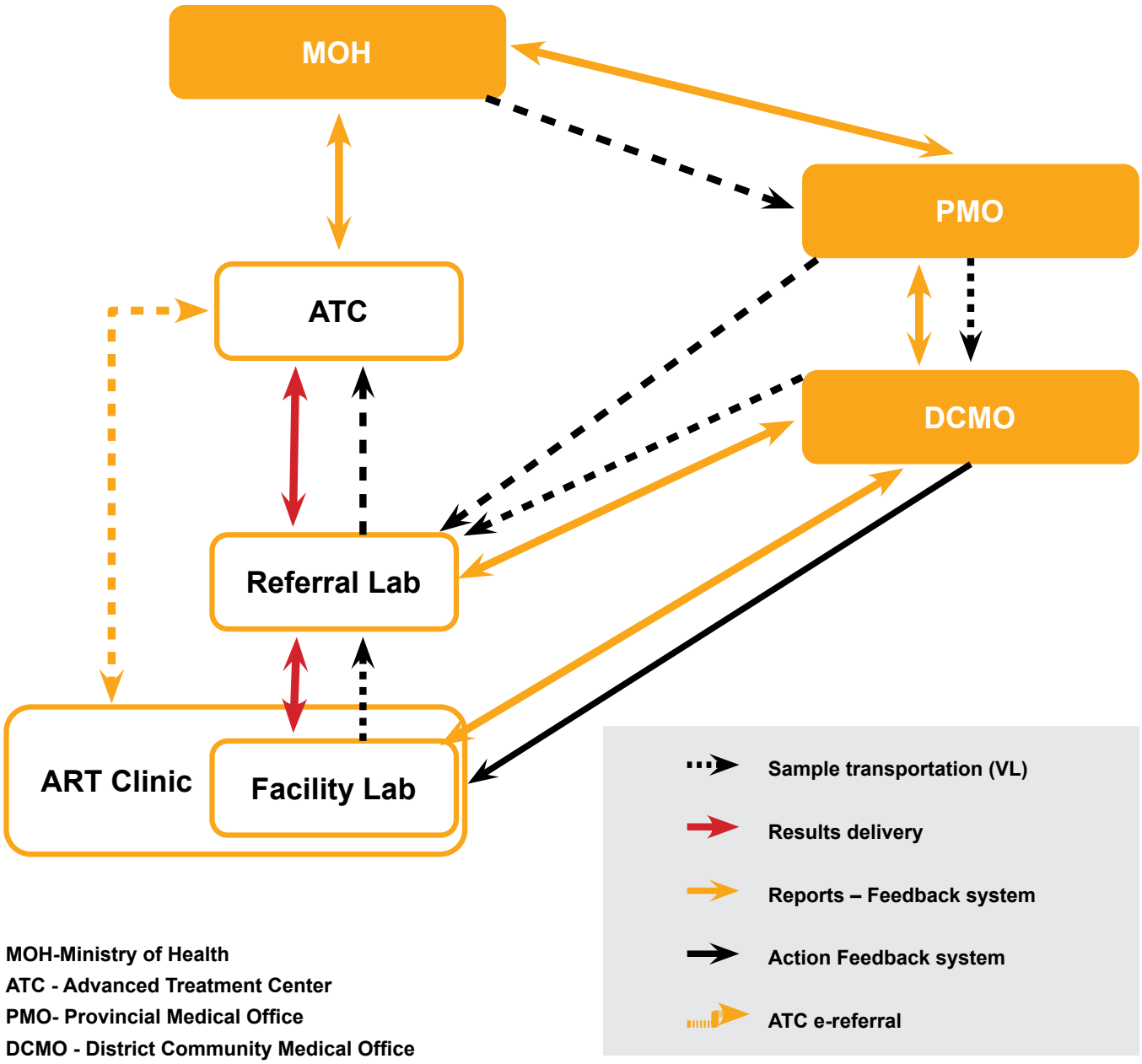


3rd Line cART: 2nd Line Treatment Failure

Provision of 3rd line cART occurs in very rare circumstances and is beyond the scope of most cART providers. All patients being considered for 3rd line cART should have:

- confirmed 2nd line cART failure (defined by a persistently detectable viral load exceeding 1,000 copies/ml [that is, two consecutive viral load measurements within a three-month interval, with enhanced adherence support between measurements] after at least six months of using 2nd line cART
- genotype (resistance) testing
  - Refer (see figure 7) 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 3rd line, establish the reason for treatment failure (e.g. poor adherence, suboptimal dosing, drug-drug interactions) and conduct intensive adherence counselling sessions until there is agreement between the patient, provider, and adherence counsellor that the patient is ready to commence 3rd 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 2nd line
  - Maraviroc: needs special tropism test prior to initiation, which is currently not available in Zambia

Figure 7: Information pathways for patients needing ATC services



MOH-Ministry of Health
ATC - Advanced Treatment Center
PMO- Provincial Medical Office
DCMO - District Community Medical Office

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.

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 counselling sessions until there is agreement between the patient, provider, and adherence counsellor that the patient is ready to commence 2nd 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.

Patient's cART history, including interruptions/discontinuations/adverse reactions, should be carefully documented on the HIV Summary Sheet as these strongly influence cART regimen choices in the future

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 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 counselling
- Non-adherence despite repeated counselling: 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 cART

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 2nd 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

Co-morbidities: TB, HBV, and Mental Illness

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 (table 16 and 17). Persons who screen negative for TB should be given TB INH Preventive Therapy (TB-IPT).

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 If renal insufficiency, ABC + 3TC + EFV
Children 3 months to <3 years old with TB-HIV co-infection	Start ATT (RHZ) immediately	ABC + 3TC + EFV Alternative regimen: ABC + 3TC + AZT
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 If renal insufficiency, ABC + 3TC + EFV
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 and continue cART. If on LPV-r, double dose of LPV-r or start rifabutin (in place of rifampicin) 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 If renal insufficiency, ABC + 3TC + EFV
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 150 mg Monday/ Wednesday/Friday.

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

Mental Illness and HIV Infection

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 initiation, consider switching EFV to NVP or LPV-r.

Immune Reconstitution Inflammatory Syndrome

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/mm3
- 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 0.5-1.0 mg/kg/day for 5-10 days

Preventive Interventions and Treatment

Four Prongs of PMTCT

Comprehensive PMTCT services includes four prongs:

- Prong I: Primary prevention of HIV among women of reproductive-age
- Prong II: Prevention of unintended pregnancies among HIV-infected women
- Prong III: Prevention of mother-to-child transmission of HIV using ARVs
- Prong IV: Provision of appropriate treatment, care, and support to women, children, and families

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 counselling and provision of a variety of family planning (FP) methods. With timely initiation of cART and adherence to cART in the HIV-infected non-pregnant women, planning for pregnancy is encouraged.

- Refer patients to Family Planning clinics, if needed, for further counselling 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) 150 mg (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

Co-trimoxazole Preventative Therapy (CPT)

CPT prevents *Pneumocystis* pneumonia (PCP), toxoplasmosis, isosporidia, 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 (table18 and 19). HIV-infected pregnant women on CPT should not be given sulfadoxine-pyrimethamine (SP; malaria prophylaxis in pregnancy).

Table 18:
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
	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
Children (5 to <10 years old)			
Adolescents	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
Adults			

[a] 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. DO NOT re-challenge

Table 19: CPT dosing for HIV-exposed children and HIV-infected children and adolescents

Sub-Population Recommended Daily Dosage (OD)	Syrup (200mg/40mg)	Child Tablet (100mg/20mg)	Single Strength Adult Tablet (400mg/80mg)
<5 kg (<6 months) 100 mg SMX/20 mg TMP	2.5 ml	1 tablet*	¼ tablet*
5 kg to <15 kg (6 months to <5 years old) 200 mg SMX/40 mg TMP	5 ml	2 tablets	1/2 tablet
15 kg to <30 kg (5 to <14 years old) 400 mg SMX/80 mg TMP	10 ml	4 tablets	1 tablet
≥30 kg (≥14 years old) 800 mg SMX/160 mg TMP	Not applicable	Not applicable	2 tablets

* Mix with feed or small amount of milk or water

Reference: WHO 2006 Guidelines on co-trimoxazole prophylaxis for HIV-related infections among children, adolescents and adults in resource-limited settings, recommendations for a public health approach
All HIV-infected individuals who are on CTX should be monitored clinically for side effects (table 20) at every visit.

Table 20: Co-trimoxazole toxicity grades and management

Toxicity Grading	Clinical Description	Management
Grade 1	Erythema	Continue CPT with close follow up Provide symptomatic treatment, such as antihistamines
Grade 2	Diffuse maculopapular rash, dry desquamation	Continue CPT with close follow up Provide symptomatic treatment, such as antihistamines
Grade 3	Vesiculation, mucosal ulceration	Stop CPT until the adverse effect has completely resolved (usually 2 weeks) and then restart or start CPT using desensitization protocol (appendix 3)
Grade 4	Exfoliative dermatitis, Stevens-Johnson syndrome or erythema multiforme, moist desquamation	Stop CPT and do not restart

Malaria Prevention in Pregnancy

All pregnant women should receive sulfadoxine-pyrimethamine (SP) as malaria intermittent presumptive therapy. HIV-infected pregnant women on CTX should not take SP since one of the many health benefits of CTX is malaria prophylaxis.

Tuberculosis Isoniazid Preventive Therapy (TB-IPT)

These guidelines focus on key interventions branded as the three Is (intensive case finding, isoniazid prophylaxis therapy, infection control 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 & 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 (table 21)
  - 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 25 mg once daily to prevent side effects of isoniazid in pregnant & breastfeeding women, adolescents, and adults

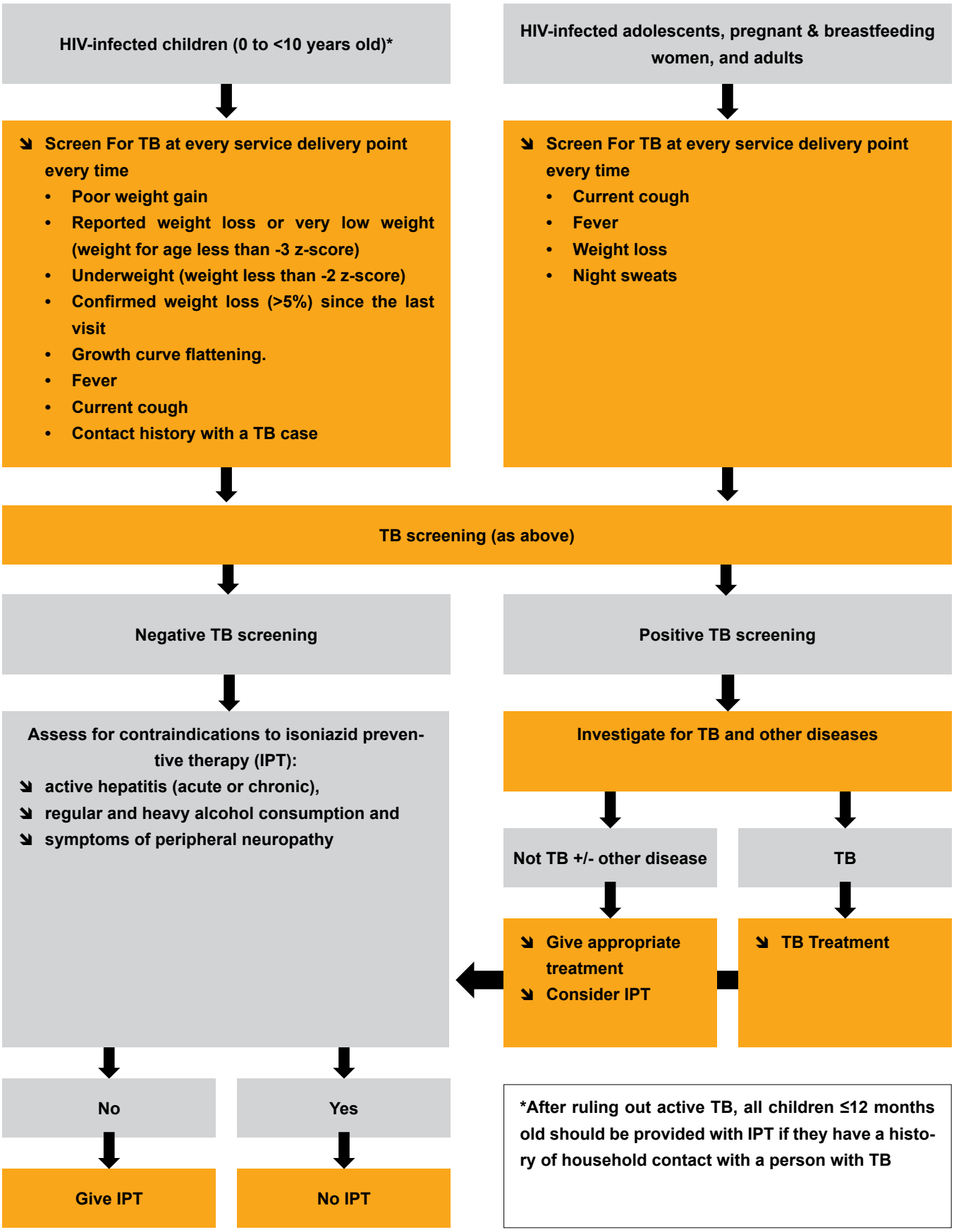
Table 21: Dosage for isoniazid preventative therapy, co-trimoxazole prophylaxis, and combination INH/CTX/B6 drugs

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

*NA = Not applicable

Screening for Active Tuberculosis

Figure 8: TB screening algorithm



Post-Exposure Prophylaxis (PEP)

Post-exposure prophylaxis is the use of cART to prevent HIV transmission. Non-occupational exposure to HIV in children is mostly due to 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 which caused the injury, injury with a large bore needle from artery or vein, and terminal HIV illness in source patient. Body fluids and materials which 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 site.
- 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 22) 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 and counselling. If HTC will likely last ≥1 hour, give first dose of PEP before HTC.
- 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. Observe 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

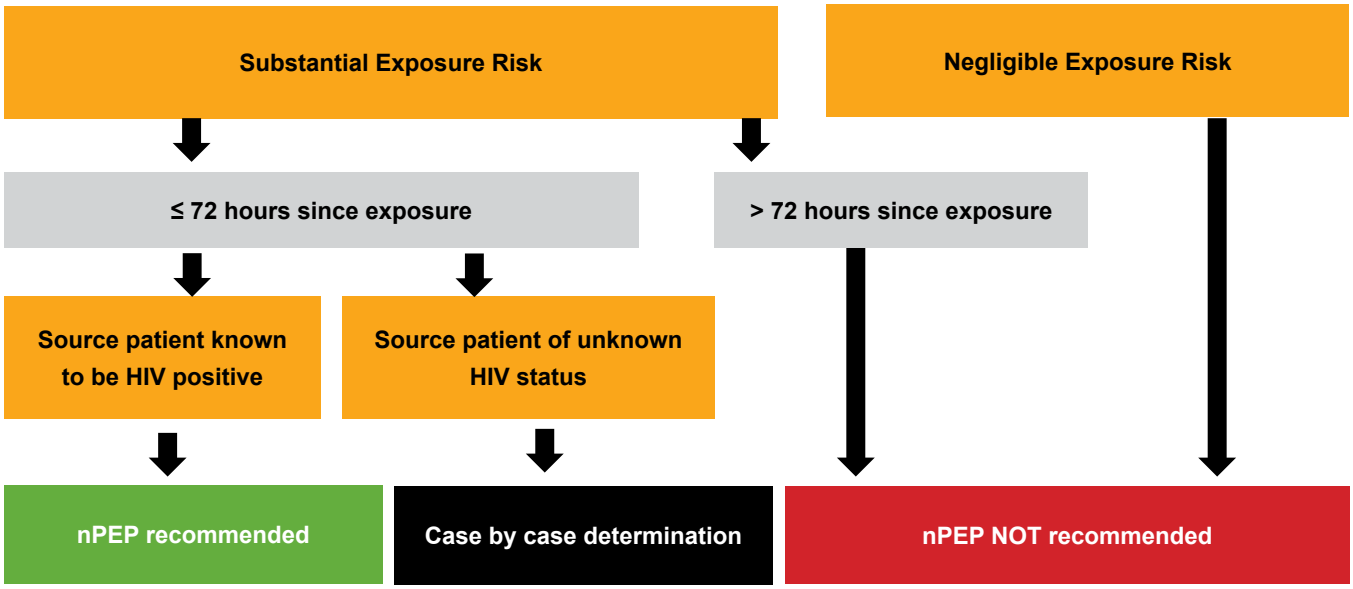
Table 22 : Post-exposure prophylaxis recommendations by risk category

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

*For GI intolerance to LPV-r, use TDF + XTC + ATV-r
For patients with CrCl <50 ml/min, replace TDF with AZT
For children <5 years old, use AZT + 3TC + LPV-r

Management of non-occupational exposure to infectious substances should be managed as shown in figure 9 below.

Figure 9: Algorithm for evaluation and treatment of possible non occupational HIV exposures



Substantial risk for HIV exposure
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

Negligible risk for HIV exposure
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

Ref MMWR 21 Jan 2005 nPEP –Non-occupational exposure

Positive Health Dignity and Prevention (PHDP)

To have a significant impact 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 counselling
  - Step 5: Give patient condoms at every visit
  - Step 6: Partner HIV testing

Community Involvement

These guidelines recognize that people spend the majority of their time in the community and not the health facility, and so the success of lifelong ART relies on a strong community network of support. These guidelines build on evidence-based community programs, such as the TB DOTS strategy and 'Reach Every Child' model for high childhood immunization coverage rates. At a minimum, the following should be done:

- At the health facility level, HCWs should engage the community
  - HCWs should identify community leaders (chiefs, headmen) and community interest groups who can serve as champions for cART adherence, retention in care and stigma reduction.
  - HCWs should sensitize community leaders and targeted groups (male groups, marriage counsellors, Safe Motherhood Action Groups) on these consolidated guidelines, specifically lifelong cART for pregnant & breastfeeding women, through already established structures, such as neighbourhood health committees.
  - HCWs are responsible for supervising and coordinating the work of community health workers (CHWs) and community health assistants (CHAs) in association with community development officers (CDOs).
  - At the client level, HCWs should support people on cART
  - HCWs should support HIV-infected individuals to disclose their status to at least one community-based treatment supporter or support group.
  - HCWs should review adherence and adherence barriers at each and every visit.

The following are key messages for providers and community health workers to communicate to clients:

- Pregnant women testing HIV positive: addressing benefits of lifelong ART
- Pregnant women testing HIV negative: addressing partner testing, risk of HIV acquisition
- Person testing for HIV:
  - Benefits of testing and treating early (normal quality and quantity of life, not progressing to acquired immunodeficiency syndrome [AIDS])
  - Community benefits of early treatment (prevention of HIV transmission to partners)
  - Options for persons testing HIV negative: male circumcision and family planning
- Other general issues:
  - PHDP
  - Family planning
  - Multiple concurrent partners

Nutrition Care and Support

Nutrition impacts the quality of life and survival of HIV-infected populations, as well as HEIs, because HIV impacts nutrient intake, absorption, metabolism, and storage by inducing a hyper-metabolic state. Furthermore, malnutrition has adverse effects on the immune system. Thus, nutritional assessment, counselling, and support are integral components to HIV care and treatment.

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 WCS, 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 %ile)
  - Stunted (height-for-age <3rd %ile)
  - Wasted (weight-for-height <3rd %ile)
- 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 23). 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 23: 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 only if AFASS	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 (<18.5 kg/m^2), normal (18.5 to 24.9 kg/m^2), overweight (25 to 29.9 kg/m^2), or obese (≥ 30 kg/m^2).
- If BMI <16 kg/m^2 or anaemia (Hb <10 g/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 >25 kg/m^2, provide nutrition counselling, including dietary advice and need for physical exercise.
- Table 24 lists some the specific BMI-related ARV drug risks

Table 24: Specific BMI-related ARV drug risks

BMI	ARV drug	Associated Risks	Recommended Actions
<18 kg/m^2	TDF	Tubular renal dysfunction Fanconi syndrome	Manage these patients with caution. Consult next level if necessary.
>25 kg/m^2	AZT	Lactic acidosis Severe hepatomegaly with steatosis	
	d4T	Lactic acidosis Severe hepatomegaly with steatosis Acute pancreatitis	

Palliative Care

Palliative care is about looking after people with illness that cannot be cured, relieving their suffering, and supporting them through difficult times. Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification, good assessment and treatment of pain and other problems, physical, psychosocial and spiritual.

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.

Managing the Programme
Documentation & Reporting

Tracking and Keeping Patients in Care

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

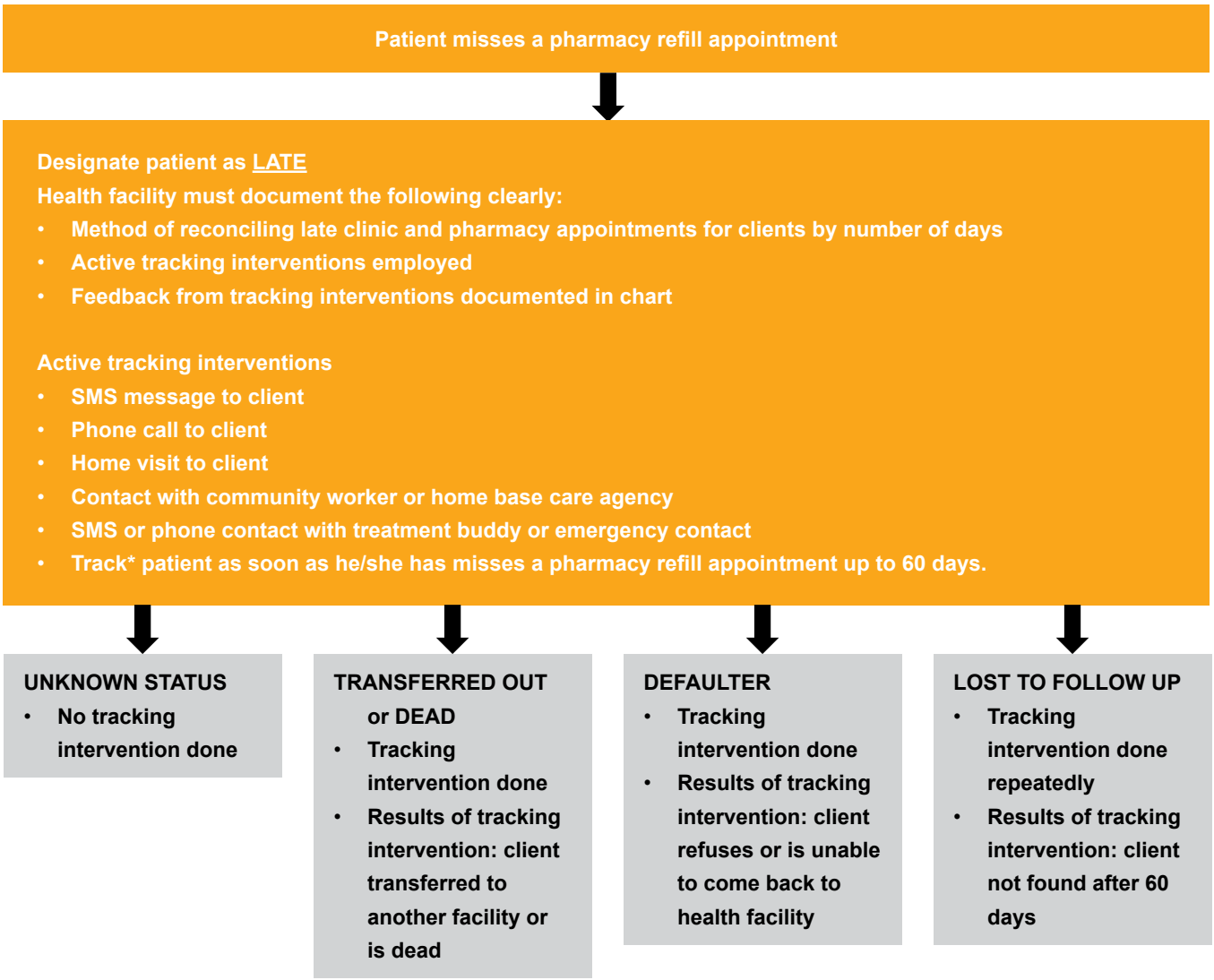
- Have a structured plan to track patients and prevent LTFU
- Monitor all missed clinic and pharmacy visits
- Create linkages with home-based care workers and volunteers
- Dedicate health facility staff to ensure patients who miss visits are contacted

Lost to Follow Up (LTFU)

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 & 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 & breastfeeding women, LTFU is defined as missing for ≥60 days after last scheduled pharmacy refill visit with inability to be traced after all active tracking mechanisms have been exhausted.
- Defaulter: HIV-infected individual has been located while late 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 10

Figure 10: Algorithm for active interventions when HIV-infected clients are late and determining their attrition status



Structured Plan for Tracking Patients

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 & 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 register
- EID register/log book/ EID lab requisition

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.

Supply Chain Management Systems (SCMS)

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

Quality Improvement

Quality improvement (QI) is a process that aims to strengthen the quality of services provided at health facilities. The QI 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 12 months old
- Percentage of all HIV positive clients retained on HIV care and treatment the last 12 months

Lifelong cART in pregnant & 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 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

Renal-adjusted ARV dosing for HIV-infected children and adults

Drug	Normal Dose	Renal Dose
Abacavir (ABC)	Adult: 300 mg BID PO Pediatrics: 8 mg/kg 12 hourly PO	No adjustment
Atazanavur (ATV) + Ritonavir (RTV)	Adult: 300/100 mg 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	Adult: 600mg OD PO Pediatrics: see pediatric dosing by weight bands.	No adjustment
Emtricitabine (FTC)	Adult: 200 mg OD PO Pediatrics: 0-3 months ols: 3 mg/kg/day (solution) 3 months – 15years old (>33kg) : 6 mg/kg.day (solution; max 240 mg daily) or capsule: 200 mg OD (capsule)	Adult: CrCl 30-49: 200 mg every 48 hours CrCl 15-29: 200 mg every 72 hours CrCl <15: 200 mg 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 (ETV)	Adult: 200 mg BID PO Pediatrics: see pediatric dosing by weight bands. Not approved for children <6 years old (approval underway for 2 months to 6 year olds).	No adjustment
Lamivudine (3TC)	Adult: 150 mg BID or 300 mg OD PO Pediatrics: 2-4 mg/kg BID PO	Adults: CrCl 30-49: 150 mg OD PO CrCl 15-29: 150 mg x1 then 100 mg OD PO CrCl 5-14: 150 mg x 1 then 50 mg OD PO CrCl <5: 50 mg x1 then 25 mg OD (50-75 mg 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: 10-13 mg/kg BID PO for lopinavir component	No dose adjustment but use with caution in patients with CrCl <50
Nevirapine (NVP)	Adult: 200 mg OD PO x 14 days then 200 mg BID PO Pediatrics: 4-7 mg/kg BID PO	No dose adjustment but give dose after dialysis

Drug	Normal Dose	Renal Dose
Raltegravir (RAL)	Adult: 400 mg BID PO.(with Rifampicin 800 mg BID PO) Pediatrics: not established for children <16 years old	No dose adjustment
Tenofovir (TDF)	Adult: 300 mg OD PO Pediatrics: 8 mg/kg OD PO	Same for adult & pediatrics: *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: 300 mg (8 mg/kg) every 48 hours CrCl 10-29: 300 mg (8 mg/kg) twice weekly CrCl <10: consider 300 mg (8mg/kg) OD PO (inadequate data) Hemodialysis: 300 mg (8 mg/kg) once weekly. To be given after dialysis. CAPD: no data
Zidovudine (AZT)	Adult: 300 mg BID PO Pediatrics: see pediatric dosing by weight bands.	CrCl 30-49: 300 BID PO CrCl 10-29: 300 BID PO CrCl <10: 300 mg OD PO in consultation with experienced clinician in renal dosing

Appendix 2

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

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

Appendix 3

Co-trimoxazole desensitization protocol for adolescents and adults

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

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

Reference:

WHO Guidelines on cotrimoxazole prophylaxis for HIV-related infections among children, adolescents and adults, 2006

Appendix 4

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

Get a good history

Ask about kidney disease, Hypertension, Diabetes, Chronic / acute diarrhea (recent or on-going)
Use of NSAIDS or herbal medications

↓

Check BP, weight, height, BMI, urinalysis, RBS or FBS

↓

Risk Factors

- History of hypertension or High or Low blood pressure
- History of diabetes mallitos or High Blood Sugar
- BMI ≤ 18.5 or less than 50kg (if > 190 years old)
- Persistent hematuria / proteinuria (2 weeks apart)
- Acutely ill patients / recently hospitalised
- Chronic use of NSAIDs or Herbs

↓

Risk factor(s) present

↓

Do not initiate based regimen without eGFR (Creatinine - serum & clearance)

↓

No risk factors

↓

Can initiate TDF based regimen

↓

Review for symptoms/signs at 2 and 4 weeks
Perform Serum Creatinine as soon as available

Appendix 5

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 =0.011312 *µmol/L
Height : [cm]

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

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)

- **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)

Notes

Notes