



Guidelines for antiretroviral therapy in Kenya



4th edition 2011 (Re-print)

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Foreword

Since the publication of the third edition of the national guideline on antiretroviral therapy in Kenya in 2005, new evidence on more efficacious, durable and tolerable HIV care and treatment options has emerged; culminating in the publication, in 2010, of World Health Organization (WHO) updates on prevention and treatment of HIV infection. The WHO recommendations, however, retained emphasis on a public health approach to the scaling up of HIV care and treatment services.

The fourth edition of the Guideline on antiretroviral therapy in Kenya has adopted these recommendations which are in line with international best practice. In addition, the Guideline provides specific emphasis on efficient and effective delivery of HIV prevention, care and treatment services. It outlines the health systems pillars that are essential to the delivery of quality HIV care and treatment services. Key areas covered include HIV diagnosis, antiretroviral therapy for adults, adolescents and children including special populations, prevention of mother-to-child transmission of HIV infection and prevention and management of common opportunistic infections as well as chronic non communicable diseases among PLHIV.

This Guideline is an important tool for use by multi-disciplinary teams of health care professionals providing care and treatment to PLHIV including doctors, clinical officers, nurses, pharmacists, pharmaceutical technologists, nutritionists, social workers and laboratory technologists among other service providers. In addition, it is presented in a simplified manner and provides a sound knowledge base for health care professionals involved in caring for PLHIV.

The development of this 4th edition of the Guideline has been done through extensive consultations and the commendable effort of multiple stakeholders, individuals and institutions led by the Ministries of Medical Services and Public Health & Sanitation.

It is our hope that this Guideline will add impetus to the rapid scale up of comprehensive HIV prevention, care, treatment and support and contribute to the achievement of universal access to quality HIV care and treatment services in Kenya.



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November 2011

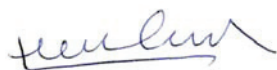
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Acronyms and abbreviations

3TC	Lamivudine
ABC	Abacavir
ADR	Adverse drug reaction
AFB	Acid fast bacilli
AIDS	Acquired immunodeficiency syndrome
ALT	Alanine transaminase
AMPATH	Academic model
ANC	Antenatal care
ANC	Absolute Neutrophil count
APV	Amprenavir
ART	Antiretroviral therapy
ARV	Antiretroviral drugs
AST	Aspartate transaminase
ATV	Atazanavir
AZT	Zidovudine
BD	Twice daily
CBC	Complete blood count
CCC	Comprehensive care centre
CDC	Centers for Disease Control and Prevention
CMV	Cytomegalovirus
CNS	Central nervous system
CrCL	Creatinine clearance
CRS	Christian Relief
CTX	Cotrimoxazole
CXR	Chest X-ray
CYP450	Cytochrome P450
d4T	Stavudine
ddC	Zalcitabine
ddI	Didanosine
DLV	Delavirdine
DMS	Director of Medical Services
DOT	Directly observed therapy
DS	Double strength
EFV	Efavirenz
EGPAF,	Elizabeth Glaiser Paediatric AIDS Foundation
EIA	Enzyme immunoassay (ELISA)
ELISA	Enzyme-linked immunosorbent assay (EIA)
EPTB	Extra pulmonary tuberculosis

F-APV	Fosamprenavir
FBC	Full blood count
FBO	Faith base organization
FDCs	Fixed dose combinations
FHI	Family Health International
FTC	Emtricitabine
GOK	Government of Kenya
HAART	Highly active antiretroviral therapy
HBC	Home based care
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HCW	Health care worker
HIV	Human immunodeficiency virus
HMIS	Health management information system
ICAP	International Centre for AIDS care and Treatment Programme
ICF	Intensified case finding
IDU	Injecting drug user
IDV	Indinavir
IEC	Information, education and communication
IPT	Isoniazid preventative therapy
IRIS	Immune reconstitution inflammatory syndrome
IU	International units
Jhpiego	Johns Hopkins Program for International Education in Gynecology and Obstetrics
KEMSA	Kenya Medical Supplies Agency
KPA	Kenya Paediatrics Association
KS	Kaposi sarcoma
LFT	Liver function test
LMIS	Logistics management information System
LPV	Lopinavir
LPV/r	Lopinavir/ritonavir
LRTI	Lower respiratory tract infection
M&E	Monitoring and evaluation
MAC	Mycobacterium avium complex
MBS	Moran of the Burning Spear
MCH	Maternal and child health
MOH	Ministry of Health
MSF	Medice
MSH/SCMS	Management science health/supply chain management system
MTCT	Mother-to-child transmission
MTRH	Moi Teaching and Referral Hospital

MUAC	Mid upper ARM circumference
NASCOP	National HIV/AIDS and STD Control Programme
NFV	Nelfinavir
NGO	Nongovernmental organization
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor
NtRTI	Nucleotide reverse transcriptase inhibitor
NVP	Nevirapine
OD	Once daily
OI	Opportunistic infection
PCP	Pneumocystis pneumonia
PCR	Polymerase chain reaction
PEP	Post-exposure prophylaxis
PGL	Persistent generalized lymphadenopathy
PI	Protease inhibitor
PLHA	People living with HIV/AIDS
PML	Progressive multifocal leucoencephalopathy
PMTCT	Prevention of mother-to-child transmission
PPE	Papular pruritic eruptions
PPP	Public private partnership
PTB	Pulmonary tuberculosis
RNA	Ribonucleic acid
RTV	Ritonavir
sdNVP	Single dose nevirapine
SQV	Saquinavir
SS	Single strength
STI	Sexually transmitted infection
TAMS	Thymidine analogue mutations
TST	Tuberculin skin test
UCSF/FACES	University of California San Francisco/Family AIDS Center and Education Services
USAID/OPH	United States Agency for International Development/Office of HIV/AIDS
WHO	World Health Organization

1. Overview of recommendations for standard prevention, care and treatment of HIV infection in Kenya

1.1 Introduction

This section contains succinct information on recommendations made throughout the “Guidelines” for quick reference. In the 4th revision of the national guidelines, emphasis has been laid on

- earlier initiation of antiretroviral treatment initiation and improved criteria for ART switching
- the use of the most potent, effective and feasible first-line, second-line and subsequent treatment regimens applicable to the majority of populations,
- the optimal management of pregnant women for their own health and for prevention of mother-to-child transmission
- the management of HIV-exposed infants including feeding options
- the management of TB/HIV and HIV/HBV co-infections as well as common chronic noncommunicable conditions in HIV infection.

1.2 Essential package of care for People living with HIV

Knowledge of HIV status is essential for one to access HIV care services. Therefore HIV testing should be offered at all service points and appropriate referrals made.

The essential package of services should be provided to all PLHIV; it includes

- Counselling and psychosocial support
- Prevention with positives
- Potrimoxazole prophylaxis
- Tuberculosis prevention and treatment among PLHIV
- Sexually transmitted and other reproductive tract infections
- Screening for cervical cancer
- Preventing malaria
- Vaccination and immunization
- Reproductive health and family planning
- Nutrition

1.3 **Antiretroviral therapy (ART) in adolescents and adults**

1.3.1 Recommendations for antiretroviral therapy in adults and adolescents

When to start ART

Antiretroviral therapy (ART) is indicated in all HIV-positive adults and adolescents with the following:

- WHO clinical stage 1 or 2 and a CD4 count ≤ 350 cells/mm³,
- WHO clinical stage 3 or 4 regardless of CD4 count,
- HIV and TB co-infection regardless of the CD4 count,
- Patients with HIV/HBV co-infection with evidence of active liver disease (elevated ALT), cirrhosis or other evidence of chronic liver disease.

What antiretroviral agents (ARVs) to start with

The recommended **first-line antiretroviral regimens** in treatment naïve adults and adolescents are:

TDF + 3TC + EFV or NVP	OR	AZT + 3TC + NVP or EFV
------------------------	----	------------------------

In pregnant women, AZT based ART is preferred due to the long experience of AZT in pregnancy and its well documented efficacy in preventing mother-to-child transmission of HIV.

As much as possible, fixed dose ARV drug combinations should be used to reduce the pill burden and encourage optimum adherence.

Stavudine phase out - patients already on a stavudine-based first-line regimen should be evaluated for adverse effects and where indicated, therapy changed appropriately. Patients who have been on stavudine for more than 6 months and are experiencing toxicity should have a viral load assessment to exclude treatment failure and to guide choice of appropriate regimen.

Recommended second-line regimens for adults and adolescents

In patients failing first-line therapy, the recommended second-line regimens are as shown in Table 1.1

Table 1.1 Recommended second-line regimens for adults and adolescents

First-line regimen	Second-line regimen
TDF + 3TC + EFV or NVP	AZT + 3TC + LPV/r or ATV/r*
AZT + 3TC + EFV or NVP	TDF + 3TC + LPV/r or ATV/r*
d4T + 3TC + EFV or NVP	TDF + 3TC + LPV/r or ATV/r*

*ATV/r is a suitable substitute when LPV/r is not tolerated.

1.4 Antiretroviral therapy in children

1.4.1 Diagnosis of HIV infection in infants and children

- All infants and young children whose exposure status is not known at the time of the first visit to a health facility should have their exposure status established through
 - counselling and then testing the mother for HIV or
 - testing the infant using an antibody test where the mother is not available or unwilling to be tested.
- All HIV -exposed infants (HIV antibody test positive/child born to HIV infected mother) should be offered routine HIV DNA PCR testing (early infant diagnosis) at the 6 weeks visit or at the earliest opportunity for infants seen after 6 weeks of age
- All HIV-exposed infants (HIV antibody test positive/child born to HIV-infected mother) should be offered cotrimoxazole preventive therapy from age 6 weeks till their HIV status is established. HIV-infected children should receive life-long cotrimoxazole prophylaxis unless contraindicated.

1.4.2 Recommendations for antiretroviral therapy in infants and children

When to start ART

- All children aged less than 24 months, confirmed HIV-infected; should be initiated on ART regardless of CD4 cell count, CD4 percentage or WHO clinical stage.
- In children older than 24 months of age, initiation of ART should be based on WHO stage and/or CD4 cell count or percentage as shown in Table 1.2 below

Table 1.2 Criteria for initiation of ART in children

Age	WHO clinical stage	CD4%	CD4 count (cells/mm ³)
<24 months	All	All	All
24–59 months	3 or 4	<25%	<1000
5–12 years	3 or 4	<20%	<500

Recommended first-line ART for infants and children

The choice of the ART regimen for use in a child is based on whether the child was exposed to nevirapine during PMTCT. The recommended first-line regimen in children depending on NVP exposure status is shown in Table 1.3.

Table 1.3 Recommended first-line ART in infants and children

Child characteristics		Recommended regimen
A. Child previously exposed to infant or maternal nevirapine for PMTCT (failed prophylaxis)		
All ages	Preferred	ABC + 3TC + LPV/r
	Alternative	AZT + 3TC + LPV/r
B. Child previously NOT exposed to Nevirapine for PMCT HIV transmission		
Age below 3 years or weight <10 kg	Preferred	ABC + 3TC + NVP
	Alternative	AZT + 3TC + NVP
Age above 3 years and weight >10 kg	Preferred	ABC + 3TC +NVP/EFV
	Alternative	AZT + 3TC + NVP/EFV

1.4.3 Prevention of mother-to-child transmission of HIV infection (PMTCT)

- All pregnant women should be encouraged to start attending antenatal care (ANC) early (as soon as they know they are pregnant; and preferably in the first trimester)
- All pregnant women should be offered HIV counselling and testing during their first ANC visit in line with testing and counselling guidelines. Those who are HIV-negative should be re-tested every 3 months until delivery.
- All pregnant women who are not tested, and opt-out or decline HIV testing during the initial ANC visit should be offered HIV counselling and testing at subsequent visit(s).
- Encourage mothers attending ANC to bring their partners for counselling and testing (couple counselling).
- Test sexual partners and children of all HIV-positive women identified at ANC.
- All HIV-positive pregnant women should be screened for TB, STIs, cervical cancer, and initiated on cotrimoxazole prophylaxis.
- All HIV-positive pregnant women should be evaluated for eligibility for ART during the first ANC visit; clinically, using WHO staging and CD4 cell count where available.
- All HIV-positive pregnant women in WHO stage 1 or 2 and with a CD4 cell count ≤ 350 cells/mm³ or in WHO stage 3 or 4 irrespective of CD4 count should be started on life-long ART as soon as possible irrespective of the gestational age.
- All HIV-positive pregnant women with CD4 cell count >350 cells/mm³ and with WHO clinical stage 1 or 2 should be provided with efficacious antiretroviral prophylaxis to prevent mother-to-child transmission of HIV infection but may be considered for lifelong ART where feasible.

All women, of unknown HIV status presenting in labour or after delivery should be offered HIV counselling and testing and managed as per the PMTCT recommendations. All HIV-exposed infants should be started on NVP prophylaxis from birth regardless of infant feeding option. Duration of NVP in the infant depends on whether the mother is on ART and whether the infant will be breastfed as follows:

- for infants whose mothers are on HAART or those who are not breastfed at all regardless of mother's treatment/PMCT intervention; NVP should be continued for 6 weeks only;
- for breastfeeding infants whose mothers are not on HAART, NVP should be given continuously from birth and continued throughout the duration of breastfeeding then stopped 1 week after complete cessation of breastfeeding.

All HIV-exposed breastfeeding infants whose mothers are not on HAART, presenting for the first time in the post-partum period up to 6 weeks of age, should be started on nevirapine prophylaxis upon presentation at the health facility. Diagnostic HIV DNA PCR testing of these infants should be done at 6 weeks of age or at the earliest opportunity thereafter. Infants with PCR negative result should be continued on nevirapine prophylaxis while those with PCR positive results should be initiated on ART.

- All HIV-exposed breastfeeding infants whose mothers are not on HAART, presenting for the first time in the post-partum after 6 weeks of age, should start on cotrimoxazole prophylaxis and have a diagnostic DNA – PCR done at the first visit. Infants with a positive PCR results should start ART while those with negative PCR results should start nevirapine prophylaxis.
- Breastfeeding infants of mothers who start ART during the post-natal period should continue nevirapine prophylaxis till one week after cessation of breastfeeding.
- Infants with a positive PCR result should have the nevirapine prophylaxis discontinued and instead started on full ART, (Refer to table 1.3 above).

1.4.4 Infant and young child feeding in the context of HIV infection

- All mothers who are HIV-negative or are of unknown HIV status should be encouraged and supported to **exclusively** breastfeed for the first 6 months and continue breastfeeding with appropriate complementary feeds introduced thereafter.
- All HIV-positive mothers should be given accurate information on available infant feeding options including the challenges and benefits of each option in order to help them make an informed decision on which infant feeding option best suits their circumstances.

For majority of HIV-positive mothers, breastfeeding with infant ARV prophylaxis is the best option. They should be encouraged and supported to exclusively breastfeed for the first 6 months and continue feeding with appropriate complementary feeds thereafter. Infants of these mothers should receive Nevirapine prophylaxis throughout breastfeeding and until one week after complete cessation of breastfeeding.

All HIV-positive mothers who choose not to breastfeed should be counselled and supported to provide exclusive replacement feeding for the first 6 months and appropriate complementary feeds introduced thereafter. Infants of these mothers should be provided with Nevirapine prophylaxis from birth until 6 weeks of age.

2. Overview of HIV infection and antiretroviral agents

2.1 Introduction

There has been unprecedented growth in the understanding of HIV in the last three decades. This has resulted in the rapid development of antiretroviral agents based on the life-cycle of the virus. This section provides an overview of the biology HIV, the effects of HIV infection on the body and available antiretroviral agents developed to manage HIV infection.

2.2 The human immunodeficiency virus (HIV)

The human immunodeficiency virus (HIV), the etiologic agent for the acquired immunodeficiency syndrome (AIDS) belongs to the family of retroviruses (retroviridae) and the genus of lentiviruses. It is an RNA virus whose hallmark is the reverse transcription of genomic RNA to DNA by the enzyme reverse transcriptase.

There are two types of HIV, namely HIV-1 and HIV-2.

2.2.1 HIV type 1 (HIV-1)

HIV- 1 is the cause of much of the global HIV pandemic and is much more infective than HIV-2. HIV- 1 is further sub-divided into different groups M, N and O; with different geographical distribution. Nine sub-types or clades (A to D, F to H, J and K) are currently recognized for group M. The commonest clades in Kenya are A and D (both subtypes of the M group), while in eastern and southern Africa subtype C is the commonest, and also accounts for over 50% of all HIV 1 infection globally. In areas where more than one HIV 1 subtype is in circulation, genetic material from the different sub-types can mix or recombine, producing recombinant or hybrid virus, which can subsequently be transmitted.

This genetic diversity of HIV 1 may be important when it comes to diagnostic tests and performance of nucleic acid based tests (such as viral load). While most currently available standard assays will detect subtypes within group M, this epidemic dynamism of HIV 1 necessitates molecular surveillance at the national level. There is evidence that different subtypes may have different genetic pathways to ART resistance. Currently the sub-type diversity of HIV 1 does not appear to have implications with regard to clinical response to recommended ARV treatment strategies.

2.2.2 HIV type 2 (HIV-2)

HIV-2 is uncommon outside of parts of West and Central Africa. Disease caused by HIV-2 progresses more slowly (a slower rate of both CD4 and clinical decline) than HIV-1 disease. HIV-2 infected individuals often have lower viral loads. Compared with HIV-1, HIV-2 is less transmissible (5- to 8- fold less efficient than HIV-1 in early-stage disease) and is rarely the cause of vertical transmission). HIV-2 is uniformly resistant to non-nucleoside reverse transcriptase inhibitors (NNRTIs) and less susceptible to some of the newer drugs (e.g. entry inhibitors).

2.2.3 Modes of transmission

HIV is present in blood, semen, vaginal secretions, breast-milk and other body fluids and secretions. The virus can be transmitted through:

- unprotected (vaginal, anal or oral) sex with someone who is HIV-infected,
- injection or transfusion of contaminated blood or blood products, donations of semen (artificial insemination), skin grafts or organ transplants taken from someone who is HIV-infected,
- vertical transmission from a HIV-infected mother to baby during pregnancy, labour and delivery or through breastfeeding,
- sharing or use of contaminated needles,
- occupational exposure (through needle stick injuries, splashing etc).

Transmission of HIV in Kenya is predominantly among heterosexual partnerships including stable partnerships. Transmission among other key populations at risk of HIV exposure, such sex workers, men who have sex with men (MSM) and injecting drug users (IDUs) accounts for about 30% of all infections. Vertical transmission also remains an important mode of transmission of HIV in Kenya.

2.2.4 Virus life cycle

HIV enters cells through interaction of an envelope glycoprotein (gp120) and the cellular receptor, CD4, and other co-receptors such as CCR5 and CXCR4. These receptors are expressed on T-helper lymphocytes (CD4 lymphocytes), macrophages, dendritic cells (in lymph nodes and mucosal surfaces) and microglial cells in the brain. Viruses that utilize the CCR5 co-receptor to gain entry into cells are referred to as R5 tropic; whereas those that use CXCR4 co-receptor are X4 tropic. Most primary HIV infections are R5 tropic; the X4 tropic virus appears late in the course of HIV infection.

The virus life cycle can be divided into a number of distinct steps, each of which is a current or potential therapeutic drug target:

1. Binding, fusion and entry

During this step, viral gp120 binds to the CD4 receptor and CCR5 or CXCR4 co-receptor on host cell surface. The binding facilitates fusion of viral and host cell membrane thereby facilitating the entry of viral nuclear material into the host cell.

2. Reverse transcription

Viral RNA is reverse transcribed into viral DNA. This process is mediated by the enzyme reverse transcriptase (RT). This enzyme has no proof-reading function, and therefore the process is error prone and responsible for rapid development of drug resistant mutations.

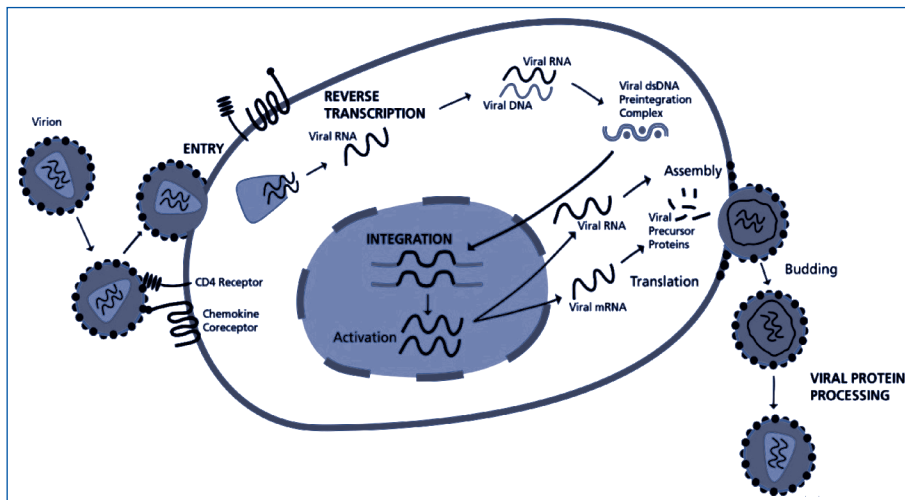
3. Integration

The pro-viral DNA is inserted into host cell chromosomal DNA using the viral enzyme integrase. This is the step that establishes replication competent virus in the body and makes HIV incurable even with effective ART. Further, drug resistant virus that occurs in patients on ART may also be archived in the same way, establishing a permanent pool of resistant viruses.

4. Transcription and translation

Host cell enzymes transcribe viral DNA into viral RNA. Viral RNA uses host cell energy and synthetic pathways to make viral proteins

Figure 2.1 The HIV life cycle and sites of action of current antiretroviral agents



5. Assembly, budding and maturation

Viral proteins and RNA aggregate on the cell surface for assembly into a mature viral particle by budding through host cell membrane.

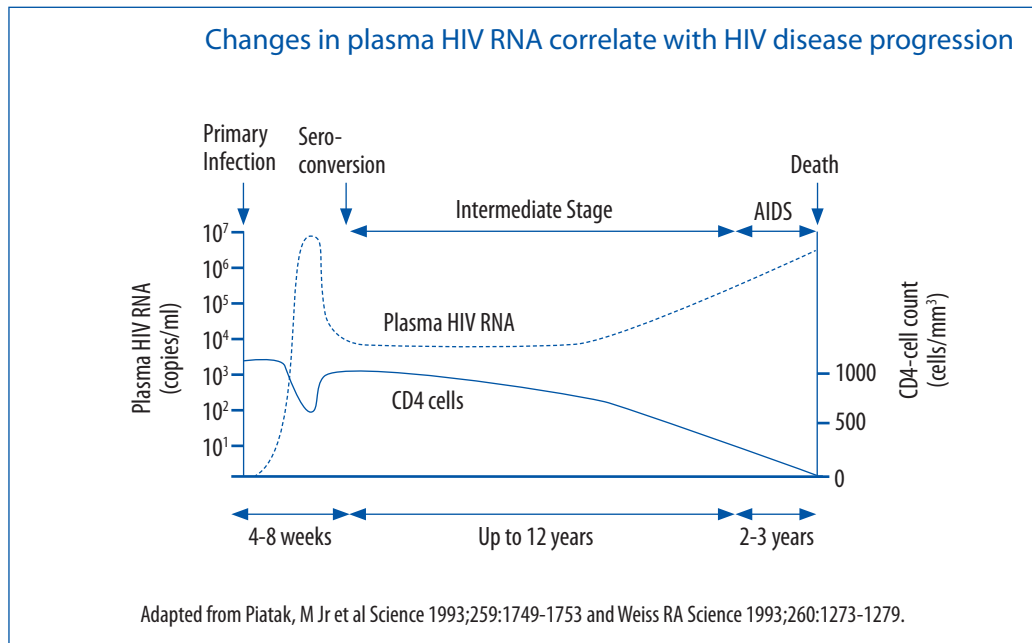
2.3 Natural history and staging of HIV infection

2.3.1 Natural history of HIV infection

Following infection with the HIV virus, there is an initial rapid rise in viral load, which may be associated with flu like symptoms (primary HIV infection). A vigorous immune response occurs within weeks of infection, with production of both antibodies and cellular mediated responses. Thus antibodies to HIV can be detected within 2 weeks of infection. The immune response inhibits HIV replication with the result that the viral load declines and stabilizes within the first 6-12 months after infection. Thereafter the patient remains asymptomatic for on average 6-10 years in the majority of patients, before the ongoing immune destruction begins to manifest in symptomatic HIV-related diseases.

At the time of initial infection with HIV, patients have a large number of susceptible CD4+ T- lymphocytes and no HIV specific immune response. Thus, there is rapid HIV replication that causes rapid destruction of CD4+ T lymphocytes over the first weeks and months after infection. Through the induction of HIV-specific immune responses, there is stabilization of CD4 cell levels and containment of viral replication, which is marked by a very slow decline of CD4+ T-cells over 6-10 year (See Figure 2.2) Eventually, in the absence of effective antiretroviral therapy CD4 cell levels decline further culminating in progressive immune deficiency accompanied by the development of HIV-associated complications (such as opportunistic infections, malignancies and neuro-cognitive dysfunction). While immunologic decline after primary infection usually occurs slowly over many years, it is worth noting that many patients will not be diagnosed until late in the course of infection, when symptoms are present and CD4 count is low .

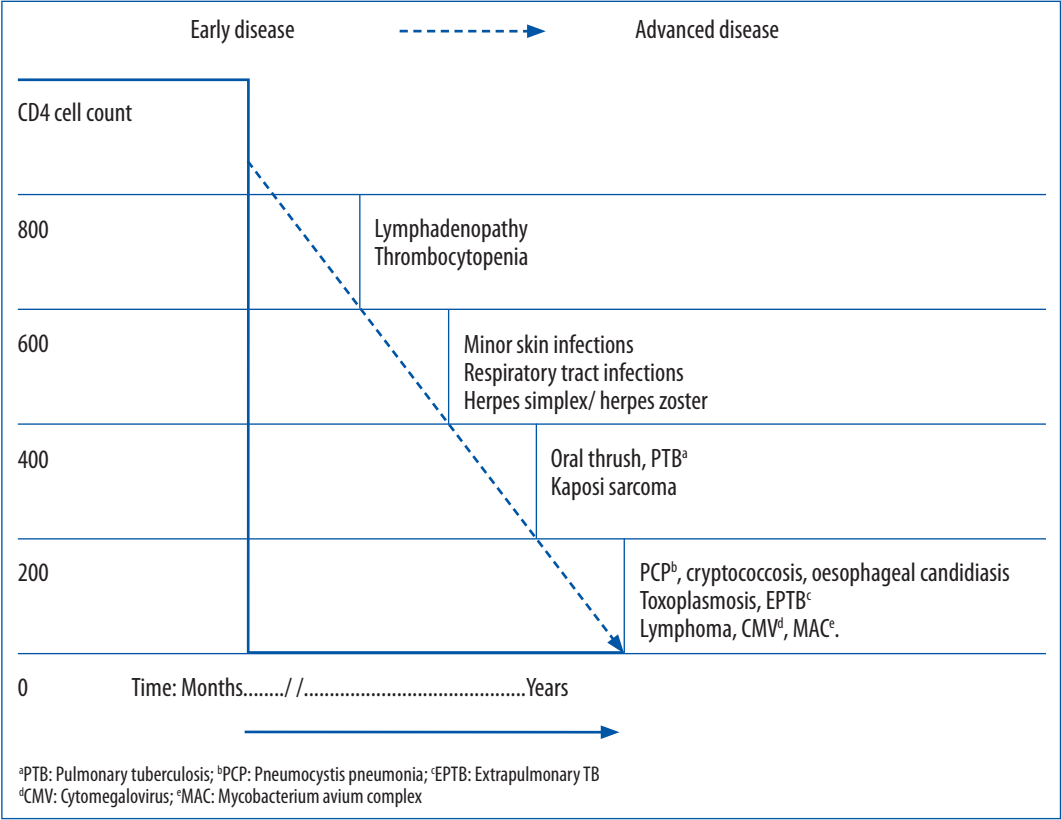
Figure 2.2 Natural history of HIV infection in untreated patients



In about 10% of patients, HIV disease progression may be very rapid, with patients presenting with AIDS within about 2 years following initial infection; In less than 10% of patients disease progression may be very slow (long term non-progressors and elite controllers), with patients maintaining low or undetectable viral load and conserved CD4 cells.

Recently, light has been shed on the role of systemic immune activation as being a key driver in the pathogenesis of HIV disease. Most of the initial HIV replication after primary infection takes place in the gastrointestinal tract, which contains a significant subset of the total body CD4⁺ cells. This results in a massive loss of memory CD4 cells in the gut associated lymphoid tissue (GALT), which persists even after the initiation of ARV therapy, and subsequent immune reconstitution. This destruction of the GALT is associated with free entry of microbes and their products into the blood stream, triggering an inflammatory cascade which contributes to the persistent immune activation of chronic HIV infection. While chronic immune activation is intended to protect, the inflammatory response results in damage to the host and may contribute to the increased risk of non-HIV-associated conditions (cardiovascular, liver and renal disease) prevalent in HIV-positive individuals.

Figure 2.3 Decline in CD4 cell count and clinical progression of HIV infection



2.3.2 Clinical staging of HIV Infec tion

The WHO clinical staging system for HIV/AIDS uses a set of clinical parameters to classify HIV infection into 4 stages; reflecting disease severity and prognosis. Clinical staging serves several functions:

- harmonize clinical case and surveillance definitions
- assist with clinical decision-making, including decisions on starting, substituting, switching and stopping ART,
- assess current clinical status of individuals in HIV care, either on ART or not on ART
- guide clinicians in assessing the response to ART - new or recurrent stage 3 or 4 events may suggest failure or inadequate response to treatment. permit the inclusion of laboratory testing, especially CD4 count, so as to guide prognosis and assist in determining the need for ART and other therapies. Some patients classified as being in WHO stage 1 or 2 may have significant immunosuppression (CD4 count below 350 cells/mm³) in spite of relatively minor or no symptoms

Only patients with confirmed HIV-infection are eligible for WHO clinical staging.

Table 2.1 WHO clinical staging of HIV/AIDS in adults and adolescents.

Clinical stage 1	
1.	Asymptomatic
2.	Persistent generalized lymphadenopathy (PGL)
Clinical stage 2	
1.	Moderate unexplained weight loss (<10% of presumed or measured body weight)
2.	Minor mucocutaneous manifestations (seborrheic dermatitis, popular pruritic eruptions, fungal nail infections, recurrent oral ulcerations, angular cheilitis)
3.	Herpes zoster
4.	Recurrent upper respiratory tract infections (sinusitis, tonsillitis, bronchitis, otitis media, pharyngitis)
Clinical stage 3	
1.	Unexplained severe weight loss (over 10% of presumed or measured body weight)
2.	Unexplained chronic diarrhoea for longer than one month
3.	Unexplained persistent fever (intermittent or constant for longer than one month)
4.	Persistent oral candidiasis
5.	Oral hairy leukoplakia
6.	Pulmonary tuberculosis
7.	Severe bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia)
8.	Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
9.	Unexplained anaemia (below 8 g/dl), neutropenia (below 0.5 x 10 ⁹ /l) and/or chronic thrombocytopenia (below 50 x 10 ⁹ /l)
Clinical stage 4	
<i>Conditions where a presumptive diagnosis can be made using clinical signs or simple investigations:</i>	
1.	HIV wasting syndrome
2.	Pneumocystis jiroveci pneumonia (PCP)
3.	Recurrent severe bacterial pneumonia (≥ 2 episodes within 1 year)
4.	Cryptococcal meningitis
5.	Toxoplasmosis of the brain
6.	Chronic orolabial, genital or ano-rectal herpes simplex infection for >1 month
7.	Kaposi sarcoma (KS)
8.	HIV encephalopathy
9.	Extra pulmonary tuberculosis (EPTB)
<i>Conditions where confirmatory diagnostic testing is necessary:</i>	
1.	Cryptosporidiosis, with diarrhoea >1 month
2.	Isosporiasis
3.	Cryptococcosis (extra pulmonary)
4.	Disseminated non-tuberculous mycobacterial infection
5.	Cytomegalovirus (CMV) retinitis or infection of the organs (other than liver, spleen, or lymph nodes)
6.	Progressive multifocal leucoencephalopathy (PML)
7.	Any disseminated mycosis (e.g. histoplasmosis, coccidiomycosis)
8.	Candidiasis of the oesophagus or airways
9.	Non-typhoid salmonella (NTS) septicaemia
10.	Lymphoma cerebral or B cell Non Hodgkin's Lymphoma
11.	Invasive cervical cancer
10.	Visceral leishmaniasis
11.	Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy

Table 2.2 WHO clinical staging of paediatric HIV/AIDS

Clinical stage 1	
1.	Asymptomatic
2.	Persistent generalized lymphadenopathy (PGL)
Clinical stage 2	
1.	Unexplained persistent hepatosplenomegaly
2.	Papular pruritic eruptions
3.	Extensive wart virus infection
4.	Extensive molluscum contagiosum
5.	Recurrent oral ulcerations
6.	Unexplained persistent parotid enlargement
7.	Lineal gingival erythema
8.	Herpes zoster
9.	Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis)
10.	Fungal nail infections
Clinical stage 3	
1.	Unexplained moderate malnutrition not adequately responding to standard therapy
2.	Unexplained persistent diarrhoea (14 days or more)
3.	Unexplained persistent fever (above 37.5°C, intermittent or constant, for longer than one month)
4.	Persistent oral Candidiasis (after first 6 weeks of life)
5.	Oral hairy leukoplakia
6.	Acute necrotizing ulcerative gingivitis/periodontitis
7.	Lymph node TB
8.	Pulmonary TB
9.	Severe recurrent bacterial pneumonia
10.	Symptomatic lymphoid interstitial pneumonitis
11.	Chronic HIV-associated lung disease including bronchiectasis
12.	Unexplained anaemia (<8.0 g/dl), neutropenia (<0.5x10 ⁹ /L ³) or chronic thrombocytopenia (<50 x 10 ⁹ /L ³)
Clinical stage 4	
1.	Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
2.	Pneumocystis pneumonia
3.	Recurrent severe bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)
4.	Chronic herpes simplex infection; (orolabial or cutaneous of more than one month's duration, or visceral at any site)
5.	Extrapulmonary TB
6.	Kaposi sarcoma
7.	Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
8.	Central nervous system toxoplasmosis (after the neonatal period)
9.	HIV encephalopathy
10.	Cytomegalovirus (CMV) infection; retinitis or CMV infection affecting another organ, with onset at age more than 1 month
11.	Extrapulmonary cryptococcosis including meningitis
12.	Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidioidomycosis, penicilliosis)
13.	Chronic cryptosporidiosis (with diarrhoea)
14.	Chronic isosporiasis
15.	Disseminated non-tuberculous mycobacterial infection
16.	Cerebral or B cell non-Hodgkin lymphoma
17.	Progressive multifocal leukoencephalopathy
18.	HIV-associated cardiomyopathy or nephropathy

2.4 Key characteristics and uses of available antiretroviral agents

Currently, there are five classes of drugs active against HIV (Table 2.3). ARV agents act by interfering with important functions in the viral life-cycle (Figure 2.3).

- I. **Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs)** also referred to as nucleoside/nucleotide analogues. NRTIs work by prematurely terminating DNA chain formation as the enzyme reverse transcriptase copies viral RNA into DNA.
- II. **Non-nucleoside reverse transcriptase inhibitors (NNRTIs)** inhibit formation of viral DNA from viral RNA by tightly binding to the reverse transcriptase enzyme.
- III. **Protease inhibitors (PIs)** bind to the viral protease enzyme and block the formation of viral proteins.
- IV. **Entry inhibitors** prevent entry of the virus into the host cell i.e. CD4
- V. **Integrase strand transfer inhibitors (INSTI)** block the integrase enzyme which incorporates/integrates pro-viral DNA into the host cell DNA.

Table 2.3 Current antiretroviral drugs by class

Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs and NtRTI)	Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	Protease inhibitors (PIs)	Entry inhibitors	Integrase strand transfer inhibitors (INSTI) ³
NRTIs Abacavir (ABC) Didanosine (ddI) Emtricitabine (FTC) Lamivudine (3TC) Stavudine (d4T) Zidovudine (AZT)	Efavirenz Nevirapine Etravirine Rilpivirine	Indinavir (IDV) Nelfinavir (NFV) Ritonavir Saquinavir (SQV) Lopinavir (LPV) Atazanavir (ATV) Fosamprenavir	Fusion inhibitor enfuvirtide	Raltegravir Elvitegravir Dolutegravir
NtRTI Tenofovir (TDF)		Tipranavir Darunavir (DRV)	CCR5 antagonist Maraviroc	

³Elvitegravir and Dolutegravir are two INSTIs that are undergoing clinical studies and may be available in the next two to three years. Elvitegravir will be used with a booster - Cobicistat.

2.4.1 Key characteristics of first and second-line antiretroviral agents

Refer to **appendices, tables 20.1 to 20.14** for more detailed information on the characteristics of the ARV agents (ARVs) for use in adults and children as well as the interactions between ARVs and other commonly used medicines.

Fixed dose combinations

Fixed dose combinations (FDCs) are the preferred formulations of the recommended regimens where available. FDCs have advantages over single drugs because they simplify procurement and drug logistics management and may be easier to take due to reduced pill burden, allowing for an increased level of adherence to treatment. See Tables 2.4 and 2.5 for FDC formulations currently available in Kenya.

Table 2.4 Adult FDC formulations

Formulation	Strength
AZT / 3TC	300 mg/150 mg
AZT /3TC/ NVP	300 mg/150 mg / 200 mg
D4T / 3TC	30 mg/ 150 mg
D4T / 3TC/ NVP	30 mg/ 150 mg / 200 mg
TDF /3TC	300 mg / 300 mg
TDF/ 3TC/ EFV	300 mg / 300 mg / 600 mg

Table 2.5 Paediatric FDC formulation

Formulation	Strength
ABC/3TC	60 mg/30 mg
AZT/3TC	60 mg / 30 mg
AZT/ 3TC/ NVP	60 mg/30 mg/ 50 mg

3. Essential package of prevention and care for people living with HIV infection

3.1 Introduction

Knowledge of HIV status remains a major limiting factor to accessing HIV prevention care and treatment services, therefore at all HIV testing sites:

- VCT services should refer patients to HIV/Comprehensive Care Clinics (CCC) as soon after diagnosis as possible.
- Provider initiated testing and counselling should be carried out aggressively at in- and out-patient service points (ANC, TB, STI, FP, MCH etc); aiming at universal access to counselling and testing in healthcare settings.
- All patients with children under the age of 15 years attending CCC should be encouraged to bring their children for HIV testing. In addition sexual partners of all adult PLHIV should also be tested as part of prevention with positive activities and identification of discordant partnerships for appropriate management.
- All community based organizations and families supporting orphans and vulnerable children should arrange to have those children whose parents may have died of HIV infection tested.

All PLHIV, whether on ART or not, should have access to a set of core interventions known to promote health, improve the quality of life, prevent further HIV transmission; and for some, delay HIV disease progression and prevent mortality. Most of these interventions are simple, relatively inexpensive and widely available. These interventions emphasize prevention of opportunistic infections and other HIV-associated illnesses. The interventions should be applied throughout the continuum of healthcare delivery from the family to the community to healthcare settings.

3.2 Essential package of services for PLHIV

3.2.1 Counselling and psychosocial support

- I. All PLHIV should be provided with counselling and psychosocial support interventions including individual and group counselling, peer support groups, family and couples counselling, and adherence support.

Counselling and psychosocial support should focus on;

- mitigation of fear, anger, self-stigma and discrimination,
 - alleviation of grief, bewilderment and stress among partners and family members,
 - behaviour change in support of healthy living and prevention of further HIV transmission,
 - disclosure and partners notification,
 - family/partner counselling to identify family members who may need care and treatment,
 - skills-building on how to live a healthy and productive life,
 - identification and treatment of depression and substance abuse. Mental illness and substance and alcohol dependence are common conditions among PLHIV. These conditions, besides affecting the quality of life of patients can cause non-adherence to prophylactic and ART regimens as well as undermine safer sex practices; and
 - youth and adolescent specific issues.
- II. PLHIV should be offered counselling and support to promote adherence to preventive interventions and treatment recommended for their care including ART
 - III. PLHIV who choose to be sexually active should be counselled on safer sex practices to prevent HIV transmission to their sexual partners and avoid acquisition of STIs and HIV re-infection; and should be provided with condoms and appropriate contraceptive services and counselling.

3.2.2 Prevention with positives

A significant proportion of PLHIV remain sexually active. Knowledge of HIV status does not always translate into behaviour change in support of prevention of HIV transmission. Healthcare workers should sensitively and non-judgmentally provide information on how to prevent HIV transmission among PLHIV. Preventive interventions among HIV-positive individuals include disclosure and partner testing and engagement in the care process; condom use; contraception; and prevention and treatment of STI.

PLHIV should be supported and encouraged to disclose their HIV status to those who need to know; particularly sexual partners.

- In Kenya, up to 7-11% of couples in stable long-term partnerships are sero-discordant. HIV-negative partners in a sero-discordant relationship are at high risk of HIV infection. Disclosure of HIV status encourages couple counselling and testing, the discussion of reproductive health issues such as desire to have children, better couple communication and condom use.
- Accumulating evidence has shown that treatment of the HIV-positive partners in a sero-discordant relationship (irrespective of CD4 cell count, and particularly in those with a CD4 cell count of 350-500 cells/mm³) markedly reduces the risk of HIV transmission to the HIV-negative partner.
- Sero-concordant couples also benefit from disclosure; thus facilitating couple counselling and testing; provision of condoms to avoid STIs and unintended pregnancies and discussion of reproductive health matters.

3.2.3 Co-trimoxazole prophylaxis (CPT)

All HIV-positive patients should be given lifelong CPT unless contraindicated.

- Cotrimoxazole is an effective prophylactic agent against a broad range of conditions and organisms including toxoplasmosis, PCP, common bacterial infections, sepsis, diarrhoea and malaria.
- In pregnancy, CPT has additional benefits of reducing chorioamnionitis, prematurity and neonatal mortality, particularly in patients with a CD4 cell count of ≤ 200 cells/mm³. During pregnancy, CPT should be initiated irrespective of the gestational age. Additional intermittent preventive therapy for malaria is not required in women already on CPT. HIV-infected breastfeeding women should continue with CPT.

Table 3.1 Dose of prophylactic cotrimoxazole

Weight (kg)*	Suspension 240 mg per 5 ml	Single strength tablet 480 mg (SS)	Double strength tablet 960 mg (DS)
1 – 4	2.5 ml	¼ SS tab	--
5 – 8	5 ml	½ SS tab	¼ DS tab
9 – 16	10 ml	1 SS tab	½ DS tab
17 – 30	15 ml	2 SS tabs	1 DS tab
>30 (adults and adolescents)	-	2 SS tabs	1 DS tab

*Dose by body weight is 24–30 mg/kg once daily of the trimethoprim-sulphamethoxazole- combination drug.

- A rash may occasionally develop, usually about 7-14 days following initiation of CTX. It is often a relatively mild maculopapular rash with or without pruritus. Infrequently, a more severe rash may develop with severe exfoliation of the skin and Stevens-Johnson syndrome.
- Patients with mild to moderate rash should stop the CTX and once recovered should undergo desensitization.
 - Patients with severe rash (edema, vesiculation of the skin, mucosal involvement) should **NOT** be desensitized; CTX should be stopped and never be re-used.
 - Desensitization is effective in the majority of patients but is not recommended in children
 - The rapid regimen can be used in situations where treatment for PCP with CTX is required.

Management of patients with cotrimoxazole allergy

- Desensitization is effective in the majority of patients. The rapid regimen (Table 3.3) can be used in situations where treatment for PCP is needed.
- Dapsone is recommended for use in patients unable to use CTX; unfortunately dapsone is not as effective a chemo-prophylactic agent as CTX and is effective against only PCP when used alone. (Ideally, pyrimethamine should be used in addition, to provide effective prevention against toxoplasmosis).

Cotrimoxazole desensitization

Table 3.2 Standard desensitization regimen (days)

Day	Dose of TMP/SMX suspension 40/200 per 5 ml
1	0.5 ml
2	1 ml
3	2 ml
4	3 ml
5	4 ml
6	5 ml
7	1 SS tablet
8	2 SS tablets/1 DS tablet per day

Table 3.3 Rapid desensitization regimen (hours)

Hour	Dose of TMP/SMX 40/200 per 5 ml
0	0.5 ml
1	1 ml
2	2 ml
3	3 ml
4	4 ml
5	5 ml
6	1 SS tablet

- **Dose of dapsone**
 - Available as 25 mg and 100 mg tabs
 - Children: **4 mg /kg per week** OR 2 mg/kg once daily; maximum dose is 100 mg.
 - Adults: 100 mg once daily.
- Dapsone should be commenced in patients with WHO stage 4 disease and/or those with a CD4 <200 cells/mm³
- Dapsone should be discontinued once the CD4 has been greater than the following values for at least 6 months.
 - 200 cells/mm³ for adults and children >5 years
 - the age specific threshold for severe immunodeficiency for younger children

Dapsone should be commenced in patients with WHO stage 4 disease and/or those with a CD4 cells/mm³ <200. It should be discontinued once the CD4 has been greater than 200 cells/mm³ for at least 6 months.

Desensitization of patients with Stevens-Johnson (i.e. blistering of skin or mucosa) should be avoided.

3.2.4 Tuberculosis prevention and treatment among PLHIV (refer to Chapter 6 for more details)

Among PLHIV, TB is the most frequent serious opportunistic infection and a leading cause of death. HIV Infection increases the risk of TB-disease ten-fold; together with a higher risk of death, recurrence and re-infection. ART substantially decreases the risk of TB disease, but additional interventions are needed to reduce the risk burden of TB-disease among PLHIV.

- I. PLHIV should receive counselling about the risk of acquiring TB, strategies for reducing exposure to TB, recognizing clinical manifestations of TB and seeking care promptly, the risk of transmission of TB to others and TB preventive therapy.

- II. PLHIV should be screened for TB at each visit with the healthcare team; persons suspected of having TB should undergo further evaluation. (figure 6.1)
- III. TB preventive therapy should be provided to all PLHIV after thorough exclusion of TB disease
 - TB screening is done based on clinical symptoms, according to the TB screening tool. CXR should only be done if indicated, and is not a pre-requisite for IPT in asymptomatic patients.
 - TB-preventive therapy should not be given to PLHIV with symptoms suggestive of TB especially those with advanced HIV disease in whom TB cannot be excluded with confidence.
 - Previous treatment for TB is not a contraindication to TB-preventive therapy; if treatment was completed more than 2 years previously IPT should be considered.
 - A tuberculin skin test is not a necessary pre-condition to imitate TB preventive therapy
 - The recommended regimen for TB—preventive therapy is isoniazid given daily for six months.

Indications for IPT

- **All** children regardless of HIV sero-status <5 years exposed to “open” PTB in a close contact, with a negative TB screen should be given IPT
 - **All children living with HIV with more than 1 year of age** in whom TB has been excluded,
 - **All** HIV-positive adult patients in whom TB has been excluded (universal use of IPT for PLHIV)
- IV. Healthcare settings present suitable conditions for transmission of TB; particularly among vulnerable individuals like PLHIV. All healthcare settings should develop and implement TB infection control strategies to reduce the risk of transmission of TB among patients, visitors and staff.

3.2.5 Sexually transmitted and other reproductive tract infections

Ulcerative and inflammatory diseases of the reproductive tract often co-exist with HIV infection, increase HIV infectiousness and shedding and some may cause serious complications like peritonitis due to pelvic inflammatory disease.

- I. At the initial assessment, a thorough history should be obtained including information on
 - Previous STIs
 - Symptoms of current STIs (discharge, pain on micturition, genital sores, dyspareunia, itching etc)

- Risky sexual practices
 - Multiple partners
 - Anonymous partners
 - Drug and alcohol abuse
 - Report of unprotected sex outside of a mutually monogamous relationship
 - Exchange of sex for drugs or money, or sex with a partner who reports these behaviours
- Contraceptive and condom use.

The history should be accompanied by a thorough physical examination, including examination of the external genitalia for ulcers and discharge. All PLHIV should receive a serological test for syphilis.

- II. PLHIV diagnosed with an STI should be managed according to national STI treatment protocols. Sexual partners should be treated as well.
- III. At initial diagnosis of HIV infection, all sex workers should be assessed for STIs and if present offered syndromic therapy.
- IV. Patients who have persistent signs and symptoms of STIs in spite of syndromic treatment should undergo diagnostic evaluation for definitive diagnosis and aetiological therapy
- V. All PLHIV should be evaluated for continued risky sexual practices and symptoms of STIs through sensitive and non-judgemental interviewing. Those with on-going risk should receive intensive counselling to reduce risky behaviour; and be provided with easy access to condoms. Sex workers should be evaluated for STIs more frequently.

3.2.6 Screening for cervical cancer

Cervical cancer is caused by the human papilloma virus (HPV) and is the most common cancer in women in Kenya, more prevalent in HIV-positive than in HIV uninfected women. Cervical cancer is a WHO stage 4 disease and therefore an indication for ART initiation.

Screening for cervical cancer results in early detection of pre-malignant lesions early initiation of treatment and curative therapy of early stage cancer. Therefore all HIV-infected women (and HIV uninfected sexually active women) should be screened for cervical cancer. Effective vaccination against HPV is now available and where possible should be offered to all eligible girls and women irrespective of HIV status.

All HIV comprehensive care clinics should integrate cervical cancer screening and management of cervical dysplasia into routine care and treatment. Women with HIV infection should be screened for cervical cancer at initial assessment and at regular intervals thereafter in line with the Division of Reproductive Health guidelines for cervical cancer screening.

The recommended screening methods are visual inspection with acetic acid (VIA); visual inspection with Lugol's iodine (VILI) or cervical cytology using Pap smear and offered appropriate therapy according to the Division of Reproductive Health Guidelines.

Some studies have reported a higher recurrence rate after treatment in HIV-positive women. Close follow up is therefore very important for these women.

HIV-positive women should be encouraged to practice primary prevention strategies to reduce likelihood of HPV infection. This includes abstinence where possible, avoidance of multiple sexual partners and condom use. It is also advisable that they avoid behaviour that predisposes to progression of HPV into cancer e.g. cigarette smoking and alcohol consumption.

3.2.7 Preventing malaria

Children and adults with HIV infection suffer more frequent and more severe malaria than HIV uninfected individuals. Further, people with advanced immunosuppression are at risk of failure of anti-malarial treatment. In pregnancy, there is increased risk of placental malaria, severe anaemia, premature delivery and perinatal mortality.

- I. Cotrimoxazole preventive therapy, as recommended for all HIV-infected patients provides effective protection against malaria infection.
- II. PLHIV should have access to insecticide treated mosquito nets or indoor residual spraying to reduce exposure to mosquito bites and malaria transmission.
- III. HIV-positive pregnant women who are taking cotrimoxazole prophylaxis should not be given sulfadoxine-pyrimethamine (SP) for intermittent preventive treatment.
- IV. PLHIV with fever and on CPT should not be treated for a presumptive diagnosis of malaria. As far as possible, laboratory confirmation of malaria should be obtained prior to initiation of anti-malarial therapy. Other causes of fever should be considered.
- V. PLHIV with malaria should receive standard anti-malarial therapy according to national guidelines. Patients on ART receiving anti-malarial therapy should be monitored closely for adverse drug reactions.

3.2.8 Vaccination and immunization

- I. When available, Hepatitis B vaccination is recommended for all HBsAg negative PLHIV.
- II. Where resources permit, response to the vaccine should be assessed with hepatitis B surface antibody (HBsAb) testing after three doses of HBV vaccine. If the vaccine response is suboptimal, revaccination with three doses of standard- or double-strength HBV vaccine should be considered when the person's immunity is improved and CD4 count is >200 cells/mm³.

- III. Pneumococcal polysaccharide vaccine may be considered for people with HIV in WHO clinical stage 1 or, if CD4 testing is available, with a CD4 count >500 cells/mm³.
- IV. PLHIV should be encouraged to receive annual influenza vaccination with the inactivated subunit influenza vaccine.
- V. The yellow fever vaccine should not be given to PLHIV in WHO stage 3 or 4 disease or with a CD4 cell count below 200 cells/mm³. The vaccine can be given to PLHIV in WHO stage 1 or 2 disease if the benefits of vaccination outweigh the risks (i.e. necessary travel to an area with a yellow fever epidemic or where the disease is endemic).
- VI. BCG vaccine protects children younger than 2 years of age against disseminated and severe TB, including TB meningitis and miliary TB. However, because of the risk of severe local reactions and disseminated BCG disease, children with symptoms of HIV infection should not receive BCG vaccine. Asymptomatic infants should be vaccinated as recommended. BCG is not recommended for adolescents and adults, including those with HIV infection, because it has little or no effect in reducing the number of adult cases of pulmonary tuberculosis
- VII. Live, attenuated oral cholera vaccine is contraindicated in HIV-infected people. The killed cholera vaccine can be offered to PLHIV at risk of cholera infection or traveling to a cholera endemic/epidemic region.

3.2.9 Reproductive health and family planning

PLHIV have reproductive health rights and needs and should therefore receive access to the full range of reproductive health services available to the general population.

- I. HIV+ women and couples living with HIV infection should be encouraged to discuss their reproductive options and those who wish to have children should be encouraged to discuss with their health care provider to ensure they go through a safe and successful pregnancy.
- II. Where pregnancy is not desired, effective contraception should be offered; if hormonal methods are chosen, dual contraception (use of both hormonal contraception and condoms) should always be encouraged and condoms provided.
- III. Effective use of contraception in HIV+ women plays an important role in the prevention of unplanned pregnancies and thus the prevention of mother-to-child transmission (PMCT) of HIV infection.
- IV. Where pregnancy is desired, a couple's status should be considered; if discordance exists, appropriate advice and support should be given. If pregnancy has occurred in a HIV+ woman, ART should be used to optimize the mother's health and prevent mother-to-child transmission of HIV. (Only if she meets the criteria for chronic care especially adherence to lifelong ART)
- V. The choice of contraceptive methods in HIV+ women is the same as in HIV uninfected women. Hormonal contraception may be used in HIV-infected women; however choice of hormonal contraception should take into account ARV drug use. HIV-

positive women on efavirenz should be informed of the risk of fetal abnormalities associated with this drug if pregnancy occurs. Effective contraception should be availed to women at risk of pregnancy if efavirenz needs to be used

3.2.10 Nutrition

HIV infection is often associated with poor nutrition due to a number of reasons including:

- Increasing energy requirements
- Decreased appetite
- Reduced intake due to painful oral and oesophageal OIs
- Malabsorption
- Unavailability of sufficient food due to household food insecurity and poverty

Low body mass index is an independent predictor of mortality in PLHIV.

- I. At the initial clinical assessment and at regular intervals thereafter, all PLHIV should receive full nutritional assessment (weight, height, BMI, MUAC, symptoms related to appetite, nausea, difficulty swallowing, diarrhoea, food drug interactions and adequacy of food intake).
- II. Clinically malnourished adults ($\text{BMI} < 18.5 \text{ kg/m}^2$) need therapeutic and supplementary feeding support until their BMI is above 18.5 kg/m^2 .
- III. Care and treatment programmes should link patients to community organizations and programmes that will assist them to achieve household food security.
- IV. PLHIV should be provided with daily micronutrient supplements (appropriate multivitamin preparation); unless their diets are determined to be adequate and diversified.
- V. The standard recommendations for nutrient intake and nutritional support for pregnant and lactating women should be followed, regardless of the woman's HIV status.

3.2.11 Safe water, sanitation and hygiene

Diarrhoeal illnesses are common causes of mortality and morbidity among PLHIV. These diseases are often due to lack of access to safe, drinking water, and improper disposal of human and animal waste leading to contamination of food and water, and poor personal hygiene.

- I. PLHIV should be counselled to wash their hands with soap after handling human or animal faeces, after using the toilet and before food preparation or eating.
- II. Facilities for proper disposal of human waste should be available to PLHIV and their households
- III. PLHIV should be trained on, and provided with household-based water treatment methods and water storage containers that prevent manual contact with drinking water.

4. Initiation of antiretroviral therapy in adults and adolescents

4.1 Introduction

The introduction of ART has transformed HIV infection from a debilitating and fatal disease to a manageable chronic disorder. The use of ART has been accompanied with reduction in death rates, hospitalization and the incidence of opportunistic infections. In spite of established efficacy and safety profiles of the ART regimens used, the medications used have some adverse drug reactions, drug-drug interactions, and emergence of drug resistance often due to sub-optimal adherence to therapy. To maximize on the benefits of ART, it is important to perform a complete clinical evaluation and to adequately prepare the patient for life-long ART.

4.2 Assessment and preparation of patients for ART

4.2.1 Pre-treatment evaluation

All patients seeking HIV care in comprehensive care centres or other health care settings should have a complete medical history taken, a thorough physical examination and as complete and appropriate a laboratory evaluation as possible carried out. The purpose of this comprehensive clinical assessment is to:

- Confirm the presence of HIV infection if not previously or reliably done
- Assess the patient for WHO clinical staging for HIV
- Detect the presence of any co-existing illnesses particularly the common and serious opportunistic infections
- Review concomitant medications including traditional therapies, alcohol, cigarette use and non-prescription drug use
- HIV-positive patients being assessed for treatment should be started on cotrimoxazole preventive therapy unless contraindicated (see section 3.2.3)

Evaluation of patient should include clinical, nutritional, laboratory and social assessment, as well as assessment of other factors that may impact on adherence.

4.2.2 Clinical assessment

The goal of clinical assessment is to identify patients who need ART and ensure they are medically ready to commence therapy. The assessment involves thorough history, screening for and treating/stabilizing any opportunistic infections (OIs), starting preventive therapy against OIs, addressing any pre-existing medical problems, WHO clinical staging and determining if ART is required.

Clinical assessment includes confirmation of the diagnosis of HIV infection: healthcare providers should obtain written documentation for the patient's HIV test result. If not available a repeat HIV test should be carried out.

1. A thorough history should be taken with the aim of;
 - establishing the patient's concerns and expectations,
 - identifying intercurrent illnesses and opportunistic infections,
 - documenting history of ARV use including use of ARV medicines for PMCT,
 - identifying important co-morbidities (HBV, diabetes, hypertension, kidney disease, tuberculosis) and medication history,
 - nutritional assessment, family, social and sexual history; sexual partners and HIV status if known; any children and their HIV status,
 - drug allergies, particularly cotrimoxazole,
 - patient's and partner's use of alcohol and other drug of recreation,
 - menstrual history; syndromic review for STIs; obstetric history;
 - mental health assessment,
 - occupational history and potential impact of treatment options on work life.

A complete physical examination should be performed as part of the initial evaluation. Important components include but are not limited to:

- general health, mood (anxiety, depression, anger), weight, height, temperature, blood pressure and respiratory rate,
- skin examination to look for significant HIV-related skin lesions; particularly PPE, herpes zoster scar, Kaposi sarcoma and fungal infections,
- oral exam to look for candidiasis, Kaposi sarcoma, oral hairy leukoplakia and gum disease,
- lymph nodes enlargement, particularly asymmetric or rapidly enlarging lymph nodes which will require biopsy or fine needle aspiration to exclude infection or malignancy,
- examination of the genitalia and anus to look for ulcers, sores, urethral discharge, condylomata (genital warts), or Kaposi lesions. Females will require speculum examination and cervical screening carried out (visual based methods as per national recommendation. Pap smear may also be done).

2. Systems examination (look for signs of respiratory, cardiac and neurologic disease and other organ enlargement or ascites in the abdomen).

The WHO clinical staging (Table 2.1 and 2.2) is designed to be used where HIV infection has been confirmed with an antibody or a virological test. The clinical assessment above will provide information to support WHO clinical staging.

The WHO clinical staging provides clinicians and patients with important information about HIV disease severity and guides clinical management. It is useful:

- a. for providing guidance as to when to start or review ARV drug therapy,
- b. in assessing clinical response to therapy in the absence of appropriate laboratory tests,
- c. for determining prognosis and monitoring patients' clinical progress.

4.2.3 Laboratory assessment

Laboratory tests provide important objective information on the clinical state of the patient in order to

- confirm HIV infection
- establish presence of common concurrent conditions especially hepatitis B, cryptococcal meningitis
- determine baseline laboratory tests prior to initiating drugs that may alter them to assess for eligibility for ART by CD4 count
- pregnancy status for female patients of reproductive age.

Laboratory assessment is not a prerequisite for ART initiation and should not cause undue delay in starting ART in patients who are eligible for ART following clinical assessment.

The comprehensiveness of laboratory tests will depend on the clinical presentation of the patient. Stable patients with no evidence of co-existing systemic illness often require minimal testing, as opposed to ill patients who may require more extensive laboratory tests to assess for and manage concurrent illnesses.

- A CD4 count at initiation of ART is essential and should be done. More than 50% of HIV-infected patients with WHO clinical stage 2 (mild HIV disease) may have a CD4 count of ≤ 350 cells/mm³. HIV-infected individuals with WHO clinical stage 1 and 2 disease should have access to CD4 testing to decide if treatment should be initiated.
- Baseline haemoglobin is recommended before starting an AZT containing regimen;
- Baseline ALT is recommended for patients initiating a NVP containing regimen and those at risk of drug-induced liver toxicity (ART naïve women with CD4 >250 cells/mm³ on NVP and patients with pre-existing liver conditions)

- HBsAg is desirable to identify patients with HIV/HBV co-infection who will preferentially benefit from TDF/3TC or TDF/FTC containing regimen.

Where available, the following laboratory tests are recommended in PLHIV prior to starting ART:

- HIV serology (when patient has no documentation of a HIV test in the records)
- CD4 cell count
- Haemoglobin concentration
- ALT
- Creatinine
- Urinalysis
- Hepatitis B surface antigen (HBsAg)
- Serum cryptococcal antigen – CRAG-(if the CD4 cell count is less than 100 cells/mm³)

It's not possible for ALL facilities providing ART services to perform all the laboratory tests required for HIV care and treatment. If a facility does not have on-site capacity to carry out any particular test, arrangements should be made to transport specimens to a local or regional reference laboratory. Facilities are encouraged to join or form regional networks of laboratory services to improve access to these tests.

4.2.4 Psychosocial assessment

The goal of psychosocial assessment and preparation is to

- begin the process of empowering the patient through education and support,
- address the patient's or caregiver's concerns raised as a result of a diagnosis of HIV infection,
- educate the patient or caregiver on HIV, disease progression and its management,
- discuss with the patient or caregiver about disclosure and its benefits,
- discuss and offer the patient or caregiver the opportunity to join support groups,
- identify (and support the patient in addressing) any factors in the patient's family and social circumstances that may impact negatively on patient's health and ART outcome,
- provide adherence education and counselling, and develop mechanisms to ensure high-level adherence; and
- ensure that the patient is ready, willing and able to start and continue with ART if clinically indicated.

The initial psychosocial assessment and preparation often takes 2-3 sessions and should be started at the earliest opportunity. Always assess patient's understanding and knowledge before giving further information.

Appointments for psychosocial assessment should not unduly delay initiation of ART. The care team should use their judgment to decide whether a patient is ready for ART; and provide ongoing psychosocial support after initiation of ART.

4.2.4 Adherence counselling and assessment

Adherence is central to the success of ART. Almost perfect adherence (rates exceeding 95%) is desirable in order to maximize the benefits of ART. This means taking the correct dose of drugs at the correct times while observing any dietary or fluid restrictions. Adherence protocols should be available in HIV Clinics and all HCWs should be familiar with them to ensure consistency of adherence messages. Organized clinic records including diaries, daily list of defaulters and tracker cards should be maintained. The clinic should have a clearly defined and prioritized system of tracing defaulting patients. Community groups and patients' support groups should be enlisted to help with adherence education support and patient tracking.

Table 4.1 Checklist to maximize adherence

1.	Patient/caregiver attended all scheduled preparation visits?
2.	Patient/care giver prepared well before ART begins? Written information provided where useful?
3.	Patient/care giver given information on and understands the benefits of ART?
4.	Patient/care giver able to demonstrate how they will take/give child their ARVs?
5.	Information about predictable and common side-effects of intended regimen.
6.	Patient/care giver knows what to do should common mild or serious side-effects occur?
7.	Has patient disclosed diagnosis? (Family members at risk, sexual contacts? Status of family/contacts at risk?)
8.	Patient advised and encouraged to identify a treatment supporter, ideally a family member?
9.	Patient informed of group sessions for education and counselling?
10.	Patient locator information and contact details up to date?
11.	Adherence preparation information recorded?
12.	Next appointment given?

4.3 When to initiate antiretroviral therapy in adults and adolescents

The optimal time to start antiretroviral therapy in patients with asymptomatic or mild chronic HIV infection continues to be a subject of ongoing intense investigation. The dilemma has been the best approach to balance the benefits of antiretroviral therapy on one side and the long term adverse effects of antiretroviral therapy together with prospects of achieving life-long (decades) of maximal adherence to ART on the other hand. However, evidence from randomized trials now supports earlier initiation of ART in asymptomatic patients as recommended in these guidelines.

Goals of ART

The goals of ART are:

- maximal and durable suppression of viral replication to prevent development of HIV drug resistance and treatment failure,
- restoration and/or preservation of immunologic function,
- reduction of HIV-related morbidity and mortality,
- improvement of the patient's quality of life including prevention of unpleasant adverse drug effects of ARVs,
- prevention of onward transmission of HIV infection.

Currently available ARVs do not completely eradicate HIV from the body once the infection is established. Life-long therapy is therefore required

Key strategies to achieve the goals of therapy include:

- I. **Provider expertise:** providers should be able to:
 - assess and prepare patients to ensure effective management of opportunistic infections and long term adherence to treatment,
 - use ARV drugs rationally and adhere to national guidelines,
 - ensure regular and adequate monitoring of patients,
 - keep complete, legible and accurate patient records to facilitate chronic care,
 - identify and manage complications of treatment and change treatment appropriately,
 - recognize personal and institutional limitations to manage particular ARV and HIV-associated complications and refer or consult appropriately, and
 - identify and manage the complications associated with drug interactions.
- II. **Patient education and preparation** to ensure long term adherence to recommended interventions, should address the following:
 - the need for life-long therapy - HIV is not curable and currently requires lifelong continuous ARV drug treatment; the expected benefits of treatment and consequences of treatment interruption should be discussed,
 - that adherence is essential for treatment success and the relationship between non-adherence and poor treatment outcome (declining health) and drug resistance,
 - current drugs, while tolerable, are not without potential side-effects and patients should be instructed on what to do in the event of such side-effects,
 - the necessity for life-long, chronic care and self-management with oversight from medical provider whether or not on ART; and
 - PLHIV on ART need to avoid alcohol, recreational drugs and substances, over-the-counter and herbal medication whose interactions with ARV drugs may be undefined or undesirable.

Principles of antiretroviral therapy.

- i. ART is only one part of comprehensive HIV care
- ii. It is recommended that opportunistic infections are addressed first before starting antiretroviral therapy.
- iii. Patients should not be denied ART based on predicted non-adherence; instead, obstacles to adherence should be identified and corrected through on-going intensified counselling, support and monitoring.
- iv. Factors to consider when selecting ART regimens include
 - ease of administration (dosing frequency, food and fluid restrictions) and therefore, better chances of adherence,
 - co-existent conditions such as tuberculosis, hepatitis B, diabetes, depression, epilepsy recreational drug use with the risks of adverse drug-drug interactions,
 - pre-existing laboratory abnormalities such as anaemia, liver enzyme elevations, proteinuria or elevated creatinine etc,
 - pregnancy or the risk thereof,
 - potential for infection with a virus strain with reduced susceptibility to one or more ARV drugs (e.g. due to prior exposure to NVP for PMTCT or transmission of drug resistant virus),
 - side-effect profile and laboratory monitoring requirements,
 - potential for preservation of future treatment options; and
 - availability and cost of ART.

Further, evidence has also shown that;

- a. patients with TB/HIV co-infection starting ART soon after initiation of anti-TB treatment have lower mortality than those delaying ART; even at higher CD4 counts. This also applies to other opportunistic infections, except for cryptococcal and tuberculous meningitis;
- b. patients starting therapy at very low CD4 cell counts take long to achieve immune-reconstitution and may never achieve a normal CD4 cell count and therefore remain at risk of HIV-associated mortality and morbidity.
- c. initiating ART at CD4 counts of ≤ 350 cells/ mm³ (as opposed to waiting until the CD4 count drops to <250 cells/ mm³) confers obvious morbidity and survival benefits;
- d. more than 50% of HIV-infected patients with WHO clinical stage 2 (mild HIV disease) may have a CD4 count of ≤ 350 cells/mm³, emphasizing the need for baseline CD4 count measurement in all PLHA entering care;
- e. patients with HIV/HBV co-infection may benefit from initiating ART earlier (with CD4 cell count >350 cells/mm³) if these patients have evidence of active hepatitis;

Accumulating evidence is showing that treatment of the HIV-positive partners in a sero-discordant relationship (irrespective of CD4 cell count; and particularly in those with a CD4 cell count of 350-500 cells/mm³) markedly reduces the risk of HIV transmission to the HIV-negative partner. Similarly, emerging evidence has shown that initiation of life-long triple therapy in pregnant mothers irrespective of CD4 cell count may confer greater benefits to the mother, as well as markedly reduce transmission of HIV infection from mother-to-child. This evidence is under consideration in Kenya for future National recommendations.

The following are the recommendations/indications for initiating ART in HIV-infected adults and adolescents with documented HIV infection (Table 4.2).

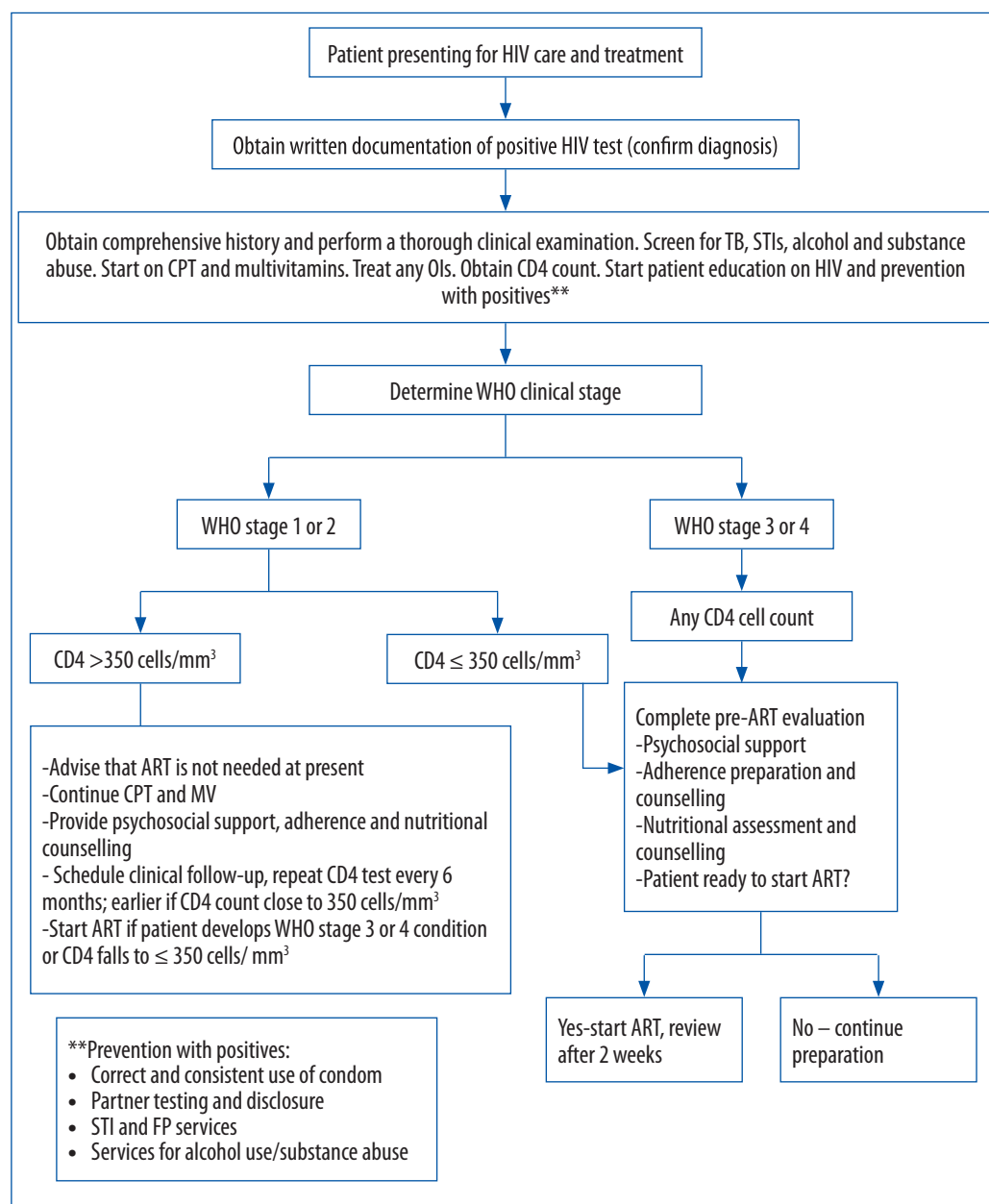
Table 4.2 Criteria for initiation of ART in adults and adolescents

WHO stage/ Clinical condition	CD4 cell count (cells/mm ³)	
	≤350	>350
1 & 2	Start ART	Defer ART
3 & 4 ¹	Start ART	Start ART
TB disease	Start ART	Start ART
HIV/HBV co-infection with evidence of active/chronic liver disease	Start ART	Start ART
HIV associated nephropathy ²	Start ART	Start ART

¹ Patients with WHO stage 3 or 4 should be started on ART irrespective of availability of CD4

²HIV associated nephropathy is characterized by proteinuria and impaired kidney function with or without peripheral oedema.

Figure 4.1 Initiation of antiretroviral therapy in adults and adolescents



4.4 What to start with – ARV drugs for treatment-naïve adults and adolescents

ARV drugs currently available do not cure HIV but suppress viral replication, thus preventing further disease progression and immune system damage. For adequate treatment potency and efficacy, antiretroviral drug therapy usually involves a combination of a minimum of three antiretroviral drugs often from at least two different classes.

4.4.1 Recommended first-line standardized national antiretroviral drug regimens

All new (treatment naïve) patients should be started on

TDF + 3TC + EFV or NVP

In pregnant women and where patients are unable to tolerate tenofovir the following is recommended:

AZT + 3TC + EFV or NVP

- The combination of TDF + 3TC is recommended as the preferred NRTI backbone in patients without contra-indications to TDF.
- The TDF and 3TC NRTI backbone is also recommended for patients with HIV/ HBV co-infection as the two agents have anti-HBV activity and should be used in combination for maximal potency and avoidance of the emergence of HBV drug resistance.
- AZT is recommended as part of the first line regimen in pregnant women because of the long term experience with it in this situation.
- Abacavir use in adult patients in Kenya should be limited to those with moderate to severe renal impairment where it is preferred above the other NRTIs.
- Stavudine use is no longer recommended as an option in patients starting first line ART. However, stavudine continues to be used by a large proportion of patients already on ART; these patients should be monitored for toxicity and treatment reviewed if present. Stavudine will continue to have a role as part of second-line therapy where AZT is not tolerated.
- With regard to the NNRTI choice, efavirenz is preferred in TB/HIV co-infection, while nevirapine is preferred in women who wish to conceive or are at risk of pregnancy and are not on effective contraception.

Table 4.3 Recommended first-line ART in treatment naïve adults and adolescents

Target population	Preferred options	Comments
Adults and adolescents	TDF+ 3TC + EFV or NVP	TDF has been associated with renal toxicity and bone mineral loss.
	AZT + 3TC + EFV or NVP	AZT has been associated with anaemia, gastrointestinal side-effects, and proximal muscle weakness.
HIV/TB co-infection	AZT or TDF + 3TC + EFV	If EFV cannot be used, use of PI/r with Rifabutin based TB medicines is the best option but AZT + 3TC + ABC/TDF* is an alternative regimen if EFV cannot be used and PI/r is not tolerated NB: AZT+3TC +ABC/TDF this regimen is inferior to standard regimens and should be changed to standard ART regimen after completion of TB treatment
HIV/HBV co-infection	TDF + 3TC + EFV or NVP	Use of 2 agents active against HBV (TDF + 3TC) recommended
Pregnant women	AZT + 3TC + NVP or EFV	EFV should not be initiated in the first trimester.
	TDF + 3TC + NVP or EFV	
First line ART regimen for women with history of exposure to nevirapine		
Nevirapine exposure within 24 months	Preferred	AZT + 3TC+ LPV/r
	Alternative	TDF + 3TC + LPV/r
Nevirapine exposure >24 months ago or no Nevirapine exposure	Preferred	AZT + 3TC + NVP/EFV*
	Alternative	TDF + 3TC + NVP/EFV*

NB: d4T can be used in patients who cannot tolerate AZT or TDF

* EFV should not be used in first 12 weeks (1st trimester) of pregnancy and should be changed to NVP if in 1st trimester of pregnant.

Table 4.4 Administration of first-line ARVs in adults and adolescents

Name	Dosage forms	Recommended adult dose	Food effect	Dose adjustment in renal failure
Zidovudine(AZT)	100 and 300 mg tablets	300 mg twice daily	more gastro intestinal effects on an empty stomach	Yes
Tenofovir (TDF)	300 mg tablets	300 mg once daily	None	Yes
Lamivudine (3TC)	150 and 300 mg tablets	150 mg twice daily or 300 mg once daily	None	Yes
Efavirenz (EFV)	200 mg(scored) and 600 mg tablets	600 mg once daily at bedtime	Take on an empty stomach or with a low fat meal	No
Nevirapine (NVP)	200 mg tablets	200 mg once daily for the first 14 days, thereafter, 200 mg twice daily	No	No
Abacavir	300 mg tablets	300 mg twice daily	No	No
Stavudine (d4T)	30 mg	30 mg twice daily	No	No

Fixed dose combination for adult are available (*refer table 2.4*).

FDCs should be used to improve adherence on ART.

Single formulations should only be used when FDCs are contraindicated.

EFV is not available as FDC with AZT/3TC and D4T/3TC.

5. Monitoring and changing antiretroviral therapy in adults and adolescents

5.1 Introduction

Patients on ART should be monitored closely in order to assess adherence to the prescribed regimen, efficacy of treatment and inter-current illnesses. They should also be evaluated for drug intolerance and side-effects.

5.2 Monitoring of patients on ART

Monitoring of therapy involves both clinical and laboratory parameters as summarized on Table 5.1

Table 5.1 Summary of clinical and lab follow up of a patient on ART

	Week		Month								
Appointment*	0	2	1	2	3	4	5	6	9	12	Stable
Clinical evaluation, Wt, Ht ¹ , ADRs	+	+	+	+	+	+	+	+	+	+	Every visit
TB screening	+	+	+	+	+	+	+	+	+	+	Every visit
Adherence check	+	+	+	+	+	+	+	+	+	+	Every visit
Hb	+		+ ²		+ ²	Symptom directed					
ALT	+		+ ^{3,4}		+ ^{3,4}	Symptom directed					
Creatinine ⁵	+	Symptom directed									
Pregnancy test ⁶ (PT)	+	If indicated									
Urinalysis	+	Symptom directed									
Fasting lipid profile & glucose ⁷	+	Annually for patients on PIs									
CD4 count	+							+		+	Every 6 months
Viral load ⁸		Targeted									

¹Weight and height should be measured in children regularly and in adults for BMI calculation at initial assessment

²Schedule when AZT is used

³Schedule when NVP is used

⁴Schedule in pregnant women: ALT should be done at baseline, 2, 4 weeks then monthly until the woman delivers; especially important in women with CD4 >250 cells/mm³ at ART initiation on NVP-based regimen

⁵All pts should have creatinine measured if available. NRTI doses may need adjustment if renal function (RF) abnormal. TDF should be avoided if RF abnormal (See Table 20.11–20.14).

⁶PT should be done at baseline if EFV is to be used; thereafter PRN

⁷Schedule if PIs used

⁸Currently viral load is indicated for suspected treatment failure cases and before substituting d4T in cases of toxicity where d4T has been used for more than 6 months.

* appointment visits should be based on patients clinical status.

Laboratory tests, while desirable, are not a prerequisite for initiation or for routine follow up of patients on ART.

5.2.1 Clinical monitoring for patients starting ART

While the recommended frequency of visits for clinical monitoring should be as described above, patients should be encouraged to attend the clinic in between appointments if they experience any problems.

Following ART initiation, patients need to be followed up closely for the first 3 months for the following reasons:

- monitoring and support for adherence is critical early after treatment initiation when the risk for ARV drug resistance development is high if adherence is sub-optimal;
- most common ARV drug adverse reactions occur within the first few months after ART initiation;
- immune reconstitution inflammatory syndrome (IRIS) is likely to present during this time and should be considered in the assessment.

The first planned visit should take place 2 weeks after initiating therapy. This appointment should focus on ensuring that the medicines are being taken and stored correctly. Any side-effects should be noted and addressed accordingly. Patients on nevirapine should have the dose of nevirapine adjusted at this point if the drug is well tolerated (Table 4.4).

- If the patient is stable, subsequent planned clinical visits should be carried out at monthly intervals for the first 6 months of ART; and the focus should be on assessing the patient's clinical progress, reinforcing adherence counselling and any other supportive counselling; and checking for any side-effects of the drugs.
- After 6-12 months following initiation of ART, clinical appointments and drug pick up may be spaced up to 3 month intervals in compliant and clinically stable patients with a good understanding
- Follow up appointments for stable patients can be devolved to a nurse suitably equipped and trained to triage patients. Estimation of the level of adherence is important during all visits.
- Patients should be informed that in case of any medical problems in between clinical appointments, they will be seen by a clinician.

At each clinical visit:

- Plot the patient's weight and note the trend,
- Determine the patient's physical condition;

- ask about and check for symptoms and signs of anticipated adverse reactions (e.g. pallor if on AZT; rash in patients on NVP; features of peripheral neuropathy or lipoatrophy in patients on d4T) and other clinical conditions,
- ask about symptoms and check for signs suggestive of TB. Based on symptom screening, further tests for TB should be carried out whenever TB is suspected. HIV-infected patients on ART are less likely to develop TB compared to untreated patients; however because of the high prevalence of TB in the local community, they remain at risk for developing TB thus the need to maintain vigilance and routine clinical screening.
- address ongoing medical problems including the possibility of treatment failure (the development of new OIs);
 - treat any inter-current infections,
 - clinicians should remember that early in the course of ART of severely immunocompromised patients before immunological restoration occurs, patients will still be at risk of various opportunistic conditions; the appearance of these within the first 6 months of treatment does not necessarily indicate treatment failure.
- Assess for immune reconstitution inflammatory syndrome (IRIS).
- Check drug dosages at each visit and adjust accordingly if there is any indication eg. Renal disease.
- Assess and support adherence at each visit.
- Encourage patients to carry their medicines to the clinic at each visit. Conduct and reconcile pill counts to assess adherence.

5.2.2 Monitoring treatment adherence

Adherence is central to the success of ART. Almost perfect adherence (rates exceeding 95%) is desirable in order to maximize the benefits of ART. This means taking the correct dose of drugs at the correct times while observing any dietary or fluid restrictions. While treatment regimens have improved tremendously with greater potency, tolerability and ease of administration, no treatment is effective unless taken appropriately. The relationship between adherence to treatment and viral suppression is well established. Poor adherence leads to continue viral replication; this leads to continued destruction of the immune system with decline in the CD4 count and subsequently development of HIV-related illnesses. As viral replication continues in the presence of ARV drugs, emergence of resistant viral strains follows, limiting treatment options in the future and adding to programme costs as patients require more expensive regimens.

Adherence monitoring

Adherence assessment should be carried out at each visit. This should include

- Discussing with the patient about how they take their pills, any difficulty experienced and any concerns about their treatment.
- A pill count should be carried out and related to the number of pills obtained at the last visit and the date of the current visit.
- In-depth discussions should be held with patients with adherence problems or excess pills, with particular reference to their home circumstances; work/school; disclosure; substance use; additional support should be arranged where necessary.
- Assessment for side-effects is important during each visit as side-effects often contributes to non-adherence
- Adherence should be related to the clinical and laboratory indicators to form a comprehensive view of a patient's progress.

The following strategies are useful in monitoring and maintaining high level adherence in HIV care clinics:

- Adherence protocols should be available in the CCC and all HCWs should be familiar with them to ensure consistency of adherence messages. These protocols should include treatment preparation and patient education as well as adherence assessment during each clinic visit
- Organized clinic records including diary, daily list of patients missing appointments, tracker cards should be maintained.
- The clinic should have a clearly defined and prioritized system of tracing defaulting patients.
- Community groups and patients' support groups should be enlisted to help with adherence education support and patient tracking.
- A robust community patient treatment support programme is essential in limiting the number of patients missing treatment or defaulting from care.

For categories of patients, pre-filled pill packs and directly observed treatment (by family member or community volunteer) may be necessary to support adherence.

Counselling and the provision of accurate information to all patients is an important determinant of treatment adherence. Information on side-effects should be provided and patients should be told what to expect from the treatment. A treatment timetable, e.g. like the TB card, should also be provided and patients and care givers should be shown how to fill out the card. Counselling should be provided at each visit and patients should be allowed to seek help between visits as well. Patients should be encouraged to bring with them all tablet containers at each visit. Providers should carry out a pill count in order to determine whether the medications have been taken as per schedules provided.

Strategies to optimize adherence include:

- Patient education and counselling
- Easy access to medication
- Convenient dosing regimen
- Pre-filled pill packs/blister packs which facilitate regular pill counts
- Medication reminders
- Treatment buddies
- E-caps
- SMS reminders
- Treatment support from family or a friend/treatment buddy

5.2.3 Laboratory monitoring of antiretroviral therapy

I. Monitoring for ART intolerance and side-effects

Laboratory tests are recommended for

- Monitoring for toxicity,
- Assessing response to and efficacy of treatment,

Laboratory tests, while desirable, are not a prerequisite for initiation or for routine follow up of patients on ART.

Tests for monitoring toxicity

All classes of antiretroviral drugs can cause varying degrees of abnormalities in laboratory tests. In order to anticipate some of the common side-effects, baseline laboratory tests are recommended, where available. The tests and its frequency is indicated in Table 5.1

Ideally, these basic tests should be available on site (especially in all level 4 and 5 facilities). If a facility does not have the capacity to carry out these tests on site, arrangements should be made to transport specimens to a regional laboratory as part of laboratory networking.

Routine haematological and biochemical monitoring is no longer recommended for patients on ART. Laboratory tests should however be accessible to support symptom-directed patient management. Symptom-directed monitoring means that the clinician orders tests on recognition of symptoms and signs of potential intercurrent illness, ART-related toxicity, occurrence of an opportunistic condition, immune reconstitution syndrome or treatment failure.

Table 5.2 Laboratory monitoring for common ART-associated toxicity

ARV drug	Major toxicity	High risk situations*	Laboratory monitoring strategy
d4T	Lipodystrophy Neuropathy Lactic acidosis	Age >40 years-old CD4 count <200 cells/mm ³ BMI >25 (or body weight >75 kg) Concomitant use with INH or ddl	Symptom directed toxicity monitoring e.g serum lactate for lactic acidosis
AZT	Anaemia Neutropaenia	CD4 count <200 cells/mm ³ BMI <18.5 (or body weight <50 kg) Anaemia at baseline	Hb at baseline, at 4-6 weeks, and 12 weeks, thereafter, as needed.
TDF	Renal dysfunction	Underlying renal disease Age >40 years-old BMI <18.5 (or body weight <50 kg) Diabetes mellitus Hypertension Concomitant use of a boosted PI or nephrotoxic drugs	Urinanalysis and CrCl at baseline, at 1 month and then every 6 months. In absence of risk factor, urinalysis and CrCl annually.
EFV	Teratogenicity	first trimester of pregnancy (do not use EFV)	Pregnancy test when indicated
	Psychiatric illness	Depression or psychiatric disease (previous or at baseline)	-
NVP	Hepatotoxicity	HCV and HBV co-infection	ALT at baseline, at 4 and 12 weeks, then as symptom-directed thereafter.

II. Laboratory monitoring for efficacy

Efficacy of ART is monitored by regular and careful clinical assessment, assessment of immunologic function as indicated by the CD4 cell count,. While CD4 testing is now almost universally accessible, viral load capacity is still limited. Currently viral load testing is recommended in the assessment of patients suspected of failing treatment (i.e. targeted viral load testing).

CD4 cell monitoring

With successful ART, the rate of increase in CD4+ lymphocyte levels depends on the initial CD4+ lymphocyte count. While the majority of patients experience a good CD4 response, a minority may not do so despite good adherence, particularly if the baseline CD4+ lymphocyte count was very low e.g. less than 50 cells/mm³. Persistently declining CD4+ lymphocyte counts as measured on two occasions is suggestive of treatment failure and warrants further assessment.

A greater than 30% decline in CD4 counts should be considered significant and a viral load carried out for confirmation of treatment failure. Variations below this cut-off may be physiological.

A CD4 count should be determined at baseline and thereafter at 6 monthly intervals for all patients on ART. Where crucial treatment change decisions are being considered, at least two tests on separate occasions should be carried out. CD4 count should not be measured during a concurrent infection; measurement should be delayed until 2-4 weeks after recovery. For consistency, CD4 measurements in a patient should be carried out in the same laboratory and preferably at the same time of day. Laboratories carrying out CD4 measurements should have established adequate internal and external quality control and assurance.

HIV viral load monitoring

The HIV viral load decreases to undetectable levels within 6 months of successful ART. However this response also depends on the initial, pre-treatment viral load; where the pre-treatment viral load is very high it may take longer than 6 months for full suppression to be attained.

The following are indications for targeted viral load testing:

- When treatment failure is suspected, either clinically or immunologically;
 - CD4 fall by >30% from (on treatment) peak,
 - new or recurrent WHO stage 3 or 4 disease as well as recurrent PPE (after 6 months of ART),
 - failure of CD4 count to rise to >100 cells/mm³ after at least 12 months of therapy (less than expected CD4 response). Some patients may however have a poor CD4 response despite full virological suppression. Once viral suppression is confirmed they should not be considered to be failing treatment and should stay on the same regimen.
- In patients with drug toxicity who may need a single drug substitution and have been on ART for more than 6 months. Viral load is recommended to rule out treatment failure before substituting single drug for toxicity. This is important for patients who have been on a stavudine based regimen and have developed toxicity after several years of therapy, requiring substitution.
- In patients on third line or salvage therapy an annual viral load is recommended
- In patients on sub-optimal regimens eg. triple nucleosides in TB /HIV co-infection
- After six months of treatment for women starting NNRTI based regimen with history of prior exposure to nevirapine

- Crucial treatment change decisions should ideally be based on at least two tests done on separate occasions. A viral load persistently ≥ 1000 copies/ml implies on-going viral replication and the possibility of non-adherence to ART and/or drug-resistant virus and therefore treatment failure.

5.3 When to substitute therapy

Indications for changing therapy include:

- Adverse drug reactions/toxicity
- Drug interactions (refer tables 20.7-20.9)
- Management of co-morbidity (refer chapter 8)
- Pregnancy (refer chapter 16)

Toxicity

Adverse events are the most common reasons for substituting or discontinuing therapy and non-adherence to medication. Adverse drug reactions (ADRs) may be precipitated or exacerbated by

- Use of concomitant medications with overlapping, additive or synergistic toxicity, e.g. d4T with ddI; ARV drugs and anti-TB treatment. Overlapping toxicity profile can also lead to confusion as to which drug is responsible when toxicity develops.
- Co-morbid conditions that may exacerbate or increase risk of developing adverse events. These include dual treatment of TB and HIV, alcoholism, hepatitis B or C co-infection all of which are likely to increase the risk of hepatotoxicity.
- Drug to drug interaction may lead to an increase in dose-related toxicities, e.g. fluconazole increases NVP levels and may increase NVP related toxicity

Although the majority of patients will tolerate treatment fairly well, adverse events have been reported with virtually all antiretroviral drugs. Most patients who experience ADRs get symptoms that can be considered “mild” (nausea, fatigue, dizziness); however to many patients these undesired effects may be very distressing especially considering that patients may have been relatively asymptomatic prior to treatment initiation. It is therefore important to inform patients of likely side-effects and actions to take should ADRs occur.

Patients should be reassured that most mild side-effects occur early in treatment and resolve within the first few weeks after treatment initiation. Supportive treatment should be given if necessary. Rarely, it may be necessary to change treatment. Less commonly ADRs are serious and may even be life threatening. These may be acute, occurring early in treatment (e.g. NVP associated rash or Steven's Johnson syndrome) or after several months of ART (e.g. lactic acidosis)

Considerations for changing therapy due to toxicity

The following points should be considered carefully before changing treatment.

- Establish whether the adverse event is due to ARV drug(s) or to other medication. For example, one should consider whether isoniazid is the cause of peripheral neuropathy in a patient on ARV drugs taking anti-TB drugs
- Not all problems that arise during treatment result from ARV drugs; therefore, consider other disease processes, for example infectious hepatitis when there is elevation of liver enzymes.
- In the setting of a good therapeutic response, the development of a clearly definable toxicity permits single drug substitutions without compromising the overall regimen. Where alternative drugs are available change of treatment due to toxicity should be prompt; this is important because some ARV-related side-effects may respond poorly to treatment discontinuation.
- For minor symptoms ART should be continued and the patient reassured and closely observed
- In some instances especially with severe ADRs, the entire drug regimen needs to be discontinued For patients who develop ARV drug toxicity after more than 6 months on treatment, treatment failure should be considered and a viral load carried out prior to a single drug substitution.
- Treatment should be stopped if severe reactions occur; the medical event should be managed prior to reintroducing ARV drugs using a modified regimen.

Table 5.3 Class adverse effects of antiretroviral Agents

NRTIs Renal impairment, bone marrow suppression peripheral neuropathy, pancreatitis, lipodystrophy, hepatitis, lactic acidosis,	PIs Lipodystrophy, GI intolerance, hyperglycemia, lipid abnormalities
NNRTIs Rash, fever, nausea, diarrhoea, hepatotoxicity,	Common adverse effects Peripheral neuropathy – d4T and ddI Bone marrow suppression – AZT Skin rash and liver toxicity – NVP CNS disturbance – EFV Diarrhoea – NFV Hypersensitivity – ABC Dyslipidemia – PIs and d4T Lipodystrophy – PIs, d4T Renal toxicity - TDF

Table 5.4 Toxicities and recommended drug substitutions

ARV drug	Common associated toxicity	Suggested substitute
TDF	<p>Asthenia, headache, diarrhea, nausea, vomiting, flatulence</p> <p>Renal insufficiency, Fanconi syndrome</p> <p>Osteomalacia</p> <p>Decrease in bone mineral density</p> <p>Severe acute exacerbation of hepatitis may occur in HBV-coinfected patients who discontinue TDF</p>	<p>If used in first line AZT (or d4T if no other choice)</p> <p>If used in second line Within a public health approach, there is no option If patient has failed AZT /d4T in first line. If feasible, consider referral to a higher level of care where individualised therapy may be available</p>
AZT	<p>Bone marrow suppression: macrocytic anaemia or neutropaenia</p> <p>Gastrointestinal intolerance, headache, insomnia, asthenia</p> <p>Skin and nail pigmentation</p> <p>Lactic acidosis with hepatic steatosis</p>	<p>If used in first line TDF (or d4T if no other choice)</p> <p>If used in second line d4T</p>
EFV	<p>Hypersensitivity reaction</p> <p>Stevens Johnson Syndrome</p> <p>Rash</p> <p>Hepatic toxicity</p> <p>Persistent and severe central nervous system toxicity (depression, confusion)</p> <p>Hyperlipidaemia</p> <p>Male gynaecomastia</p> <p>Potential teratogenicity (first trimester of pregnancy or women not using adequate contraception)</p>	<p>NVP</p> <p>boosted PI (bPI) if intolerant to both NNRTIs</p> <p>Triple NRTI if no other choice</p>
NVP	<p>Hypersensitivity reaction</p> <p>Stevens Johnson Syndrome</p> <p>Rash</p> <p>Hepatic toxicity</p> <p>Hyperlipidaemia</p>	<p>EFV</p> <p>boosted PI (bPI) if intolerant to both NNRTIs</p> <p>Triple NRTI if no other choice</p>
LPV/r	<p>GI intolerance, nausea, vomiting, diarrhoea</p> <p>Asthenia</p> <p>Hyperlipidemia (especially hypertriglyceridaemia)</p> <p>Elevated serum transaminases</p> <p>Hyperglycaemia</p> <p>Fat maldistribution</p> <p>Possible increased bleeding episodes in pts with haemophilia</p> <p>PR interval prolongation</p> <p>QT interval prolongation and torsade de pointes</p>	ATV/r
ATV/r	<p>Indirect hyperbilirubinaemia</p> <p>Clinical jaundice</p> <p>Prolonged PR interval—first degree Symptomatic AV block in some pts</p> <p>Hyperglycaemia</p> <p>Fat maldistribution</p> <p>Possible increased bleeding episodes in individuals with haemophilia</p> <p>Nephrolithiasis</p>	LPV/r

Table 5.5 ARV related adverse events and recommendations (symptom-directed management of toxicity)

Adverse events	Major first line ARVs	Recommendations
Acute pancreatitis	d4T	Discontinue ART. Give supportive treatment with laboratory monitoring. Resume ART with an NRTI with low pancreatic toxicity risk such as AZT or TDF
Drug eruptions (mild to severe, including Stevens-Johnson syndrome or toxic epidermal necrolysis)	NVP, EFV (less commonly)	In mild cases, symptomatic care. EFV rash often stops spontaneously after 3-5 days without need to change ART. If moderate rash, non-progressing and without mucosal involvement or systemic signs, consider a single NNRTI substitution (i.e. from NVP to EFV). In moderate and severe cases, discontinue ART and give supportive treatment. After resolution, resume ART with a boosted PI (bPI)-based regimen or tripled NRTI if no other choice.
Dyslipidaemia	All NRTIs (particularly d4T) EFV	Consider replacing the suspected ARV
Anaemia and neutropaenia	AZT	If severe (Hb <7.0 g/dl and/or ANC <750 cells/mm ³), replace with an ARV with minimal or no bone marrow toxicity (e.g. d4T or TDF) and consider blood transfusion.
Hepatitis	All ARVs (particularly NVP)	If ALT is at more than five times the basal level, discontinue ART and monitor. After resolution, restart ART replacing the causative drug (e.g. EFV replaces NVP)
Lactic acidosis	All NRTIs (particularly d4T)	Discontinue ART and give supportive treatment. After resolution, resume ART, with TDF
Lipoatrophy and lipodystrophy	All NRTIs (particularly d4T)	Early replacement of the suspected ARV drug (e.g. d4T for TDF or AZT).
Neuropsychiatric changes	EFV	Usually self-limited, without the need to discontinue ART. If intolerable to the patient, replace NVP with EFV or boosted PI (bPI). Single substitution recommended without cessation of ART
Renal toxicity (renal tubular dysfunction)	TDF	Dosage adjustment for individuals with altered creatinine clearance (refer to section 5.2.3) Consider substitution with AZT
Peripheral neuropathy	d4T	Replacement d4T with AZT, TDF Symptomatic treatment (amitriptyline, vitamin B6)

Management of NRTI toxicities

TDF associated toxicity

TDF may cause renal impairment, in about 1-4% of patients on long term treatment. The impairment is characterized by elevation in creatinine, presence of proteinuria and glycosuria, and rarely, acute renal failure. Renal toxicity is often asymptomatic, but is more likely in patients with

- pre-existing renal disease (elevated creatinine or proteinuria at baseline),
- low CD4 cell count,
- advanced age (>35 years at initiation of therapy); and
- concurrent use of nephrotoxic agents.

Ideally, all patients should have a baseline urinalysis and serum creatinine (and an estimated creatinine clearance calculated) prior to initiation of TDF. Follow up should be symptom directed. Patients who develop significant renal impairment should have a creatinine clearance estimated and the decision on the NRTI component of the treatment (including TDF) made per the table below:

Calculating creatinine clearance (Cockcroft-Gault equation):

In men	In women
$\text{CrCl (ml/min)} = \frac{1.23 \times (140 - \text{age}) \times \text{weight}}{\text{Cr } (\mu\text{mol/l})}$ <p>(Age in years, weight in kg)</p>	$\text{CrCl (ml/min)} = \frac{1.04 \times (140 - \text{age}) \times \text{weight}}{\text{Cr } (\mu\text{mol/l})}$ <p>(Age in years, weight in kg)</p>

Table 5.6 Antiretroviral drug dose adjustment in renal impairment

Drug	Daily dose	Mild renal failure (GFR 20-50)	Moderate renal failure (GFR 10-20)	Severe renal failure (GFR <10)
AZT	600 mg	Unchanged	Unchanged	300 mg OD
d4T	60 mg	20 mg daily	20 mg daily	15 mg daily
3TC1	300 mg	150 mg daily	100 mg daily	50 mg daily
ddl >60/<60kg	400/250 mg	200/125 mg daily	125/100 mg daily	125/75 mg daily
TDF	300 mg	300 mg 48 hourly	Do not use	Do not use
ABC	600 mg	Unchanged	Unchanged	Unchanged
FTC	200 mg	200 mg q48h	200 mg q72h	200 mg q96h
PIs	Standard dose	Unchanged	Unchanged	Unchanged
NNRTIs	Standard Dose	Unchanged	Unchanged	Unchanged

For patients with moderate to severe renal failure, abacavir should be used as the preferred NRTI; dose adjustment is not required in renal impairment.

Figure 5.1 Management of AZT-associated bone marrow suppression

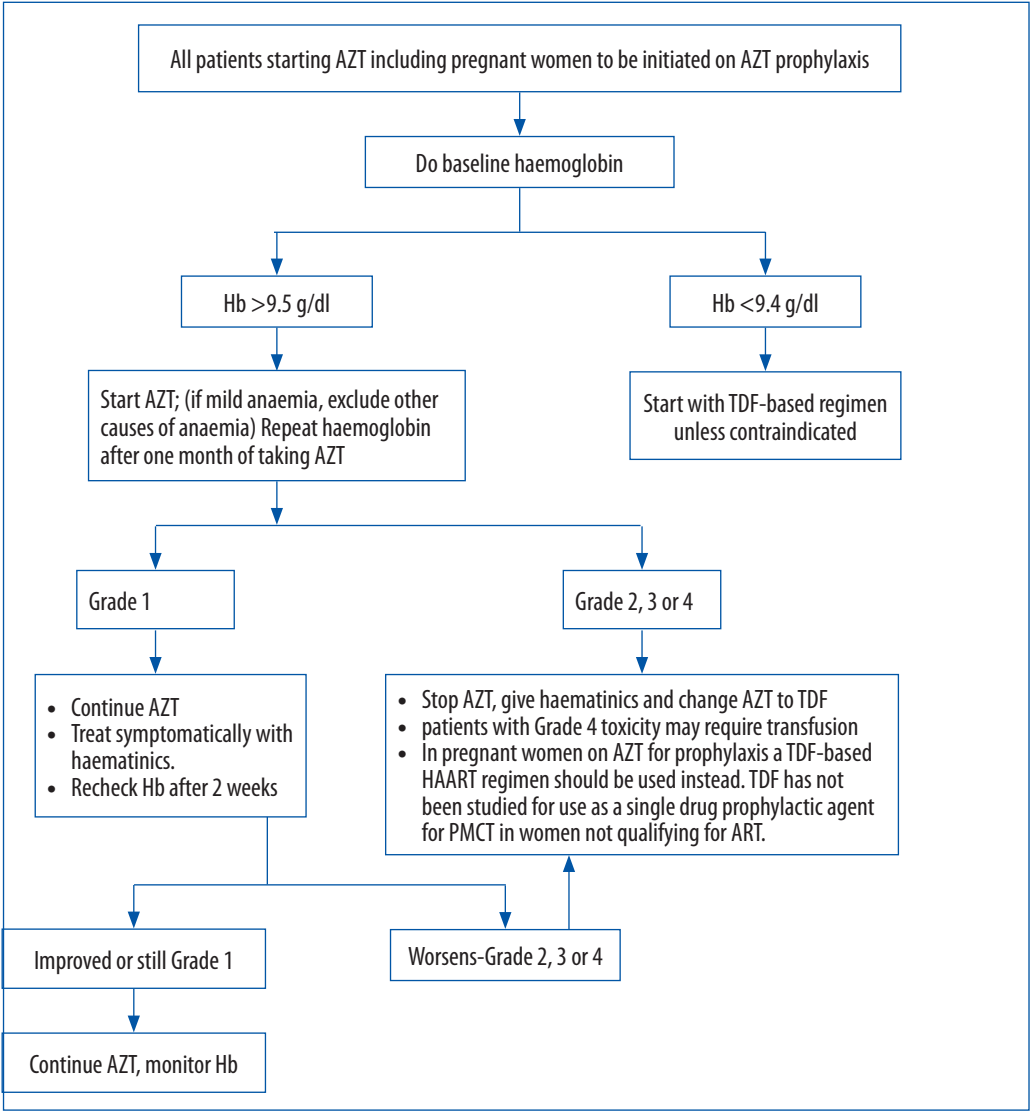
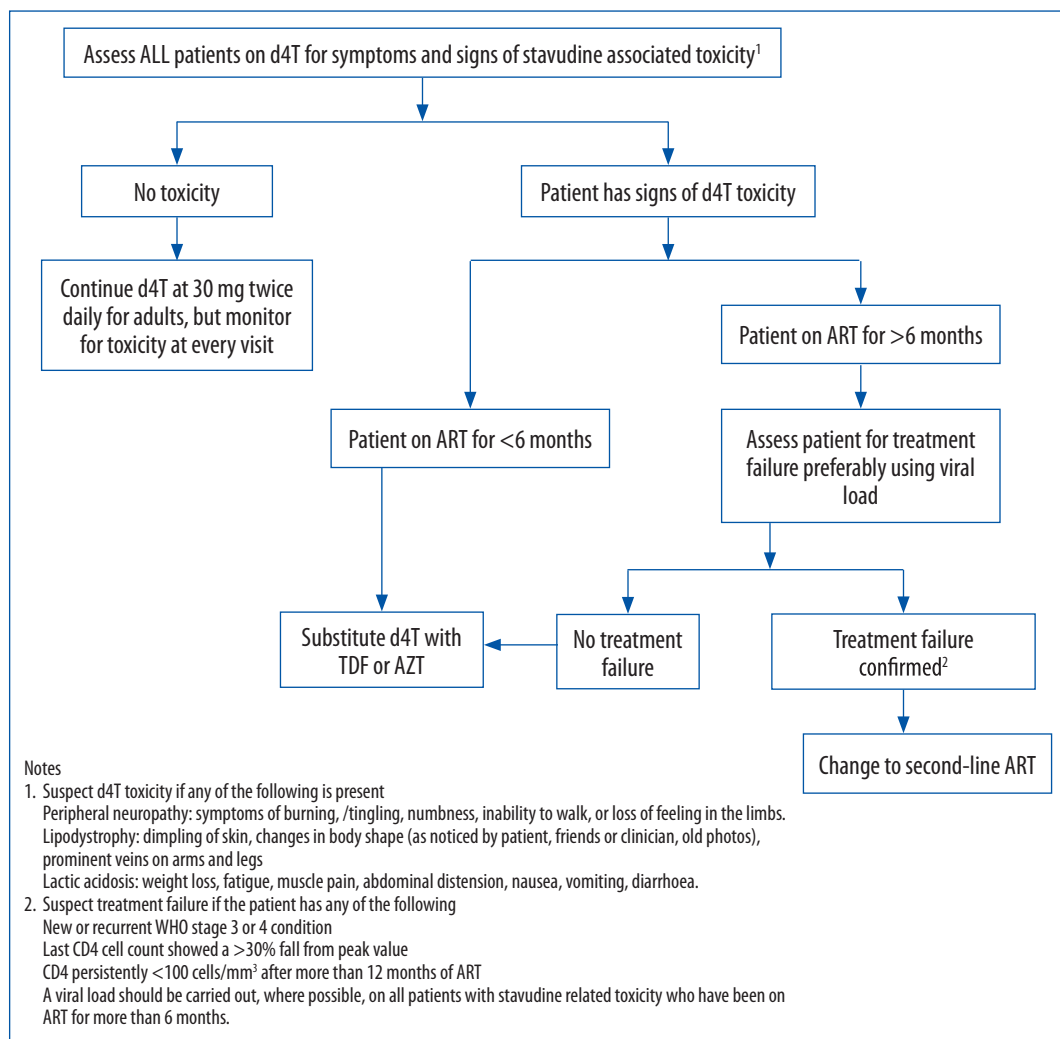


Table 5.7 Clinical grading of AZT-associated bone marrow suppression

Indices	Grade 1	Grade 2	Grade 3	Grade 4
Hb (g/dl)	8.5 – 9.4	7.5 – 8.4	6.5 – 7.4	<6.4
Neutrophil count (cells/ml)	1000 – 1300	750 – 999	500 – 749	<500

Patients with moderate or severe anaemia starting a first line regimen should ideally be started on a TDF-based or ABC-based regimen.

Figure 5.2 Assessing and managing d4T phase-out



Management of NNRTIs associated toxicity

- NNRTIs have a long half-life. As a result, if treatment is discontinued, therapeutic drug levels may persist for up to 2-3 weeks during which time viral rebound occurs. This means that if the NRTI backbone (which consists of drugs with relatively short half lives) is also discontinued at the same time, the patient will effectively be on NNRTI monotherapy and is therefore likely to develop NNRTI drug resistance. There is emerging evidence that if NRTIs are continued for some time after stopping the NNRTI, the proportion of patients developing drug resistance can be reduced. It is therefore recommended that in the event that an NNRTI is likely to be used again in the future, on discontinuation of either EFV or NVP, the NRTI backbone (e.g. 3TC + d4T/AZT/TDF) should be continued for a period of 2 weeks where possible.

Figure 5.3 Management of a nevirapine associated rash

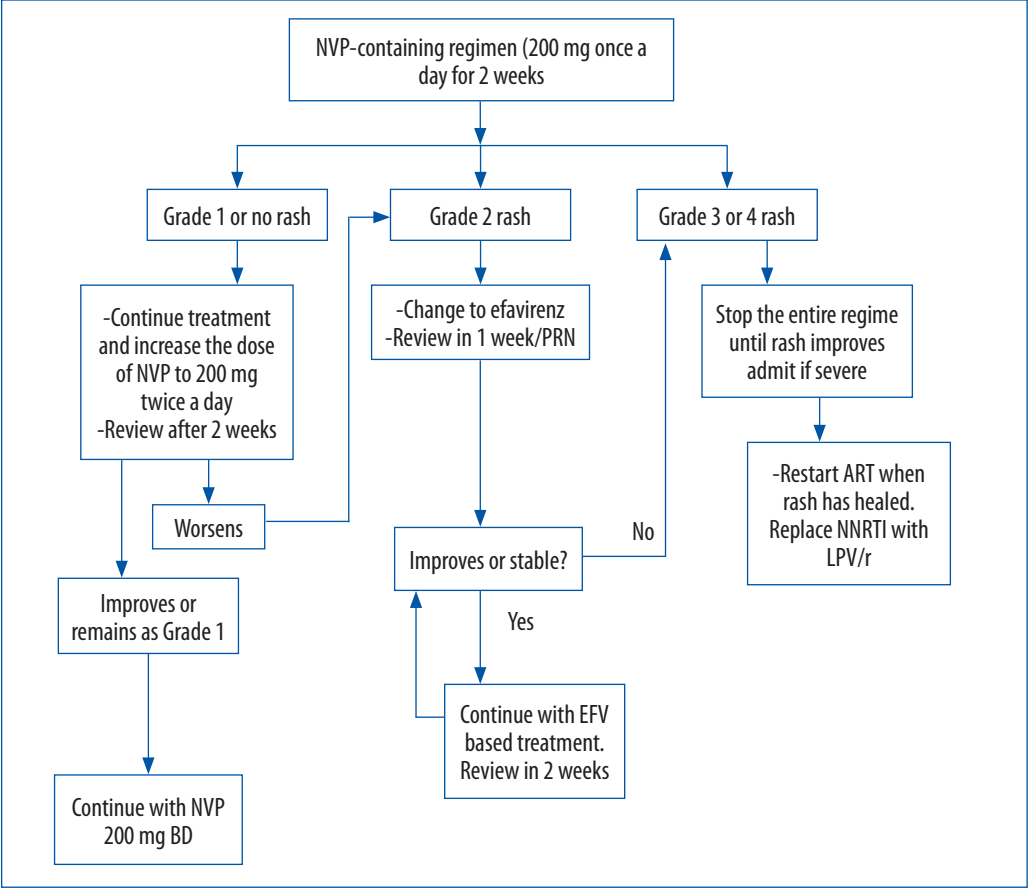


Table 5.8 Clinical grading of ARV associated rash

Rash	Grade 1	Grade 2	Grade 3	Grade 4
	Erythema, pruritus affecting <50% body surface area	Diffuse maculo-papular rash OR dry desquamation affecting >50% of body surface area	Vesiculation OR moist desquamation OR ulceration	Mucous membrane involvement, Stevens Johnson, erythema multiforme

Greatest risk of rash is in first 6 weeks; consider other drugs as potential causes in patients who develop a rash after 2 months of ART initiation

In managing nevirapine toxicity, care should be taken to avoid periods of suboptimal therapy with the NNRTI class of drugs.

5.4 Treatment failure

5.4.1 Definition

Antiretroviral treatment failure occurs when there is sub-optimal response to ART. Treatment failure can be defined clinically, immunologically and virologically.

Clinical failure is indicated by:

- New onset of significant OIs or malignancy, usually a WHO stage 3 or 4 condition.
- Recurrence of previously treated OIs after at least six months of ART. It should be noted that TB may occur at any time in the course of HIV infection, even in those responding to ART. Furthermore, early in the course of treatment, TB and other OIs may develop as part of the immune reconstitution and inflammatory syndrome (IRIS) or because of an immune system that is yet to recover, leaving the patient vulnerable to OIs. A diagnosis of treatment failure therefore should not be considered in adherent patients who develop OIs and have been on treatment for <6months.
- Downgrading of WHO classification in the course of follow up
- Unintentional weight loss in a patient who was doing well on ARVs without any overt signs and/or symptoms should trigger suspicion of regimen failure.

Clinicians are advised to follow up such patients closely, assess nutrition and investigate them for possible regimen failure.

Immunological failure

Immunological failure is defined as a persistent decline in CD4 count after a period of immune reconstitution.

immunological failure is present if the CD4 count

- falls to or below pre-ART level OR
- falls by 30% or more from on treatment peak value OR
- remains persistently below 100 cell/mm³ after at least 12 months of effective ART.

All patients should have a CD4 count done every 6 months, to avail a series of readings allowing trends to be observed. Thus a drop in the CD4 count or percentage should always be viewed in the context of previous readings in addition to any repeat tests.

In patients with intercurrent illness, a significant transient decrease in CD4 may occur. Change of ART should not be based on a single CD4 assessment or one done during intercurrent illness.

In patients with severe immune suppression at treatment initiation with very low CD4 counts, CD4 recovery may be very slow and/or less than expected. Care should therefore

be taken that such patients, if stable and adherent, should not have their treatment changed unnecessarily.

Virological failure

Virological failure may be defined as viral load >1000 copies/ml in any of the following scenarios:

- Incomplete viral suppression: the HIV viral load (plasma HIV-1 RNA level) remains high following initiation of ART. A viral load of >1000 copies/ml after 12 months of therapy is indicative of incomplete viral suppression.
- Viral rebound: increase in viral load after initial viral suppression when adherence to medication is adequate. Repeated detection of HIV viral load level above 1000 copies/ml after an initial period of viral suppression is indicative of virologic failure.

5.4.2 Causes of treatment failure

- Non-adherence to treatment
- Pre-existing drug resistance to one or more drugs (e.g. after single dose nevirapine for PMCT)
- Regimens with low potency
- Impaired drug absorption
- Altered drug pharmacology including drug-drug and drug food interactions

Non-adherence is the main cause of treatment failure.

Factors that increase the risk of treatment failure should be explored at every visit; and supportive counselling intensified. These include:

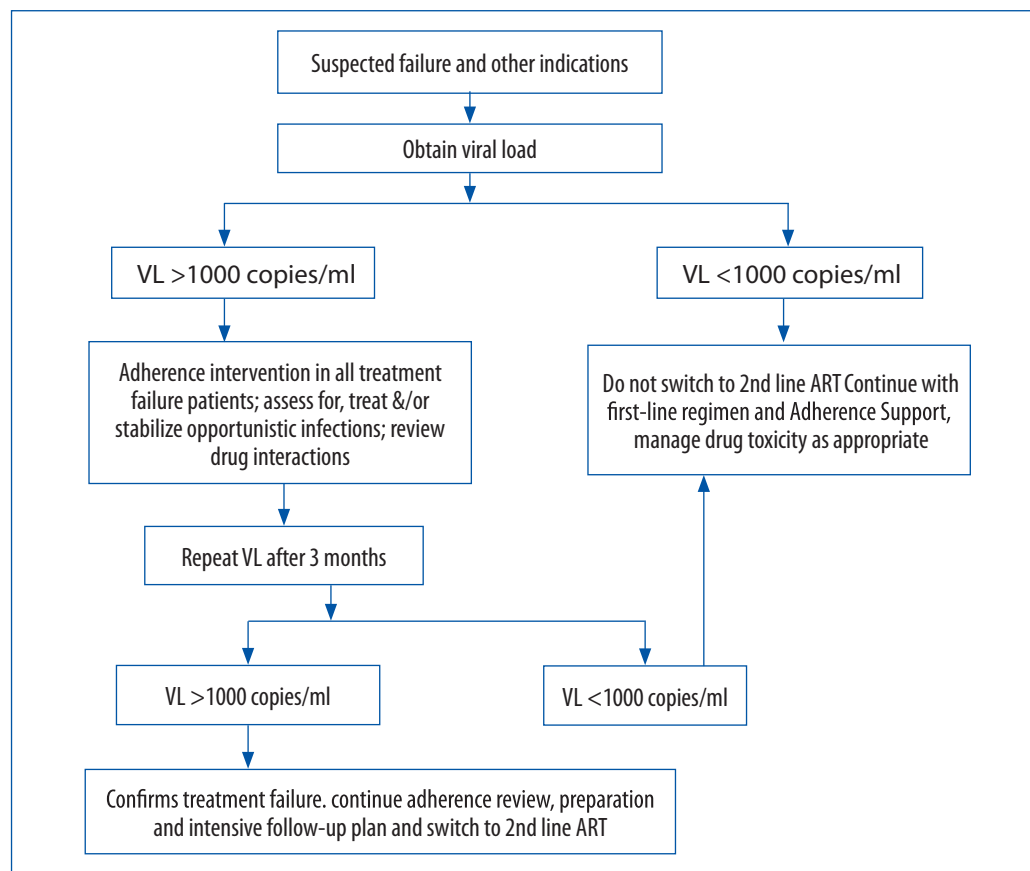
- Factors that affect adherence such as lack of psycho-social support, depression, treatment regimen (pill burden, frequency, food or fluid restrictions)
- Poor patient-provider relationship
- Development of intolerance or toxicity
- Financial barriers to care
- Substance abuse including alcohol abuse

5.4.3 Management of patients with suspected clinical or immunological failure

- Adherence history should be reviewed; it should be noted that even in patients with a previously good adherence, life events may precipitate a period of non-adherence. Non-adherence should be addressed, particularly in the context of potential cause of treatment failure.
- If treatment failure on clinical grounds is suspected; then the CD4 cell count should be checked, adherence reviewed (and intensified if sub-optimal).

- Any OIs should be treated promptly, and patient reviewed for other OIs, HIV-associated malignancy and adequacy of nutrition
- The CD4 trends should be reviewed and a repeat done if this is the first time the CD4 count has dropped and the patient is suspected of failure.
- Treatment failure is unlikely to be responsible for symptoms in an adherent patient in the first 6 months of treatment since immune recovery is still on-going and the patient may still be at risk of OIs or immune recovery inflammatory syndrome (IRIS).
- Because of the limited specificity of immunologic or clinical criteria to predict true virologic failure, in patients with suspected failure on the basis of new clinical features or a drop in CD4 count, it is recommended that a viral load test be done to confirm the diagnosis of treatment failure whenever possible, to avoid unnecessary switch to more expensive second line treatment. Where viral load testing is not available on site, arrangements should be made to transport specimens and results to and from identified laboratories within the national network.

Figure 5.4 Targeted viral load testing for the diagnosis of 1st line treatment failure



5.4.4 Considerations for switching (changing a failing regimen) regimen

As with the initiation of antiretroviral therapy, the decision to change regimens should be approached with careful consideration of several complex factors, which should be taken into account prior to switching treatment.

- Do not rush into second-line therapy. As much as possible, patients who need to change therapy should be discussed in a multi-disciplinary team and the reasons for failure discussed.
- When changing therapy, determine whether poor adherence was responsible for the failure.
- If it is not possible to improve adherence, attempt directly observed therapy with a health worker, family member or a friend
- The new therapy should include as many active drugs as possible
- Class cross resistance should be considered; with triple combinations of drugs, at least two of the drugs selected should be drugs that are not subject to anticipated cross-resistance to drugs given previously.
- When changing therapy review all other medications for possible drug interactions
- In patients with weight loss always consider TB as a possible cause. HIV-positive patients on treatment continue to be at risk for developing TB; this may therefore not necessarily be a result of treatment failure
- Do not discontinue the failing regimen until the new regimen becomes available

5.5 Recommended second-line ART regimens in adults and adolescents

Table 5.9 Recommended second-line regimen

First-line regimen	Second-line regimen
TDF + 3TC + EFV or NVP	AZT* + 3TC + LPV/r or ATV/r**
AZT* + 3TC + EFV or NVP	TDF + 3TC + LPV/r

* Stavudine may be used in patients unable to tolerate AZT

** If the patient is intolerant to LPV/r, boosted atazanavir (atazanavir/ritonavir) can be used instead.

**For patients who initiate a PI based regimen as their first line regimen (e.g. severe rash with the NNRTI class) and subsequently fail treatment, national therapeutic committee should be consulted

Table 5.10 Drug dosages for second-line regimens ARVs

Generic name	Forms	Dosing recommendation	Food effect
Didanosine (ddl)	Enteric coated(EC): 125, 200, 250 or 400 mg Buffered tabs: 25, 50, 100, 150, 200 mg	Body weight >60: 400 mg OD (buffered or EC capsules) or 200 mg BD (Buffered tabs) Body weight <60 kg: 250 mg OD (Buffered tabs or EC capsule) or 125 mg BD (buffered tabs)	Take ½ - 1 hour before or 2 hours after meal. Levels decrease 55%;
Abacavir (ABC)	300 mg tablets	300 mg per dose twice daily	Take without regard to meals. Alcohol increases ABC levels to 41%
Stavudine	Tablets/capsules 15 mg, 20 mg, 30 mg	Weight <30 kg: 1 mg/kg/dose twice daily Weight >30 kg: 30 mg/dose twice daily	Take without regard to meals
LPV/r	LPV 200mg/ RTV 50mg	LPV/r 400/100mg BD	Take with food, moderate fat increases bioavailability
Atazanavir (ATV)	Capsules 100 mg, 150 mg, 200 mg, 300 mg	Treatment naive ATV 300 mg with RTV 100 mg once daily	To be taken with food

NB: Refer Table 4.4 for other ARV drug dosages

5.6 Management of patients failing second-line ART in adults and adolescents

To avoid the need for post second-line (salvage) ART, health care workers should work together with patients to ensure maximum durability of the first- and where this fails the second-line regimens. Patient education and adherence support cannot be over-emphasized. Managing highly treatment experienced patients in resource-limited settings will be a considerable challenge because these patients require:

- individualized approach to treatment,
- costly regimens which are unlikely to be widely available;
- increased adherence demands for the patients;
- costly and less readily available monitoring tools (viral load and resistance testing) and healthcare worker expertise; and
- greater likelihood of drug interactions.

For these reasons, clinicians and their patients should aim to get the maximum benefit out of initial treatment.

To facilitate effective management of patients failing second-line therapy the following framework is being developed by NASCOP:

- Establishment of a technical working group (TWG) to provide guidance on the management of complex patients including patients failing second-line ART,
- Under this framework, all patients suspected of failing second-line ART should have a viral load done as per the algorithm below(Figure 5.6)

- The detail clinical and ART history, adherence and psychosocial assessment and laboratory results should be sent to National ARV Therapeutics TWG.

The committee will advise on further management of such patient including drug resistance testing and treatment plan for the patient.

General principles for the management of patients failing second-line

- Maintain the patient on the failing regimen until a full third-line regimen is available as recommended by the national TWG
- Third-line regimens should contain at least two fully active drugs for durable, potent virologic suppression

Third-line regimen choice must be guided by resistance testing

Figure 5.6 Suspected second-line treatment failure

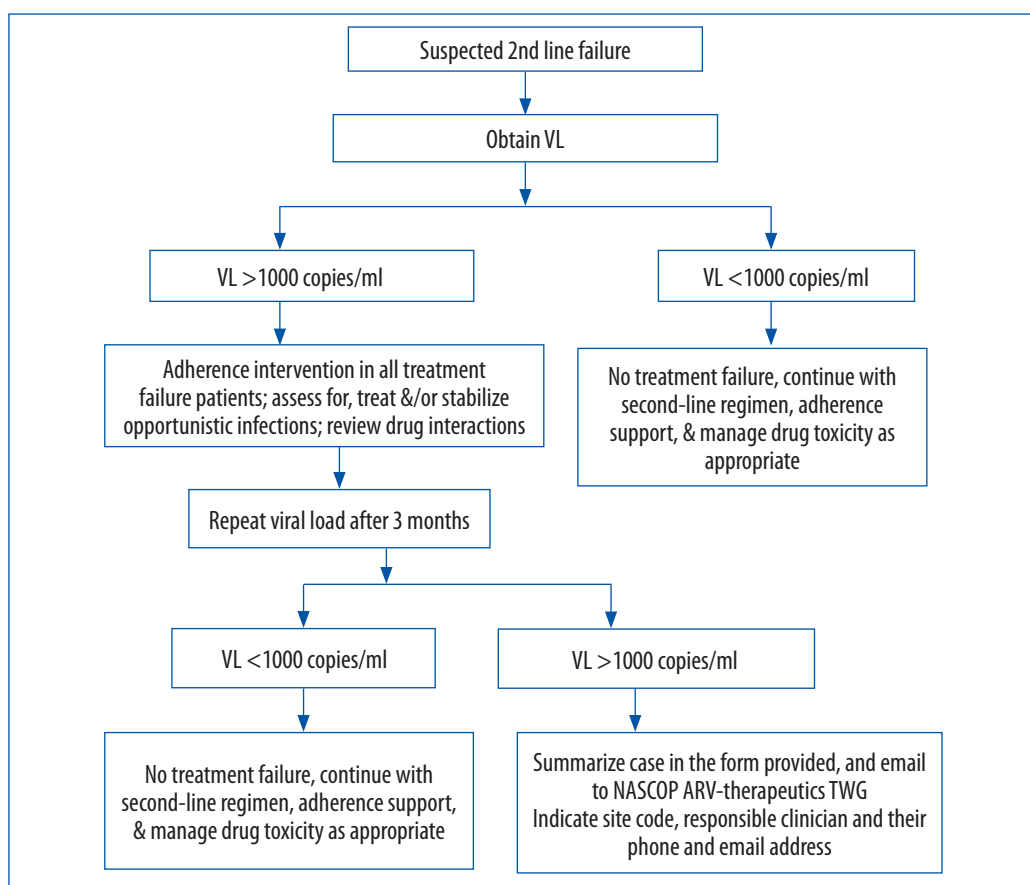


Table 5.11 Possible third-line ART agents for adults and adolescents

Class	Drug	Remarks
Protease inhibitor	Darunavir (DRV)	Formulation: tablets 75 mg, 150 mg, 400 mg or 600 mg. Recommended dose for adults and adolescents with no DRV resistance substitutions (V11I, V32I, L33F, I47V, I50V, I54L, I54M, T74P, L76V, I84V and L89V) is 800 mg together with 100 mg of ritonavir once daily with food. In the presence of one of the DRV resistance substitutions, DRV is given as 600 mg with 100 mg of RTV twice daily with food.
Integrase inhibitor	Raltegravir (RAL)	Formulation: tablets 400 mg. Recommended dose in adults is 400 mg twice daily. In patients on rifampicin, the dose is increased to 800 mg twice daily.
Recycling drugs that confer benefit	Lamivudine, Tenofovir (3TC, TDF)	Standard dsoing used in 1st or 2nd line ART
Non nucleoside reverse transcriptase inhibitor	Etravirine	It is second generation NNRTI. Patients who failed an initial NNRTI based first line regimen are unlikely to benefit from Etravirine, as part of the third line treatment. The use of Etravirine in our setting should therefore be guided by further understanding of NNRTI resistance at first line failure. Recommended dosing is 200 mg twice daily

Lamivudine associated resistant viruses have poor replication capacity compared to wild type virus, and should be maintained in patients requiring third-line regimens

Patients failing TDF may still benefit from continuation of TDF despite the presence of the characteristic TDF mutation.

Based on current standardized treatment regimens, majority of patients are likely to achieve full virologic suppression with a regimen of DRV/r plus RAL plus 3TC +/- TDF

Follow up of patients on a third-line/salvage regimen

Currently there are no other treatment options beyond the drugs recommended for third-line treatment. As such, patients should be made aware that this really is the last opportunity for an effective regimen. Adherence to this treatment must be supported to the largest extent possible, both at facility and community levels. The following is therefore recommended:

- Patients should not start third-line drugs unless fully prepared and are ready for the treatment.
- Monitoring requirements are the same as for other patients. The first visit should be at 2 weeks and thereafter monthly.
- Directly observed therapy should be instituted for the first 3 months of treatment. This should involve engaging a family member or a community health worker to provide support.
- Adherence must be reviewed at each visit, both with the CHW/family member and with the patient.

5.7 Immune reconstitution inflammatory syndrome (IRIS) after ART initiation

5.7.1 Definition

Individuals with human immunodeficiency virus infection who commence antiretroviral therapy are susceptible to immune reconstitution disorders. The most common disorders are the various forms of immune restoration disease (IRD) that appear following restoration of a dysregulated immune response against pathogen-specific antigens. Any pathogen that can cause an opportunistic infection as a result of cellular immunodeficiency can provoke IRD when pathogen-specific immune responses recover during antiretroviral therapy. The most significant of these include *Mycobacterium tuberculosis* and *Cryptococcus neoformans* as well as herpetic flare-ups. IRD associated with these pathogens is characterized by severe inflammatory responses and is often referred to as immune reconstitution inflammatory syndrome. IRIS is not a side-effect of ART, but a consequence of improving immunity after initiation of ART.

5.7.2 Conditions associated with the IRIS

Common disease conditions associated with the IRIS include

- Tuberculosis
 - Common cause of IRIS; rarely severe enough to cause IRIS-related death
- Cryptococcal meningitis
 - Often presents as severe headache
 - A potentially deadly cause of IRIS
- Toxoplasmosis
- Cytomegalovirus retinitis
- Pneumocystis pneumonia (PCP)
- Others
 - Kaposi sarcoma
 - Skin and mucous membranes: most common sites of IRIS reactions
- Folliculitis, zoster, molluscum contagiosum
- Genital lesions: Genital herpes simplex virus (HSV) and warts (human papilloma virus, HPV)

5.7.3 Risk factors (predictors) for IRIS:

- Low CD4 count before starting ART; CD4 less than 100 cells/mm³ in adults and CD4% less than 15% in children
- Patients with evidence of undiagnosed and/or untreated opportunistic infections; Patients with severe weight loss patients (at high risk of TB and other infections), chronic cough, fever, headache, lymphadenopathy and other symptoms of WHO stage 4 conditions.
- Failure to screen patients for OIs before ART
- Initiating ART soon after starting therapy for an OI (e.g. TB and cryptococcus)

All patients should have a thorough history and examination looking for opportunistic infections before starting ART. Patients at risk of IRIS should be followed up closely.

Before ART, if there's any suspicion of an OI, thorough investigation and treatment for the OI should be offered before ART is started.

Table 5.12 Clinical presentation of IRIS

Responsible condition	Clinical presentation of IRIS
TB	<ul style="list-style-type: none"> • TB-IRIS often presents in the first 1-6 weeks of starting ART • Commonly high fever, cough, dyspnoea; new or increased lymphadenopathy (peripheral or mediastinal); lymph node abscesses; worsening of pulmonary disease with new or increased infiltrates or effusion; new or worsening CNS presentation; other new extrapulmonary lesions
Herpes zoster	<ul style="list-style-type: none"> • Presents within the first 4 months of ART initiation. Presents with herpes zoster (new or recurrent)
Cryptococcus	<ul style="list-style-type: none"> • Presents 1 week to 11 months after ART initiation. • Fever, worsening headache, lymphadenitis, new or worsening signs of meningitis; pulmonary disease and skin lesions.
PCP	<ul style="list-style-type: none"> • Fever, cough, dyspnoea in patients on treatment, those recently treated or those undiagnosed. The chest radiograph may show a worsening radiographic picture
Skin	<ul style="list-style-type: none"> • New or worsening PPE, eosinophilic folliculitis, new presentation or chronic mucocutaneous herpes lesions
Malignancies	<ul style="list-style-type: none"> • New or worsening KS lesions
Hepatitis B	<ul style="list-style-type: none"> • Worsening hepatitis, confirmed by rising ALT or AST.

5.7.4 Management of IRIS

Best approach to the IRIS is the prevention, primarily by initiating ART earlier within current ART guidelines and by carrying out a thorough assessment to identify OIs prior to ART initiation

After diagnosing IRIS;

- Investigate appropriately if new OI is suspected/undiagnosed and treat.
- Continue treatment of OI.
- Continue ART. Rarely, patients may have to stop ART because of severe symptoms.
- Most patients just require analgesics and basic supportive symptom management. Role of corticosteroids in management of IRIS;
 - a. Some patients have very severe symptoms of inflammation, so corticosteroids may be necessary to control the IRIS response.
 - b. Corticosteroids are indicated in the presence of certain types of OIs; TB meningitis, TB pericarditis, toxoplasmosis, cryptococcal meningitis
 - c. Start prednisolone 1-2 mg/kg every day, taper(lower) the dose of prednisolone over several weeks as symptoms improve
 - d. Non-steroidal anti-inflammatory drugs (NSAIDS) such as ibuprofen and aspirin may be used in non- severe cases.

6. Management of TB/HIV co-infection

6.1 Introduction

HIV infection exponentially increases the risk of active tuberculosis in co-infected individuals. Additionally, TB continues to be a major cause of HIV-associated morbidity and mortality. Patients with HIV continue to be at a higher risk of developing TB; though the risk of TB disease decreases with successful ART, it remains higher than in HIV uninfected individuals. For this reason TB/HIV co-infected should be identified and managed.

6.2 Managing TB/HIV co-infection

The aim of management of TB/HIV co-infection is to reduce the burden and impact of TB in PLHIV. Early diagnosis of HIV infection in patients suspected to have TB is the most important first step in providing comprehensive care to the TB/HIV co-infected patient. Active screening, early diagnosis and treatment of TB reduces morbidity and mortality in PLHIV.

6.2.1 HIV counselling and testing

All patients with confirmed or with symptoms suggestive of active tuberculosis should be offered HIV counselling and testing as standard care.

In many patients, a diagnosis of tuberculosis is often the first indication of underlying HIV infection. HIV counselling and testing should be carried out in all TB suspects as part of the investigations for TB). A diagnosis of HIV infection at the earliest opportunity possible has several benefits:

- The patient will enter into HIV care and treatment (including cotrimoxazole preventive therapy and ART); both of which will greatly improve TB treatment outcomes.
- HIV-positive TB patients may have household members with undiagnosed HIV infection. Using either a family-cantered approach to/or couple HIV counselling and testing, these infected family members can be identified and referred for care and treatment as well. Detection of sero-discordance will provide opportunities for prevention of HIV transmission.
- Using the family- centred approach; household contacts of sputum positive TB patients are screened for TB, and those with active TB are offered prompt treatment. This will also provide the opportunity to provide isoniazid preventive therapy to eligible household contacts with no active disease.

6.2.2 Intensified case finding

Adults and adolescents living with HIV should be screened for TB (at every visit to the healthcare facility and in community care settings) with a clinical algorithm (Figure 6.1).

Intensified case finding (ICF) for TB refers to the regular screening of all people with or at high risk of HIV or in congregate settings (prisons, military barracks, and informal settlements) for the symptoms and signs of TB, followed promptly with diagnosis and treatment, and then doing the same for household contacts.

ICF allows for rapid diagnosis of TB and triage procedures to avoid or reduce transmission in congregate settings. In addition it provides an opportunity for provision of isoniazid preventive therapy in those without active TB.

6.2.3 Isoniazid preventive therapy (IPT)

Preventive therapy against TB is the use of anti-TB drugs(s) in individuals with latent *Mycobacterium tuberculosis* infection in order to prevent progression to active disease.

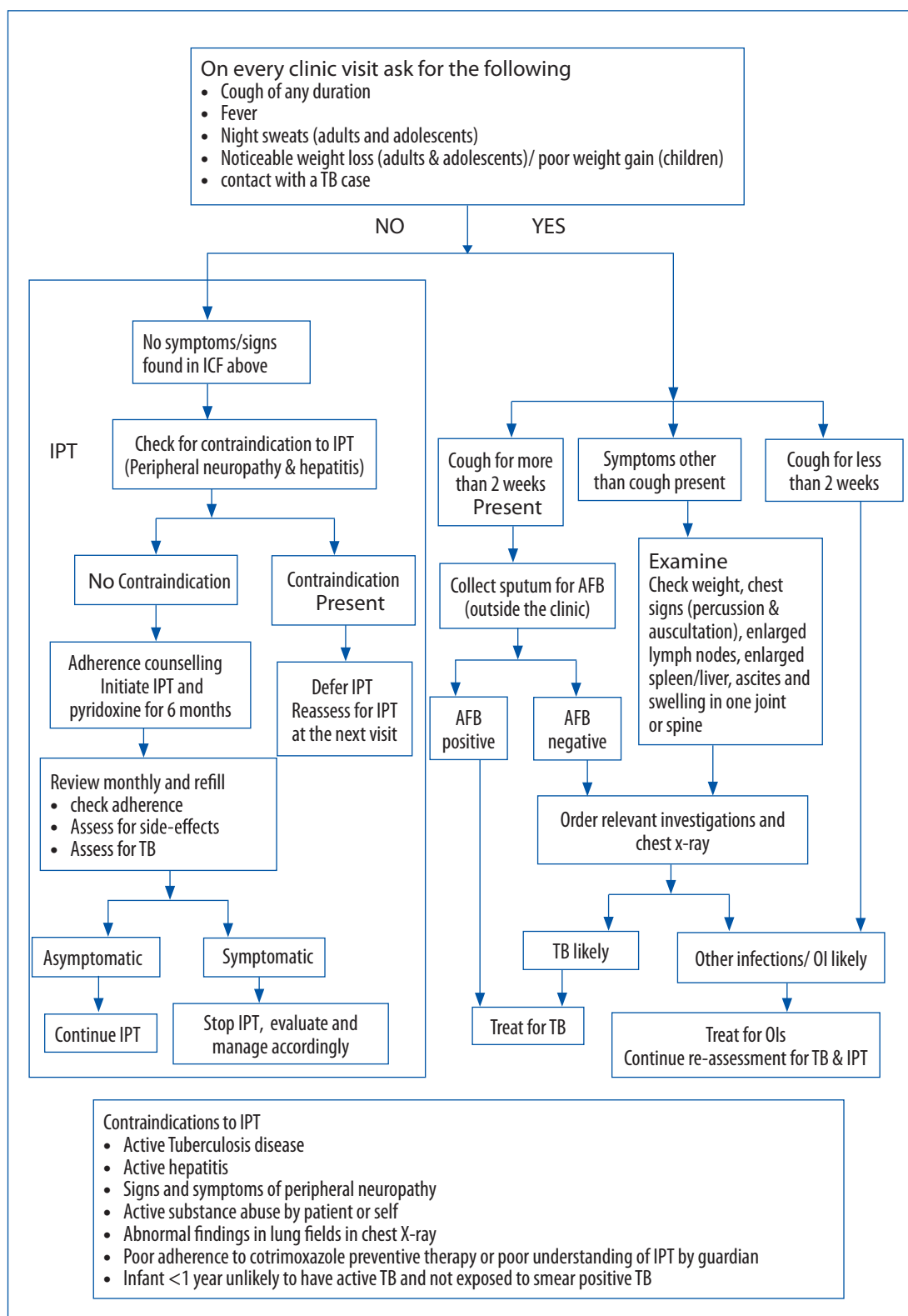
TB preventive therapy with INH is safe and effective in people living with HIV, reducing the risk of TB by 33–62%. Recent evidence has shown that the use of IPT together with ART significantly reduces the incidence of tuberculosis.

Tuberculin Skin Test (TST) is not a requirement for initiating IPT in people living with HIV.

I. IPT in adults and adolescents

- Adults and adolescents living with HIV (including pregnant women) should be screened for TB with a clinical algorithm (Figure 6.1) and those who do not report any one of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered IPT.
- IPT should only be used in patients in whom active TB has been excluded, when active patient follow up is possible and a high level adherence can be attained,

Figure 6.1 Screening for TB and isoniazid preventive therapy in HIV care settings



IPT is recommended for all adults and adolescents living with HIV (including pregnant women) in whom active TB disease has been excluded.

Dose and duration of INH for IPT in adults and adolescents >25 kg weight

300 mg/day for 6 months

Pyridoxine at a dose of 25–50 mg daily is recommended for prophylaxis against peripheral neuropathy by INH during duration of INH prophylaxis.

II. IPT in Children

- Children living with HIV who are more than 12 months of age and who are unlikely to have active TB on symptom-based screening, and have no contact with a TB case should receive six months of IPT (10 mg/kg/day) as part of a comprehensive package of HIV prevention and care services.
- In children living with HIV who are less than 12 months of age, only those who have contact with a TB case and who are evaluated for TB (using investigations) should receive six months of IPT if the evaluation shows no TB disease

Dose and duration of INH for IPT in children

INH 10 mg/kg/day for 6 months (maximum 300 mg/day). PLUS pyridoxine 25 mg/day

Table 6.1 Dose of INH for IPT

Weight	Dose in mg/day	Number of 100 mg, INH tablets	Number of 300 mg (adult) tablets
<5	50	½	-
5.1 – 9.9	100	1	-
10-13.9	150	1½	½
14-19.9	200	2	-
20-24.9	250	2½	-
>25 and adults	300	3	1

6.2.4 Infection prevention and control

Infection control refers to measures taken to prevent droplet nuclei containing *M. tuberculosis* from being generated in healthcare and community settings, thereby reducing exposure of patients, staff and other people to TB. Please refer to the *Guidelines for tuberculosis infection prevention in Kenya* for full details on this subject.

There are three main ways of achieving infection control:

- Work practice and administrative control measures
- Environmental control measures
- Use of personal protective gear

6.2.4.1 Work practice and administrative control measures

Work practice and administrative control measures have the greatest impact. These include:

- Infection control plan;
- Administrative support for procedures in the plan, including quality assurance;
- Training of staff;
- Education of patients and increasing community awareness; and
- Coordination and communication with the TB programme.

Each facility should have a written TB infection control plan that outlines a protocol for the immediate recognition, separation, provision of services, investigation for TB and referral of patients with suspected or confirmed TB disease.

Recognition: a member of staff should be designated to identify patients with prolonged cough. Such patients should be triaged, and fast tracked through registration, consultation, investigation and treatment without waiting on the queue with other patients.

Separation: whenever possible, such patients should have a separate well ventilated waiting bay be provided with a face mask and taught cough hygiene.

Investigation of TB and referral: as each facility should appoint one person to serve as the infection control officer. Larger facilities should have an infection control committee.

It is the responsibility of the infection control officer/committee to write a TB infection control plan, monitor its implementation and coordinate healthcare workers' training.

Investigation of TB and referral: as part of treatment literacy in HIV care clinics, patients should receive information on recognizing symptoms of tuberculosis and seeking care promptly, and how to protect themselves and others from tuberculosis.

6.2.4.2 Environmental control measures

Environmental control measures include ventilation, filtration and ultraviolet germicidal irradiation.

Healthcare facilities should be designed to maximize on natural ventilation, and the infection control plan will ensure measures to for environmental control (such as open windows and doors) are implemented at all times.

When patients are asked to **provide sputum specimens for TB diagnosis** onsite, they should always do so in an adequately ventilated booth or **outside** in the open air and away from other people, not in small rooms such as toilets or other enclosed areas.

6.2.4.3 Use of personal protective gear

Respiratory protective device used in health care setting which fits over the mouth and nose and are designed to protect against transmission of *M. tuberculosis* by reducing the number of inhaled infectious droplet nuclei.

Respiratory protection is an important aspect for protecting HCWs against TB nosocomial infection. It should be implemented hand in hand with administrative and environmental measures. Some approaches to respiratory protection include;

I. Use of respirators

Respirators are a special type of device that provide filtration for 0.3-0.4 micrometer particles and are closely fitted to the face to prevent leakage around the edges. They are highly efficient in preventing inhalation of infectious droplet nuclei and are recommended for use by health care workers working in high risk areas.

These face-piece respirators are disposable but can be re-used repeatedly for several weeks for TB, if they are properly stored. Some commercially available respirators include CDC/NIOSH-certified N95 (or greater) and CEN-certified FFP2 (or greater) filtering face-piece respirators.

II. Use of surgical or procedure masks

Surgical masks prevent the spread of microorganisms from the wearer (e.g. TB patient,) to others. They may provide a limited level of protection to the wearer; however, they are not designed to be of high filtration efficiency.

Surgical masks should be considered for suspect and known infectious TB patients leaving isolation rooms for medically-essential procedures. However it must be considered that surgical or procedure masks may serve to identify TB patients thus increase stigma. Patient and HCW education regarding the importance and appropriate use of wearing surgical or procedure masks should accompany their distribution.

It is important to remember that a surgical or procedure mask worn by HCWs may not adequately protect them from inhalation of air contaminated with *M. tuberculosis*. Respirators are the preferred device to reduce the concentration of *M. tuberculosis* bacilli inhaled.

6.3 TB treatment in TB/HIV co-infection in adults and adolescents

TB/HIV services should be integrated to ensure effective delivery of care.

TB/HIV co-infected patients should be started on immediate TB therapy; at the same time, they should also be offered comprehensive HIV care and treatment

The duration of TB treatment in HIV-infected patients is the same as in HIV-negative TB patients

In HIV-positive patients, cotrimoxazole preventive therapy should be started (unless contraindicated) at the time of initiation of TB treatment and continued co-trimoxazole preventive therapy reduces the risk of mortality in HIV-positive TB patients irrespective of CD4 cell count.

6.3.1 When to start antiretroviral therapy in TB/HIV co-infection

For ALL ART-naïve patients with TB/HIV co-infection, after starting TB therapy; ART should be initiated irrespective of CD4 cell count and as soon TB treatment is tolerated (at least within the first two to eight weeks).

Recent evidence has shown that early initiation of ART in TB/HIV co-infection is associated with reduced mortality, improved TB outcomes

6.3.2 Recommended first-line ART adolescents

ART in HIV/TB co-infection is complicated by

- complex rifampicin drug interactions with NNRTIs and PIs,
- increased pill burden which could negatively affect adherence,
- overlapping drug toxicity,
- risk for and consequences of developing the immune reconstitution syndrome

Therefore, closer monitoring and supportive counselling are recommended for patients on ART and tuberculosis treatment.

The preferred regimen to start HIV-infected treatment naïve patients with active TB is

- **TDF + 3TC + EFV**

In pregnant women and where patients are unable to tolerate tenofovir, the following is recommended:

- AZT + 3TC + EFV

Use of triple nucleoside analogues in TB/HIV co-infection

AZT + 3TC + TDF or AZT + 3TC + ABC

The triple nucleoside regimens should only be used in the event that a patient cannot tolerate EFV or in case of concurrent treatment of TB and HIV infection during the first trimester in pregnant women. Such treatment should be given with the advice and supervision of a senior clinician or after discussion with the multidisciplinary ART team. The patient should be put back on an NNRTI based regimen as soon as possible after completion of TB treatment and after the first trimester.

Triple nucleoside ART should NOT be used in TB/HIV co-infected patients who have previously failed ART

6.3.3 Recommendations for ART in TB/HIV co-infected patients unable to use NNRTI

These patients would normally be on ART containing a protease inhibitor. Rifampicin induces the metabolism of PIs lowering the plasma concentration of standard boosted PIs by 75 to 90%. Therefore, the concomitant use of rifampicin with standard boosted PIs is contraindicated.

The preferred regimen is the use rifabutin instead of rifampicin as part of TB therapy. Rifabutin is used at a dose of 150 mg three times weekly (Table 6.2).

Table 6.2 Treatment of TB/HIV co-infection in adults and adolescents on a PI based regimen

Phase of TB treatment	Dose of rifabutin	Other TB medications
Intensive phase (first two months)	Rifabutin 150 mg three times weekly	Isoniazid 5 mg/kg (max 300 mg) + Pyrazinamide 25 mg/kg (max 1600 mg) + Ethambutol 20 mg/kg (max 800 mg); all given orally once daily
Continuation phase (next 4 months)	Rifabutin 150 mg three times weekly	Isoniazid 5 mg/kg (max 300 mg)

The commonest adverse events of rifabutin are reduction in white cell count, elevation of liver enzymes, rash and gastrointestinal complaints. Uveitis is a rare complication; but the risk is higher in case of concomitant administration with fluconazole and clarithromycin.

Summary of management of TB HIV co-infected patients

1	ART naive adult PLHIV not on ART and newly diagnosed with TB	Initiate TB treatment Initiate EFV based ART* as soon as TB treatment is tolerated within 2-4 weeks
2	Adult PLHIV on 1st line NNRTI based ART and develops TB	Initiate anti TB treatment If on NVP based ART, change NVP to EFV
3	Adult PLHIV on PI based ART and develops TB	Initiate rifabutin based TB treatment Continue same ART

* The triple nucleoside regimens should only be used in the event that a patient cannot tolerate EFV or in case of concurrent treatment of TB and HIV infection during the first trimester in pregnant women.

Triple nucleoside ART should NOT be used in TB/HIV co-infected patients who have previously failed ART

7. HIV/hepatitis B co-infection

7.1 Introduction

Chronic hepatitis B virus (HBV) infection is an important cause of chronic liver disease. In Kenya, the average rate of chronic hepatitis B, indicated by hepatitis B surface antigen (HbsAg) carrier status varies between 7-11%. The modes of transmission of hepatitis B are similar to HIV; however HBV is a more infectious virus therefore more efficiently transmitted than HIV through bodily fluids such as saliva blood and genital secretions. HBV may become more important as a cause of morbidity and mortality in patients as universal access to ART is achieved.

In Kenya, most of HBV transmission occurs in children (<5years of age) mostly through horizontal transmission from household contacts. Vertical transmission is important; but this is likely to change with increasing availability of hepatitis B vaccination with the rates of HBV carriage likely to fall. Adult HBV transmission also occurs, primarily through sexual transmission but also in the occupational setting such as among unvaccinated health care workers, waste handlers and prison.

Over 90% of susceptible neonates and 20-30% of young children under 6 years develop chronic infection after acute infection; whereas adults are much less likely (<5%) to progress to chronic infection after exposure.

While HBV does not alter the natural history of HIV, the natural history of HBV in HIV patients is different from that in HIV uninfected patients in the following ways:

- Acute HBV resolves in the majority of patients including PLHIV; however HIV reduces chances of clearance of HBV (chronic hepatitis more likely)
- HIV accelerates HBV disease
- HBV is a risk factor for hepatotoxicity with ARV drugs.
- Immune response to ART may exacerbate the host response to HBV, leading to acute flair up of hepatitis (especially if agents that are active against HBV (TDF and 3TC) are discontinued abruptly.

7.1.1 Markers of hepatitis B

- HBsAg: hepatitis B surface antigen – the first marker to appear and its persistence for more than 6 months indicates chronicity of infection
- Anti-HBs antibody: Hepatitis B surface antibody – confers immunity to the virus; it appears when HbsAg disappears, and is the sole detectable serological marker in vaccinated individuals.

- Anti-HBc antibody: hepatitis B core antibody – develops when exposed to the hepatitis virus, but is not protective. The IgM antibody is a marker of acute disease while the IgG antibody indicates chronic disease
- HBeAg: hepatitis B e antigen – is a marker of viral replication, usually correlates with higher viral loads. A subset of patients with chronic infection are infected with a mutant virus not expressing HBeAg despite ongoing viral replication (these are the so called e antigen negative chronic hepatitis B patients)
- Anti-HBe: hepatitis B e antibody – indicates reduced viral replication HBV-DNA: ideally is the marker of active disease in hepatitis B and the level of viremia, when available, should be taken into account when considering and following treatment

HBsAg is readily available and can be used to screen for hepatitis B infection and if HBsAg persistent is diagnostic of chronic infection

7.1.2 Screening for HBV infection

Screening for hepatitis B should be done in all HIV-positive patients whenever possible with HBsAg testing. Otherwise, testing should be performed when clinically indicated: signs of liver disease (jaundice, ascites, abnormal liver on palpation, and other signs of cirrhosis) and patients with unexplained and persistent ALT elevation. Diagnosis of chronic hepatitis B requires a positive HbsAg persisting for more than 6 months.

7.1.3 Vaccination

HIV-positive patients without evidence of prior infection with hepatitis B (both negative HbsAg and HBsAb negative) should be vaccinated against hepatitis B with the standard vaccination course.

7.1.4 Alcohol and hepatitis B

HIV-positive patients co-infected with hepatitis B should be counselled to abstain from consuming alcohol. HIV, HBV and alcohol interact synergistically to accelerate liver damage.

7.2 Treatment of HIV/HBV co-infection

The optimum time to initiate ARV therapy in patients with HIV/HBV co-infection is not clear. The presence of a chronic co-infection with HIV and HBV increases the risk of progression to chronic active hepatitis by 3-6-fold, as well as increasing the risk of cirrhosis and hepatocellular carcinoma. Treatment is therefore recommended earlier in HIV-infected patients with signs of chronic active hepatitis B as the risk of progression of liver disease may be reduced.

All HIV-positive patients co-infected with hepatitis B (HBsAg positive) with elevated liver enzymes or evidence of chronic liver disease should be treated with ART, irrespective of CD4 count.

7.2.1 What to use in treatment of HIV/HBV co-infection

Standard first-line ARV drug regimen containing both TDF and 3TC is recommended; this is because treatment with 3TC alone results in rapid development of resistance of the hepatitis B in 25% of cases at 1 year and 90% at 4 years.

7.2.2 Follow-up and monitoring of therapy

Follow up of ALT/AST is recommended in HIV/HBV co-infected patients when starting ART and subsequently at 1 and 3 months. Subsequent follow up should be determined by the transaminase levels as well as the patient's clinical condition.

The presence of co-infection increases the risk of drug-related hepatotoxicity from all antiretroviral drugs by 3-5 times, especially when anti-TB and ART are given simultaneously. Also, hepatic flare as part of the immune reconstitution syndrome (AST >5 times normal value) is possible and most cases occur in the initial 3 months. ALT elevations 5-10 times normal can be tolerated in the first 3 months of ART as long as the patient is not severely symptomatic, there is no evidence of synthetic dysfunction (normal INR, glucose, and albumin), and remains stable without progression.

7.2.3 Stopping treatment, treatment interruptions

ART should never be abruptly stopped in a patient with HIV and hepatitis B as this may result in a flare-up of the hepatitis B. If the regimen must be stopped and another alternative for suppressing hepatitis B cannot be found, liver enzymes should be monitored and treatment re-instated as soon as possible.

7.3 Second line for HIV/ HBV co-infected

HIV/HBV co-infected patients failing standard first-line regimen should retain both TDF and 3TC as part of the second-line treatment (refer to Chapters 4 and 5).

8. Common noncommunicable diseases in HIV infection

8.1 Introduction

With effective ART, HIV infection is now largely a chronic, manageable disease, with patients living longer as a result of reduced mortality. However, this positive impact of ART has been accompanied with the emergence of chronic noncommunicable diseases like cardiovascular disease, diabetes, chronic liver and kidney disease among PLHIV, either as a consequence of aging, due to undesirable effects of ART, as a direct consequence of HIV infection or as a result of the pro-inflammatory effects of HIV infection. Increasingly PLHIV will present to health care providers with the dual challenges of treatment of HIV in the setting of multiple co-morbid NCD conditions.

In addition, mental health issues are also highly prevalent among PLHIV, although data on mental health and HIV in Kenya is still limited. Because of the direct association of mental illness and poor patient outcomes in HIV-infected patients, it is important that health care providers identify this population and provide them with appropriate treatment. Depression is one of the commonest psychiatric illnesses in the world. Chronic illness (like HIV/AIDS) is a major risk factor for depression

8.2 Mental illness: Depression

The prevalence of depression in HIV-infected persons has been estimated to be 22 to 45%. Untreated, depression can contribute to non-adherence to treatment, care and prevention interventions including ART as well as unhealthy lifestyle such as substance abuse and risky sexual practices. Depression has been found to independently affect the immune system. Though effective therapy for depression is available, evidence shows that less than 30% of patients have access to treatment.

It is recommended that ALL HIV-infected patients enrolled into chronic care assessed for the presence of depression and if present offered appropriate therapy.

8.2.1 Diagnosis of depression in primary care settings

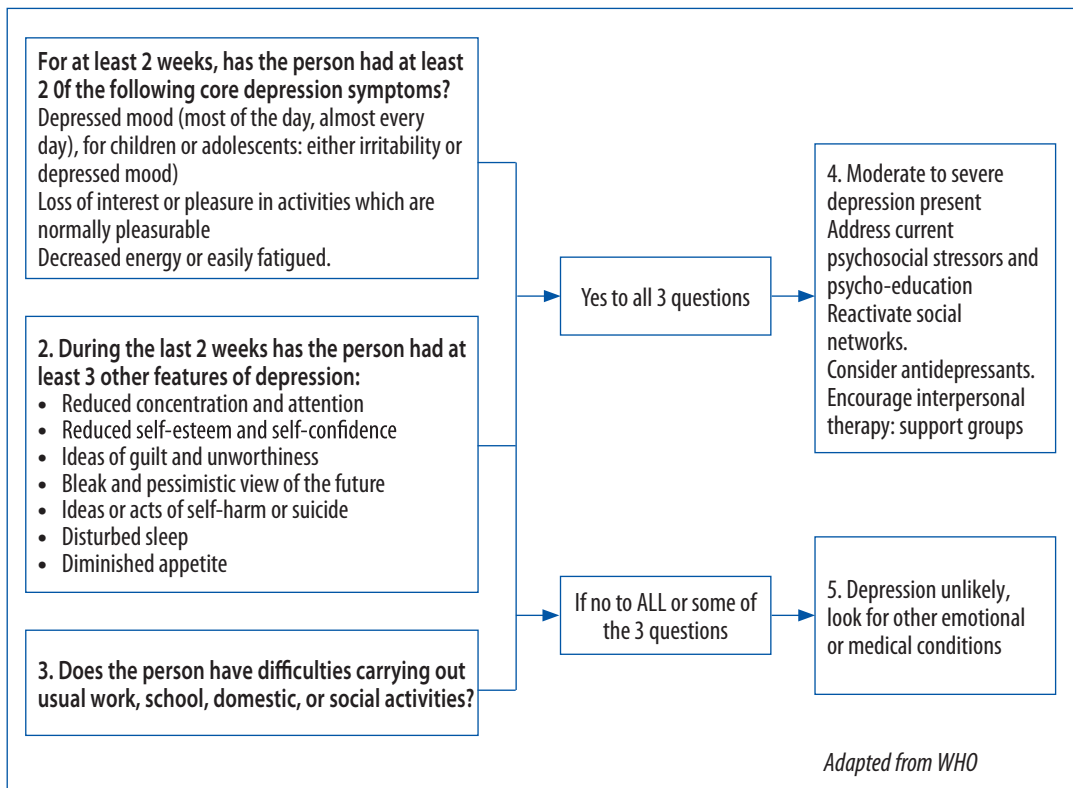
Patients with depression will present with the following (DSM-IV):

1. Depressed mood for most of the day
2. Low interest or pleasure in all or most activities that used to be interesting or enjoyable most of the day

3. Significant involuntary weight loss or gain or decreased or increased appetite
4. Agitation or slowing down
5. Fatigue or loss of energy
6. Feelings of worthlessness and/or excessive guilt
7. Multiple symptoms with no clear physical cause (e.g. aches and pains, palpitations, numbness)
8. Diminished ability to think or concentrate or indecisiveness
9. Difficulties in carrying out usual work, school, domestic or social activities
10. Recurrent thoughts of death or self harm (suicide) suicide plan or suicide attempt.

A diagnosis of depression is made in the presence of three or more of these symptoms (including at least one of #1 or #2).

Figure 8.1 Diagnosis and management of depression in primary care settings



8.2.2 Non-pharmacological management

1. Psycho-education (targeting the patient and trusted caregiver/family)
 - Depression is common and can happen to anyone
 - Depressed people tend to have unrealistic negative opinions about themselves, their life and their future.
 - Effective treatment is possible. It tends to take at least a few weeks before treatment reduces the depression. Adherence to any prescribed treatment is important.
 - Encourage the patient to
 - Continue with activities that used to be interesting or give pleasure
 - Maintain a regular sleep cycle
 - Continue with regular physical activity
 - Regular social and community activity
 - Recognize thoughts of self-harm or suicide and return or call for help when these occur
 - Continue with ART and other therapy.
2. Address psychosocial stressors
 - Offer the patient opportunity to talk, preferably in private, ask the patient to identify causes of current feelings
 - Ask about possible psychosocial stressors; assist design a problem-solving strategy, link to appropriate social/community support
 - Assess and manage spousal abuse, maltreatment, neglect
3. Reactivate/refer to social networks: particularly peer support groups of other PLWH
4. Offer regular follow-up

8.2.3 Pharmacological management

Minor depression often responds to supportive counselling (as above). Patients with moderate to severe depression may benefit from antidepressant medication. It takes least 6 to 8 weeks of antidepressant medication to see benefit in most patients; and it should be continued for at least 6 months. The patient on antidepressant medication should be on regular follow-up by phone, clinic or home visits.

Amitriptyline and fluoxetine are the two antidepressant medications in the Kenya Essential Drug List. In selecting the appropriate antidepressant to use, consider the drug's side-effect profile and the potential for drug interactions especially with antiretroviral agents and other OI medication.

Tricyclic antidepressants – TCAs (amitriptyline) cause drowsiness, dry mouth, tremors and sweating. Overdosing produces refractory, and sometimes, fatal arrhythmias. The usual dose is 50 mg given at night.

Amitriptyline levels are increased by ritonavir co-administration. To adjust the dose of amitriptyline to avoid toxicity, therapeutic drug monitoring (TDM) is required. The co-concomitant use of ritonavir and amitriptyline should therefore be avoided unless TDM is available. If the concomitant use of TCAs and boosted PIs cannot be avoided, the lowest dose of the TCA should be used and the dose then adjusted according to response.

Fluoxetine is a selective serotonin re-uptake inhibitor (SSRI), is better tolerated (but can also cause anorexia, weight loss, nausea, anxiety, agitation, insomnia, drowsiness, dry mouth, diarrhoea, acute dystonia and motor restlessness). It is given in doses of 10 to 40 mg once daily; in the morning. Ritonavir minimally increases blood levels of fluoxetine. No dose adjustment is required.

8.2.4 Indications for specialist referral

- Suicidal intent
- Risk of harm to others
- Disabling disease
- Severe physical deterioration attributable to depression
- Manic symptoms
- Specialized medication required

8.3 Cardiovascular disease, hypertension, diabetes and chronic kidney disease

8.3.1 Introduction

While the widespread availability of ART has resulted in dramatic reduction in HIV-associated morbidity and mortality, morbidity and mortality from non-HIV-related causes has remained unchanged, and in some populations increased. Partly as a reflection of general population trends, with longer survival of HIV-infected patients, the prevalence of chronic noncommunicable diseases will increase. Emerging evidence shows that the burden of noncommunicable diseases is higher among the HIV-infected population compared to age and sex-matched controls.

The causes of increased non-infectious disease burden in HIV infection are multi-factorial including immune activation, inflammation and disorders of coagulation, ART itself and persistent immunodeficiency.

Healthcare workers involved in the care of HIV-infected patients should be knowledgeable in the prevention, diagnosis and treatment of chronic NCDs in HIV-infected patients. In particular, they should be aware of the potential for drug-drug interactions between the drugs used to manage some of the NCDs and ART. Furthermore, co-management of NCDs and HIV infection will result in increased pill burden, and hence the risk of non-adherence ART.

Table 8.1 Screening for noncommunicable co-morbidities

	Evaluation	Initial visit	At start of ART	Follow-up On ART	In care
1. History	History of DM, HBP, renal disease Family history (e.g. premature CVDa, diabetes, hypertension, CKD) Concomitant medications (anti-hypertensive and antidiabetic agents) Current lifestyle ^b (alcohol use, smoking, diet, exercise)	√	√	Every visit	Every visit
2. Examination	Weight, height, BMI, BP, PR, lipodystrophy assessment	√	√	Every visit	Every visit
3. Hypertension	BP measurement	√	√	Every visit	Every visit
5. Dyslipidaemia	Total cholesterol, HDL-cholesterol, LDL-cholesterol, Triglycerides	√	√	Bi-annually for patients on PIs and those at risk of CVD	Annual
6. Diabetes	Blood glucose	√	√	Biannually for patients on PIs	Annual
7. Renal disease	Risk assessment, CrCl Dipstick urinalysis	√	√	Annually for patients on TDF	Annually

Notes

History

- Premature cardiovascular disease: occurring in first degree relative male <55 years, female <65 years.
- If adverse life-style factors are identified, appropriate counselling/treatment/advice should be offered, and re-assessment done more frequently.
- For patients at risk of end-organ disease, laboratory assessment may be required more frequently than shown in the table.

2. Examination

Lipoatrophy assessment: in patients on NRTIs (d4T and AZT), assess for lipoatrophy every follow up visit. Management is by switching to either TDF or ABC. Exclude treatment failure before single drug substitutions.

8.3.2 Lifestyle interventions to prevent CVD in HIV

Smoking cessation

- Provide clear unambiguous statements on the need to stop smoking
- In patients who are not ready or motivated to stop smoking, try to encourage them to consider stopping by enumerating positive short-term and long-term benefits of smoking cessation
- If the patient is ready to stop, try agree on a date, and provide a reward system
- Prescribe pharmacotherapy (such as nicotine replacement therapy and/or bupropion) and explain its use. Efavirenz and boosted PIs decrease the blood levels of bupropion; with the possibility of decreased effects of bupropion.
- Anticipate relapses, explain these as part of weaning

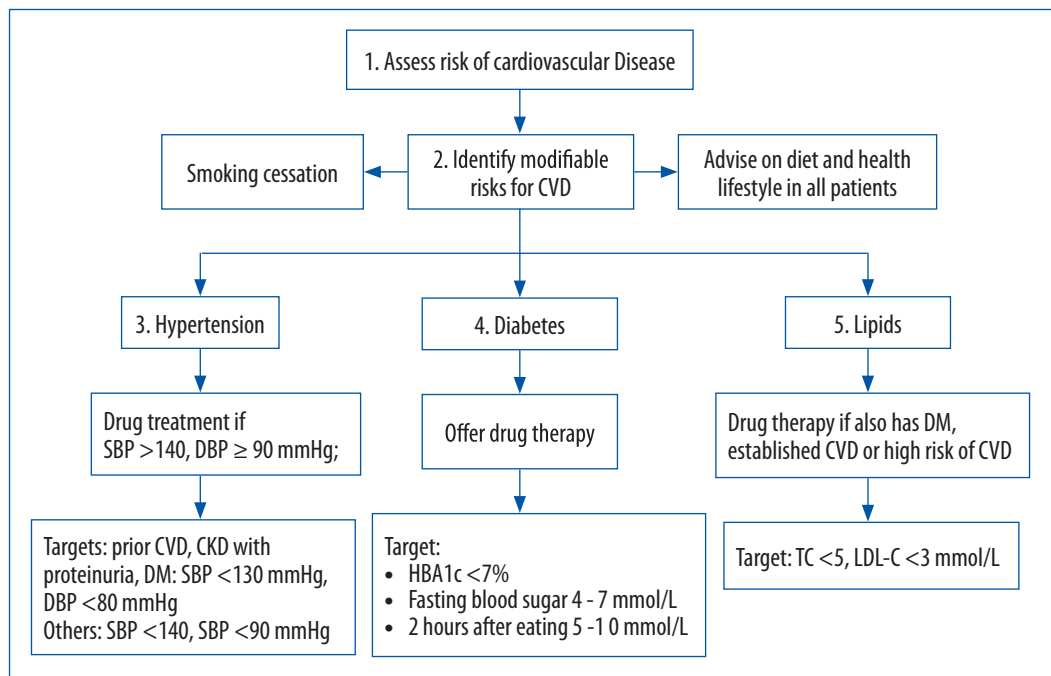
Dietary counselling

- Dietary intervention should not interfere with the dietary requirements required for appropriate absorption of ART drugs
- Keep caloric intake balanced with energy expenditure
- Limit intake of saturated fat, cholesterol and refined carbohydrates
- Reduce total fat intake to <30% and dietary cholesterol to <300 mg/day
- Emphasize intake of vegetables, fruits, grain products with fibre
- Emphasize consumption of fish, poultry (without skin) and lean meat
- Consider referral to dietician, one week food and drink diary to discover 'hidden' calories
- Avoid binge eating
- In patients with HIV-related wasting and dyslipidaemia address wasting first and consider referral to dietician

Physical activity

- Encourage the patient to adopt an active lifestyle to prevent and treat obesity, hypertension and diabetes
- Encourage self-directed moderate level physical activity (take the stairs, cycle or walk to work etc)
- Emphasize regular moderate-intensity exercise rather than vigorous exercise to achieve cardiovascular fitness (e.g. 30 minutes brisk walking >5 days a week)

Figure 8.2 Preventing cardiovascular disease



8.3.3 Treatment of hypertension in HIV Infection

Hypertension is an independent, reversible risk factor for cardiovascular, cerebrovascular and renal disease. PLHIV have high prevalence of hypertension, in addition to other cardiovascular risk factors.

- BP should be measured and recorded in the patient's chart at every clinic visit
- In patients with elevated BP, use a combination of lifestyle changes and pharmacotherapy to achieve treatment targets of BP <140/90 mmHg if the patient has no other cardiovascular risk factors, and <130/80 mmHg in patients with concurrent diabetes, chronic kidney disease or left ventricular dysfunction (overt heart failure or left ventricular hypertrophy)
- Lifestyle changes include
 - Diet high in fruits, vegetables, lean protein, low fat dairy products, nuts and fibres; and low in lean meats and sugars; and low sodium diet (≤ 2.4 g/day)
 - >30 minutes of brisk walking per day or equivalent aerobic activity
 - Reduction/avoid alcohol use
 - Weight management (to maintain BMI at 18.5 to 24.9 kg/m²)

Drug therapy

The following antihypertensive agents in the Kenya Essential Medicines List 2010:

- Amlodipine,
- Atenolol,
- Enalapril,
- Hydrochlorothiazide (HCTZ).

In newly diagnosed patients, start with a calcium channel antagonist (amlodipine) or diuretic (HCTZ). Review for control after 2 to 6 weeks before adjusting therapy. If the target has not been achieved, add an angiotensin converting enzyme inhibitor (enalapril). Patients who require more than 3 agents for control of blood pressure should be referred for specialist evaluation.

Amlodipine: start at 2.5 mg OD; maximum 10 mg once daily.

Metabolism of CCBs is inhibited by PIs; if CCBs must be used with PIs, use the smallest dose possible at initiation of treatment and titrate up while monitoring for side-effects (e.g. hypotension and peripheral oedema).

Metabolism of CCBs may be induced by the NNRTIs EFV and NVP, leading to blunted antihypertensive effect.

Atenolol: start at 25 to 50 mg once daily or divided twice daily; to maximum dose of 100 mg per day. No dose adjustment is required for standard first and second-line therapy. Atazanavir may increase the plasma levels of atenolol; but dose adjustment is not necessary.

Enalapril: start with 2.5 mg once daily; usual maintenance dose is 20 mg once daily; maximum dose is 40 mg per day. There are no significant interactions with ARVs.

Hydrochlorothiazide: start at 12.5-25 mg OD; may increase up to 50 mg OD, though dosages higher than 25 mg carry the risk of hypokalemia with no added benefit. There are no significant interactions with ARVs.

8.3.4 Treatment of diabetes in HIV infection

The risk of diabetes for HIV-infected patients consists primarily of traditional factors, with some added risk from the use of PIs and NRTIs, which may exacerbate underlying diabetes risk.

Screen for impaired glucose tolerance using a fasting blood sugar at entry into care, before starting ART and annually (biannually for those on PIs).

If there is impaired glucose tolerance, initiate lifestyle changes including nutritional counselling and repeat FBS every 3 to 6 months.

Patients with lipodystrophy are at a higher risk of diabetes and impaired glucose tolerance.

Table 8.2 Diagnosis of diabetes

	Fasting plasma glucose mmol/L	Oral glucose tolerance test (OGTT) 2-h value mmol/L
Diabetes	≥ 7.0	≥ 11.1
Impaired glucose tolerance (IGT)	<7.0	7.8 – 11.0
Impaired fasting glucose (IFG)	6.1 – 6.9	<7.8

Start with lifestyle and dietary interventions and when these are not sufficient; prescribe metformin 500 BD or 850 mg OD, to a maximum of 3 g/day. Monitor for at least 1 week before each dose adjustment.

A sulphonylurea is indicated if baseline glucose is very high.

If monotherapy fails, use combination therapy such as metformin/sulphonylurea or metformin/pioglitazone (the preferred regimen). Before starting metformin, the patient's creatinine should be checked for potential nephropathy, as nephropathy is common in patients with diabetes mellitus, and metformin can be nephrotoxic.

Treatment goals: HbA1c <6.5–7% (without hypoglycaemia); fasting plasma glucose 4–7 mmol/L

8.3.5 Treatment of hyperlipidaemia in HIV infection

Elevated LDL cholesterol increases the risk of CVD. The antiretroviral agents that cause the greatest rise in total cholesterol are boosted lopinavir, boosted fosamprenavir and efavirenz, when used in combination with NRTIs. TDF has a marginally protective effect.

The mainstay of treatment of lipid therapy is lifestyle changes such as smoking cessation, diet and weight management. When these measures do not work, change of the ART regimen and drug therapy may be required. Pravastatin and atorvastatin are the first-line statins to use in HIV infection:

- Pravastatin 20 to 80 mg once daily
- Atorvastatin 10 to 80 mg once daily

Start with the lower dose and adjust according to response and tolerability. When using atorvastatin with LPV/r, the maximum dose of atorvastatin is 40 mg once daily. Side-effects of statins include GI intolerance, headache and (rarely) rhabdomyolysis.

The use of simvastatin with protease inhibitors is contraindicated.

8.3.6 Managing chronic kidney disease in HIV infection

Kidney disease is a frequent complication and/or co-morbidity in HIV infection; affecting up to 30% of HIV-infected persons. The risk factors for kidney disease in HIV infection include:

1. African descent
 2. Low CD4 counts (<200 cells/ml)
 3. High viral load (>4000 copies/ml)
 4. Low BMI
 5. Co-morbidities especially diabetes, hypertension, hepatitis B and C infection and cigarette smoking
 6. Use of nephrotoxic drugs
- All HIV-infected patients should be screened for kidney disease at the time of HIV diagnosis or entry into care. Patients with additional risk factors or exposure to nephrotoxic medications should be screened annually. Individuals without risk factors may be rescreened based on clinical signs and symptoms.
 - Screening tests: dipstick urinalysis, calculated estimate of renal function (using the Cockcroft-Gault Equation – refer Chapter 5)
 - If screening shows creatinine clearance (CrCl) or estimated GFR (eGFR) <60 ml/min/1.73 m², or proteinuria ≥1+ on urine dipstick analysis consultation with a specialist physician is advised.

Figure 8.3 Screening for kidney disease in HIV infection

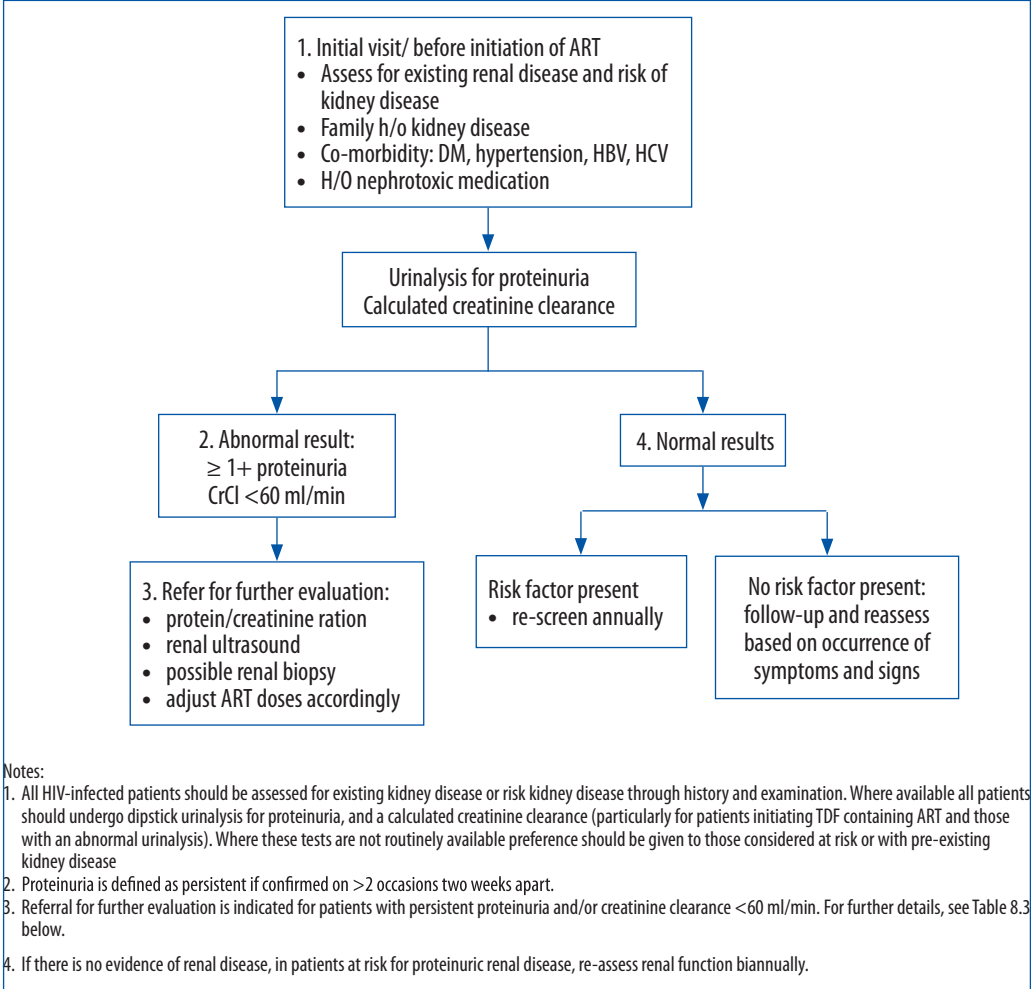


Table 8.3 Management of Kidney disease in HIV infection

Intervention	Comments
General measures -Treat dehydration promptly and aggressively -Avoid nephrotoxic drugs -Life style measures (smoking, weight, diet) -Treat dyslipidaemia and diabetes, hypertension -Adjust drug dosages where necessary	Refer for further evaluation patients with <ul style="list-style-type: none"> • Persistent proteinuria, • CrCl <60, • HBC/HCV co-infection
Start ACE inhibitors if: a) Hypertension, and/or b) Proteinuria	Target BP SBP <130, DBP <80 mmHg
ART	Start ART in ALL HIV-positive patients with persistent proteinuria and oedema irrespective of CD4 count

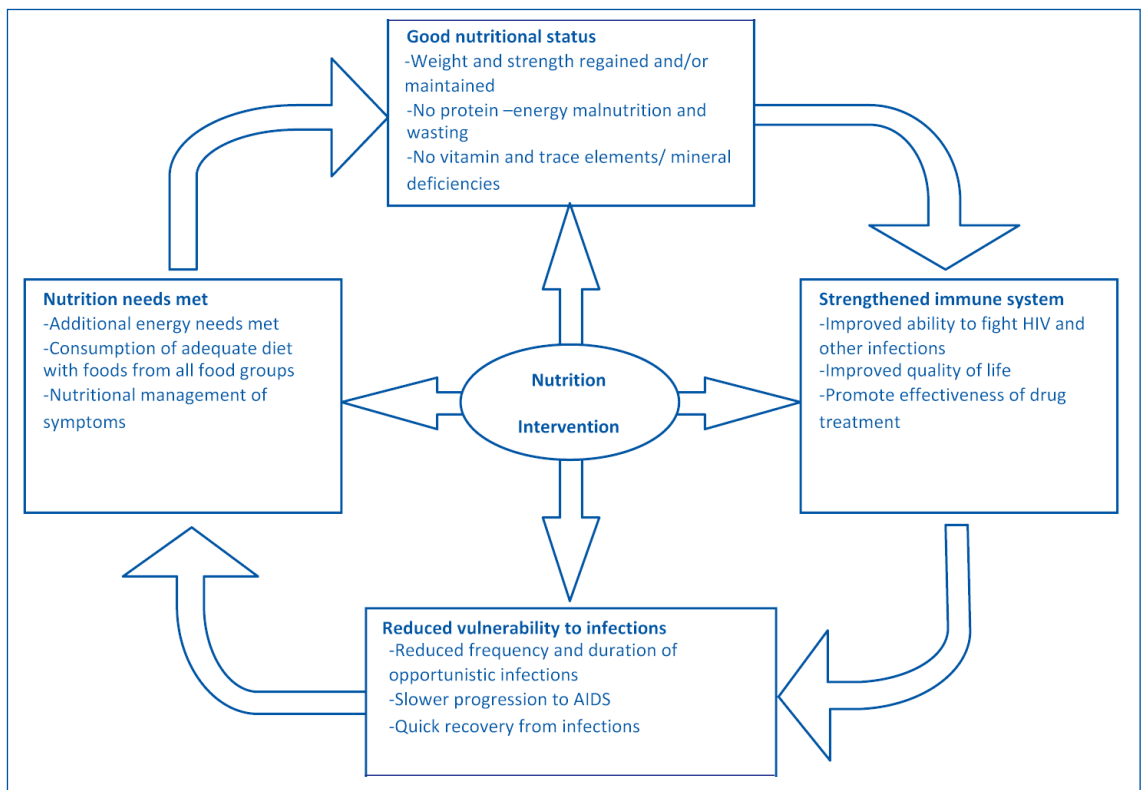
9. Nutritional support of adults and adolescents living with HIV infection

9.1 Introduction

Malnutrition leads to immune impairment, worsens the effects of HIV, and contributes to more rapid progression of HIV disease. HIV infection affects the nutrition status of an individual through increased energy requirements, breakdown of muscle proteins and sub-cutaneous fat, usage of vitamins, trace elements and minerals; and malabsorption. Thus, malnutrition both contributes to and is a result of HIV disease progression.

A well-nourished person has a stronger immune system for coping with HIV and fighting illness. Figure 9.1 illustrates the benefits of improving and maintaining good nutrition in HIV-infected adults. Timely nutritional interventions can help strengthen the immune system, thereby reducing the incidence of infections, preventing loss of weight and preserving lean body mass, and delaying disease progression.

Figure 9.1 Benefits of nutrition intervention for HIV-infected adults



9.2 Nutritional requirements for people living with HIV/AIDS

Moderately active healthy non-pregnant/lactating HIV-uninfected adults require 1990–2580 kcal/day. People living with HIV infection (PLHIV) have increased resting energy expenditure (REE). The following are recommended energy requirements for PLHIV;

- 10% more energy if in WHO stage I (i.e. no AIDS-related symptoms); equivalent to about 210 additional kcal/day (this translates to 1 cup of thick porridge)
- 20-30% more energy in WHO stages II, III and IV (depending on severity of symptoms) and is equivalent to about 420-630 kcal/day (this translates to 4-6 cups of thick porridge)

Protein, fat, vitamins, trace elements/minerals (micronutrients) and water requirements for physiologically normal PLHIV are the same as in HIV-negative individuals. However, PLHIV are vulnerable and require adequate intake of all nutrients at all times.

During episodes of acute infection and in advanced HIV disease, higher protein intake (1.2–1.5 g/kg body weight/day) is required. In addition, extra caution is required to ensure safe drinking water and good food hygiene.

Inadequate intake of energy and other nutrients to support the altered metabolism leads to malnutrition (under nutrition and wasting). Common causes of inadequate food intake include loss of appetite (anorexia) which may occur as a side-effect of medications or due to infections, stress and depression. Other causes include diarrhoea, constipation, fever, nausea and vomiting, and pain in the mouth or throat due to opportunistic infections such as thrush.

Food insecurity makes the situation worse by limiting available food to meet increased nutrient needs of PLHIV.

9.3 Nutrition assessment, diagnosis and interventions

The algorithm below gives an overview of nutrition assessment, diagnosis and management of malnutrition among PLHIV (Figure 9.2).

9.3.1 Assessment

Nutritional assessment refers to the process of determining a person's nutritional status, situation, and vulnerability to malnutrition by asking questions related to dietary intake, symptoms and barriers to adequate food intake (listed above), signs of weight loss such

as loosening of clothes; and household food security. Assessment also includes enquiring about the drugs that the patient is taking, use of nutritional supplements and herbal preparations.

The second component of assessment comprises of anthropometric measurements, physical examination for clinical signs, muscle function tests and dietary recall. Patients with protein energy malnutrition will invariably have one or more micronutrient deficiency disorders. Health care workers should look for signs of common micronutrient deficiencies, among them pallor due to possible iron, folic acid and vitamin B12 deficiencies (nutritional anaemia); ocular signs of vitamin A deficiency such as night blindness, conjunctival dryness (xerosis), lesions such as Bitot's spots, corneal xerosis and keratomalacia; signs of scurvy such as easy bruising and gum bleeding due vitamin C deficiency; signs of pellagra such as dermatitis, diarrhoea and dementia due to vitamin B3 (niacin) deficiency; and neurologic signs associated with vitamin B1 (thiamine) deficiency among others. Zinc and selenium are crucial in development and maintenance of the immune system as well as gastrointestinal and cutaneous health.

The following specific assessments are recommended;

1. Anthropometric assessment: weight at every visit, height at enrolment for adults and quarterly for adolescents (up to age 18), and mid-upper left arm circumference (MUAC) for pregnant women, adolescents, bed ridden patients. (Refer to the Ministry of Health Guidelines on the Integrated Management of Acute Malnutrition.)
2. Clinical assessment: bilateral pitting oedema, muscle wasting, hair colour/texture changes and fat distribution.
3. Functional tests: handgrip, morbidity, days bedridden for in-patients and patients on nutrition therapy
4. Dietary assessment: food recalls (24 hr, or 3-5 day recall for advanced conditions) to provide information on food frequency by type of food, and household food security.
5. Laboratory investigations: Haemoglobin concentration, blood glucose levels and electrolytes for early detection and grading of risk and severity of deficiencies and metabolic disturbances.

9.3.2 Diagnosis

Diagnosis of malnutrition or over nutrition is based on cut-off points of body mass index (BMI). BMI is equal to weight (kg)/height (m²) or MUAC (cm). Table 9.1 shows the cut-off points used for categorizing malnutrition and over nutrition. In addition to BMI, the waist and hip measurements are useful especially for individuals who are overweight or obese in determining fat distribution and attendant risk of chronic life-style disease. A ratio of waist to hip ratio (WHR) >1 in men and >0.8 in women calls for appropriate dietary counselling and exercise interventions.

Micronutrient deficiency disorders such as anaemia are also categorized into different grades of severity based on cut-off points or type of the signs observed. Generally, they are graded as mild, moderate or severe. In the case of anaemia, Hb less than 11 g/dl indicates mild anaemia, while Hb less than 7g/dl severe anaemia.

Table 9.1 Reference values for anthropometric measurements

Diagnosis/classification	Adults (not pregnant) BMI (kg/m ²)	Adults (not pregnant) MUAC (cm)	Pregnant and early postpartum MUAC (cm) ¹
Severe acute malnutrition	<16	<16 cm	<19 cm
Moderate acute malnutrition	16–17	16.0–18.5 cm	19–<22 cm
Mild acute malnutrition	17.1–<18.5	18.5–23 cm	22–23 cm
Normal	18.5–<25	—	—
Overweight	25–30	—	—
Obese	>30	—	—

¹ Early post-partum in this context is the first 6-8 weeks.

The diagnostic category should trigger specific actions (counselling, nutritional treatment and referral services) through specific pre-determined eligibility (entry and exit) criteria for therapeutic or supplemental nutritional therapy and support services such as food assistance.

9.3.3 Management

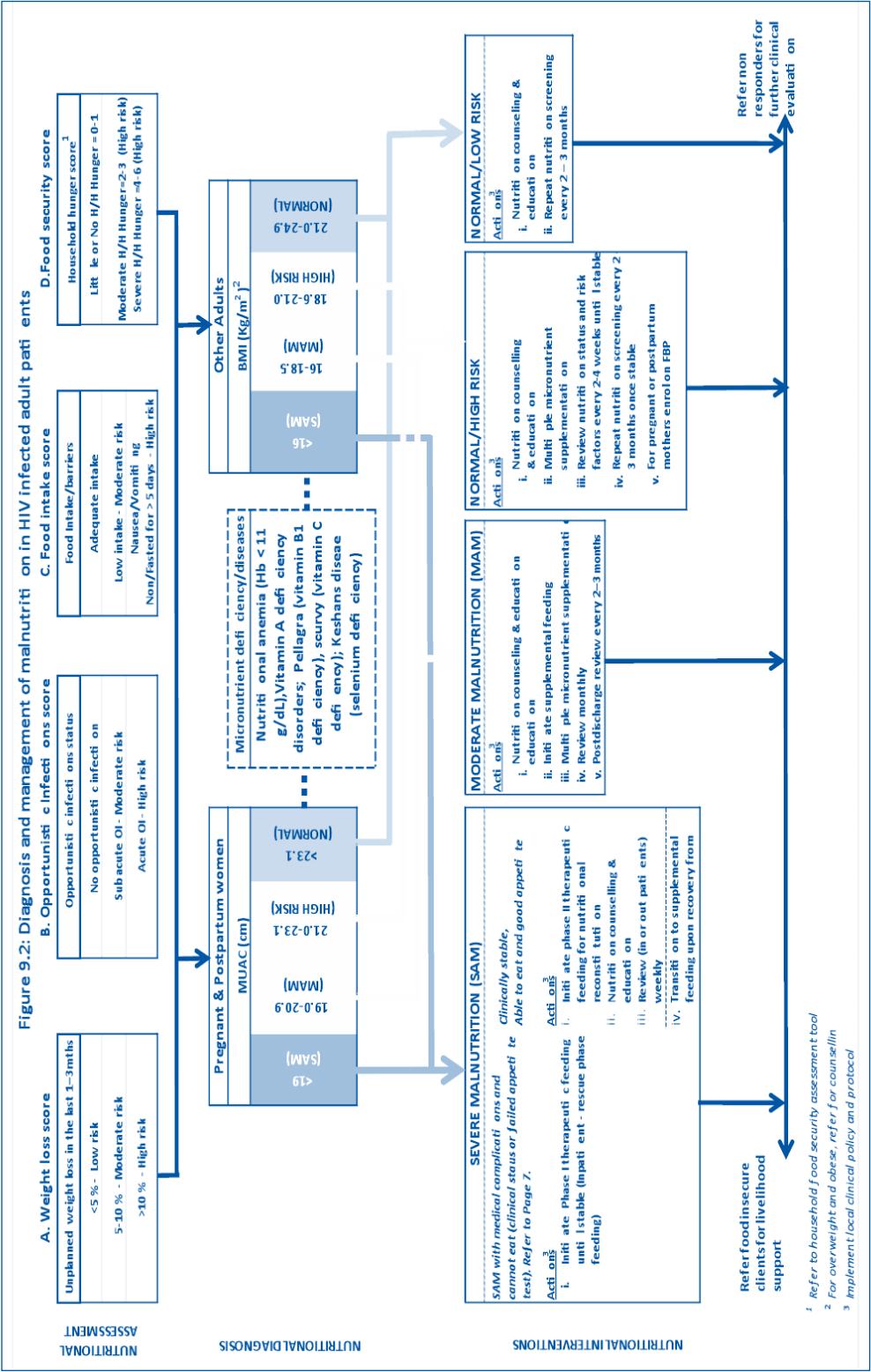
All stable PLHIV and their care givers, irrespective of nutrition status (normal, malnourished or over nourished) should received quality nutrition counselling and education. Clinically malnourished patients and their care givers should also receive specific nutritional therapies and adherence counselling.

Nutrition counselling – critical nutrition practices

The following key nutrition counselling and education messages should be provided to influence individual or family nutrition practices:

1. The patient should have periodic (every 2-3 months) nutritional status assessments, especially weight.
2. The patient has increased energy needs depending on the disease stage. To achieve required energy, the patient should eat sufficient amounts of balanced foods in three meals and one or more snacks between meals per say.
3. The patient should maintain high levels of sanitation, food hygiene and use safe water at all times.
4. The patient should practice positive living behaviours, including safe sex practices, avoidance of alcohol and tobacco, avoidance or moderation in consumption of high fat, refined foods and seek help in management of stress and depression.

Figure 9.2 Diagnosis and management of malnutrition in HIV infected adult patients



5. Physical activity is important to strengthen or build muscles and increase appetite and improve health. Progressive resistance exercise is required for recovery of malnourished patients.
6. Recommend drinking of plenty of clean, safe water (at least 8 glasses of filtered and boiled or treated water) and using the same to swallow medicines, preparation of juices and cleaning of fruits and salads before eating.
7. The patient should seek prompt treatment for all opportunistic infections and other diseases, and manage mild symptoms with dietary practices, especially for illnesses that may interfere with food intake, absorption and utilization.
8. If the patient is on medicine, such as ARV agents, manage drug-food interactions and diet-related side-effects. Encourage patients taking traditional herbs or nutritional supplements to inform the clinician.

Nutritional treatment

The aim of treating clinical malnutrition is to stop further weight loss, facilitate weight gain and nutritional reconstitution. Overall, management of clinical malnutrition requires supplemental or therapeutic interventions depending on the severity. Patients with severe malnutrition and life threatening medical complications; or unable to feed orally are managed as inpatients. Stabilization of hypoglycaemia, hypothermia, dehydration, electrolytes balance and infection control is required before in addition to nutrition therapy. Appropriate hospital feeding protocols and feeds should be used to ensure gradual increase in energy intake to allow the patient to physiologically stabilize before full loading with energy and nutrient requirements (Refer to Guidelines on Integrated Management of Acute Malnutrition, 2009).

Stable in-patients with uncomplicated severe malnutrition are managed with oral nutrition therapeutic or supplemental regimens of ready to use therapeutic food (RUTF) which are continued at home upon discharge. These foods are lipid based pastes, powders or bars and may be combined with supplemental food formulations to improve acceptability. Commonly available formulations include, lipid based peanut-milk powder paste and cereal-milk powder and plant protein based solid bars. Supplemental food formulations are nutrient dense fortified blended foods (FBF) or composites of staple foods.

Majority of adult patients with severe acute malnutrition weigh less than 45 kg. The recommended energy intake should be gradually increased from 25-30 kcal/kg body weight/ day over a period of 5-10 days to help normalize the physiologic and biochemical body functions. Patients in this phase of treatment should receive 100 mg of thiamine (vitamin B1) along with complete multi-micronutrients in the therapeutic food. Thiamine plays an important role in the regulation of glucose metabolism and pancreatic beta-cell functioning. Patients entering the rehabilitation phase should be provided with full loading of therapeutic food regime to meet about 100% energy, proteins, lipids and micronutrients requirements and extra to enhance repletion (Section 9.2). Patients should be encouraged

to eat normal foods with or after therapeutic food to facilitate transition to regular home diets upon recovery. With good adherence, patients should reach the exit cut-off point for moderate malnutrition shown in Table 9.1 in 4 to 8 weeks. Upon reaching moderate malnutrition stage, patients should be transitioned to oral supplemental food prescriptions alone.

Supplemental foods such as FBF and ready to use supplemental foods (RUSF) are designed to provide about 50% of energy (section 9.2), over 70% of whole protein and lipids along with approximately one recommended dietary allowance (RDA) of key micronutrients.

An RDA is the average daily dietary intake of a nutrient that is sufficient to meet the requirement of nearly all healthy persons. Oral supplemental foods are used for stable patients with moderate and mild acute malnutrition in out-patient and inpatient settings. Oral nutrition therapeutic and supplemental regimens are currently provided under food by prescription (FBP) programme and outpatient therapeutic programme (OTP) protocols in some settings. Alternative supplemental food formulations are required for diabetic patients.

Oral nutrition therapeutic foods provide therapeutic/pharmacological doses of multi-micronutrients to restore physiological levels and replenish body stores (Table 9.2). Oral nutrition supplemental foods contain levels of multi-micronutrients formulations at approximately one RDA to correct mild deficiencies and prevent development of deficiencies in moderately and mildly malnourished patients. Patients whose diet is not adequate with respect to recommended daily allowances and patients who have borderline nutrition status (high risk) are also supplemented with one RDA multi-micronutrients formulations until their dietary intake is considered adequate and stable.

Table 9.2 Nutritional composition multi-micronutrient formulations

Nutrients	Therapeutic (multiply by number of grams prescribed per day) ¹	Daily (1 RDA)
Vitamins		
Vitamin A	0.8 to 1.1 mg/100 g	700-900 µg
Vitamin D	15 to 20 µg/100 g	10 µg
Vitamin E	20 mg/100 g minimum	10 mg
Vitamin C	50 mg/100 g minimum	60 mg
Vitamin K	15 to 30 µg/100 g	80 µg
Vitamin B1 (thiamine)	0.5 mg/100 g minimum	1.5 mg
Vitamin B2 (riboflavin)	1.6 mg/100 g minimum	1.7 mg
Vitamin B3 (niacin)	5 mg/100 g minimum	2.0 mg
Vitamin B6 (pyridoxine)	0.6 mg/100 g minimum	2.0 mg
Vitamin B12 (cobalamin)	1.6 µg/100 g minimum	1.7 µg
Folic acid	200 mcg/100 g minimum	193 µg
Pantothenic acid	3 mg/100 g minimum	2.85 mg
Biotin	60 µg/100 g minimum	60 µg
Minerals		
Iron	10 to 14 mg/100 g	18 mg
Zinc	11 to 14 mg/100 g	15 mg
Copper	1.4 to 1.8 mg/100 g	2.0 mg
Selenium	20 to 40 µg	70 µg
Iodine	70 to 140 µg/100 g	150 µg
Sodium	290 mg/100 g maximum	<276 mg
Potassium	1100 to 1400 mg/100 g	1022 mg
Calcium	300 to 600 mg/100 g	276 g
Phosphorus	300 to 600 mg/100 g	276 g
Magnesium	80 to 140 mg/100 g	84.6 mg

1 Source: World Health Organization/World Food Programme/United Nations System Standing Committee on Nutrition/The United Nations Children's Fund, 2007

To overcome acute persistent barriers to oral intake of food requires clinical assessment to establish underlying causes. In addition to psychosocial support, symptoms such as acute anorexia, nausea and vomiting, pain from oral-pharyngeal lesions, pharmacological treatments is required. For patients who do not have heart ailments, diabetes and chronic bronchitis, short course of metopine a non-hormonal anabolic, 3-5 mg in 5-10 ml oral suspension before main meals is useful. Metopine is combined with the B-complex vitamins and amino acids lysine and carnitine to enhance carbohydrate metabolism. Relief to persistent nausea and vomiting may be provided through short course of antiemetics. Oral sores should be treated promptly by use of antifungal agents (for oral thrush), antiviral agents (viral infections) and local analgesics (aphthous ulcers). Adjunctive nutrition actions shown in Table 9.3 are key to successful management of mild barriers to adequate food intake and prevention of malnutrition.

Table 9.3 Nutritional management of common symptoms of HIV/AIDS

Symptom	Nutritional management	Things to avoid
Anorexia	<ul style="list-style-type: none"> • Eat foods high in fibre content • Drink plenty of fluids 	Processed or refined foods
Nausea or vomiting	<ul style="list-style-type: none"> • Eat small quantities of food at frequent intervals • Drink after meals, limit drinking fluids with meals • Eat dry foods • Avoid spicy/salty foods • Take sips of ORS if vomiting occurs • Rest between meals 	Avoid staying with an empty stomach
Diarrhoea	<ul style="list-style-type: none"> • Drink plenty of fluids (clean, boiled/treated water) • Prepare and drink ORS regularly • Take soluble fibre foods (like oranges and mangoes) • Seek medical advice if diarrhoea is severe or if there is blood in stool) 	Foods cooked in plenty of oil Fried foods
Dry mouth	<ul style="list-style-type: none"> • Rinse mouth with warm water, a pinch of salt may be added • Maintain good oral hygiene • Seek medical advice if there is pain on swallowing or there are oral sores or spots 	Very hot or spicy foods Excess caffeine beverages such as tea or coffee and effervescent drinks
Fever	<ul style="list-style-type: none"> • Drink plenty of fluids • Eat energy and nutrient rich foods • Eat small but frequent meals • Seek medical advice 	
Change or loss of taste	<ul style="list-style-type: none"> • Chew food well and move it around in the mouth • Eat flavoured foods (spicy) as tolerated. 	

9.4 Community nutrition services for PLHIV

Efforts should be made to improve outreach and follow up, which include strengthening the links between facility and community services including complementary food programmes and livelihood support initiative, as well as reinforcing referral and tracking systems between facilities and communities. The community strategy initiative provides a framework for strengthening outreach activities using community health extension workers and collaborating with community based systems such as community based organizations and community health workers. Capacity building of community health workers to carry out screening using MUAC and home based care support are useful strategies in the prevention and management of malnutrition.

Community therapeutic care (CTC) that improve access to nutrient dense food formulations for the vulnerable at community level may be especially useful in supporting HIV affected families.

9.5 Quality improvement of nutrition services for PLHIV

Qualitative and quantitative analysis of the nutrition care of PLHIV is important in developing approaches that improve efficiency and identifying areas for improvement to make services more responsive and effective. Continuous objective monitoring and evaluation of the quality and appropriateness of protocols should be carried out on regular basis, monthly and quarterly, and substantive audit every 6 months are necessary. Identification of robust quality control indicators and development of tools to facilitate monitoring and audit at national level should be adapted by all nutrition service points. Of particular importance are overall conformance with nutrition assessment and counselling of all patients and use of FBP protocol in the management of clinical malnutrition, volume and type of facility-community referrals, incidence of clinical malnutrition and wasting (BMI <20 kg/m²) among ART and pre-ART adult patients, rates of recovery of malnourished patients on FBP, adherence to ART and treatment of opportunistic infections, mortality, quality of life, relapse rates after recovery from malnutrition.

10. Care of adolescents living with HIV/AIDS

10.1 Introduction

The World Health Organization defines adolescence as the age range from 10 to 19 years. The term “young people” refers to individuals aged 10-24 years. Young people aged 15–24 years account for 63% of people living with HIV/AIDS in sub-Saharan Africa.

Adolescence is characterized by dramatic physical, emotional, cognitive, and social change. Key attributes of this age period are summarized below.

1. Developmental markers
 - the formation of a sexual identity
 - the propensity for taking risks
2. Physical, psychological, social, cultural and economic attributes
 - Economically dependent
 - social inexperience/limited life skills
 - limited literacy on sexuality and protection from infection,
 - limited access to health care

10.2 Stages of adolescent development

Physical, emotional and cognitive development during adolescence can be divided into 3 stages:

- Early adolescence
- Mid-adolescence
- Late adolescence

Physical development

Physical development of adolescents is based on Turner’ staging of sexual maturation as shown in Table 10.1 on next page:

Table 10.1 stages of physical development in adolescents

stage	Physical characteristics	Emotional characteristics	Cognitive characteristics
Early (10–13 years)	Girls- breast bud, downy pubic hair near labia, peak growth velocity Boys- darkening and enlarging scrotal sac, testicular growth, downy pubic hair	Wide mood swings, intense feelings, low impulse control	Concrete thinking Little ability to anticipate long term consequences of their action Literal interpretation of ideas
Mid (14–16 years)	Girls- further growth of breasts, increased pigmentation of pubic hair, menarche Boys further increase in size of testes, enlargement of penis, growth	Sense of invulnerability, risk taking behaviour peaks	Able to conceptualize abstract ideas such as love, justice, truth and spirituality
Late >17 years	Mature physical development	Sense of responsibility for one's health, increasing sense of vulnerability, able to think of others and suppress ones needs, less risk taking	Ability to understand and set limits Understands other's thoughts and feelings

10.3 Package of care for the HIV-infected adolescent

There are two groups of the HIV-infected adolescents:

- Long term survivors of perinatally acquired HIV (vertically acquired HIV infection)
- Adolescents infected during childhood or adolescence (horizontally acquired HIV infection)

Challenges facing HIV-infected adolescents

- Stigma
- Self esteem
- Body image
- Peer pressure with excessive activities which contributes to lack of ability to prioritize health issues
- Substance/drug abuse
- Relationships
- Unstable living condition
- Lack of social support
- Coping with the disease in school/ college
- Simple refusal or lack of readiness for initiation of ART
- Coming to terms with a chronic illness
- Lack of youth friendly services
- Other mental health issues

The following package of care should be provided to the HIV-infected adolescent;

1. Confirmation/documentation of HIV infection
2. Growth and development assessment and monitoring (physical, emotional and cognitive)
3. Preventing opportunistic infections including co-trimoxazole and INH prophylaxis (details provided as in chapters 2 and 5)
4. Nutritional care.
5. Psychosocial assessment and counselling
 - disclosure
6. Health education including amongst others:
 - Developmental changes
 - Sexuality
 - Basic fact of HIV and AIDS.
 - Primary and secondary abstinence and safer sex practices.
7. Sexual and reproductive health care
 - For pregnant adolescent (refer to Chapters 16 and 17)
 - STI screening and treatment,
 - Provision of appropriate contraception, Cervical cancer screening for sexually active adolescents
8. Ensure that immunization is up to date and educate on appropriate vaccine schedules particularly for HPV and HBV vaccination.
9. staging of HIV disease (clinical and immunological)
10. Prompt Treatment of infections including opportunistic infections
11. Counselling for and provision of ART
12. Regular follow up schedule; provide for flexible follow-up dates to accommodate schooling.
13. Providing comprehensive care for adolescent and family
14. Planning for/providing long-term HIV care and follow up including community support

10.4 Psychosocial assessment and support in adolescents

SHADASS assessment tool¹

The SHADSSS assessment is a quick and effective tool for gaining insight into an adolescent's world. It provides a framework for discussions of all areas of the adolescent's life. All health workers should be conversant with the following dynamic aspects of the adolescent life in order to provide comprehensive care;

- S=School
- H=Home

¹ Source: Rudy B, J. Textbook of Pediatric HIV Care 2005

- A=Activities
- D=Depression/Self-esteem
- S= Substance abuse
- S=Sexuality
- S=Safety

Disclosure

Disclosure of HIV status is not a one-time event, but rather a process, involving ongoing discussions about the disease as the adolescent matures cognitively, emotionally, and sexually.

Why is HIV disclosure important?

- Helps to increase an adolescent's willingness to adhere to treatment
- Helps the adolescent understand the illness
- Avoids accidental disclosure (e.g. child overhears caregiver discussing it)
- helps to decrease behaviour problems – such as stress, depression, truancy etc
- helps to improve social functioning and school performance.

When should the disclosure process begin?

- Discussions between the clinical team and caregivers should begin early in the patient's childhood
- The disclosure of HIV infection status to school – aged children should be individualized.
- Whenever possible, disclosure should occur when child is clinically and emotionally stable and the caregiver is ready

Timing of disclosure

Disclosure process should not be rushed, but timing of disclosure becomes a pressing need as child nears adolescence.

Disclosure will depend on:

- Caregiver's acknowledgment of the disease and readiness to disclose
- Child's cognitive skills and emotional maturity (including ability to maintain confidentiality) It usually achieved by 8 years of age.

Collaborating with families to develop a disclosure plan

- Address caregivers' concerns about disclosure
- Discuss the importance of ongoing communication with the adolescent regarding health issues.
- Discuss the benefits and risks of disclosing the diagnosis of HIV infection to the adolescent
- Discuss the potential harm that can result from long-term non-disclosure.

Factors to consider when developing an individualized disclosure plan

- Adolescent's age, cognitive ability, and developmental understanding of illness and mortality
- What the adolescent has already been told and what she already knows about medications or doctor visits
- Clinical status of the adolescent
- Other disclosures that may need to be made (e.g. adoptive status, paternity issues, or parental HIV diagnosis)
- Caregivers' thoughts about disclosure
- Cultural influences
- Family/social circumstances
- Anticipated response of the adolescent on learning about the diagnosis
- Effect on HIV-infected and non-infected siblings
- Types of support available to the child and family once disclosure occurs (e.g. counselling, peer support groups)

Supporting adherence in the adolescents

Adherence counselling is an ongoing process by which counsellors support the adolescents and their caregiver in maintaining compliance to treatment. He or she should understand the treatment, know the importance of treatment and decide to take treatment. **Refer Chapter 18 for more information on adherence.**

Adolescent sexual and reproductive health services

By age 18, about half of women (47%) and slightly more than half of men (58%) have had sexual intercourse. Young women in the age groups 15 to 19 and 20 to 24 years are twice as likely to be infected with HIV as males in the same age groups. It is estimated that about 20% of all reported HIV patients are young people aged 21 to 24 years.

Adolescents living with HIV and AIDS have just as much need for sexual and reproductive health (SRH) services as non-infected adolescents.

SRH services need to be tailored to the needs of both sexually active and inactive adolescents and should be provided at a cost that is affordable to the adolescent.

Adolescents should be provided with information on where to access contraception counselling, STI treatment and PMTCT.

Adolescents should be given information and skills so that they can protect themselves from the negative consequences of sexuality. The health care worker should provide young people with correct information on their sexual feelings, sexual physiology, sexual relations, risk of STIs, family planning and should actively promote and support abstinence.

Family planning: All methods of family planning can be used safely in HIV-infected adolescents. However, a hormonal contraceptive increase genital shedding of HIV and therefore puts the sexual partner at higher risk of HIV. Hormonal contraception increases the female's vulnerability to bacterial and viral STIs including HIV, thus sexually active adolescents should use dual contraception – a condom plus an effective contraceptive method.

Prevention of STIs/ HIV in the sexually active adolescent

Prevention of STIs and HIV is key to reducing new infections in adolescents.

- Health care workers should promote correct and consistent use of condoms,
- STI including HPV screening, cervical cancer screening and provision of the HPV vaccine
- Sexually transmitted diseases should be treated in a timely manner according to the national guidelines
- Development of life-skills e.g. avoidance intergenerational sex and being faithful to one partner.

Prevention of HIV transmission among HIV-infected adolescents

Adolescents are more vulnerable to HIV/AIDS infection. Because HIV transmission in Kenya occurs predominantly through heterosexual intercourse between an infected and a non-infected person, age at first intercourse marks the time at which most individuals first risk exposure to the virus. It is necessary for HIV-infected adolescents to know that they can transmit HIV to their sexual partners and to their un-born child and hence target HIV transmission prevention messages at this special population.

HIV preventive measures among adolescent/youth include:

- Abstinence

Being faithful to one sexual partner and correct and consistent use of condoms

- Delay of sexual debut
- Counselling and testing of sexual partners
- Contact tracing and follow-up
- Early diagnosis and effective treatment of STIs
- Adherence to antiretroviral treatment
- Provision of family planning services

Life skills

These are skills that help the adolescent to adjust and operate appropriately within the society namely; self help skills, social skills and cognitive skills.

Self help skills include personal hygiene, personal grooming, culinary skills (how well can you cook), domestic chores and adherence to care and treatment.

Social skills help to build harmonious interaction with other people and include; greetings, apology, being receptive and helpful, assertive skills and anger management.

Cognitive skills help one to appraise a situation and make appropriate decisions and include one's performance in school, ability to think and act in an appropriate manner in challenging situations, conflict resolution and problem solving.

Adolescent friendly clinic

An adolescent clinic should endeavour to have the following;

- Spacious, well lit and appealing for adolescent consultation and services
 - Adolescents are booked to be seen on their own
 - Clinician trained to provide adolescent care
 - Unrushed consultations
- Adolescent friendly rooms with adequate recreational activities e.g. pool, reading material, music, TV/video
- Health care providers who are;
 - skilled and dynamic/acceptable to the youth
 - Good listening skills
 - Friendly
 - Non-judgemental
 - Dedicated to their work
- Clinics with programmes that allow for regular outings and retreats.
- Psychosocial support groups led by trained staff (counsellor, peer educator), during which
 - Share experiences about stigma in the home, school, community
 - Can express themselves through drama and song
 - Discuss pertinent issues on their illness (treatment literacy)
 - Discuss issues on life skills- sexuality, disclosure, careers, finances, drug abuse, pregnancy
- Caregivers psychosocial support group
 - Equip care givers with skills to support the adolescents to discuss issues e.g. disclosure, sexuality, prevention with positives, adherence to treatment etc
 - Prepare them for transition to adult hood and adult clinic

Community linkages

Strong community linkages play a key role in adolescent HIV care and treatment.

These linkages will ensure referral of adolescents from the community to the facility for HIV counselling and testing. Community health extension workers (CHEWs), community owned resource persons (CORPs) and even specific school teachers need to be trained on adolescent care and support. The minimum kit they will require is a training curriculum for the youth on life skills including psycho-social issues, reproductive health, drug and substance abuse.

CHEWs, CORPs and trained school teachers will equip the youth (in and out of school) with knowledge and life skills, and facilitate a supportive environment to enhance adoption of healthy lifestyles for the youth and the community. They will initiate comprehensive community based, youth friendly centres in collaboration with other stakeholders; raise awareness on disease causation, control and prevention, in particular STI/HIV/AIDS and provide family life education.

Other community based treatment and prevention support activities include:

- Defaulter tracing for adolescents lost to follow up on care and treatment;
- Promotion of community support groups which organize community events e.g. sports days, cultural events etc.
- Condom distribution in the community.

10.5 ART in adolescents

In the selection of ARV drugs for treatment of the adolescent, the following should be considered:

- sexual developmental stage (Turner's staging)
- mode of acquisition of HIV, and if perinatally acquired, whether there was exposure to nevirapine
- paediatric regimens and doses are used for early adolescence (Turner's staging 1 & 2)
- adult regimen and doses are used in the treatment of the mid and late adolescent i.e. Turner's stage 3 to 5;
- For the sexually active female adolescent who is at risk of becoming pregnant, nevirapine is preferred over efavirenz.

Requirement for initiating HAART

- Knowledge of their disease and available treatment.
- Adequate social support and stability
- Acceptance of HIV-status and need to start care and treatment
- Access to supportive health care providers
- Meets clinical and/or laboratory criteria for initiation

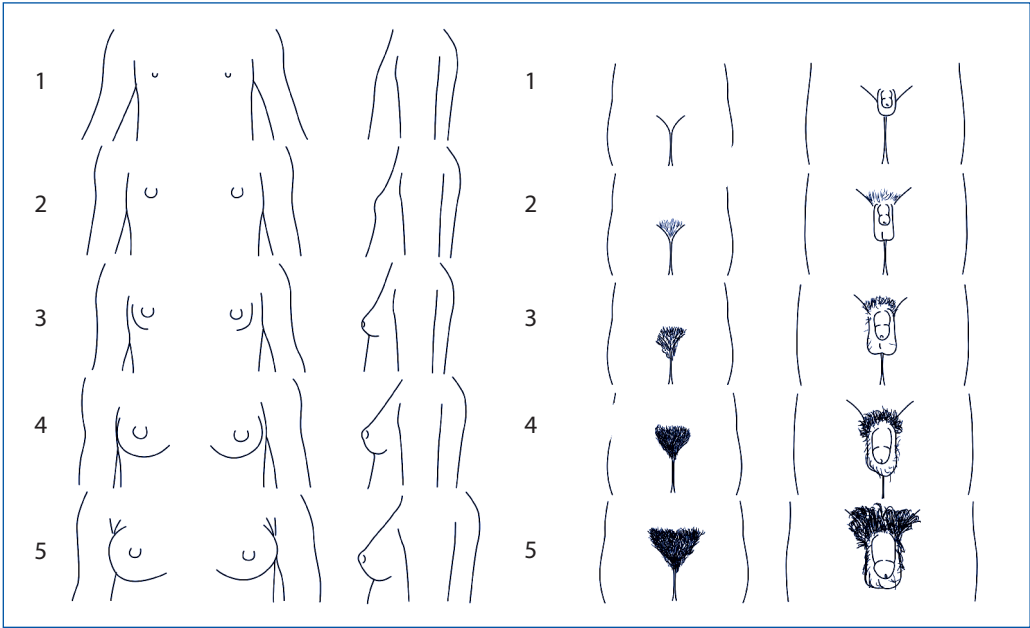
10.6 Transition from paediatric to adult services

Adolescents living with HIV need support to “graduate” into adult services when she/he “ages out” of paediatric -specific care. The timing of transition to adult clinics depends on developmental readiness, complexity of their health needs, and their social support. The assessment and preparation for readiness of transition is a process which should be carried out jointly by clinicians, counsellors and the family.

As a minimum, the following need to be accomplished during transition.

1. Cognitive and emotional assessment is carried out and a transition plan formulated
2. Full disclosure should take place before transition
3. Successful transition from a paediatric to an adult ART regimen with more use of fixed dose combinations to further promote adherence to treatment.

Figure 10.1 Tanners staging



Tanners staging is a uniform, accepted method used to describe the onset and progression of pubertal changes as indicated in the pictures above. Boys and girls are rated on a 5 point scale. Girls are rated for breast development and pubic hair growth and boys are rated for genital development and pubic hair growth.

11. Overview of HIV in children

11.1 Introduction

Globally, 3.2 million children live with HIV infection; and approximately 1500 children are born with HIV infection daily. More than 90% of HIV-infected children live in sub-Saharan Africa. Most children acquire HIV infection in-utero, during delivery or through breastfeeding. For most infants who acquire HIV infection in-utero or around delivery, disease progression occurs rapidly in the first few months of life, often resulting in severe opportunistic infections, failure to thrive and death. By two years of age, more than 50% of perinatally HIV-infected children have died. Improving access to optimal interventions that prevent mother-to-child HIV transmission has the potential to reduce transmission from 40% to less than 2%, and contribute to the eventual elimination of paediatric HIV infection.

In Kenya, an estimated 70 000 to 100 000 infants are exposed to HIV (born to HIV-infected mothers) every year. With current coverage of interventions to prevent mother-to-child HIV transmission (PMTCT), there are still an estimated 7000–10 000 children newly infected with HIV in Kenya each year.

11.2 Package of care for the HIV-exposed and the HIV-infected child

There are two groups of children with respect to HIV infection:

- (a) HIV-exposed children: children born to HIV-infected mothers but the HIV status of the child is not yet known
- (b) HIV-infected children: child whose HIV infection is confirmed

Services to prevent HIV infection for HIV-exposed children start before conception though to the childhood. The following 10 steps summarizes the package of care to be provided to HIV-exposed children:

1. Provision of essential prenatal, delivery and postnatal care for women
2. Provision of ARV to mother and child for prevention of mother-to-child transmission of HIV
3. Early infant diagnosis (early testing for HIV infection)
4. Health education and counselling of the child's caregiver on:
 - a. Infant feeding
 - b. HIV-related symptoms
5. Preventing opportunistic infections through co-trimoxazole and isoniazid prophylaxis
6. Monitoring growth and development

7. Immunization
8. Nutritional care, supplementation and advice
9. Regular presumptive de-worming every 6 months
10. Regular follow-up, with a clearly communicated a follow up schedule – birth, week age 2, 6, 10, 14 weeks, then monthly in the first year, quarterly in second year, 6 monthly thereafter or at least annually till age 5 years) and on regular basis for all HIV-positive children.

The impact of HIV infection on child survival can be minimized through these additional pillars of care:

- Confirmation / documentation of HIV infection
- staging of HIV disease
- Prompt treatment of infections including opportunistic infections
- Cotrimoxazole preventive therapy
- Prevention of tuberculosis through isoniazid prophylaxis counselling for and providing antiretroviral therapy
- Providing comprehensive care for the child, mother and other family members.
- Planning for/providing long-term HIV care and follow up including community support

11.3 Diagnosis and staging of HIV infection in infants and children

Diagnosis of HIV infection in a child often means that the mother is HIV-infected and her partner and other siblings may be HIV-infected as well. This provides an opportunity to provide counselling and support to the family and to link infected family members to care and treatment services.

11.3.1 Identification of the HIV-exposed child

Routine HIV testing should be universal in all well child clinic settings (during routine immunization and growth monitoring visits), as well as for all sick child settings, such as paediatric wards and paediatric out-patient settings (casualties, maternal and child health, sick child visits, paediatric out-patient clinics and TB clinics) in order to maximize opportunities for early HIV diagnosis. Parents with TB or with HIV infection should be encouraged to bring their children for HIV testing.

All infants and young children of unknown HIV-exposure status at the time of the first visit to a health facility should have their exposure status established through:

- Counselling and HIV antibody testing of the mother and/or
- Testing the infant using a HIV antibody test where the mother is unavailable or unwilling to be tested

A positive HIV antibody test of mother and/or child confirms that the child is HIV-exposed.

Children exposed to HIV infection should be identified as early as possible to enable interventions to prevent MTCT or to allow entry into care.

11.3.2 Diagnosis of the HIV-infected child

I. HIV diagnosis in children 18 months and older

The diagnosis of HIV infection in children who are 18 months and older is confirmed by a positive HIV antibody test (rapid test). Refer to the national HIV testing and counselling guidelines for the rapid HIV testing algorithm.

II. HIV diagnosis in children younger than 18 months (refer to figure 11.1)

Children under 18 months have maternal HIV antibodies passively transferred to them in utero, which persist in infant blood for 9–18 months. In this age group a positive HIV serological test detects HIV antibody, however it is not possible to determine if this is maternally transferred antibody, or antibody generated by the infant. The positive antibody test before age 18 months therefore does not confirm HIV infection, but is an indication of maternal HIV infection and therefore HIV exposure of the child.

In order to confirm HIV diagnosis in children <18 months of age it is necessary to perform a test that detects HIV virus using “virologic tests” such as HIV DNA PCR assay. A positive HIV PCR test confirms that the child is HIV-infected.

A virological test at 6 weeks of age identifies more than 95% of infants infected in utero and in the peri-partum period.

- HIV diagnosis in a child under 18 months is confirmed through two steps:
1. A positive HIV antibody test (shows HIV exposure)
 2. A confirmatory positive virologic test such as HIV DNA PCR (or HIV RNA PCR) assay.
- All HIV-exposed children under 18 months (infant or mother positive by HIV antibody test) should be offered routine confirmation of HIV diagnosis using HIV DNA PCR testing at the 6 week immunization visit or at the earliest opportunity for infants seen after 6 weeks of age.
 - For those children who present sick to health services and are not yet tested for HIV, should be offered HIV diagnostic testing as a routine test through provider initiated testing and counselling (PITC).
 - This early infant diagnosis enables any infected child less than 18 months to access life-saving antiretroviral therapy and other aspects of comprehensive HIV care.
 - Failure to diagnose and treat HIV early results in 50% of these infected infants dying before age 2 years.

In the absence of virologic tests, a presumptive HIV diagnosis can be made by using a combination of laboratory and clinical criteria.

Table 11.1 Diagnosis of HIV-infection in infants and children

Age	HIV diagnosis confirmed as follows
18 months and older	Positive HIV antibody test (rapid HIV antibody test)
Below 18 months	Positive HIV PCR after age 1 month
Below 18 months <i>If HIV DNA PCR not available</i>	Presumptive HIV diagnosis as shown in Table 11.2

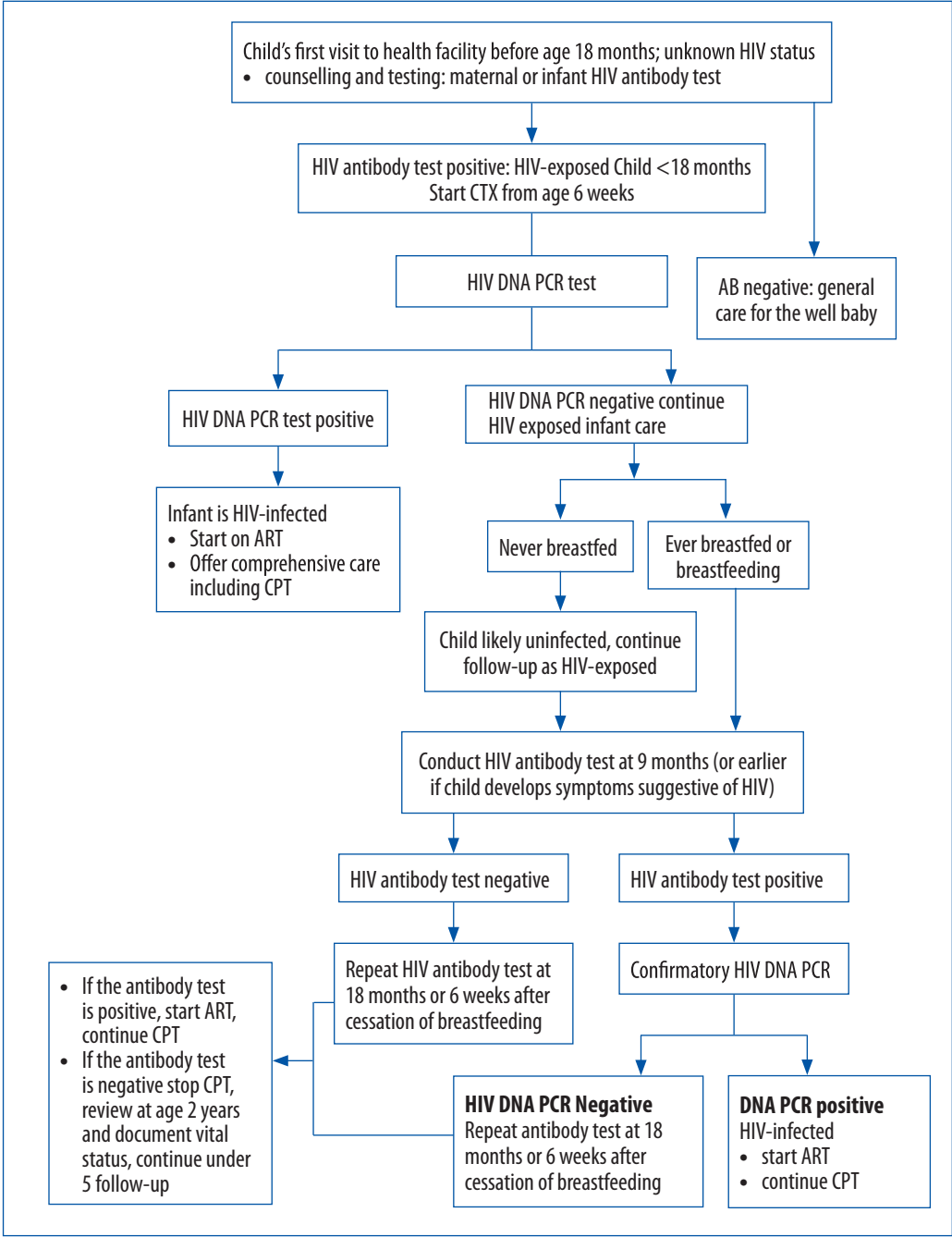
* Available HIV PCR tests: (i) HIV DNA PCR (test reported as positive or negative for HIV DNA), (ii) HIV RNA PCR which reports viral load (reports number of copies of virus/ml of blood).

III. Diagnosis of HIV infection in breastfeeding infants

An HIV-exposed breastfeeding infant is at risk of HIV infection throughout the breastfeeding period. A positive HIV DNA PCR test at any age is indicative of HIV infection. On the other hand, a negative HIV DNA PCR test does not constitute a final diagnosis, as the infant continues to be at risk of HIV transmission through ongoing breast milk exposure.

This risk is <5% if ARV prophylaxis is given either to the baby or to the mother throughout breastfeeding to prevent breast milk transmission. In these infants, the final diagnosis is determined 6 weeks after cessation of all breastfeeding, at which time a final PCR test should be done (or if the child is already above 18 months, an antibody test). Only then can a negative HIV test be indicative of no HIV infection in the infant or child.

Figure 11.1 Early infant diagnosis of HIV infection before age 18 months



Presumptive diagnosis of severe HIV disease in children less than 18 months – when a virologic HIV test is not readily available

Occasionally, children less than 18 months of age will present to healthcare facilities with severe disease suggestive of HIV infection. In some cases lack of immediately available virologic test confirmation of HIV infection could result in undue delay in instituting life-saving ART. In such cases, a **presumptive diagnosis of severe HIV disease** should be made based on the criteria in Table 11.2 below, and prompt ART initiated. However, the diagnosis should be confirmed by HIV DNA PCR (or serological tests for children >18 months of age) as soon as is feasible.

Table 11.2 Presumptive diagnosis of severe HIV disease in children under 18 months

Presumptive diagnosis of severe HIV disease in children less than eighteen months old where virologic confirmation of HIV infection is not readily available
Child <18 months of age; HIV antibody test positive and symptomatic with:
2 or more of the following:
<ul style="list-style-type: none">• oral candidiasis/thrush• severe pneumonia• severe sepsis
OR
An AIDS defining condition*
Other factors that support the diagnosis of clinical stage 4 HIV infection in this infant are recent maternal death or advanced HIV disease in mother; and/or child's CD4% <20%

* AIDS defining conditions include any of the diseases listed in the WHO clinical stage 4 in the Appendices Table 20.17.

11.3.3 Staging of HIV infection in infants and children

The next step in management of the child in whom HIV infection has been diagnosed, is to stage how advanced the child's disease progression is. This is done through history, and physical examination, and where necessary through a few simple laboratory assays. Disease is staged using a World Health Organization (WHO) staging system into asymptomatic, mild, moderate or severe HIV disease (Table 11.3 and table 2.2)

Table 11.3 World Health Organization clinical staging of HIV disease in children

Severity of HIV clinical disease	WHO clinical stage
Asymptomatic	1
Mild	2
Advanced	3
Severe	4

12. Initiating antiretroviral therapy in children

12.1 Introduction

Introduction of ART has transformed HIV infection from a killer disease in children to a manageable chronic disease. With increased access to paediatric HIV care and treatment, perinatally-infected children are living longer. The use of ART has been accompanied with reduction in the incidence of opportunistic infections, hospitalization and death rates. Children on HAART may experience some adverse drug reactions, drug-drug interactions, and emergence of drug resistance due to sub-optimal adherence to therapy. To maximize on the benefits of ART, it is important to perform a complete clinical evaluation and to adequately prepare the patient for life-long ART. Frequent patient visits and intensive follow up during the initial months after HAART initiation are necessary to support and educate the family to assure proper administration of medications and to evaluate clinical as well as drug adherence concerns.

12.3 How to prepare a child for antiretroviral therapy

Prior to initiating the child on ART, thorough baseline medical and psychosocial assessments should take place. These assessments that may be done at the first and second visit are crucial to ensuring proper preparation of the child and caregiver for lifelong uninterrupted therapy. However, every effort should be made to start the child on ART within 2 - 4 weeks of making the diagnosis, as delay may result in further deterioration of the child's health status. HIV disease progresses rapidly in children, and rapid access to ART is life-saving.

In some situations where a child is severely ill, laboratory tests are readily available, and limited personnel limit the speed of psychosocial preparation, it may be necessary to **begin ART** and continue medical and psychosocial preparation during the early weeks of treatment. For more severely ill children, this approach may be life-saving.

For all children being initiated on ART it is essential that the provider ensures that all the components of essential package for HIV-positive are addressed (for details refer to Chapter 11, Section 11.2). Initiate cotrimoxazole prophylaxis in all children unless it is contraindicated (for dosing, refer to Table 3.1). Screen for TB (refer to TB screening algorithm (Table 6.1, Chapter 6) Among those without active TB disease above age 1 year start isoniazid preventive therapy (IPT) 10 mg/kg once daily for 6 months (maximum dose 300 mg/day)

Cotrimoxazole should be administered routinely to:

- All HIV-exposed children from the age of **6 weeks** until their HIV status is determined.
- All HIV-infected children regardless of their age, immune status or clinical stage; continued while they are on ART.

12.3.1 Medical preparation

The following medical assessment should be done in preparation to start ART in a child.

- Clinical assessment:
 - Assess nutritional status (weight, height) and provide nutritional support
 - Milestones of development (normally achieve head support by 3 months, sitting without support by 7 months, standing with support by 10 months, walking by 12 – 15 months)
 - Assess for and treat inter-current illness
- Baseline laboratory tests:
 - CD4 count and/or CD4%
 - Hb (where possible do full blood count)
 - ALT
 - Creatinine

12.3.2 Health education and psychosocial preparation

The parent/guardian should be assisted to fully understand their role in the treatment success of the child.

Health education of parent/guardian

Provide the parent/guardian with the following information:

- HIV disease and the consequences of HIV infection
- On ART
 - Actions of ARV drugs to suppress the virus, restore immunity and the health of the child
 - Goals of ART
 - Lifelong nature of therapy, and importance of adherence to ART
 - When and how to administer the drugs
 - Possible adverse effects of the ARV drugs, how to recognize them and what to do should they arise
- Importance of monitoring and the need to attend the clinic regularly as required
- Carers should be encouraged to return the child to the clinic if they have concerns or the child becomes ill.

Psychosocial preparation

This includes:

- Supportive counselling to come to terms with the diagnosis and live positively
- Adherence counselling
- Assessment of the family situation and counselling support to address family psychosocial issues.
- Disclosure to child; determined by level of understanding of the child (depending on severity of illness, this may begin before ART, or proceed while child is already on therapy)

12.4 When to start antiretroviral therapy in children

Any child diagnosed to have HIV infection (as outlined above) who fulfils any of the criteria shown below should start ART as soon as possible:

Clinical criteria:

Age <24 months:

- Children with positive DNA PCR should start ART regardless of WHO clinical stage, CD4 count or CD4%.

Age 24 months and above:

The indications for starting ART in children aged above 24 months are the following:

- Children in WHO stage 3 or 4 regardless of CD4 count.
- Age related CD4 count as shown in table 12.1

Viral load is not recommended as a criterion for ART initiation as it is highly variable in young children, and levels that predict rapid disease progression are not well defined in children.

Table 12.1 Recommendations for when to start ART in infants and children

Age	WHO clinical stage	CD4%	CD4 count (cells/mm ³)
≤ 24 months	ALL	ALL	ALL
25–59 months	3 or 4	<25%	<1000
5–12 years	3 or 4	<20%	<500

Psychosocial criteria

For children who fulfil the medical criteria for initiation of ART, every effort should be made to avail adequate psychosocial support to ensure treatment success;

- An identifiable parent or guardian who is
 - Able to understand the treatment requirements
 - Consistently and correctly administer the child's medication.
 - Able to attend the HIV clinic appointments regularly.
- Sustainable long-term access to antiretroviral drugs (either through programmes providing ART, or financially able to purchase ARV drugs).

A child who fulfils the above medical and psychosocial criteria for ART initiation should start ART as soon as possible.

12.5 Recommended first-line antiretroviral therapy in children

Antiretroviral drugs should always be given as a combination of at least three drugs simultaneously (combination antiretroviral therapy (HAART) also called highly active antiretroviral therapy – HAART). The critical determinants of the choice of first-line antiretroviral regimen are age and prior exposure to antiretroviral agents for PMTCT. ARV drugs are available in paediatric formulations in liquid for HIV-exposed children for PMTCT and tablet/capsules as paediatric dual or triple fixed dose combinations (FDC).

First-line ART in children are as shown below.

NRTI class	NNRTI class	Protease inhibitor class
Abacavir (ABC) Zidovudine (AZT) Tenofovir (TDF) Lamivudine (3TC) Stavudine (d4T)	Nevirapine (NVP) Efavirenz (EFV)	Ritonavir boosted Lopinavir (LPV/r)

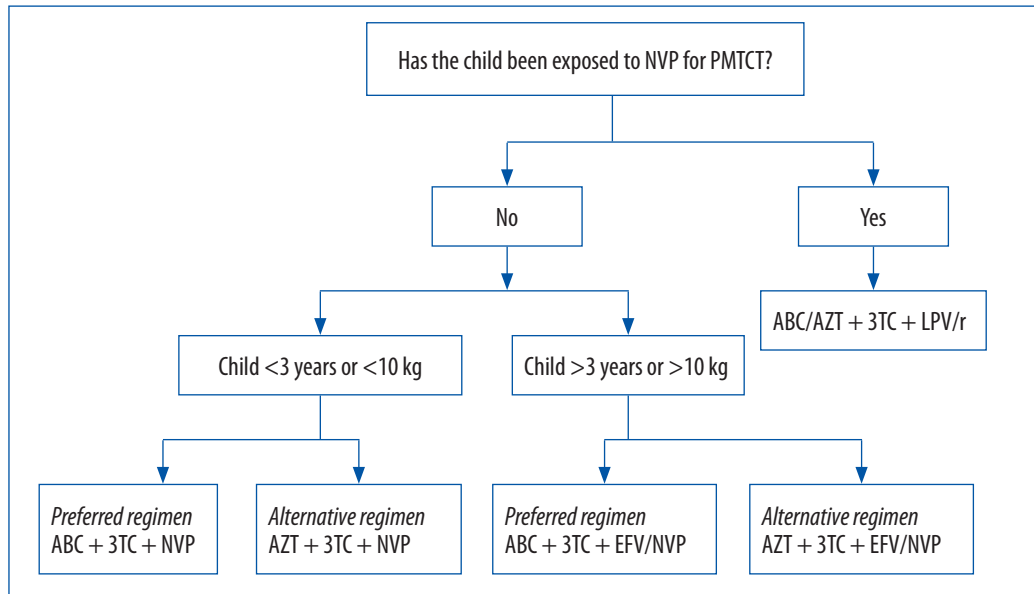
Careful consideration has gone into the selection of first line regimens for children; these considerations include availability, palatability/taste, simplicity (availability of FDCs and frequency of dosing) and durability of regimen.

Stavudine should be phased out from use among children

No new patients should be initiated on d4T based ART while the existing patients on d4T should be transitioned out to appropriate regimen

The recommended first-line regimens for infants and children in Kenya are shown in Figure 12.1 below.

Figure 12.1 Recommended first-line ART for children and infants



- ABC is preferred as first choice, especially if a child has severe anaemia (Hb <7.5 g/dl) or neutropenia (neutrophil count <0.5 x 10⁹/l). ABC is also the drug of choice in case of renal impairment.
- Nevirapine should be started once daily for 14 days, then stepped up to twice daily on day 15. Efavirenz dosing is not established for children age <3 years, or of weight <10 kg.
- Evidence shows that >60% of children exposed to single drug NVP develop NVP resistant virus and as a result do not respond well to a NNRTI-based HAART regimen, and require a protease inhibitor based regimen.
- LPV/r liquid formulation requires refrigeration and has a bitter taste. *The lopinavir/ritonavir(200/50 mg) heat stable tablet SHOULD BE SWALLOWED WHOLE and NOT crushed or broken.*

12.6 Calculating dosages and paediatric ARV drugs

Children's ARV drug dosages are always calculated according to the child's body weight in kilograms.

Tables 20.15 (appendices) provides paediatric drug dosage charts which show the appropriate dose in tablets, capsules or ml of syrup required according to the weight of the child. These charts aid the health worker to prescribe the correct dose and should be used to ensure correct prescriptions to children.

12.7 Antiretroviral therapy in HIV-infected children with tuberculosis

Tuberculosis is an increasingly common opportunistic infection in HIV-infected children. HIV infection increases a child's risk of progressive primary tuberculosis and reactivation of latent TB in the older child.

The pill burden in TB/HIV co-infection is large. Intensive adherence support and monitoring should be offered. The risk of adverse drug reactions is increased during concomitant therapy. Perform a full clinical evaluation at every clinic visit and if there are symptoms suggestive of adverse drug reactions, particularly liver toxicity, do the appropriate laboratory tests.

If significant problems are experienced, either severe drug intolerance, or erratic adherence, continue the anti-TB, but *consider interrupting ART*. Resume after the problem has been adequately addressed (may occasionally have to wait until completion of anti-TB therapy).

The principles of treatment of tuberculosis in HIV-infected children are similar to those in HIV-negative children, and the same regimens should be used as those used in HIV-negative children. Recent data suggest that early initiation of HAART early in TB treatment reduces TB morbidity and mortality, without excess adverse events.

Any child with active tuberculosis should begin TB treatment immediately; and begin ART as soon as the TB treatment is tolerated; i.e. no nausea or vomiting and no on-going or evolving adverse drug events, usually 2 to 8 weeks into TB therapy

Rifampicin interacts with both PIs and NNRTIs, reducing their blood levels, therefore reducing their effectiveness, therefore when treating TB and giving concurrent ART the ART regimen may require adjustment.

ART options with rifampicin are limited and are based on the various scenarios as indicated.

- EFV based ART
- Super boosted LPV with ritonavir during TB treatment and **revert to the normal LPV/r dosing after completion of TB treatment.**
- Triple nucleosides - triple nucleoside ART is a weak ART combination. Use of AZT +ABC+3TC may lead to accumulation of mutations including M184V and thymidine analogue mutations among others. It should be used only when other options are not indicated or available or when preferred option is not tolerated.

After completion of TB treatment with triple nucleoside ART, **never restart NNRTI based ART regimen instead the child should be changed to LPV/r based ART.**

Scenario A: Child develops TB before initiating ART

Start anti-TB treatment as soon as possible and ART within 2–8 weeks of starting anti-TB therapy.

- a child who is severely ill needs to be started on ART sooner (within 2 weeks)
- a child who is less severely ill may be started on ART within 2 - 8 weeks.
- The ART options are as shown below.

Table 12.2 Child develops TB before initiating ART

NVP exposed	NVP non-exposed	
Irrespective of age and weight	<3 years and <10 kg	>3 years and >10 kg
Preferred option: ABC/AZT + 3TC + LPV/r + RTV(add extra dose of RTV to make the LPV/RTV ratio 1:1-super boosted LPV)	Preferred option: ABC/AZT + 3TC + LPV/r + RTV(add extra dose of RTV to make the LPV/RTV ratio 1:1-super boosted LPV)	ABC/AZT+3TC+EFV
After completion of the TB treatment, continue child on ABC/AZT+3TC+LPV/r normal dosage	After completion of the TB treatment, continue child on ABC/AZT+3TC+LPV/r normal dosage	Continue ART

Scenario B: Child develops TB during the first 6 months of first-line ART

Start TB treatment immediately and also change ART regimen as indicated below.

Table 12.3 Child develops TB during the first 6 months of first-line ART

NVP exposed	NVP non-exposed	
	<3 years and <10 kg	>3 years and >10 kg
Preferred option: ABC/AZT + 3TC + LPV/r + RTV (add extra dose of RTV to make the LPV/RTV ratio 1:1-super boosted LPV)	If child on NVP based regimen change to regimen below: Preferred option: ABC/AZT + 3TC + LPV/r + RTV (add extra dose of RTV to make the LPV/RTV ratio 1:1-super boosted LPV)	ABC/AZT+3TC+EFV
Continue on ABC / AZT +3TC+ LPV/r after completion of TB treatment	After completion of the TB treatment, continue child on ABC/AZT+3TC+LPV/r normal dosage	Continue ART

Scenario C: Child develops TB while on 1st line ART for more than 6 months

There is the possibility that this new episode of TB is an indication of poor response to ART due to non-adherence or of ARV treatment failure or both.

Manage as follows:

1. Initiate anti-TB treatment immediately.
2. Evaluate adherence to ART and ensure that any problems in adherence have been addressed before embarking on a second-line regimen ART (refer to Chapter 14)
3. Evaluate for treatment failure for all.

The ART options are as shown below:

Table 12.4 Child develops TB while on first-line ART for more than 6 months

NVP exposed		NVP non-exposed	
Irrespective of age and weight		<3 years and <10 kg	>3 years and >10 kg
Preferred option: ABC/AZT + 3TC + LPV/r + RTV(add extra dose of RTV to make the LPV/RTV ratio 1:1-super boosted LPV)		If child on NVP based regimen change to regimen below: Preferred option: ABC/AZT + 3TC + LPV/r + RTV (add extra dose of RTV to make the LPV/RTV ratio 1:1-super boosted LPV)	If no treatment failure use ABC/AZT+3TC+EFV If failing treatment change to second line: ABC/AZT + 3TC + LPV/r + RTV (add extra dose of RTV to make the LPV/RTV ratio 1:1-super boosted LPV)
Continue on ABC/AZT +3TC+ LPV/r after completion of TB treatment		After completion of the TB treatment, continue child on ABC/AZT+3TC+LPV/r normal dosage	After completion of the TB treatment, manage accordingly
If child is confirmed to have failed first line LPV/r based ART, continue failing regimen and consult therapeutic committee for future ART options.			

Scenario D Child develops TB while on 2nd line ART regimen

Anti-TB therapy should be started immediately.

There is the possibility that this new episode of TB is an indication of poor response to ART due to non-adherence, or of ARV treatment failure, or both. If treatment failure is confirmed, do not discontinue ART. In addition their future management of ART should be discussed with a senior consultant with expertise in the management of HIV infection and the National ARV therapeutics TWG.

The ART option is as shown below:

Table 12.5 Child develops TB while on 2nd line ART regimen

Scenario	ART options
Child on second line LPV/r based ART	Preferred option: ABC/AZT + 3TC + LPV/r + RTV (add extra dose of RTV to make the LPV/RTV ratio 1:1–super boosted LPV. Change to normal LPV/r dose after completion of TB treatment
	Alternative option: 3TC monotherapy. Restart original ART after completing TB treatment.

Triple nucleoside ART should NOT be used in TB/HIV co-infected patients who have previously failed ART

13. Monitoring and substituting ART in children

13.1 Introduction

Children on ART should be monitored closely in order to assess adherence to the prescribed regimen, efficacy of treatment and inter-current illnesses. They should also be evaluated for drug intolerance and side-effects. The frequency of visits, and the schedule of clinical and laboratory monitoring that should be performed during each visit is indicated table 13.1 below.

Table 13.1

	Week		Month								
Appointment*	0	2	1	2	3	4	5	6	9	12	Stable
Clinical evaluation ¹	+	+	+	+	+	+	+	+	+	+	Every visit
TB screening	+	+	+	+	+	+	+	+	+	+	Every visit
Adherence check	+	+	+	+	+	+	+	+	+	+	Every visit
Hb ³	+		+ ³		+ ³	Symptom directed					
ALT ⁴	+		+ ⁴		+ ⁴	Symptom directed					
Creatinine ⁵	+	Symptom directed									
Pregnancy test (PT) ⁶	+	If indicated									
Urinalysis	+	Symptom directed									
Fasting lipid profile & Glucose ⁷	+	Annually for patients on PIs									
CD4 count	+							+		+	Every 6 months
Viral load ⁸		Targeted									

¹ clinical evaluation includes history and physical exam to evaluate:

- Growth (weight and height, plot on growth charts)
- Development (neuro-developmental milestones – sitting by 7 months, standing by 10 months, walking by 15 months, speech, school performance)
- Presence of intercurrent illnesses
- Presence of adverse drug effects (e.g. anaemia, rash, jaundice, nausea-vomiting-diarrhoea, neuropathy)

² Hb (or full hemogram) if on AZT or looks pale.

³ ALT scheduled when Nevirapine is used

⁴ Greater than 95% adherence is necessary to prevent the emergence of drug resistance and ensure long-term good virological response with the first line regimen. If a child misses more than 1 dose in ten days it implies <95% (suboptimal) adherence, and the health-worker should counsel parent or guardian to identify causes of missed doses and how to avoid this in the future.

⁵ All pts should have creatinine measured if available. NRTI doses may need adjustment if renal function (RF) abnormal. TDF should be avoided if RF abnormal (see Table 20.11-20.14).

⁶ For pregnant adolescent girls, provide prophylaxis or combination ART to those who are in need of it for their own health and/or to prevent vertical transmission. (refer to PMTCT Guidelines)

⁷ Scheduled when patient on protease inhibitors

⁸ Targeted VL can be used for suspected clinical or immunological ART failure prior to switching treatment regimen

*The appointment schedule given here is a general guide, appointments should be arranged as per the individual patient need.

13.2 Antiretroviral drug toxicity in children

At every clinic visit children on ART should be monitored clinically for toxicities using appropriate history (history of symptoms that suggest toxicity) and physical examination (relevant signs). Laboratory monitoring at intervals may also be used to identify specific toxicities. The main types of toxicities with ART in children include: hepatotoxicity, hematologic, mitochondrial dysfunction, lipodystrophy and metabolic complications, and allergic reactions.

Before considering drug toxicity related to ART considers other causes of the symptoms: this includes: other drugs e.g. anti-TB drugs for a child who develops jaundice, other disease processes e. g viral hepatitis. All toxicities should be graded as described in the next section.

13.2.1 Grading toxicities

Toxicities should be graded as mild, moderate, or severe.

Table 13.2 Principles of management for various grades of toxicity

Grade of toxicity	Drug discontinuation	Supportive care
Mild	Not indicated	Yes, e.g. antihistamine for skin rash
Moderate	Switch only the offending drug, do not stop all ARVs	
Severe	Discontinue ALL ARVs, stabilize the patient, then introduce modified regimen	Intensive, may include hospitalization

A more detailed grading for each specific type of drug toxicity is provided in Chapter 5.

13.2.2. Management of toxicities

Due to limited number of available ARV agents, substitutions should be limited to situations with moderate to severe drug toxicity. If a single drug within a regimen can be identified to be responsible for toxicity, the particular offending drugs should be replaced by a different drug, preferably from the same class but with different toxicity profile e.g. efavirenz CNS toxicity, replace with nevirapine which does not have CNS toxic effects.

Table 13.3 Suggested first-line ARV substitutions for common toxicities.

Toxicities (symptoms)	Main drugs implicated	Suggested 1st-line replacement
Acute hepatitis	Nevirapine (less common efavirenz)	Efavirenz (alternative third NRTI, or Protease Inhibitor)
GI symptoms • Severe diarrhoea, nausea, vomiting	Zidovudine Protease Inhibitors	Nevirapine or efavirenz
Pancreatitis (nausea, vomiting, abdominal pain)	Stavudine (less frequent ddl, 3TC)	Temporarily stop all ARVs, stabilize patient, then re-start ART, substituting offending drug
Bone marrow toxicity • Severe anaemia ($Hb < 7.5 \text{ g/dl}$) • or neutropenia (neutrophils $< 500/\text{mm}^3$) • or thrombocytopaenia (platelets $< 50\,000/\text{mm}^3$)	Zidovudine	Abacavir
Severe or life-threatening rash (Stevens–Johnson syndrome) <i>Extensive rash with desquamation and angioedema, involving mucus membranes</i>	Nevirapine (less common Efavirenz)	stop all ARVs until resolution and consider switch to new class (PI or triple NRTIs)
• Severe central nervous system toxicity (hallucinations, psychosis) • Potential teratogenicity	Efavirenz	Nevirapine
Peripheral neuropathy (tingling, burning sensation, weakness, distal numbness)	Stavudine (less frequent ddl, 3TC)	Zidovudine or abacavir
• Lipoatrophy/metabolic syndrome • Dyslipidaemia (Recent changes in body shape) <i>cholesterol, blood glucose, triglycerides.</i>	Stavudine Zidovudine Protease inhibitors	Abacavir
Lactic acidosis (recent or current symptoms of weight loss, fatigue, muscle pain, abdominal pain, hepatomegaly)	Stavudine Less common AZT	Abacavir Consider protease Inhibitor based regimen
Hypersensitivity reaction <i>Acute onset fever, myalgia, nausea, vomiting, abdominal pain, pharyngitis and cough with or without skin rash</i>	Abacavir (less common, nevirapine)	Zidovudine

13.3 Immune re-constitution inflammatory syndrome (IRIS)

Children on antiretroviral therapy may develop the immune reconstitution inflammatory syndrome (IRIS). IRIS presents clinically as worsening of pre-existing conditions or development of new conditions. IRIS is more likely to occur during the first 3 months of treatment and is more common in children with very low pre-treatment of CD4 counts. IRIS has also been found to be more common in younger children. **(Refer to Chapter 5 for more details on IRIS).**

14. Antiretroviral treatment failure in children

14.1 Introduction

Many children can remain on a stable antiretroviral therapy (ART) for several years. However regular re-assessment of the ART becomes necessary to monitor the efficacy of HAART treatment failure is defined as suboptimal response or a lack of sustained response to therapy using clinical, immunologic and virologic criteria. Not all cases of treatment failure may require immediate change in ART; a careful assessment of the causes of the treatment failure especially non adherence and drug interactions should be done and these causes managed appropriately.

The goal of treatment for all patients; whether on initial, second or third line regimen is complete virologic suppression, combined with the recovery or maintenance of immunologic function as well as improvement in clinical status of the patient.

The approach to treatment failure in children failing second line regimen is often more complex than in those failing first line regimen. Children failing second line regimen therefore, should be managed in collaboration with the national ART therapeutic committee.

14.2 Definition of antiretroviral treatment failure

Treatment failure refers to clinical, immunologic or virologic deterioration after a child has received ART for an adequate period. At least 6 months of ART should be given before consideration of treatment failure. Clinical, immunologic or virologic deterioration often occur together, however a child may deteriorate in one domain earlier than in a different domain. For instance a child may develop clinical symptoms suggestive of treatment failure several months before the CD4 counts decline.

Clinical failure is defined by the presence of any of the following:

- Detection of *new* or *recurrent* severe clinical events (WHO clinical stage 3-4) including opportunistic infections and HIV-associated malignancies.
- Growth failure despite adequate nutrition.
- Neuro-developmental deterioration including loss of existing developmental milestones, or stagnation /failure in achieving new milestones. (Appendices, Table 20.18 contains normal developmental milestones).

- Lack of clinical improvement from the baseline condition which the child presented with to care.

Clinical failure is the most urgent form of treatment failure that is associated directly with mortality. Therefore presence of symptoms and signs suggestive of clinical failure should result in prompt evaluation.

Immunologic failure is defined by the presence of any of the following:

- Sustained decline in CD4% (child of any age) or CD4 count (older children >5 years) to age-related CD4 thresholds or to below pre-treatment levels after initial rise. The table below provides the age-related CD4 thresholds.
- Incomplete immunologic response: CD4 % fails to rise by 5 percentiles (or CD4 count fails to rise by at least 50 cells/mm³) during the first year of HAART.
- CD4 count drops by more than 50% of the peak achieved on HAART.

Table 14.1 Age related CD4 thresholds that define immunologic failure

Age	Immunologic failure
2-5 yrs	Return to <500 cells/mm ³ or <15%
>5 yrs	Return to <350 cells/mm ³
All (infant to 12 years)	Drop to less than half of peak CD4 count achieved on HAART

It is recommended that CD4 testing always be confirmed with repeat testing before a decision is reached on immunologic failure. The repeat test should be performed at least 2 weeks after the initial test and the child should not have an active opportunistic infection (OI) at the time of testing. The presence of an OI often results in temporary decline in CD4 count. In addition the presence of infections that lead to lymphocytosis may result in abnormally low CD4 percentage.

Virologic failure refers to any of the following scenarios:

- *Incomplete viral suppression*: the HIV viral load (plasma HIV-1 RNA level) remains high following initiation of ART. A viral load of >1000 copies/ml after 12 months of therapy is indicative of incomplete viral suppression.
- *Viral rebound*: increase in viral load in a child who initially achieved viral suppression to undetectable levels after initiation of ART. Repeated detection of HIV viral load level above 1000 copies/ml after an initial period of viral suppression is indicative of virologic failure.

14.3 Causes of treatment failure

- Non-adherence to treatment
- Pre-existing drug resistance to one or more drugs (e.g. after single dose nevirapine for PMCT)
- Regimens with low potency
- Impaired drug absorption
- Altered drug pharmacology including drug-drug and drug food interactions

Non-adherence is the main cause of treatment failure

Factors that increase the risk of treatment failure should be explored at every visit; and supportive counselling intensified. These include:

- Factors that affect adherence such as lack of psycho-social support, depression, treatment regimen (pill burden, frequency, food or fluid restrictions)
- Poor patient-provider relationship
- Development of intolerance or toxicity
- Financial barriers to care

14.4 Management of patients with suspected clinical or immunological failure

- Adherence history should be reviewed; it should be noted that even in patients with a previously good adherence, life events may precipitate a period of non-adherence. Non-adherence should be addressed, particularly in the context of potential cause of treatment failure.
- Any OIs should be treated promptly, and patient reviewed for other OIs, HIV-associated malignancy and adequacy of nutrition
- If treatment failure on clinical grounds is suspected; then the CD4 cell count should be checked, adherence reviewed (and intensified if sub-optimal).
- The CD4 trends should be reviewed and a repeat done if this is the first time the CD4 count has dropped and the patient is suspected of failure.
- Treatment failure is unlikely to be responsible for symptoms in an adherent patient in the first 6 months of treatment since immune recovery is still on-going and the patient may still be at risk of OIs or immune recovery inflammatory syndrome (IRIS).
- Because of the limited specificity of immunologic or clinical criteria to predict true virologic failure, in patients with suspected failure on the basis of new clinical features or a drop in CD4 count, it is recommended that a viral load test be done to confirm the diagnosis of treatment failure whenever possible, to avoid unnecessary switch to more expensive second line treatment. Where viral load testing is not available on site, arrangements should be made to transport specimens and results to and from identified laboratories within the national network.

Approaches to managing a child with suspected treatment failure

Only children who have received HAART for at least 6 months may be considered to have treatment failure. This is in order to ensure that children with Immune reconstitution inflammatory syndrome are not misdiagnosed to have treatment failure. The key steps in the approach of a child with suspected treatment failure include:

- Verification that the child has actually been adherent to ART (**deterioration may be due to failure to take medicine as required and non-adherence to HAART is the most common and most likely cause of treatment failure**).
- Exclusion of immune reconstitution inflammatory syndrome (IRIS) especially in the first few months ART (see Chapter 5).
- Evaluation and management of specific OIs.
- Adequate nutrition (in cases of growth failure).
- Continue on failing regimen until switch to second line without a break in between.
- Multi-disciplinary team approach

14.4.1 Evaluate and address adherence

Before considering a switch in the ARV regimen, adequate adherence should be ensured. It is critical to assess adherence in children by asking the following questions:

- **Who** gives the medication?
- Which medications are given? The caregiver should physically show *the health worker medications including the dosages taken*.
- **When** are medications taken?
- Are there **missed doses**?
- Are there concomitant medications that may lead to significant drug-drug **interactions**?
- Is there **intolerance** to the medication?

Also consider family dynamics including change in caregiver, disclosure between parents or other caregiver of the child, and disclosure to the older child and adolescent. A child who is brought to the clinic by a different caregiver each time is more likely to experience non-adherence. The pharmacy refill records and the appointment keeping of the child are important indicators of adherence to HAART. For instance a child who regularly misses clinic appointments is likely to have non adherence regardless of the answers given to the above questions.

Intensive counselling and support provided to children with non-adherence may result in virologic, immunologic and clinical improvement and a switch in ART regimen may not be necessary. In addition switching ART regimens in a child with non-adherence is likely to be of little benefit since the problem will most likely persist and possibly worsen.

14.4.2 Management of specific HIV-related illnesses including TB and malnutrition

Certain OIs especially **tuberculosis** may result in signs and symptoms suggestive of clinical failure. A diagnosis of tuberculosis should therefore be considered in children with suspected clinical failure (see algorithm for TB diagnosis in children Chapter 6) and management with anti-tuberculous drugs.

In addition, among children who initiate HAART at very low CD4 counts (and %), a single OI including pneumonia or pulmonary tuberculosis is not necessarily indicative of treatment failure and should be treated before consideration of a treatment switch. This is because immune dysfunction may persist for a few months after initiating ART.

It is also important to recognize that children with severe end-organ damage at baseline (before ART initiation) may not dramatically improve and this does not necessarily constitute treatment failure. This includes children with cor-pulmonale and HIV-associated cardiomyopathy as well as severe neurologic impairment.

Severe malnutrition is capable of limiting CD4 response in children and is in itself a cause of immune suppression. Therefore severe malnutrition should be managed accordingly.

14.4.3 Continue (maintain) failing regimen until second line is available

Children with suspected or confirmed failure to first-line ART should remain on the failing 1st line regimen while preparations are made towards switching to second-line. The baby as indicated above.

14.2.4. Multi-disciplinary approach

The evaluation and management of a child with suspected or confirmed treatment failure should be undertaken by a multidisciplinary team as much as possible. This team may be led by the clinician and contain a pharmacist, counsellor, primary care nurse and nutritionist.

14.5 Switching from first-line to second-line ART regimens

14.5.1 Indications for switching from first to second line ART regimens

Switch from first line to second line antiretroviral therapy in the following situations:

1. **Clinical failure:** new recurrent, severe WHO stage 3-4 conditions especially if the CD4 count/percent is dropping to below age-specific thresholds. Clinical failure is the

most serious form of treatment failure that requires urgent change of a failing regimen to avoid mortality.

2. **Immunologic failure:** persistent dropping CD4 count/percent to below age –specific thresholds, or drop to below pre-treatment levels. A child with immunologic failure is likely to develop clinical deterioration and serious events in the near future.
3. **Virologic failure:** If viral load is available and persistently above 1000 copies/ml after 12 months of therapy, this should warrant treatment switch. The rationale of switching in virologic failure is to avoid development of further resistance mutations that may undermine the future second line regimen.

14.5.2 Decision-making process for switching from first-line to second-line

Treatment failure based on clinical and immunological criteria should be confirmed with viral load test. (refer to figure 5.4).

14.5.3 Choice of second-line ARV regimen in children

The purpose of switching a failing regimen is to achieve durable viral suppression that results in immunologic and clinical improvement. We therefore aim to have AT LEAST TWO fully active agents in the second-line regimen. This will often necessitate changing to at least ONE NEW class of ARV not previously used by the child. Adherence should be addressed before a regimen is switched, since incomplete adherence is likely to undermine success of second line regimens.

Retention of lamivudine in second line ART regimens

Lamivudine (3TC) should be retained as an integral part of second–line ART regimen. This is informed by the fact that a common mutation, M184V that selects for high level resistance to 3TC is associated with reduced viral replication ability. Hence retaining 3TC results maintains a relatively weak HIV virus.

a) Second line regimens for children failing NNRTI based first-line HAART

For children who fail on a first-line regimen containing 2NRTIs and an NNRTI the table below gives the recommended approach to switching individual drugs.

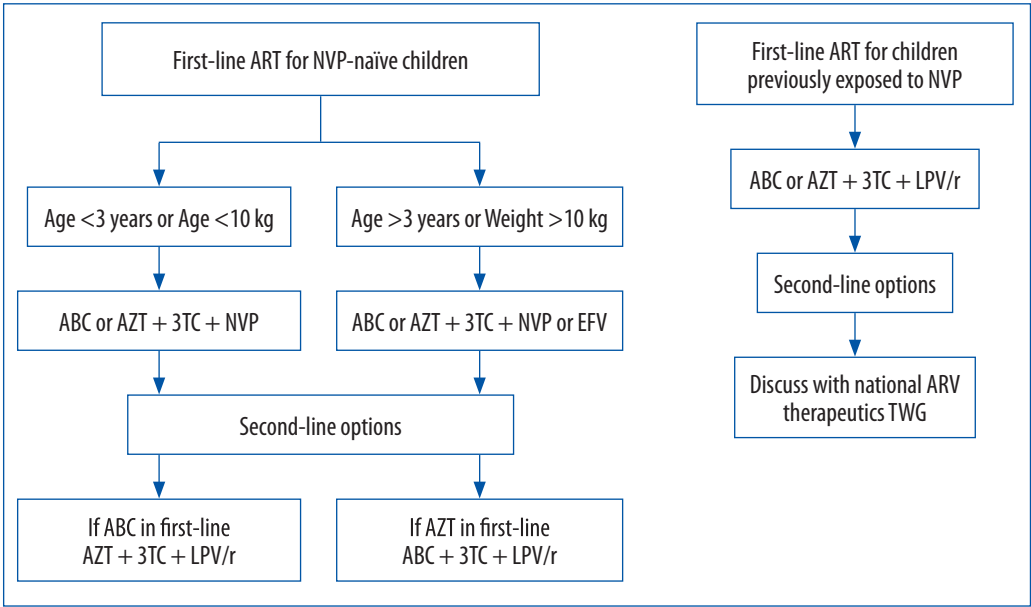
Table 14.2 Recommended second-line ARV drug replacement

Current first-line ARV drug	Recommended replacement drug for second-line regimen
ABC	AZT
AZT (or d4T)	ABC
3TC	3TC
NVP or EFV	Boosted PI (LPV/r)

b) Second line options for children failing a protease inhibitor-based first-line regimen (single dose NVP-exposed at PMCT)

For children failing on first-line regimen is LPV/r +2NRTI the choice of an appropriate second –line regimen is more complex. In the event that such children fail treatment consultation should be done with senior clinicians experienced in paediatric HIV care.

Figure 14.1 Recommendations for second line ART in children



14.6 Monitoring of children on second line ART regimen

The child on second-line ART should be monitored using clinical and immunologic (CD4) parameters.

Monitoring follows the same guidelines as for first line ART, however shall be more intense as follows:

- Child should be seen by a clinician more frequently (preferably every month) for clinical assessment
- Evaluation of adherence and counselling support should be offered at every visit
- Laboratory tests to monitor response to second-line therapy shall include:
 - CD4 testing every 6 months or when indicated (during presentation and recovery from major illness)
 - Targeted viral load (in children suspected to be failing therapy)
- Laboratory tests to monitor for adverse effects of the second-line drugs should be regular, especially lipid profiles every 6 months

14.7 Third line ARV therapy – children who have failed second-line therapy

There is a small but increasing number of HIV-infected children on second line therapy who are experiencing treatment failure. This group of children requires careful approach and should be managed in consultation with senior clinicians experienced in HIV treatment. For these reasons, clinicians and their patients should aim to get the maximum benefit out of early treatment.

To facilitate effective management of patients failing second-line therapy the framework is being developed by NASCOP (Figure 5.6, Chapter 5).

15. Nutritional support for the HIV-exposed and infected child

15.1 Introduction

Besides the risk of transmission of HIV from the mother to the child during pregnancy, delivery and through breast milk, children born to HIV-positive women are more likely to be underweight, to suffer malnutrition and to be at increased risk of disease and childhood mortality.

- I. HIV-infected children should receive routine nutritional assessment (including care-giver practices, food hygiene, family food security, weight, height and mid-upper arm circumference) and support (counselling, health education, nutrition therapy, healthy eating, avoidance of under-nutrition and obesity, referral to food support programmes).

HIV infection undermines nutritional status by increasing nutrient and energy requirements by the body, reducing intake due to a variety of reasons such as reduced appetite, painful oral sores and household food insecurity; besides increased nutrient loss through diarrhoea and vomiting.

- II. HIV-infected children on ART or in care who are symptomatic (with opportunistic conditions) or have weight loss or poor weight gain should receive 25 – 30% additional calories per day.
- III. HIV-infected children who are severely malnourished should be provided with 50-100% additional energy through calorie-dense food preparations (refer to National Guidelines for Integrated Management of Acute malnutrition, 2009).
- IV. All HIV-infected children should receive one recommended daily allowance (RDA) of micronutrients daily
- V. HIV-infected children between 6 and 59 months of age should receive high-dose vitamin A supplementation every 6 months (6-11 months; 100 000 IU at once, 12-59 months, 200 000 IU every 6 months)

15.2 Infant and young child feeding options in HIV infection

Two main infant feeding options are recommended for HIV-exposed infants:

- i. exclusive breastfeeding with ARVs,
- ii. exclusive replacement feeding.

15.2.1 Exclusive breastfeeding with ARV

Exclusive breastfeeding involves giving the baby only breast milk with no other liquids (including water) or solids for the first six months of life. Giving of vitamins, mineral supplements or medicines are permitted. Mixed feeding during this period is associated with malnutrition and significantly higher risk of mother-to-child of HIV transmission, diarrhoeal and respiratory tract illnesses among other consequences; and should be prevented at through ongoing counselling and support to promote exclusive breastfeeding.

To further minimize HIV transmission risk during exclusive breastfeeding periods, the mother and/or the baby should be on ARVs throughout the breastfeeding period. Refer to PMTCT guidelines (Chapter 16) for further details.

- I. Exclusive breastfeeding is recommended for **HIV-positive** women for the first 6 months of life unless exclusive replacement feeding (15.2.2 below) is acceptable, feasible, affordable, sustainable and safe. After 6 months, appropriate complementary feeds should be introduced and breastfeeding continued for the first year of life of the infant. Thereafter, breastfeeding may be stopped gradually if a nutritionally acceptable and safe diet can be provided.
- II. All HIV-exposed breastfeeding infants (irrespective of maternal ARV prophylaxis) should be given daily NVP prophylaxis from birth and continued throughout the breastfeeding period until one week after complete cessation of breastfeeding.
- III. All HIV-exposed breastfeeding infants whose mothers are on triple ART should be started on NVP prophylaxis from birth until 6 weeks of age. Thereafter, the mother should continue breastfeeding during at least the first 12 months of the infant's life. Breastfeeding should be stopped gradually only if a nutritionally acceptable, adequate and safe diet can be provided.
- IV. For infants and young children **known** to be HIV-infected, mothers should be encouraged to exclusively breast-feed for the first 6 months and thereafter to continue breastfeeding (in addition to introduction of appropriate complementary feeds) up to 2 years and beyond (as recommended for the general population)

15.2.2 Exclusive replacement feeding

Exclusive replacement feeding involves giving the baby only commercial breast milk substitutes. Replacement feeding requires time, safe water, fuel and utensils for its preparation and administration and adequate finances to ensure continuity of supply.

Table 15.1 Approximate amount of milk needed to feed a baby each day

Baby's age	Number of feeds per day	Amount of milk or formula per feed per day	Total milk or formula per day
Birth to 1 month	8	60	480 ml
1 to 2 months	7	90	630 ml
2 to 4 months	6	120	720 ml
4 to 6 months	6	150	900 ml

The amount of milk the baby requires will be calculated based on the baby's weight. A baby requires 150 ml per kg body weight.

15.2.3 Complementary feeding

Complimentary feeding means giving other foods to complement breast or formula milk. Complimentary feeds provide additional nutritional value to meet the child's increasing nutritional needs for growth. Furthermore, complementary feeding helps the child to gradually become accustomed to eating family foods while breastfeeding or replacement feeding continues to be an important source of nutrients.

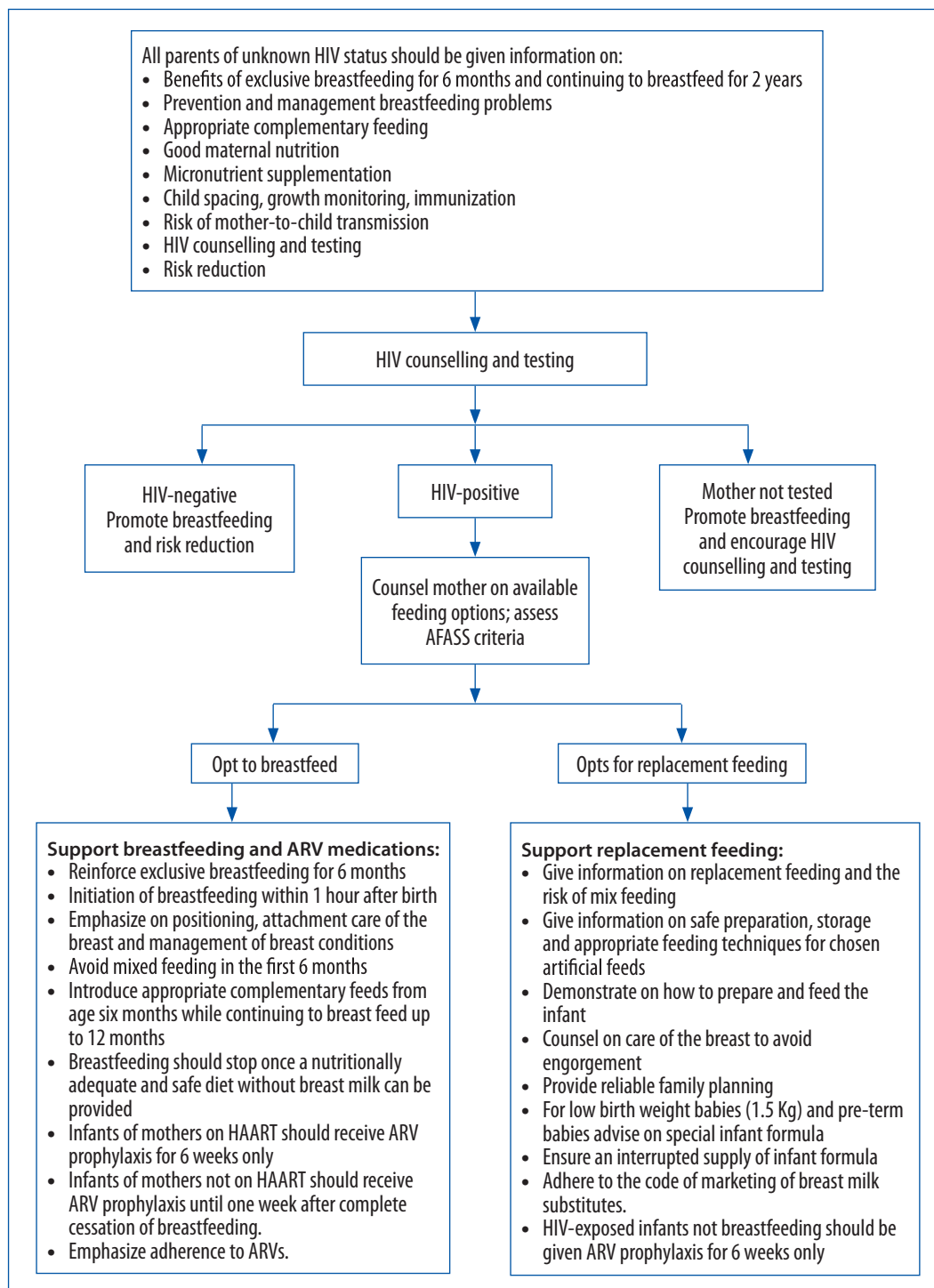
Exclusive breastfeeding or replacement feeding alone should continue up to 6 months of age. Complementary feeding should be introduced after 6 months until the child is weaned from breast or replacement feeding.

Table 15.2 Complementary feeding recommendations

Age (months)	Texture	Frequency	Amount per meal
6-8	Start with thick porridge, well mashed foods. Continue with mashed family foods	2-3 meals per day plus breastfeeds \pm 1-2 snacks	Start with 2-3 tablespoons per feed increasing gradually to half of a 250 ml cup
9-11	Finely chopped or mashed foods, foods that the baby can pick up	3-4 meals per day plus breastfeeds \pm 1-2 snacks	Half of a 250 ml cup/bowl
12-23	Family foods, chopped or mashed if necessary	3-4 meals per day plus breastfeeds \pm 1-2 snacks	$\frac{3}{4}$ to one 250 ml cup/bowl

A baby that is not breastfed should get additional 1-2 cups of milk and 1-2 extra meals per day.

Figure 15.1 Infant feeding in the context of HIV infection



All parents of unknown HIV status should be given information on

- Benefits of exclusive breastfeeding for 6 months and continue breastfeeding for 2 years
- Risks of mother to mother-to-child transmission of HIV
- Prevention and management of breastfeeding problems
- Appropriate complementary feeding
- Promotion of good maternal nutrition and self care
- Importance of micronutrients
- Counsel on child spacing
- Prompt treatment of infections
- Importance of HIV counselling and testing
- Reinforcing risk reduction to couples
- Counsel on adherence to growth monitoring and immunization services

Key information and action to take to support safe breastfeeding:

- Reinforce the benefits of breastfeeding
- Give information on exclusive breastfeeding, including early initiation and appropriate complementary feeding and the risk of mix feeding
- Give information on care of the breast as well as prevention and management of breast conditions
- Reinforce information the need for ARV prophylaxis for the baby to be continued until one week after complete cessation of breastfeeding or where the mother is on ART; the need for adherence to her therapy.
- Provide relevant antiretroviral for the baby during the breastfeeding period.
- Reinforce information on maternal nutrition

Key information and action to take to support safe replacement feeding:

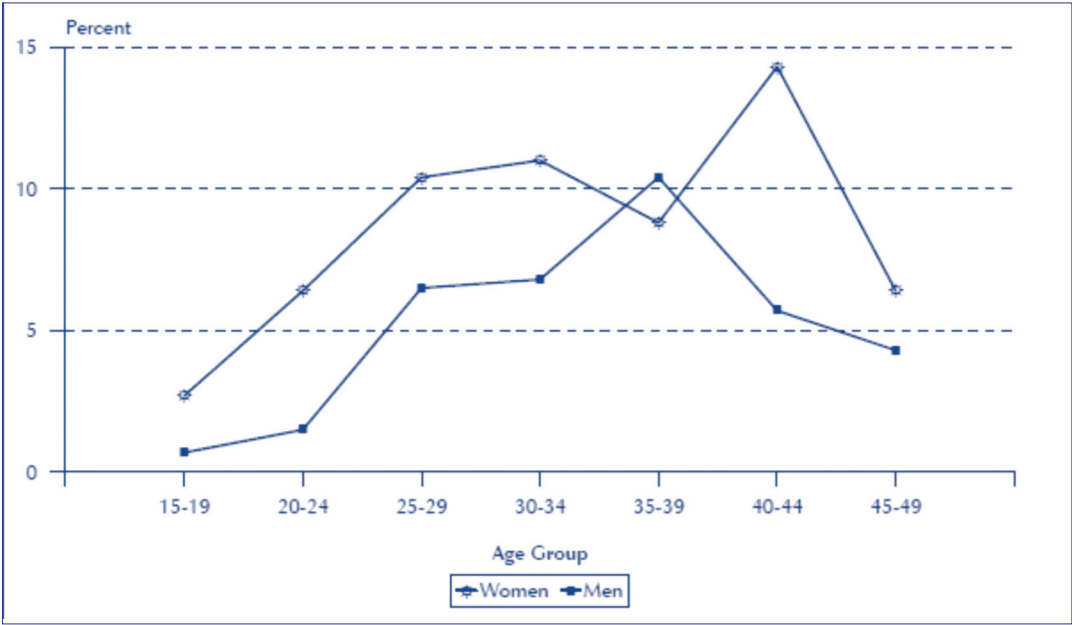
- Give information on replacement feeding and the risk of mix feeding.
- Give information on safe preparation, storage and appropriate feeding techniques for chosen replacement feeds.
- Demonstrate on how to prepare the feeds.
- Demonstrate on how to feed the infant.
- Discuss on the recommended duration of providing formula.
- Counsel on care of the breast to avoid engorgement.
- Provide reliable family planning.
- For low birth weight babies (1.5 kg) and preterm babies provide special infant formula.
- Ensure an interrupted supply of infant formula within the facility.
- Code of marketing of breast milk substitutes should be strictly adhered to.
- Give information on what to do if the child develops diarrhoea.
- Provide ORS for initial home management of diarrhoea.
- Support with infant formula for 9 months and safe water kit. (If available in health facility.)
- Counsel on appropriate hygiene and sanitation practices.
- Give information on appropriate complementary feeding.

16. ARV therapy in the management of HIV-infected pregnant women

16.1 Introduction

The prevalence of HIV infection in women is almost twice that in men: women 8 percent compared to 4.3 percent for men (KDHS 2008-09). Young women (aged 15-24 years) have prevalence four times higher than young men in the same age group: 4.5 percent against 1.1 percent (KDHS 2008-09).

Figure 16.1 HIV-prevalence by age group and gender



Although the prevalence of HIV infection is declining, these data suggest that mother-to-child transmission (MTCT) will remain a significant source of infection for children in Kenya unless effective interventions are used to prevent it. In Kenya, MTCT accounts for more than 90% of HIV infection in children.

Without any interventions, the risk of an HIV-infected mother passing the virus to her infant during pregnancy, labour and delivery or in the postnatal period is 1 in 3. In other words, out of 100 infants born to women with HIV/AIDS, 60-75 of them will not get infected. Of the one-third who become infected, about 5-10 infants will be infected during pregnancy, 15 will be infected during labour and delivery while 5-15 will be infected during breastfeeding, largely being dependent on breastfeeding practices and the duration of breastfeeding.

The comprehensive implementation of prevention of MTCT of HIV interventions including universal testing of all pregnant women, use of combined ART, scheduled Caesarean delivery and safer infant feeding practices has reduced MTCT of HIV infection to less than 2% in developed economies.

16.2 Impact of HIV infection on pregnancy

Though pregnancy does not appear to affect the natural history of HIV infection, the impact of HIV infection on pregnancy is profound. Complications of pregnancy in HIV infection include:

- i. Increased pregnancy loss (spontaneous abortions)
- ii. Increased incidence of pre-term deliveries with the accompanying increase in perinatal mortality
- iii. Low birth weight
- iv. Increased rate of still-birth deliveries
- v. Increased occurrence of HIV-associated and non-HIV-associated conditions such as bacterial pneumonia, urinary tract infections, tuberculosis and Kaposi sarcoma during the antenatal and postnatal periods

16.3 Mother-to-child transmission of HIV infection

More than 90% of paediatric HIV infections are as a result of MTCT. In the absence of any intervention, the risk of MTCT is 15–30% in non-breastfeeding populations and 20–45% among women who practice prolonged breastfeeding without antiretroviral prophylaxis. The greatest risk of transmission is during labour and delivery due to the increased exposure of the newborn to HIV contaminated blood and body fluids. Higher viral load (≥ 1000 copies/ml), lower CD4 count (≤ 350 cells/mm³), rupture of amniotic membranes for more than 4 hours before delivery and prolonged breastfeeding all increase the risk of MTCT. Prematurity, low birth weight, mastitis and genital tract infection are some additional factors that may further increase the risk.

Table 16.1 Risk factors for mother-to-child transmission of HIV

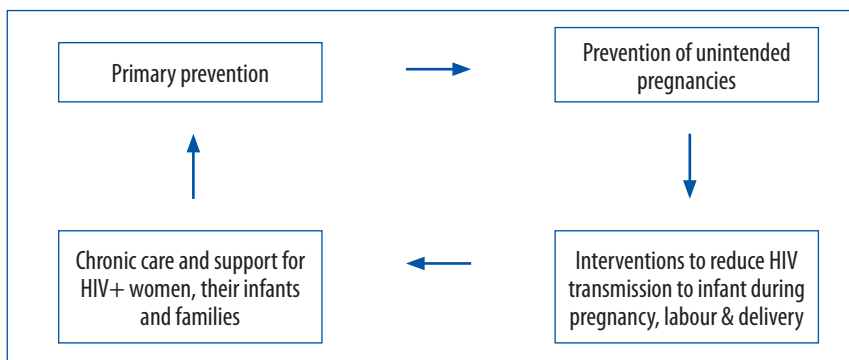
Period	Risk factor
Preconception, antenatal	<i>Maternal factors</i> <ul style="list-style-type: none"> • High HIV viral load • Advanced maternal HIV disease (WHO stage 3 or 4 or CD4 count <350 cells/mm³) • Genital tract infections • Under-nutrition and micronutrient deficiency • Cigarette smoking and unsafe sexual practices
Intra-partum	<i>Obstetric factors</i> <ul style="list-style-type: none"> • Vaginal delivery with high viral load. • Prolonged rupture of membranes >4 hours • Placental infection (chorio-amnionitis) • Intra-partum haemorrhage, invasive foetal monitoring and instrument assisted delivery • Presence of STI
Postnatal	<i>Maternal factors</i> <ul style="list-style-type: none"> • There is increased risk during breastfeeding with: <ul style="list-style-type: none"> ◦ High HIV RNA viral load ◦ Low CD4 count ◦ Advanced maternal HIV disease (WHO stage 3 or 4) ◦ Mixed feeding ◦ Mastitis ◦ Cracked nipples ◦ Breast abscess ◦ No ARVs prophylaxis <i>Infant factors</i> <ul style="list-style-type: none"> • Prematurity (<37 weeks) • Low birth weight • Oral candidiasis/sores

16.4 Interventions to reduce MTCT

Interventions to reduce MTCT should target each of these key areas and include the four prongs of PMTCT:

1. Prevention of HIV Infection among all women of reproductive age group from getting HIV
2. Prevention of unintended pregnancies among HIV-positive women
3. Effective interventions to reduce HIV transmission to infants during pregnancy, labour and delivery and post-delivery
4. Chronic care and support for the HIV-infected women, their infants, partners and families

Figure 16.2 The four prongs of comprehensive prevention of mother-to-child transmission



Attendance of ANC especially in early pregnancy is critical to the provision of PMTCT services. The KAIS 2007 revealed that of the women who gave birth between 2003 and 2007, knowledge of each mode of MTCT was much higher among women who attended ANC compared to those who had not. Knowledge of antiretroviral preventive therapy for PMTCT was also higher among women who attended ANC (76.3 percent) compared to women who had not (58.3 percent). For details on the four prongs of PMTCT, refer to the PMTCT Guidelines and the PMTCT Training Package available at <http://nascop.or.ke/library/pmtct/Training%20Curriculum/>

16.5 Rationale for use of ARVs in pregnancy for PMTCT

Antiretroviral therapy provides the opportunity to significantly reduce maternal HIV viral load therefore to decreasing the risk of HIV transmission by the mother to her child. A reduction in HIV transmission is achievable using more efficacious regimens (dual- or triple-drug combinations). Observational studies have shown that the more potent the ARV drug regimen used, the more effective the reduction in MTCT. In countries where effective interventions against MTCT have been successfully implemented, new HIV infections in children is now extremely rare. This has largely been achieved through the universal access to counselling and testing and use of effective ARV drugs both for prevention of MTCT and treatment in HIV-positive pregnant women.

In Kenya, till 2006, single dose nevirapine (sd-NVP) was effectively the method of choice for PMTCT mainly for reasons of cost, acceptability and ease of use. Although single dose nevirapine is efficacious, it has significant drawbacks. These include failure to prevent transmission in about 50% of instances and development of drug resistance thus limiting future treatment options for mothers and infants in whom prophylaxis fails.

16.6 Use of antiretroviral agents for prevention of mother-to-child transmission of HIV

16.6.1 Recommendations for care of HIV-positive pregnant women

- I. All HIV-infected women who desire pregnancy should receive preconception care to optimize their health status prior to pregnancy (details are found in the PMTCT training curriculum)
The care for such women should be provided by a multidisciplinary team from the HIV clinic (comprehensive care clinic), the maternal and child health (MCH) clinic, the family planning clinic and community healthcare workers. A complete package of care should be provided to the patient to optimize maternal health before conception.
- II. All pregnant women should be encouraged to start attending antenatal care (ANC) as soon as they know that they are pregnant, **preferably in the first trimester**. Recent evidence has shown that earlier initiation of ARV prophylaxis for PMTCT is associated with lower rates of MTCT of HIV.
- III. All pregnant women should be offered HIV counselling and testing during their first ANC visit in line with testing and counselling guidelines. Those who are HIV-negative should be re-tested after 3 months.
- IV. All pregnant women who are not tested or opt-out or decline HIV testing during the first ANC visit should be offered continued counselling and testing in the subsequent visit(s).
- V. Health care workers should offer counselling and testing to all sexual partners of ANC clients and children of all HIV-infected ANC clients. HIV-positive partners in discordant relationships should be evaluated for ART eligibility.
- VI. If a woman is HIV-positive at the time of enrolment into ANC or becomes pregnant while in care; a full baseline assessment should be performed including clinical, psychosocial and laboratory assessment including CD4 cell counts and eligibility for ART initiation determined.
- VII. Where available, all HIV-infected pregnant women should be screened for hepatitis B virus infection and managed accordingly (refer to Chapter 7 for more details)
- VIII. Labour and delivery management should follow optimal obstetric management guidelines. (Refer to PMTCT Curriculum and Guidelines and the WHO IMPAC Care Manual)
- IX. There are two categories of management of HIV-positive women in pregnancy. Those eligible for ART and those that are not (requiring ARV prophylaxis). All HIV-infected pregnant women (irrespective of ART eligibility status) should be enrolled into care and continue to receive the full package of antenatal care and comprehensive HIV care including cotrimoxazole prophylaxis, TB screening, micronutrient and multivitamin supplementation, insecticide treated mosquito nets in malaria endemic areas, treatment of sexually transmitted diseases, prevention with positives interventions and psychosocial support.

16.6.2 Use of antiretroviral drugs for treating HIV-positive pregnant women for their own health (those eligible for ART)

I. When to start antiretroviral therapy

The criteria for initiating ART for pregnant women are similar to that for non-pregnant women (Table 16.2). In pregnant women who meet the criteria for antiretroviral therapy for their own health, it is also the most effective method of preventing MTCT. By improving the general health of the mother; ART also offers the best chance of survival to children born to HIV-positive women. Recent evidence has demonstrated that these group of women account for about 80% of MTCT hence making it critical to identify and treat them.

- Lifelong ART in eligible pregnant women should be initiated as soon as feasible irrespective of gestational age and continued throughout pregnancy, during delivery, breastfeeding and throughout life
- Though ART should be initiated expeditiously in eligible pregnant women; adequate patient preparation through patient education, counselling and support is important to avoid non-adherence and treatment failure. Many of these patients are likely to be relatively healthy; the motivation to deliver a healthy baby means that patient preparation can be successfully fast-tracked.

Table 16.2 When to initiate ART in pregnant women

WHO clinical stage	CD4 testing not available	CD4 testing available
1	Offer efficacious ARV Prophylaxis	Treat if CD4 <350 cells per mm ³
2		
3	Treat with ART	Treat with ART
4	Treat with ART	Treat with ART

Note: Lifelong ART may be initiated in HIV-infected pregnant women, irrespective of CD4 cell count or WHO stage, if the conditions for lifelong ART are met.

A. Choice of ART regimen in pregnant women who require treatment and have had prior exposure to antiretroviral agents for PMTCT

Available data suggests that initiating women on an NNRTI-based (NVP or EFV) regimen within 24 months of sd-NVP exposure is associated with high rates of virological failure. A protease inhibitor based ART regimen should be used in women who have had prior exposure to sd-NVP within 24 months while an NNRTI based regimen should be used in women whose exposure to sd-NVP was more than 24 months ago. Viral load testing is however recommended after 6 months of treatment for women starting NNRTI based regiment with history of prior exposure to nevirapine. If the viral load is >1000 copies/ml, a switch to a boosted PI (PLV/r) based regimen is recommended.

Table 16.3 First line ART regimen for women with history of exposure to nevirapine

Nevirapine exposure within 24 months	Preferred	AZT + 3TC + LPV/r
	Alternative	TDF + 3TC + LPV/r
Nevirapine exposure >24 months ago or no Nevirapine exposure	Preferred	AZT + 3TC + NVP/EFV*
	Alternative	TDF + 3TC + NVP/EFV*

* EFV should not be used in the first 12 weeks (1st trimester) of pregnancy and should be changed to NVP if in first trimester

B. Choice of ART regimen in pregnant women who require treatment and have no history of prior exposure to antiretroviral agents for PMTCT

Table 16.4 First-line ART regimens in pregnant women with no history of prior exposure to ARVs

Regimen and dose	
Preferred	AZT + 3TC + NVP/EFV
Alternative	TDF + 3TC + NVP
	TDF + 3TC + EFV

1. In pregnant women eligible for ART with HBV co-infection, the recommended regimen is TDF + 3TC + EFV

2. In pregnant women intolerant to both AZT and TDF, alternative substitutes include ABC,

- If a woman receiving EFV is recognized as pregnant before 8 weeks of gestation, EFV should be stopped and substituted with NVP but if she is diagnosed as pregnant after 8 weeks of gestation, EFV should be continued. There is no indication for termination of pregnancy in women exposed to EFV in the first trimester of pregnancy. NVP dosing should be given as twice daily with no lead-in dosing when substituting for EFV
- It is recommended that zidovudine (AZT) be part of any regimen for treatment of a pregnant woman, unless there is a documented history of severe AZT-related toxicity or AZT resistance. Baseline assessment of Hb is recommended.
- The combination of d4T and ddI has been linked to increased risk of lactic acidosis, and fatalities during pregnancy; and should therefore be avoided.
- There is increased risk of rash and hepatotoxicity in women initiating a NVP-containing regimen with a CD4 count of >250 cells/mm³. When NVP is used as part of a regimen in these women, more frequent monitoring for toxicity is recommended and appropriate management instituted. Women on an effective NVP based ART regimen prior to pregnancy should continue with the same regimen irrespective of CD4 count at diagnosis of pregnancy.
- There is increased risk of nephrotoxicity with use of TDF. Renal function assessment is recommended before starting TDF and in the first 12 weeks of ART.

16.6.3 ARVs for PMTCT in mothers who are not eligible for ART (women needing ARV prophylaxis)

Pregnant women who are not eligible for ART should be started on ARV prophylaxis. They should be initiated on AZT (300 mg BD) from 14 weeks of pregnancy or as soon as possible thereafter. At the onset of labour, give AZT 600 mg PLUS 3TC 300 mg PLUS NVP 200 mg at once followed by AZT (300 mg BD) and 3TC (150 mg BD) should be for seven days post-delivery.

Single dose NVP given at the beginning of labour has the ability to rapidly decrease intracellular and extracellular HIV viral levels and to act synergistically with AZT and 3TC. However, to reduce the risk of development of NVP resistance following sd-NVP, a 7-day post partum regimen of AZT and 3TC is given to the mother after delivery. This is called OPTION A of ARV prophylaxis.

However, in settings with the capacity to initiate and monitor triple therapy on HIV-infected pregnant women, triple ARV prophylaxis can be used. This is called option B. Due to the risk of NVP-associated hepatic toxicity in women with a CD4 count >250 cells/mm³, it may be necessary to use LPV/r-based triple therapy. Emerging evidence has shown increased morbidity and mortality in patients who interrupt ART hence women who are initiated on triple ARV prophylaxis (OPTION B) for PMTCT should continue with lifelong therapy irrespective of CD4 count or WHO clinical stage or breastfeeding status.

- Remember, that all HIV-infected pregnant women (irrespective of ART eligibility status) should be enrolled into care and continue to receive the full package of antenatal care and comprehensive HIV care including cotrimoxazole prophylaxis, TB screening, micronutrient and multivitamin supplementation, insecticide treated mosquito nets in malaria endemic areas, treatment of sexually transmitted diseases, prevention with positives interventions and psychosocial support.
- Though ARV prophylaxis should be initiated from 14 weeks or at first contact thereafter, adequate patient preparation through patient education, counselling and support is important to avoid non-adherence. Although many of these patients are likely to be relatively healthy, the motivation to deliver a healthy baby means that patient preparation can be successfully fast-tracked.

16.6.4 Monitoring of pregnant women on antiretroviral therapy for their own health or for prevention of MTCT

- Pregnant women initiating therapy should be followed up every 2 week for the first 8 weeks, then monthly thereafter or as clinically indicated.
- This is particularly important in those on a nevirapine containing regimen. In such patients, ALT (or preferably a full LFT) should be evaluated at week 2 and 4 and subsequently monthly until delivery. Patients should be asked to report to the health facility promptly if they experience ART related symptoms; particularly those associated with liver disease (nausea, vomiting, abdominal pain and jaundice).

Hyperemesis gravidarum may sometimes necessitate temporary discontinuation of ART in women receiving treatment prior to the pregnancy.

Table 16.5 Managing antiretroviral therapy in pregnant mother with anaemia

Haemoglobin g/dl	Grade	Remarks
8–10	Mild	Look for treatable causes and manage, give haematinics irrespective of gestation
6–8	Moderate	AZT contraindicated. Initiate ART with TDF in place of AZT i.e. (TDF+3TC+NVP/EFV). Transfuse if ≥36 weeks gestation and if <36 weeks gestation give haematinics
<6	Severe	AZT contraindicated. Initiate ART with TDF in place of AZT i.e. (TDF+3TC+NVP/EFV). Transfuse irrespective of gestation

16.7 Infant ARV prophylaxis

16.7.1 HIV-exposed infants of women on ART

- HIV-exposed infants of women on ART (for their own health or for PMTCT - option B) should receive 6 weeks of daily nevirapine irrespective of breastfeeding practices.

16.7.2. HIV-exposed infants of mothers NOT on ART:

- Infants who are breastfeeding whose mothers are not on ART should receive daily nevirapine until one week after complete cessation of breastfeeding.
- Infants who are not breastfeeding should receive 6 weeks of daily nevirapine.

Table 16.6 Infant nevirapine prophylaxis for HIV-exposed infants

Age	Nevirapine dose
0 – 6 weeks	Birth weight <2500 g – 10 mg (1 ml) once daily Birth weight >2500 g – 15 mg (1.5 ml) once daily
6 weeks – 14 weeks	20 mg (2 ml) once daily
14 weeks to 6 months	25 mg (2.5 ml) once daily
6 months – 9 months	30 mg (3 ml) once daily
9 months – 12 months	40 mg (4 ml) once daily
>12 months	50 mg (5 ml) once daily

Note:

- AZT 15mg/kg twice daily for 6 weeks is an alternative for infants who are not breast fed or whose mothers are on ART/triple prophylaxis
- 3TC is an alternative for infants with severe NVP toxicity (grade 3 or 4)/or if baby is on TB treatment with rifampicin containing regimen

Table 16.7 Infant lamivudine prophylaxis for infants who cannot take NVP

Age	Dosage
0-4weeks	2 mg/kg twice daily
>4 weeks	4 mg/kg twice daily

Table 16.8 Infant AZT prophylaxis dosage for HIV-exposed infants

Birth weight	Dosage
<2500 g	10 mg/kg twice a day
>2500 g	15 mg/kg twice a day

Table 16.9 Antiretroviral prophylaxis for prevention of mother-to-child transmission of HIV infection-antenatal

Mother's presentation (scenario)	Is the mother on ART?	Antenatal and intra-partum interventions – mother	ARV intervention – infant	Follow up after delivery
Asymptomatic (stage I or II) or/ and CD4>350 cells/mm ³ ; presents before onset of labour	No	<ul style="list-style-type: none"> Start CPT, micronutrient and multivitamin supplementation, standard ANC package <p>ARV prophylaxis: Option A</p> <ul style="list-style-type: none"> start on AZT 300 mg BD from 14 weeks or at first contact thereafter and In labour and delivery give AZT 600 mg PLUS single dose NVP 200 mg and 3TC 300 mg all at once 	<p>If breastfeeding</p> <ul style="list-style-type: none"> Daily NVP (from birth until one wk after all exposure to breast milk has ended) <p>If not breastfeeding</p> <ul style="list-style-type: none"> Daily NVP* for 6 weeks 	<ul style="list-style-type: none"> Mother to continue both AZT 300 mg BD and 3TC 150 mg BD for one week. Provide the mother with comprehensive HIV care as per national guidelines Subsequent follow-up of infant care for HIV-exposed Infant
		<p>Option B ((triple ARV prophylaxis):</p> <p><i>Preferred</i> AZT+3TC+EFV</p> <p><i>Alternative</i></p> <ul style="list-style-type: none"> AZT/TDF + 3TC + NVP TDF+3TC+EFV 	Daily Nevirapine for 6 weeks irrespective of breastfeeding practices.	<ul style="list-style-type: none"> Provide the mother with comprehensive HIV care as per national guidelines Subsequent follow-up of infant care for HIV-exposed Infant <p>Pregnant women starting triple ARV prophylaxis should not stop</p>

Table 16.10 Antiretroviral prophylaxis for prevention of mother-to-child transmission of HIV infection – early and late labour

Mother's presentation (scenario)	Is the mother on ART?	Intra-partum interventions – mother	ARV intervention – infant	Follow up after delivery
Scenario 2 Mother presents in early labour (>1 hour before delivery)	No	Single dose NVP 200 mg plus AZT 600 mg and 3TC 300 mg all at once	If breastfeeding <ul style="list-style-type: none"> Daily NVP (from birth until one wk after all exposure to breast milk has ended) If not breastfeeding <ul style="list-style-type: none"> Daily NVP for 6 weeks 	<ul style="list-style-type: none"> Mother to continue both AZT 300 mg BD and 3TC 150 mg BD for seven days. Enrol mother into comprehensive care. Subsequent follow-up of infant care as per HIV-exposed infant
Scenario 3 Mother presents in late labour (<1 hour before delivery) or <72 hours post delivery	No	Mother's HIV status not known <ul style="list-style-type: none"> carry out counselling and rapid HIV test out as soon as possible to enable infant PEP to be administered 	HIV-exposed Infant If breastfeeding <ul style="list-style-type: none"> Daily NVP (from birth until one wk after all exposure to breast milk has ended) If not breastfeeding <ul style="list-style-type: none"> Daily NVP for 6 weeks 	<ul style="list-style-type: none"> Enrol mother into comprehensive care. Subsequent follow-up of infant care as per HIV-exposed infant

Table 16.11 Antiretroviral drugs for prevention of mother-to-child transmission of HIV infection – the postnatal period

Mother's presentation (scenario)	Is the mother on ART?	Intra-partum interventions – mother	ARV intervention – infant	Follow up after delivery
Scenario 4 Mother becomes eligible for ART post-partum	Yes	Prepare mother for ART as per adult recommendations	HIV-exposed infant if breastfeeding <ul style="list-style-type: none"> Continue infant NVP prophylaxis till one week after cessation of breastfeeding. Encourage cessation of BF at 1 year 	N/A
Scenario 5 Infant presents after delivery up to 6 weeks of age	No	Mother's HIV status not known <ul style="list-style-type: none"> carry out counselling and rapid HIV test as soon as possible to enable infant PEP to be administered 	HIV-exposed infant if breastfeeding <ul style="list-style-type: none"> Start daily NVP and continue until one week after all exposure to breast milk has ended At 6 weeks perform PCR and start CTX Follow EID algorithm and recommendations for ART initiation in children 	N/A
Scenario 6 interrupted NVP prophylaxis for infant	No		<ul style="list-style-type: none"> Restart NVP prophylaxis Re start CTX, Do DBS, review the child with DBS results 	
Infants presenting >6 weeks after delivery	No		<ul style="list-style-type: none"> Start CTX, Do DBS, review the child with DBS results, If PCR negative – start NVP prophylaxis for the duration of BF, If PCR pos – start ART. 	

17. Post-exposure prophylaxis

17.1 Introduction

Management of infectious diseases of public health concern has traditionally involved different approaches including avoiding exposure, immunization, prophylaxis and treatment. With particular regard to prophylaxis, drug treatment has been used successfully in different settings to prevent infection from developing following exposure. The same principles have been applied in the prevention and control of HIV infection.

About 100 documented and 200 possible cases of HIV infection in health care workers (HCWs) have been reported worldwide. The risk of transmission has been estimated on average to be 0.3% after a percutaneous exposure to HIV-infected blood, and 0.09% after a mucous membrane exposure; the risk can be higher following an exposure to a large volume of blood or to a high titre of HIV.

Health care workers are at risk of exposure to HIV through contact with contaminated blood and other body fluids containing HIV through

- needle stick injuries and injuries by other sharp objects
- non-intact skin and mucous membranes

The risk of exposure to HIV contaminated blood or body fluids should be minimized by using universal precautions. This means that all blood should be treated **as if contaminated with HIV**. The same conditions apply to hepatitis B & C which are also blood borne viruses. To avoid exposure to these viruses precautions should be taken when handling possibly contaminated body fluids by including the use of appropriate barriers such as gloves, gowns and goggles; care with sharps including minimizing blind surgical procedures and proper handling and disposal of sharps; safe disposal of contaminated waste; safe handling of soiled linen; adequate disinfection procedures and universal Hepatitis B vaccination of non-immune at risk groups including HCWs, police, prison staff and rescue workers.

The case for providing antiretroviral treatment as post-exposure prophylaxis after sexual exposure is an extension of the case for providing it in occupational settings.

17.2 Considerations for post exposure prophylaxis

- Local capacity to offer treatment as soon as possible after risk exposure
 - Once the decision to give PEP has been made, treatment should be started as soon after the exposure as possible preferably within 1 hour of exposure and administered for 4 weeks.)

- PEP should be discouraged after 72 hours of exposure as there is no benefit. (Ensure early referral to nearest centre offering PEP if there are no local services)
- Pre-existing medical conditions and any current medications being used by an exposed individual.
- Choice of an efficacious simplified regimen preferably in a fixed dose combination whenever possible to increase adherence by reducing number of pills and frequency of dosing.
- Capacity to follow up the exposed individual, provide on-going counselling and monitor treatment
 - After initiating treatment, constitutional adverse reactions that may develop can be managed symptomatically. This could enhance adherence to the prescribed regimen with the ultimate goal of achieving treatment completion in the exposed individual.
 - Linkage to a unit where ART is provided should this be necessary in the HCW (as well as source)
 - Recording and reporting of data

PEP may be considered following RTA where there has been exposure to other people's blood; among police and prison staff who may be injured in the course of their work and in discordant couples following condom accidents.

17.3 Post-exposure management

17.3.1 Post-exposure management in occupational exposure comprises of

- Immediate care to exposure site
 - Encourage bleeding from the site but do not scrub or cut the site, washing it with soap and water
- Determine risk associated with exposure
 - Evaluate the source and exposed person
 - Assess the potential risk of infection
 - Both the source and exposed person need to be counselled for HIV-testing. A known source should be tested for HIV; if the source person is not willing to be tested, he/she should not be coerced into having the test.
 - Discarded sharps/needles should not be tested
- The exposed person should not receive ARV drugs without being tested. *However, where immediate testing is not feasible, treatment should not be delayed* since HIV testing can be carried out the following day or soon thereafter. Counselling and support should be provided to the exposed and for those who decline to be tested, they should be offered further appropriate support.

- HIV test should be done at baseline, at 3 months and at 6 months for person exposed. Other baseline tests to be carried out where feasible include: FBC, LFT and renal function.
- Offer PEP as appropriate (see below)
- Treatment should not be continued if status of exposed individual remains undetermined
- Hepatitis B vaccination should be offered to non-immune where available.
- Review staff health and safety: evaluate exposure and determine whether local preventive procedures could be improved
- Provide follow up testing and counselling for the exposed person
- Proper documentation and reporting of event and patient management
- Post exposure prophylaxis is not indicated
 - If the exposed person is HIV-positive, post exposure prophylaxis is not indicated
 - Exposure to intact skin with potentially infectious material, any exposure to non-infectious material (e.g. faces, urine, saliva and sweat)
 - If the exposure occurred more than 72 hours previously

17.3.2 Post exposure management of sexual assault

- Provide appropriate first aid and emotional support
- Provide baseline and follow up counselling for HIV test
- Offer PEP as appropriate
- The first doses should not be delayed by baseline HIV Testing
- Treatment should not be continued if status of patient remains undetermined
- Offer emergency contraception in women at risk of pregnancy
- Document clinical evidence of assault, take appropriate swabs and forensic specimens should be handled appropriately (see Guidelines on PEP)
- Provide STI prophylaxis and consider hepatitis B vaccination if indicated
- Offer trauma counselling
- Alert authorities as appropriate
- Refer as appropriate for legal services

17.4 Indications for and considerations prior to prescribing PEP

17.4.1 Indications for and considerations prior to prescribing PEP in health care settings.

Antiretroviral prophylaxis is prescribed after an occupational exposure to HIV is based risk assessment, which takes into account the type of exposure, the characteristics of the source patient and the material to which the HCW is exposed, as summarized in the table below:

Table 17.1 Risk assessment following exposure to various body fluids

	Low risk	High risk
Type of exposure	Intact skin	Mucus membrane/ non-intact skin Percutaneous injury
Source	HIV-negative	HIV status unknown; clinically well/unwell
Material	Saliva, tears, sweat, faeces, urine, sputum, vomit	Semen, vaginal secretions, synovial, pleural, pericardial, peritoneal, amniotic fluids Blood and bloody bodily fluids; CSF; viral cultures in labs

Of particular high risk are deep injuries, those involving hollow needles with visible blood and those involving patients with high viral loads (recent HIV infection, late stage HIV disease).

17.4.2 Indications for and considerations prior to prescribing PEP in sexual assault

- The argument to offer PEP is based on a comparison of per-exposure risks. Transmission rates in men receiving unprotected anal sex or a woman's exposure during rape or receptive vaginal intercourse with a partner likely or known to be HIV-positive are comparable to transmission rates associated with most needle-stick injuries

Table 17.2 Probability of HIV acquisition after different exposures

Exposure	Probability of disease acquisition (%)
Receptive anal intercourse	0.008-0.032 (0.8-3.2)
Receptive vaginal	0.0005-0.0015 (0.05-0.15)
IVDU	0.0067 (0.67)
Needle stick injury	0.0032 (0.32)
Insertive vaginal intercourse	0.0003-0.0009 (0.03-0.09)

The risk of HIV transmission is probably significantly higher in rape because of trauma forceful penetration. Other factors that increase transmission risk include disease status of rapist (risk increases with viral load) and presence of STIs in the source or the person assaulted.

NB: in a high HIV prevalence population rapists should be assumed to be HIV-positive unless proven otherwise

17.5 Choice of ARVs regiment

PEP is recommended following exposures judged to be of high risk.

The choice of ARV drugs used for PEP should be made only after careful assessment of the nature of the exposure and the source's characteristics including previous and current ART history.

The prophylaxis is given for 28 days

ARV prophylaxis options in occupational exposure

TDF/AZT + 3TC + LPV/r

PI-based triple regimens are preferred for high risk exposure and in the patient care setting where patients are likely to be on ART and possibility of resistance exists. Dual ARV prophylaxis should only be considered where clients cannot tolerate a protease inhibitor.

- Exposures involving source patients on ART should be discussed with a clinician experienced in HIV management; however treatment should be started even while awaiting this.
- NNRTI-based regimens are NOT recommended for PEP. (Severe NVP toxicity has been reported and should be anticipated in the immunocompetent. There is no biological reason why EFV should not be used; however EFV and the risk of teratogenicity in early pregnancy and short term toxicity may pose problems. Furthermore, these drugs are part of standard first line treatment and should therefore not be used in circumstances where PEP may be used following exposure to patients on NNRTI treatment, HIV sero-conversion may occur or treatment discontinuation is likely to be high.)

Use FDCs if available, to reduce pill burden and increase adherence.

ARV prophylaxis options in sexual assault

All HIV exposures through sexual assault are considered to be high risk and should be treated as indicated.

TDF + 3TC +LPV/r (adults only)

Or

AZT + 3TC +LPV/r (for adults and children)

Dosing of these drugs is same as in ART. For children, use the dosing wheel to calculate the dose based on the weight of the child.

Table 17.3 Summary of medical management of HIV-post exposure prophylaxis

Eligibility	Exposure within 72 hours Exposed individual not HIV-infected High risk exposure Source individual HIV-positive or of unknown HIV status
Counselling and testing the exposed individual	Offer information on risks and benefits Verbal consent adequate Base-line HIV test in HIV-exposed person Voluntary testing for both exposed and source individuals
ARV agents for PEP	Occupational exposure: TDF or AZT + 3TC + LPV/r
	Sexual assault (adult): TDF or AZT + 3TC + LPV/r
	Sexual assault (children): AZT or ABC + 3TC + LPV/r
Time of initiation	As soon as possible after exposure, but no later than after 72 hours
Duration of therapy	28 days
Dose of PEP	Same as indicated for ART, use dosing wheel for children for age appropriate dosing.
Follow-up	Follow-up HIV testing at 3 and 6 months after exposure Pregnancy testing Hb (if AZT-containing regimen used for PEP) Hepatitis B and C screening (if available) Management of side-effects
Counselling	Adherence counselling, risk reduction, trauma and mental health problems, social support and safety, safe sex practices
Additional services for sexual Assault	<ol style="list-style-type: none"> 1. Emergency contraceptives for child bearing non-pregnant women 2. STI prophylactic treatment to all <ul style="list-style-type: none"> Adult non-pregnant: PO Doxycycline 100mg BD x 7 days + PO Norfloxacin 800mg stat Adult pregnant: IM inj. Spectinomycin 2gm stat + PO Erythromycin 500mg QID x 7 days Children: PO Amoxycillin 15mg / kg / dose TDS x 7 days + PO Erythromycin 10 mg / kg / dose QID x 7 days 3. Document clinical evidence of an assault 4. Refer for legal services

18. Psychosocial support

18.1 Introduction

People diagnosed with HIV experience many emotional psychological reactions which include shock, disbelief, denial, fear, anger, hopelessness, shame, anxiety, depression and guilt.

The level of distress felt by a person as a result of disclosure of HIV diagnosis may depend on method of acquiring the infection, personality characteristics and lifestyle, degree of support available, knowledge of and experience with AIDS-related issues, accessibility of care and treatment services, and self-evaluated risk of exposure to HIV.

Psychological support helps individuals, couples, and families affected by HIV to cope with their emotions and psychosocial needs. Awareness of these unique psychosocial needs is crucial in effecting timely and appropriate interventions.

Psychosocial support addresses the ongoing psychological and social problems of HIV-infected individuals, their partners, families and caregivers. The ultimate objective of psychosocial care is to prolong survival of patients, assist them to attain quality of life and to enable them to achieve their full potential in society.

Why is psychosocial support important?

- HIV infection affects all dimensions of a person's life: physical, psychological, social and spiritual.
- HIV infections often results in stigma and fear for those living with the infection, their carers and families.
- Psychosocial care can assist people to make informed decisions, cope better with illness and deal more effectively with discrimination.
- Psychosocial support can contribute towards improving the quality of life of PLHIV and prevent further transmission of HIV infection.
- With adequate support, PLWHA will be less likely to develop serious mental health problems.

18.2 Types of psychosocial interventions

Psychosocial interventions include:

- Counselling - support to adapt to HIV status, promote healthy lifestyles e.g. adherence, behaviour change
- Disclosure - to whom, how and when
- Education on - sex education, HIV infections and opportunistic infections, nutrition, caregiver's skills
- Practical support and assistance - condom provision, home visits, legal assistance
- Psychotherapy and psychiatric support

Table 18.1 Providing psychosocial support

Patient education	<ul style="list-style-type: none"> • Facts about HIV and modes of transmission, • Prevention including safer sex, use of condoms, abstinence, • Disease progression, • Positive living
Patient preparation and psychosocial eligibility assessment	<ul style="list-style-type: none"> • Readiness assessment: evaluate the patients functioning (schooling, occupation, interest and mood) • Discuss and encourage disclosure to family members, confidants, sexual partners • Promote partner and family testing • Assess and discuss family history and functioning; i.e. family relationships, social support networks, family dynamics such as domestic violence, separation, substance abuse and sources and adequacy of family income
Address the patients concerns and issues	The patient should be encouraged to share their fears and feelings arising from the presenting issue. (This should be addressed at every stage of the psychosocial process.)
Adherence counselling	<ul style="list-style-type: none"> • Discuss with the patient about keeping clinic appointments • Treatment regime • Side-effects and their management • How to take the medications • Challenges anticipated by the patient towards their treatment • Potential barriers to adherence • Support system i.e. caregiver for children, relatives, teachers etc. • Substance abuse, cultural and religious beliefs • Positive living: good nutrition, hygiene, exercises, safer sexual practices etc.
Supportive and ongoing counselling	<ul style="list-style-type: none"> • Individual counselling • Group counselling • Psychosocial support groups
Special consideration	
Children	<ul style="list-style-type: none"> • The very young i.e. infants and toddler <5 years • Where disclosure has not been done to a child • Children living with grand parents • Orphaned living in homes or foster homes • Physically and mentally challenged children • Children who have gone through sexual and emotional abuse
Adolescents	Sexuality and teenage pregnancies <ul style="list-style-type: none"> • Schooling • Self concept: self esteem, body image, self image and idea self • High risk practices: indiscriminate sex, substance abuse, tattooing, sex toys • Life skills-negotiation and assertiveness
Drug and substance abuse	<ul style="list-style-type: none"> • Assess the use of alcohol • Injecting drug • Locally available drugs and substances
Truck drivers and nomadic communities	<ul style="list-style-type: none"> • Due to their constant movement this group should be considered
Health care providers	<ul style="list-style-type: none"> • Have difficulty accessing care due to stigma • Foster empathy in the course of providing service • Skills to provide quality health care and emotional support
Referrals and linkages to appropriate providers	<ul style="list-style-type: none"> • Have a directory with addresses and contact persons i.e. CBOs, NGOs, health care professionals etc

Figure 18.1 Disclosure of HIV status to children

Step 1: Assess eligibility for disclosure			
Developmental age of child, at least ≥ 5 years	No severe physical or psychological illness	Caregiver willing to disclose	
Step 2: Readiness assessment counselling			
School performance	Family and peer relationships and support	Interest and activity	Mood and behaviour
Step 3: Disclosure counselling			
Guided by caregiver and supported by healthcare provider			
Step 4: Post-disclosure assessment and counselling			
(Reduced interest and activity in the following indicators suggests maladjustment after disclosure)			
School functioning	Family and peer relationship	Interest and activity	Mood and behaviour
Step 5: Referral and support			
Multi-disciplinary team	Counsellor	Psychiatrist	

19. Health System Strengthening in Support of HIV Care and Treatment

19.1 Introduction

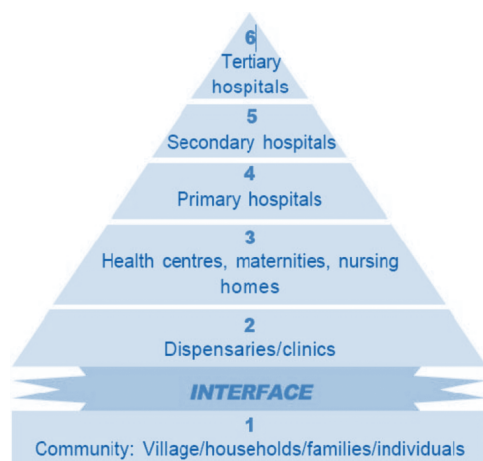
World Health Organization (WHO) defines service delivery as the way inputs¹ such as money, staff, equipment and drugs are combined to allow the delivery of a series of interventions such as HIV care and treatment. Hence, health system strengthening for delivery of HIV care and treatment should focus on facilitating the following:

- Appropriate management of all inputs required for service delivery
- Appropriate organization of services (i.e. ensure access, coverage and quality)
- Appropriate influencing of providers and users (i.e. provider incentives and demand creation)

This section focuses on planning, managing and monitoring service delivery (i.e. organization of services); managing service delivery inputs e.g. human resources, medicines and supplies, infrastructure and equipment; and managing partnerships with providers and communities. The overall goal of this section is to provide the necessary guidance that will facilitate improved, accessible and responsive services for HIV care and treatment across all levels of health services delivery in the country

19.2 Service delivery organization

In Kenya, health services are delivered through six complementary levels. These are:



1. Level 1: Community
2. Level 2: Dispensary
3. Level 3: Health centre
4. Level 4: Sub-district and low volume district hospital (primary hospitals)
5. Level 5: Provincial general hospitals and high volume DHs
6. Level 6: National referral and teaching hospitals

Figure 19.1 The levels of health service delivery in Kenya

(Source: MOPHS Strategic Plan 2008-2012)

¹ Core inputs necessary for health service delivery are financial resources, competent health care staff, adequate physical facilities and equipment, essential medicines and supplies, current clinical guidelines, and operational policies. These inputs must be available, accessible and used properly to produce desired health outputs.

The Ministry of Health in Kenya has adopted WHO's definition of HIV care and treatment which encompasses all interventions provided to PLHIV, including:

- Palliative care
- Prevention of illnesses among PLHIV through vaccinations, malaria prevention, water, sanitation and hygiene initiatives.
- Prevention, diagnosis and treatment of opportunistic infections and HIV-related conditions including intensified TB case finding and management, co-trimoxazole prophylaxis, reproductive tract infections management, prevention of fungal infections and management of other HIV-related cancers.
- Prevention of mother-to-child transmission of HIV;
- Provision of antiretroviral therapy
- Laboratory diagnostics to support antiretroviral therapy (ART)
- Nutritional support
- Reproductive health counselling and support including family planning and cervical cancer screening
- Psychosocial counselling and support for adherence, disclosure and partner notification, testing and counselling
- Prevention with positives (PwP) education and support

Not all health facilities provide all recommended services.

HIV care and treatment services organization

HIV care and treatment services in the Kenya are organized through central sites, satellites, standalone sites and the community level. Central sites are levels 6 to 4 facilities that have satellite sites. There are some level 3 facilities that also function as central sites. Satellite sites are level 3 and 2 facilities supported by central sites. Stand-alone sites could be at any level of service delivery. See Decentralization Guidelines (MOMs, 2008) for more information.

Central sites: are facilities providing comprehensive HIV care and treatment services to a large population. They include provincial, district and high volume sub-district hospitals and other hospitals (faith-based or private). Central sites supervise, mentor and provide logistical support to satellite sites e.g. drug ordering, lab specimen handling, etc. Hence, central sites are expected to have capacity to adequately supervise, mentor and provide logistical support to satellite sites.

Stand-alone sites: are facilities providing comprehensive HIV care and treatment services to a large population like the central sites. However stand-alone sites do not support any satellite site. They order for their ARVs and OI medicines directly from the central level. They have adequate human resources, pharmaceutical and laboratory capacity to function appropriately.

Satellite sites: are mainly health centres and dispensaries including some small sub-district hospitals offering HIV prevention and care services under the supervision of a central site. Satellite sites provide a minimum of ART continuation with varying levels of other complimentary HIV services. The level of services provided by a satellite site is likely to change over time and satellite sites may graduate to become central site.

Community: includes groups of people living with HIV (PLHIV), families, community-based organizations, NGOs, churches, leaders, schools, community health extension workers (CHEWS), community health workers (CHWs) or other volunteers who promote or facilitate mobilisation of clients, patient referral, follow-up, adherence monitoring, defaulter tracking, palliative care and treatment literacy and integration of HIV issues into other community-based programmes e.g. microfinance. Community action on HIV care and treatment is more effective when linked a health facility and delivered in line with MOH community strategy.

Referral system

Existing levels of care are tied together by a referral system. Referral can occur from community to any facility, a facility to another, and from facility to the community. This can take the form of patient referral, specimen referral or exchange of information. For **patient referral** or transfer, the following minimum recommendations should be followed:

- Use of referral forms that fully capture patient's management information that would enable another site to offer continued care and treatment.
- For patients being transferred from one site to another; a copy of a well maintained and completed patient card (blue card) should be transferred with the patient. Where electronic medical records are in use, this should be generated.
- The referral form should have space for feedback notes to and from the facilities and patients and this should be completed
- Referring clinic/health facility is expected to support required referral logistics for the client e.g. transport costs and user fees to be paid where patients are being referred to. If not able to directly support, the referring clinic should explain these requirements and only proceed with the referral if the client is able to meet these on their own.

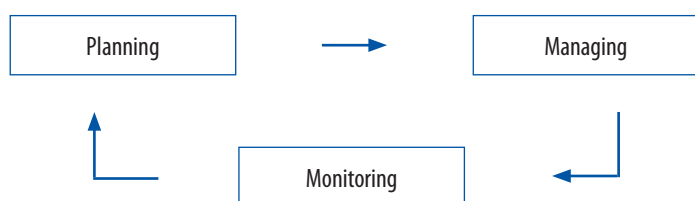
For **laboratory specimen/sample referral**, the following minimum recommendations should be followed:

- A system for timely transportation of the specimens and return of results should be in place and functional
- All specimens should be collected, handled and appropriately documented using provided protocols and forms.
- Clients should be booked for receipt of results at a given definite date based on the performance of the specimen referral system. Where this is not possible, client contact details should be taken and clients should be contacted when results have come.

For the **information exchange**, this may not require standardized forms, instead non-standardised documentation or verbal information may be used. Privileged medical information should only be included in such communication if it involves clinical referral or with the client's informed consent. As is for referral, clear feedback mechanisms should be put in place.

19.3 Service delivery planning, managing and monitoring

This is a cyclical process involving the following:



a. Planning

HIV care and treatment services should be appropriately planned at all levels of service delivery in public, private and faith based sub-sectors.

Appropriate planning requires that all stakeholders in HIV care and service delivery be actively involved in the planning process. For the public sector, the annual operations plan (AOP) should be used for planning HIV care and treatment interventions at community, facility, district, provincial and national level. The AOP planning guide and specific guides from NASCOP provides the necessary steps for HIV care and treatment planning through AOP including required situation/response analysis, target setting, range of activities to be considered at each level, etc.

b. Managing

Managing HIV care and treatment service delivery involves translating policies, strategies and guidelines into how services are organized and how inputs are used to deliver interventions as well as having overall oversight and making necessary adjustments to the service delivery processes to maintain set standards or service delivery goals. Proper management will ensure quality service delivery and promote sustainability. At the facility level, managers are expected to organize clinics in such a way that they promote good patient flow, integration, utilization and efficiency.

c. Monitoring

Continuous monitoring and quality improvement are required for HIV care and treatment. Continuous monitoring and quality improvement is part of the management process for health services delivery. It is done at client, service, programme and institution level. It involves routine collection and interpretation of service delivery

statistics or periodic surveys or assessments. Continuous monitoring and quality improvement feeds into ongoing adjustments that managers are expected to make to service delivery process as well as development of plans that guide service delivery.

Monitoring of HIV programmes, services and patients should adhere to the national guidelines for standard data collection, analysis and reporting.

19.4 Infrastructure and equipment

Appropriate infrastructure is required for efficient utilization of human resources and provision of health services. The broad components of health infrastructure include buildings, equipment, transport, information and communication technologies (ICTs). The type of infrastructure in any facility is determined by the level of care as proposed in the Kenya Norms and Standards for Health Service Delivery (MOH, 2006 p 14-16).

Generally facilities providing HIV care and treatment services should have following minimum essential infrastructure requirements:

- **Space:** adequate waiting and examination area; consultation space with adequate privacy, counselling area, adequate and secure space for storage of medicines and supplies.
- **Equipment:** each facility should have the following equipment as a minimum: desk, chair, cabinet and examination bed
- **Water:** each facility should have access to water for drinking, washing hands and sanitation. Additional hygiene practices and safe waste management should be put in place for infection control.

19.5 Health workforce

A multidisciplinary team of healthcare providers are involved in provision of HIV care and treatment services at the different levels of health care. The staff should work as a team and where task shifting of duties is required prior capacity building should be undertaken to improve the skills of staff taking on more responsibilities. The roles for each team member are described in Table 19.1 on next page.

Table 19.1 Summary of the roles and responsibilities of staff in ART central sites

Health cadre	Roles and responsibilities
Medical officers	Clinical supervision and facility/district management Management of HIV patients in all aspects
Clinical officers	Clinical management of HIV patients in all aspects Service management
Nurses	Nursing care Triage of patients Continuation of clinical care of stable patients Adherence counselling Supervision and training of community and home treatment support workers Post pharmacy counselling
Nutritionists	Nutritional assessment and counselling
Laboratory Technologist/technician	Phlebotomy Laboratory services Laboratory commodities management
Counsellors, including lay counsellors	Diagnostic and voluntary testing counselling patient education Adherence counselling
Community health workers	Community and home treatment support including defaulter management
Health records information officer/ data clerks	Patient record management
Accountant/finance clerk	Receiving of cost sharing fund Financial management
Pharmacist/pharmaceutical technologist	Drug adherence counselling, rational use of ARVs, ARVs Dispensing and effective commodity/inventory management
Store keeper	Commodity management (in conjunction w/ laboratory and pharmaceutical staff)
Social worker and/or Community health co-workers and/or Defaulter tracing personnel	Adherence support Patient assessment for waiver Defaulter tracing Establishing/maintaining community linkages for patient support

The current prescribed staffing levels under KEPH are adequate to provide expected HIV care and treatments services as detailed above. However, the actual staffing are often different from the norms at the different service delivery points, hence staff delivery should be adapted according to the available staffing levels including use of task-shifting, support supervision and staff rotation.

To offer quality HIV care and treatment, all staff is expected to have undergone a basic training in HIV care and treatment (including ART). Guidelines and health worker aids should be provided to support consistent implementation of HIV care and treatment services. The core competencies of staff providing HIV care and treatment services are under development and should inform staffing and training needs when finalized.

ART sites should liaise with the respective HMT, DHMT or PHMT and for assistance with capacity building either directly or through linkages to other partners. This will ensure that appropriate human and institutional capacity building including training and mentorship opportunities are identified to ensure that gaps in systems, skills, and/or knowledge are adequately addressed.

19.6 Information management, monitoring and evaluation

Kenya’s health information system (HIS) includes routine service data; census and vital statistics; surveys; surveillance; other population-and facility-based statistics and research; and management statistics. However, across these components, integration and interoperability is limited. In addition, information feedback loops and use of information for management and decision-making is variable across health system levels and across management units.

There are standardized data collection and monitoring tools that have been developed for collection and reporting of HIV care and treatment data. These tools are based on the WHO recommended tools that contain a recommended minimum data set for HIV management. In its efforts to integrate care, Kenya is adopting the WHO 3-interlinked tools aimed at facilitating co-management (and co-supervision) of HIV care/treatment, TB, maternal and child care services at primary health care level as summarised below:

Table 19.2 Patient care and health records collection tools

	HIV care/ART	MCH/PMTCT	TB-HIV
Patient-held cards	HIV card/appointment card	Maternal/child health card Mother child booklet	TB identity card
Facility-held cards	HIV care/ART card ('blue card')	Partogram card/form (labour record)	TB treatment card
Registers tracking diagnostic tests	HTC register (replaces PITC/VCT registers)	ANC and L&D registers (contains PMTCT data)	TB laboratory and suspect registers
Longitudinal care and treatment registers	Pre-ART and ART registers	ANC and L&D registers HIV-exposed infant register	BMU TB register
Reporting tools	Monthly summary form (CCC) Monthly dashboard MOH 711 form Cohort reporting form	MOH 711 form	MOH 711 form

Other data collection tools available at the facilities include:

- a. commodity management tools used for ordering HIV care/treatment commodities and documenting drugs dispensing
- b. appointment registers
- c. referral forms
- d. supervision checklists, etc.

Given the human resource deficiencies in most clinics, the responsibility of completing patient held cards, registers, reporting tools and others such as HIV care/ART related clinic profile primarily rests with the nurse-in-charge of the HIV care/ART clinic. However, where more staff is available, this responsibility can be shared as follows:

Records clerks: issuing cards/registers, filling patients' demographic data in cards, extracting register data into reporting tools, filling/retrieval of patient's records and submitting reports.

Care/treatment providers (including nurses, clinicians, nutritionists, social workers, etc): completion of HIV care/treatment and counselling information on patient held cards and registers, preparation of cohort summaries or any other case summaries and completing patient referral where necessary.

Pharmacist/pharmacy assistant: completing drug inventory records, completing drug dispensing details for each patient and preparing/submitting supplies orders. Where continuing stable patients go straight to pharmacy for drug refills, the pharmacist/pharmacy assistant also becomes responsible filling patient card and register for continuing patients.

It should however be noted that the nurse-in-charge of the HIV care/ART clinic remains overall in-charge of ensuring that all tools are properly and fully completed and that reports are accurate and submitted in time.

At district level, the District AIDS/STD Coordinator (DASCO) is responsible for preparing district programme report which captures district HIV care/treatment profile information, summary of facility reported data (services, commodities, etc.) and summary of district wide programme activities, e.g. training, supervision and mentorship.

19.7 Commodity management: managing medicines and supplies

A successful antiretroviral therapy, care and treatment programme requires a host of various inputs and resources including drugs, reagents, equipment and other consumables and supplies. The overall management of these resources includes ensuring supplies are in the right place at the right time, in the right quantities, at the lowest possible cost, with minimal or no waste. This is a daunting but critical management task.

The national supply chain management mechanisms are designed to create a balance of responsibility and authority between the facility and the distributors

The entire chain should be monitored for performance on a regular basis and biannual evaluations should be undertaken to measure progress and re-affirm or change future action steps. Benchmarking against best practices in the industry, within the sector and from other sectors is an essential part of this work.

As a point of emphasis, the long term sustainability of supply chain systems for ART commodities, and indeed any other health commodities, will largely depend on how strong institutional systems for managing these commodities are at user institutions – in this case hospitals, clinics and other health care facilities.

In a comprehensive HIV/AIDS programme, the rational use and availability of commodities is central in supporting either the preventive or treatment interventions. These commodities are crucial as they affect demand and quality for HIV care services as continuous availability of the same guarantee adherence and hence treatment success.

The national level

Kenya has articulated the commodity flow and information pipeline that is mapped on the decentralized model to support continued and expanded access to safe, efficacious and cost effective health commodities (See Annex 11). The selection of the commodities should be grounded by evidence based national policies, standards and guidelines. In addition procurement, supply, storage and distribution systems should ensure uninterrupted availability and minimize leakages.

The facility level

Effective management of these commodities by relevant health care workers is critical in not only ensuring continuous availability but also important in ensuring programme quality. Commodities for HIV care and treatment are very costly and difficult to procure and hence need for proper and prudent management.

The staff involved should promote good inventory management practices and rational use of commodities utilizing all the necessary tools and standard operating procedures.

a. Ordering/requesting of commodities

The facility is responsible for ordering for commodities in an appropriate and timely manner based on facility specific requirements. Quantities to be ordered should be determined by past consumption and amount anticipated to be used in the future.

b. Receiving, storage and issuing of commodities

Medicines and related supplies are expensive and valuable, especially medicines and diagnostics for HIV/AIDS. They need care otherwise they may deteriorate. If they deteriorate, they may lose their potency, have the wrong effects on patients or, in the case of test kits, they may produce incorrect results.

Therefore, items in stock should always be stored in a proper storage place. The store should be secure, in good condition and be well organized. All supplies should be kept in the store and requisitions made for what is required for dispensing. If your facility does not have a room to use as a pharmacy store, improvise with a lockable cupboard with shelves to serve as your “store”.

Receipt, storage and issuance of commodities should follow set down government standard operating procedures.

c. Dispensing of medicines

When a medicine is given to a patient, it is important that the patient receives: the correct medicine, the correct quantity of the medicine, the correct information on how to take the medicine, the correct information on how to store the medicine,

Good dispensing is dependent on availability of reference materials (ART national guidelines, manuals and BNFs), dispensing Aids, dispensing envelopes, counting trays, appropriate dispensing environment, and continuous and reliable supply of commodities. Health care workers should promote rational use of medicines and should monitor document and report adverse drug reactions.

19.8 Pharmacovigilance

In the last decade, global initiatives to address public health priorities in developing countries such as HIV/AIDS, Malaria and Tuberculosis have resulted in increased access to medicines. Other factors such globalization, consumerism, free trade and increased cross border communication as well as the internet have also contributed to changes in access to medicinal products including herbals². Increased access to medicinal products

² World Health Organization. The Importance of Pharmacovigilance. Safety Monitoring of Medicinal Products. WHO, Geneva; 2002

often raises concerns about safety and effects however, there has been little attention to monitoring drug safety in the developing world although some momentum is now evident.³

To promote medicine safety, the Kenya Pharmacy and Poisons Board, the medicines regulatory authority established a pharmacovigilance department whose mandate was to establish a system for surveillance and monitoring of medicines in the Kenyan market. The Kenya pharmacovigilance system targets all medicines including anti-retrovirals and engages all sectors.

Pharmacovigilance refers to the science of collecting, monitoring, researching, assessing and evaluating information from healthcare providers and patients on the adverse effects of medicines, biological products, herbals and traditional medicines. Pharmacovigilance is an arm of patient care whose aim is to promote patient safety by identifying new information about hazards, and preventing harm to patients.

What is the scope of pharmacovigilance?

- Substandard and counterfeit medicines
- Product development
- Medication error reporting
- Adverse interactions of medicines with
 - chemicals, other medicines, and food reports
 - Assessment of drug-related mortality
 - Abuse and misuse of medicines reports
 - Efficacy monitoring
 - Off-label use of medicines
 - Case reports of acute and chronic poisoning

What is an Adverse Drug Reaction?

The World Health Organization defines an adverse drug reaction (ADR) as “A response to a drug which is noxious and unintended, and which occurs at doses normally used or tested in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function”.

Why monitor adverse drug reactions?

Before registration and marketing of a medicine, its safety and efficacy experience is based primarily on clinical trials. Some important adverse reactions may not be detected early or may even be rare. In addition, controlled conditions in clinical trials may differ from real practice for instance when patients have taken multiple medicines for various ailments. A continuous post-marketing monitoring system is therefore essential.

3 Ambrose O Talisuna, Sarah G Staedke, Umberto D'Alessandro. Pharmacovigilance of antimalarial treatment in Africa: is it possible? *Malaria Journal* 2006, 5:50

What is a poor quality medicinal product?

This refers to any medicinal product that does not meet the required quality standards in terms of physical appearance, level of active ingredients, packaging, labeling and others. This includes:

- Colour change
- Separating of components
- Powdering / crumbling
- Caking
- Moulding
- Change of colour / odour
- Mislabeling
- Incomplete pack
- Suspected contamination
- Questionable stability
- Defective components
- Poor packaging / poor labeling
- Therapeutic failures (lack of efficacy)
- Receiving expired medicines

Pharmacovigilance of antiretrovirals

Like other medicines, there is substantial experience with use of ARVs in the developed world compared to the developing countries. ARVs have been associated with safety concerns including serious ADRs, short and long term adverse effects which include altered fat distribution (lipodystrophy), anemia, hepatotoxicity, hypersensitivity reactions to mention but a few.

Healthcare workers should be vigilant in identifying, documenting and reporting poor quality medicines and adverse drug reactions. Patients and the public should visit the nearest health facility or healthcare to report medicine –related problems. Healthcare workers should educate patients on importance of identifying of ADRs and reporting them to their medical practitioners and/or nearest health facility.

How are adverse drug reactions, poor quality medicines, sub-standard medicines and counterfeit medicines monitored after a medicine has been marketed?

Reports are voluntarily submitted by health care providers and consumers and are coordinated by the Division of Medicines Information, Department of Pharmacovigilance (PPB).

Reports on **adverse reaction to a medicine** should be made using a “yellow form” (Form for Reporting Suspected Adverse Drug Reactions) which is available at <http://www.pharmacyboardkenya.org/assets/files/Suspected ADR Notification Form.pdf>

Reports on **poor quality medicine, sub-standard medicine** or counterfeit medicine, should be made using a “pink form” (Form for Reporting Poor Quality Medicinal Products) which is available at <http://www.pharmacyboardkenya.org/assets/files/Form for Reporting Poor Quality Medicinal Products.pdf>

The reporter will also be required to send the appropriate amount of sample of the poor quality medicinal product to PPB for further evaluation. All reports are individually reviewed by an Expert Safety Review Panel (ESRP) comprising of trained medical and para-medical professional staff.

What happens to an adverse reaction report?

When reports are received, they are reviewed and entered into the national adverse drug reaction database. The data is then analyzed to identify safety signals. A signal is a preliminary indication of a medicine-related safety issue and by itself does not indicate a causal association.

A detailed evaluation is undertaken to establish whether a true causal association exists between the medicine and the adverse drug reaction.

What actions can be taken by the Pharmacy and Poisons Board on establishment of a true causal association?

Possible regulatory actions vary from continuing observation to cancelling the registration of the drug. Other possibilities include:

- Additional investigations into the use of the medicine in Kenya
- Informing health care professionals and consumers about the risks of medicines
- Re-assessment of the benefit-risk profile of a medicine in Kenya
- Directing product labeling changes (such as the addition of contraindications, warnings and boxed warnings, precautions and adverse reaction information to the Product Information and Consumer Information documents)
- Change in the schedule of the medicine
- Requesting post-marketing studies
- Other regulatory and health promotion interventions as the situation may warrant including withdrawal and recall of the medicine.

Support to pharmacovigilance system strengthening is everybody's business and the key role taken by healthcare workers ensures that medicine safety and ultimate patient safety is promoted

19.9 Access and equity (financing)

Scale up of HIV care and treatment in Kenya started with large hospitals and gradually worked down to lower level facilities and the community level. At present, only a few of the existing health centres and dispensaries provide comprehensive HIV care and treatment services including ART. As a result, a considerable number of clients needing HIV care are forced to travel long distances, often away from nearest health facility to access services.

NASCOP recognizes this challenge and is aggressively pushing for decentralization of HIV care and treatment services. The *Decentralization Guidelines* developed under the auspices of NASCOP details the strategies being employed for decentralization. These strategies include:

- Progressive introduction of HIV care and treatment services (including ART) in all facilities providing PMTCT and/or TB services and eventually covering all service delivery points.
- Continued training of nurses (and clinical officers where available) and task shifting to enable them take the central role of providing HIV care and treatment services (including ART initiation and continuation) at lower level facilities
- Organization of support groups, including PLHA groups to complement facility level interventions and provide supportive functions of peer support, treatment literacy, defaulter tracing and client mobilisation

To further make services more accessible to the population, the Government of Kenya with support from partners is providing ARVs, laboratory equipment/reagents, patient documentation tools and other drugs such as cotrimoxazole free of charge to public health facilities. Some private sector facilities have also been a beneficiary of this as a way of encouraging them to waive all user fees for accessing HIV care and treatment services (including ART).

Mobilization

The Ministry of Health has identified the most-at-risk populations to HIV infection in Kenya. This population should be targeted with preventive messages. In addition, the youth and other population groups such as sex workers may not always have access to HIV care and treatment services due to factors such as societal perceptions including stigma, service hours and friendliness of the service. Health facility staff should develop strategies to actively mobilize clients to access services and deliver preventive education.

Financing for HIV services

HIV, being a chronic illness requiring long-term follow up and medication, may be financially intensive. Clients seeking HIV services should be made aware of the options available for financing their health care.

Various health-financing options are available in Kenya. These include medical insurance schemes and the National Health Insurance Fund.

Health providers should educate all clients on these options and guide them on how best to access financing.

19.10 Leadership and governance

Delivering HIV care and treatment is complex and requires clear leadership and accountability arrangements at all levels. The National AIDS and STI Control Programme (NASCOP) provide national leadership on implementation of HIV prevention, care and treatment activities. NASCOP is represented at the provincial level by the PASCO and by the DASCO at the district level. The PASCOs and DASCOs work with PHMT and DMHT teams respectively to facilitate the implementation of HIV activities at the peripheral levels. With introduction of counties, county coordinators will be introduced to coordinate HIV/AIDS service delivery within each county. Below are roles and responsibilities assigned to each level:

NASCOP

- Assess the HIV epidemiological and health service delivery patterns in the country.
- Develop national level strategic plans for HIV/AIDS and planning guides for lower levels.
- Support resource mobilization and appropriate utilization of resources for HIV/AIDS.
- Setting of national targets and provision of guidance on targets setting at lower levels.
- Development of policies, service delivery frameworks and guidelines for HIV/AIDS.
- Support procurement and distribution of health commodities for HIV/AIDS.
- Coordination of stakeholders and partners on HIV/AIDS in health sector.
- Consolidation, analysis and dissemination of routine and survey data on HIV/AIDS.
- Support, monitor and evaluate programme implementation at the peripheral levels.
- Build the leadership and management capacity of health managers in HIV/AIDS.

PHMT (with the PASCO as the focal person):

- Support districts in planning and setting targets for HIV-related activities.
- Support implementation of HIV/AIDS related activities at district level.
- Provincial coordination of partners and HIV/AIDS service delivery organizations.
- Advocating for additional resources for local health care needs.
- Monitoring distribution of resources between districts (e.g. human resources and services).
- Consolidation of routine and assessment data from the various districts.
- Identification and accreditation of central and satellite sites in collaboration with DHMTs.
- Support supervision, mentorship and training support of DHMTs and level 4 facilities.
- Monitoring service delivery to ensure quality and responsiveness to local needs.

DHMT (with the DASCO as the focal person):

- Plan and set targets for district needs and support facilities to plan and set targets.
- Coordinate partners and HIV/AIDS service delivery organizations at district level.
- Support implementation of HIV/AIDS related activities at district level.
- Ensure equitable distribution of resources and health services within the district.
- Plan and build the capacity of health service providers in HIV/AIDS service delivery.
- Supervise, mentor and train service providers in HIV/AIDS service provision.
- Consolidate and submit (to provinces) routine and assessment data from health facilities.
- Identify, set-up and strengthen activities of central, stand alone and satellite sites.
- Support facilities in organising integrated service delivery systems for HIV/AIDS.
- Establish, support and maintain patient care networks.
- Facilitate community involvement in HIV/AIDS care and treatment.
- Monitor delivery of services to ensure quality and responsiveness to local needs.

Facility management team (through facility management team and staff in-charge of HIV service delivery points):

- Planning and managing utilization of available resources for service delivery
- Supervision, mentorship, training and logistical support to satellite sites
- Management of inputs including staff, facilities/equipment and pharmaceuticals
- Routine monitoring of client outcomes, service coverage, quality and responsiveness
- Development and maintenance of health worker teams and team working
- Establishment and maintenance of community linkages with support from CHEWs
- Organising service delivery (including client flow) that facilitate integration of services

Community unit (through the community strategy)

- Mobilization of clients, patient referral, follow-up and defaulter tracing
- Provision of palliative care and treatment literacy information
- Integration of HIV issues into other community-based programmes e.g. microfinance

19.11 Health systems for HIV care and treatment in emergency and humanitarian settings

Introduction

This section focuses on planning, implementing and monitoring service delivery; managing human resources and commodity supplies and reporting mechanism for providing HIV care and treatment among displaced population both in emergencies and humanitarian settings.

Displacement leads to emergence of challenges ranging from:

- 1) Hard to reach and hard to identify
- 2) Easy to reach – hard to identify
- 3) Easy to reach and easy to identify

Above three categories depends on whether the displaced population move to camps, transit centres, host families in rural areas or are in hiding due to heightened vulnerabilities. Some may be in open view but in hard to reach areas due to heightened insecurity or ensuing calamities.

With all these complexities, the HIV care and treatment needs of displaced population need to be assured to prevent new infections and mortalities.

The effectiveness of the interventions will depend on prior preparedness, extent of disruptions and supportiveness of “therapeutic” community (the extent to which the hosting community is therapeutic) for quick recovery.

Service delivery

Other than for the fact that this is a displaced population with increased vulnerabilities, the HIV needs for care and risk reduction are similar to those for the general population.

However, having been displaced from homes and familiar grounds, their vulnerabilities are increased at a time when access to services is disrupted by displacement.

Furthermore, failure to timely intervention always leads to negative coping mechanism that increases HIV transmission, new strains and complications.

With good prior planning, HIV care and treatment for this population can easily be provided within the national structure through **central sites, satellites and the community** depending on where the displacement takes place or location where the population seeks safety /asylum. However, the keys most important structures are the satellites and community level services.

In line with MOH community health strategy, communities need to be empowered and provided with resources so that they fully participate in HIV care and treatment services.

The prior capacity of displaced population is critical as it defines the level at which they start when disaster strikes. In addition, the capacity of hosting population and local socio-economic dynamics are equally critical as it defines the extent of existing local capacity to support others as well as the possible positive or negative coping mechanism that can be adopted by the displaced population.

It is therefore important to look at the whole spectrum of prior empowerment as a core ingredient of effective HIV care and treatment during displacement. This include establishment of structures that facilitate community active surveillance for patients (and co-morbidity) identifications, treatment support, referral of patients, defaulter management and psychosocial counselling and support. The capacitating includes ensuring evidence based HIV prevention interventions are well understood well in advance. E.g. HIV prevention education including PWP, behaviour change communication, and condom distribution in the community; advocacy and stigma reduction; and integration of HIV care services with other community-based programmes livelihood and coping mechanisms e.g. microfinance, agriculture, etc.

Prior preparations help to ensure that interventions do not increase vulnerabilities, stigma exposure and security risk of the beneficiaries.

Within acceptable time frame (usually not more than 3 months), there is need to have in place a good referral mechanism between the communities and health facilities or strengthening the level of care at the community level.

For example in IDP and refugee camps with possibility of longevity, the strategy will be to improve the quality of care with enhanced proper coordination with national system.

Co-services to HIV care and treatment

Besides treatment and addressing co-morbidity and nutritional needs of PLHIV, their protection, legal and special needs ought to be address. Displacement increases vulnerabilities while place where they move to could make it better or worse.

Often, populations run from danger with no belongings and at times having lost their social identities and identifications. Establishing a prior mechanism through which displaced PLHIV can be identified even if they lose their identification documents is critical. Lose of privacy exposes some to disclosure need which they may have not thought about before.

Planning, managing and monitoring service delivery to displaced populations

d. Planning

HIV care and treatment services should be part of national/humanitarian emergency preparedness and response.

e. Managing

Anchoring of HIV care and treatment to emergency response and national resource (financial, human, information) planning is an integral part of effective management when situation arises. Although initial services is quite often provided by emergency/humanitarian response team/agencies, the timely overall coordination by national mechanism is critical for prevention of new infections, deaths and ensuring one national coordination and monitoring framework.

f. Monitoring

Early warning signs should trigger activations of preparedness plans and empowering at risk populations in potential hot spots and possible flight sites. During emergencies, continuous monitoring, evaluation and quality improvement are required for quality HIV care and treatment. This should be done at the national level (NAS COP), regional and facility level.



20. Appendices

Table 20.1 Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs & NtRTI) for adults

(Refer to Table 20.15 for Paediatric dosing)

Drug name	Dose	Dietary restrictions	Major side-effects	Comments
Stavudine (d4T) Available in 30mg tablet and as FDC with 3TC and 3TC/NVP	Adults – 30 mg BD	Take without regard to meals	Peripheral neuropathy; Pancreatitis; Lipodystrophy; Lactic acidosis and severe hepatomegaly with steatosis (fatal cases have been reported); Headache; gastrointestinal disturbances; skin rashes;	Avoid combination with ddI especially in pregnancy. Decrease dosage in patients with renal impairment
Zidovudine (AZT or ZDV) Available in 300mg tablets and as FDC with 3TC and 3TC/NVP	300mg/dose BD	Take without regard to meals	Haematological toxicity (bone marrow suppression), including Anaemia; Granulocytopenia; Headache; gastrointestinal intolerance; myopathy; myositis; liver toxicity; discoloured nails; Lactic acidosis and severe hepatomegaly with steatosis (fatal cases have been reported).	Monitor for anaemia in the first 3 months of treatment
Lamivudine (3TC) Available in 150mg tablet and as FDC with AZT and AZT/NVP, D4T and D4T/NVP and with TDF and TDF/EFV	150 mg/dose BD	Take without regard to meals.	Headache; fatigue; nausea; diarrhoea; skin rash; Pancreatitis; Peripheral neuropathy; Liver disease/hepatitis; Lactic acidosis and severe hepatomegaly with steatosis (rare fatal cases have been reported).	A well-tolerated drug. Adjust dose in renal impairment. Can also be used in the treatment of chronic Hepatitis B. Ideally, patients should be screened for chronic Hepatitis B virus (HBV) before starting therapy; exacerbation of Hepatitis B has been reported in patients on discontinuation of 3TC.

Didanosine (ddI) Available in 25mg, 50mg, 100mg, 200mg tablets Enteric coated tablets: 12.5mg, 250mg, 400mg	>60 kg: 200 mg/dose BD or 400 mg/dose OD <60 kg: 125 mg/dose BD or 250 mg OD	Take on an empty stomach at least 30 minutes before or 2 hours after eating (food decreases absorption). For EC tablets take with no regards to food	Pancreatitis; Peripheral neuropathy; Nausea; Diarrhoea; Abdominal pain and vomiting; Lactic acidosis and severe hepatomegaly with steatosis (fatal cases have been reported); Hyperuricaemia; electrolyte abnormalities;	Avoid combination with d4T especially in pregnancy. Do not use with Tenofovir; high virological failure rate and increased toxicity. Requires dosing separation from most Pls
Abacavir (ABC) Available in 300 mg tablets	300 mg/dose BD	Take without regard to meals. Alcohol increases ABC levels to 41%	Hypersensitivity reaction (potentially fatal) whose symptoms include fever, fatigue, malaise, nausea, vomiting, diarrhoea and abdominal pain or respiratory symptoms such as shortness of breath, lymphadenopathy, ulceration of mucous membranes and skin rash. Patients suspected of having hypersensitivity reaction should have ABC stopped and never be restarted. Pancreatitis; Lactic acidosis with hepatic steatosis is rare.	Educate patient on hypersensitivity reaction. Once hypersensitivity has occurred, the patient should never be re-challenged on ABC. Avoid alcohol while on ABC.
Emtricitabine (FTC) Available in 200mg capsules and as FDC with TDF and TDF/EFV	200 mg/dose OD	Take without regard to meals.	Well tolerated. Lactic acidosis and severe hepatomegaly with steatosis (fatal cases have been reported); headache; diarrhoea; nausea; rash; skin discoloration.	Effective against Hepatitis B. Ideally, patients should be screened for chronic Hepatitis B virus (HBV) before starting therapy; exacerbation of Hepatitis B has been reported in patients on discontinuation of FTC. Decrease dosage in patients with renal impairment Monitor renal function if combined with TDF. When used in combination with TDF, should not be given to patients with a creatinine clearance of <30ml/min. Should not be used with or after failure of 3TC
Tenofovir disoproxil fumarate (TDF) Available in 300mg tablets and as FDC with 3TC and 3TC/EFV	300 mg/dose OD	Take without regard to meals.	Lactic acidosis and severe hepatomegaly with steatosis (fatal cases have been reported with nucleoside analogues); renal toxicity; Pancreatitis	Should not be used with ddI. Should never be used in triple nucleoside combinations with 3TC+ddI/ABC. Renal function should be monitored while on TDF. Ideally, patients should be screened for chronic Hepatitis B virus (HBV) before starting therapy; Exacerbation of Hepatitis B has been reported in patients on discontinuation of TDF. When used in combination with 3TC, should not be given to patients with a creatinine clearance of <30ml/min. When used with ATV levels of ATV reduced significantly therefore combine with

Table 20.2 Non-nucleoside reverse transcriptase inhibitors (NNRTIs) for adults

Drug name	Dose	Dietary restrictions	Major side-effects	Comments
Nevirapine (NVP) Available in 200mg tablets and as FDC with AZT/3TC and D4T/3TC	200 mg/dose OD for first 2 weeks then 200 mg/dose BD	Take without regard to meals.	Skin rash (may be severe, requiring hospitalization, and life-threatening, including Stevens-Johnson syndrome, toxic epidermal necrolysis); hepatitis; fever, nausea, headache.	Use with caution in women with baseline CD4 > 250 or in men with baseline CD4 > 400. Liver function tests in the first 3 months of treatment. Should not be used with Rifampicin in TB patients. Avoid NVP in patients requiring prolonged treatment with Fluconazole because of increased NVP levels with possibility of increased toxicity. Use alternative antifungal drugs for treatment of oral candidiasis in patients on NVP
Efavirenz (EFV) Available in 200mg & 600mg tablets and as FDC with TDF/3TC	600 mg OD Best given at bedtime	Can be given with food, but avoid high fat meals which increase absorption. Preferably taken on an empty stomach.	CNS symptoms (somnolence, insomnia, abnormal dreams, confusion, hallucination, amnesia, etc. Avoid in patients with history of psychiatric disease); Skin rash; avoid use in during the first trimester	Can be used with Rifampicin in TB patients
Etravirine Available in tablets of 200 mg	200 mg BD	To be taken with food	Severe but rare: SJS and erythema multiforme Common & minor: Rash, nausea, vomiting, diarrhoea, abdominal pain, hepatotoxicity, dyslipidaemia and CNS disturbances (less than EFV)	Avoid concurrent use with rifampicin, and boosted tipranavir

Table 20.3 Protease inhibitors (PIs) for adults

Drug name	Dose	Dietary restrictions	Major side-effects	Comments
Lopinavir/ritonavir (LPV/r, Kaletra) Available as 200mg + 50mg RTV	2 tablets BD i.e [LPV 400 mg + RTV 100 mg] BD	Take with food. Moderate fat increases bioavailability.	GI intolerance; nausea; vomiting; diarrhoea	Tablets should be swallowed whole
Indinavir (IDV) Available as 200mg, 400mg capsules	800mg/dose TDS With RTV: IDV 800mg BD + RTV 100mg BD preferred	For unboosted IDV: Take on an empty stomach, one hour before or two hours after meals; may take with skim milk or low-fat meal. For RTV-boosted IDV: Take with or without food Plenty of fluids to be taken (> 2 litres per day)	Nephrolithiasis; exacerbation of chronic liver disease; fat redistribution and lipid abnormalities; nausea; abdominal pain; headache; metallic taste; dizziness; asymptomatic hyperbilirubinaemia	Separate dosing if given with ddl Ritonavir-boosted IDV preferred because of better pharmacokinetics; no food restrictions and increased efficacy
Saquinavir (hard gel formulation) (SQV) Available as 200mg capsules	Only for combination with Ritonavir in dose of SQV 1000mg and RTV 100g	Take within 2 hours of a meal	Exacerbation of liver disease; fat redistribution and lipid abnormalities; diarrhoea; abdominal discomfort; headache; nausea; paraesthesia; skin rash; spontaneous bleeding episodes in haemophiliacs.	Unboosted SQV not recommended.
Saquinavir (soft gel formulation) (SQV) Available as 200mg capsules	Not recommended un-boosted 1,200mg TDS or 1,600mg BD With RTV: • (RTV 100 mg + SQV-sgc 1,000 mg) two times/day	Take with large meal.	As above	Refrigerate or store at room temperature (< 25°C) for up to 3 months)

Ritonavir (RTV) Available as 100 mg capsules Capsules should be refrigerated until dispensed; stable at room (up to 25°C) for 30 days	WHO recommends that RTV be used only as a booster for other PIs at low dosage.	Administration with food increases absorption and helps reduce gastrointestinal side effects.	Exacerbation of liver disease; fat redistribution and lipid abnormalities; diarrhoea; abdominal discomfort; headache; nausea; paraesthesia; skin rash; spontaneous bleeding episodes in haemophiliacs.	Potent CYP450 inhibitor, thus its use as a booster of other PIs
Atazanavir (ATV) Available in 100mg, 150mg, 200 mg capsules Available as FDC with RTV	ATV 300mg /RTV 100mg OD	Take 2 hours before or 1 hour after antacids and buffered medications such as buffered ddi (reduced ATV concentrations if administered together) Take with food.	Jaundice; headache; fever; depression; nausea; diarrhoea and vomiting; paraesthesia; spontaneous bleeding episodes in haemophiliacs.	Indirect hyperbilirubinaemia. When used with TDF should always be given with RTV. Experienced patients should also be given ATV/RTV.
Fosamprenavir (f-APV) Available as 700mg tablets	ARV-naïve patients: f-APV 1400mg BD (without RTV); f-APV 1400mg + 200mg RTV OD; f-APV 700mg + 100mg RTV BD PI-experienced pts (once daily regimen not recommended): f-APV 700mg + 100mg RTV BD	Take with or without food. Take 1 hour before or 1 hour after antacids or ddi use	Fat redistribution and lipid abnormalities; Life-threatening rash, including Stevens-Johnson syndrome in 1% of patients;	Dosage adjustment in hepatic insufficiency recommended

Table 20.4 Fusion Inhibitors and Integrase Strand Transfer Inhibitors (INSTIs)

Drug name	Dose	Dietary restrictions	Major side-effects	Comments
Enfuvirtide (T-20) Available in 108mg injection (when reconstituted, delivers 90mg/ml)	90mg (1ml) BD injected subcutaneously into upper arm, anterior thigh or abdomen.	N/A	Local injection site reactions; increased rate of bacterial pneumonia; hypersensitivity reactions including fever, nausea and vomiting.	Mainly for salvage treatment. Store at room temperature (up to 25°C). Reconstituted solution should be stored under refrigeration at 2°C to 8°C and used within 24 hours.
Raltegravir (Ral) Available in 400mg tablet, chewable tablets 100mg and 25mg	ADULT and CHILD over 12 years, 400 mg BD 6-12 years of age chewable tablets 6mg/kg to maximum 300mg BD	Can be taken with or without food	Nausea, Vomiting, diarrhoea, flatulence, constipation Severe skin (SJS and TEN) and hypersensitivity reactions have been reported	Mainly for salvage treatment Contraindicated in breast-feeding mothers Safety in paediatric patients has not been established

Table 20.5A Pharmacokinetic properties of antiretroviral drugs – reverse transcriptase inhibitors

Drug	Oral bioavailability	Serum half-life	Intracellular half-life	Elimination
Stavudine	86%	1.0 hour	3.5 hours	Renal excretion 50%
Zidovudine	60%	1.1 hours	3 hours	Metabolized to AZT glucuronide (GAZT). Renal excretion of GAZT
Lamivudine	86%	3-6 hours	12 hours	Renal excretion
Didanosine	30–40%	1.6 hours	25–40 hours	Renal excretion 50%
Abacavir	83%	1.5 hours	3.3 hours	Metabolized by alcohol dehydrogenase and glucuronyl transferase. Renal excretion of metabolites 82%
Tenofovir	25% in fasting state; 39% with high-fat meal	17 hours	10–50 hours	Primarily renal excretion by glomerular filtration and active tubular secretion
Nevirapine	>90%	25–30 hours	Data not available	Metabolized by cytochrome P450 (3A inducer); 80% excreted in urine (glucuronidated metabolites; <5% unchanged); 10% in faeces
Efavirenz	Data not available	40–55 hours	Data not available	Metabolized by cytochrome P450 (3A mixed inducer/ inhibitor); 14%–34% excreted in urine (glucuronidated metabolites, <1% unchanged); 16%–61% in faeces.

Table 20.5B Pharmacokinetic properties of antiretroviral drugs – protease, fusion and integrase inhibitors

Drug	Oral bioavailability	Serum half-life	Route of metabolism
Indinavir	65%	1.5-2 hours	P450 cytochrome 3A4 inhibitor (less than ritonavir)
Nelfinavir	20-80%	3.5-5 hours	Cytochrome P450 (3A4 inhibitor; less than ritonavir)
Saquinavir (soft gel capsules)	4% erratic	1 – 2 hours	Cytochrome P450 (3A4 inhibitor (less than ritonavir)
Ritonavir	Not determined	3 - 5 hours	Cytochrome P450 (3A4 > 2D6; Potent 3A4 inhibitor)
Amprenavir	Not determined in humans	7.1 – 10.6 hours	Cytochrome P450 (3A4 inhibitor (less than ritonavir; similar to indinavir, nelfinavir)
Lopinavir/ritonavir	Not determined in humans	5 – 6 hours	Cytochrome P450 (3A4 inhibitor)
Enfuvirtide	84.3%	3.8 hours	Expected to undergo catabolism to its constituent amino acids, with subsequent recycling of the amino acids in the body pool
Raltegravir	32%	9 hours	Hepatic metabolism

Table 20.6 Drug-drug interactions: overlapping drug toxicity

Bone marrow suppression	Peripheral neuropathy	Pancreatitis	Nephrotoxicity	Hepatotoxicity	Rash	Diarrhoea	Ocular effects
Amphotericin B	Didanosine	Didanosine	Indinavir	Abacavir	Abacavir	Atovaquone	Cidofovir
Cotrimoxazole	Isoniazid	Lamivudine in children	Acyclovir (IV, high dose)	Amprenavir	Amprenavir	Clindamycin	Didanosine
Dapsone	Stavudine	Stavudine	Adefovir high dose	Atazanavir	Atazanavir	Didanosine	Ethambutol
Flucytosine	Zalcitabine	Cotrimoxazole	Aminoglycosides	Atovaquone	Atovaquone	(buffered formulations)	Linezolid
Ganciclovir		Ritonavir	Amphotericin B	Cotrimoxazole	Cotrimoxazole	Lopinavir/	Rifabutin
Hydroxyurea		Pentamidine		Dapsone	Dapsone	Ritonavir	Voriconazole
Interferon-		Zalcitabine	Cidofovir	Delavirdine	Delavirdine		
Primaquine			Foscarnet	Efavirenz	Efavirenz	Nelfinavir	
Pyrimethamine			Indinavir	Fosamprenavir	Fosamprenavir	Ritonavir	
Zidovudine			Pentamidine	Nevirapine	Nevirapine		
			Tenofovir	Sulfadiazine	Sulfadiazine		
				Voriconazole	Voriconazole		

Table 20.7 Drug-drug interactions requiring dose modification or cautious use- NRTIs

Drugs affected	Zidovudine (ZDV)	Stavudine (d4T)	Didanosine (ddI)	Tenofovir (TDF)
Methadone	ZDV AUC increase 43%. Monitor for ZDV related adverse effects.	Levels: d4T ↓ 27%, methadone unchanged. No dose adjustment.	Levels: EC ddI unchanged. Buffered ddI AUC ↓ 63%, methadone unchanged. Dose: No change EC ddI. May consider buffered ddI dose increase or maintain standard.	No change in methadone or TDF levels
Ribavirin	Ribavirin inhibits phosphorylation of ZDV; this combination should be avoided if possible or closely monitor virologic response.	No data	Co-administration not recommended. Ribavirin increases the intracellular levels of the active metabolite of ddI and may cause serious toxicities.	Level: Ribavirin unchanged, no data on TDF level
Didanosine	No significant interactions	Peripheral neuropathy, lactic acidosis, and pancreatitis seen with this combination; use with caution and only if potential benefit outweighs potential risks.	No data	Levels: ddI EC AUC ↑ by 48-60%, Cmax ↑ by 48-64%. Monitor for ddI-associated toxicities; For patients >60 kg, 250 mg/day of ddI EC is recommended.
Atazanavir (ATV)	ZDV: No change in AUC but 30% ↓ in Cmin. Significance unknown	No data	Buffered ddI + ATV simultaneously: Level: ↓ AUC of TV 87%; take ATV (with food) 2 hrs before or 1 hr after buffered ddI. No interaction is expected with ddI-EC; however, dosing should be at different times at TV should be taken with fold and ddI-EC on an empty stomach.	ATV 400 + TDF 300 Levels: ATV AUC ↓ 25% and Cmin ↓ by 40%. TDF AUC was by ↑ 24%. Avoid concomitant use. ATV + RTV 300/100 mg QD + TDF 300 mg QD. Levels: ATV AUC was ↓ by 25% and Cmin by 23%; ATV Cmin was higher with RTV than ATV without RTV; Consider ATV + RTV (300/100 mg QD) For Co-administration with TDF (300 mg QD); however, pharmacokinetic, safety and virologic data are limited.
Indinavir (IDV)	No significant PK interaction.	No significant PK interaction.	Buffered ddI and IDV simultaneously: Levels: ↓ AUC of IDV; take IDV 1 hr before or after buffered ddI. Enteric coated ddI can be taken together with IDV	Levels: IDV Cmax ↑ 14% Dose: Standard

Lopinavir/ ritonavir (LPV/r)	No data	No data	No data	LPV/r 400/100 AUC ↓ 15%; TDF AUC ↑ 34%; clinical significance of interaction is unknown; monitor for tenofovir toxicities
Cidofovir, valganciclovir	Ganciclovir + ZDV: no significant changes in levels for either drug Potential increase in haematological toxicities	No data	ddl + oral ganciclovir (GCV): ddl AUC ↑ 111%; GCV AUC ↓ 21%; Appropriate doses for the combination of ddl and oral GCV have not been established	Serum concentration of these drugs and/or tenofovir may be increased; Monitor for dose-related toxicities.

Table 20.8 Drug interactions requiring dose modification or cautious use – NNRTIs

Drugs affected		Efavirenz (EFV)		
Antifungals				
Ketoconazole	Levels: ketoconazole ↓ 63% NVP ↑ 15 – 30% Dose: Not recommended	No data		
Voriconazole	Metabolism of Voriconazole may be induced by NVP. Voriconazole may inhibit NNRTI metabolism. Frequently monitor for NNRTI toxicity and antifungal outcome.	Levels: EFV ↑ 44% Voriconazole ↓ 77% This combination is not recommended.		
Fluconazole	NVP Levels: Cmax, AUC, and Cmin ↑ 100% Fluconazole Levels: No change Risk of hepatotoxicity may increase with this combination. If concomitant use is necessary, recommend monitoring NVP toxicity.	No clinically significant changes in EFV or Fluconazole concentrations.		
Anti-mycobacterials				
Rifampicin	Levels: NVP ↓ 20%–58%. Virologic consequences are uncertain; the potential for additive hepatotoxicity exists. Use of this combination is not recommended; however, if used, co administration should be done with careful monitoring.	Levels: EFV ↓ 25%. Dose: Consider ↑ EFV to 800 mg QD.		
Clarithromycin	Levels: NVP ↑ 26%. Clarithromycin ↓ 30%. Monitor for efficacy or use alternative agent.	Levels: Clarithromycin ↓ 39%. Monitor for efficacy or use alternative agent.		

Oral contraceptives		Levels: ethinyl estradiol ↓ approx 20%. Use alternative or additional methods.	Levels: Ethinyl estradiol ↓ 37%. No data on other components. Use alternative or additional methods.
Lipid-lowering agents			
Simvastatin		No data	Levels: Simvastatin AUC ↓ by 58%; EFV unchanged Dose: Adjust simvastatin dose according to lipid responses, not to exceed the maximum recommended dose
Atorvastatin		No data	Levels: Atorvastatin AUC ↓ 43%; EFV unchanged. Dose: Adjust atorvastatin dose according to lipid responses, not to exceed the maximum recommended dose.
Pravastatin		No data	No data
Anticonvulsants			
Carbamazepine		Unknown	Use with caution.
Phenobarbital		Use with caution.	Monitor anticonvulsant levels.
Phenytoin		Monitor anticonvulsant levels.	
Methadone		Levels: NVP unchanged. Methadone ↓ significantly. Opiate withdrawal common when this combination is used. Increased methadone dose often necessary. Titrate methadone dose to effect.	Levels: Methadone ↓ 60%. Opiate withdrawal common, increase methadone dose often necessary. Titrate methadone dose to effect.
Miscellaneous		No data	Monitor warfarin when used concomitantly.

Table 20.9 Drug-drug interactions requiring dose modification or cautious use - PIs

Drugs affected	Indinavir (IDV)	Ritonavir (RTV)	Saquinavir (SQV)	Nelfinavir (NFV)	Lopinavir (LPV)
Antifungals					
Itraconazole	Level: When IDV 600 mg q8h given with Itraconazole 200 mg bid, IDV AUC similar to IDV 800 mg q8h Dose: IDV 600 mg q8h; Itraconazole: do not exceed 200 mg bid.	No data, but potential for bi-directional inhibition between Itraconazole and RTV, monitor for toxicities. Dose: dose adjustment for patients receiving >400 mg Itraconazole may be needed, or consider monitoring Itraconazole level.	Bi-directional interaction between itraconazole & SQV has been observed. Dose: Not established, but decreased itraconazole dosage may be warranted. Consider therapeutic drug monitoring for both SQV (if unboosted) and Itraconazole.	No data, but potential for bi-directional inhibition between itraconazole and PIs, monitor for toxicities.	Levels: itraconazole ↑ when administered with LPV/r. Dose: itraconazole – consider not to exceed 200 mg/day or monitor level and toxicity
Ketoconazole	Levels: IDV ↑ 68%. Dose: IDV 600 mg TDS.	Levels: Ketoconazole ↑ 3X. Dose: Use with caution; do not exceed 200 mg ketoconazole daily.	Levels: SQV ↑ 3X Dose: No dosage adjustment necessary.	No dose adjustment necessary.	Levels: LPV AUC ↓ 13% Azole ↑ 3-fold. Dose: Use with caution; do not exceed 200 mg ketoconazole daily.
Anti-mycobacterials					
Rifampicin	Levels: IDV (unboosted) ↓ 89%; IDV (boosted) ↓ 87%; Contraindicated.	Levels: RTV ↓ 35%. Dose: No change. Increased liver toxicity possible. Co-administration may lead to loss of virologic response is RTV sole PI. Alternate anti-mycobacterial agents, such as rifabutin, should be considered.	Levels: SQV ↓ 84%. Contraindicated. Marked elevation of transaminases was seen in a pharmacokinetic study where healthy volunteers received a combination of rifampicin 600 mg QD + RTV 100 mg/SQV 1000 mg BID. This combination should not be used.	Levels: NFV ↓ 82%. Should not be co administered.	Levels: LPV AUC ↓ 75%. Should not be co administered as a safe and effective dose of LPV/r that can be given with rifampicin has not been established.Σ

Clarithromycin	Levels: Clarithromycin ↑ 53%. No dose adjustment.	Levels: Clarithromycin ↑ 77%. Dose: Adjust clarithromycin dose for moderate and severe renal impairment.	Levels: Clarithromycin ↑ 45%. SQV ↑ 177%. No dose adjustment.	No data	Levels: ↑ Clarithromycin AUC 77%. Dose: Adjust clarithromycin dose for moderate and severe renal impairment.
Oral contraceptives					
	Levels: norethindrone ↑ 26%. Ethinyl estradiol ↑ 24%. No dose adjustment.	Levels: Ethinyl estradiol ↓ 40%. Use alternative or additional method.	No data	Levels: Norethindrone ↓ 18%. Ethinyl estradiol ↓ 47%. Use alternative or additional methods.	Levels: Ethinyl estradiol ↑ 42%. Use alternative or additional method.
Lipid-lowering agents					
Simvastatin Lovastatin	Levels: Potential for large increase in statin levels. Avoid concomitant use.	Levels: potential for large increase in statin levels. Avoid concomitant use.	No data	Simvastatin AUC ↑ 505%. Potential for large increase in lovastatin AUC. Avoid concomitant use.	Levels: Potential for large increase in statin levels. Avoid concomitant use.
Atorvastatin	Levels: potential for increase in AUC Use lowest possible starting dose of atorvastatin with careful monitoring.	Levels: 450% ↑ when administered with SQV/RTV combination. Use lowest possible starting dose of atorvastatin with careful monitoring.	Levels: 450% ↑ when administered with SQV/RTV combination. Use lowest possible starting dose of atorvastatin with careful monitoring.	Atorvastatin AUC ↑ 74%-use lowest possible starting dose of atorvastatin with careful monitoring.	Atorvastatin AUC ↑ 5.88-fold. Use lowest possible starting dose of atorvastatin with careful monitoring.
Pravastatin		Levels: 50% ↓ when administered with SQV/RTV combination. Dose: Pravastatin dosage adjustment based on lipid response.	Levels: 50% ↓ when administered with SQV/RTV combination. No dose adjustment needed. Dose: pravastatin dosage adjustment based on lipid response.	No data	Pravastatin AUC ↑ 33%; no dosage adjustment necessary.

Anticonvulsants					
Carbamazepine Phenobarbital Phenytoin	Carbamazepine markedly ↓ IDV AUC. Consider alternative agent or monitoring IDV level.	Carbamazepine; ↑ serum levels when co-administered with RTV. Use with caution. Monitor anticonvulsant levels.	Unknown, but may markedly ↓ SQV levels. Monitor anticonvulsant levels and consider obtaining SQV level.	Unknown, but may decrease NFV levels substantially. Monitor anticonvulsant levels and virologic response. Consider obtaining NFV levels.	Many possible interactions: Carbamazepine: ↑ levels when co-administered with RTV. Use with caution. Monitor anticonvulsant levels. Phenytoin: levels of LPV, RTV, and ↓ levels of Phenytoin when administered together. Avoid concomitant use or monitor LPV level.
Methadone	No change in methadone levels.	Methadone ↓ 37%. Monitor and titrate dose if needed. May require ↑ methadone dose.	Methadone AUC ↑ 20%. When co-administered with SQV/RTV 400/400 mg BID. Dose: No adjustment for this PI regimen, but monitor and titrate to methadone response as necessary.	NFV may decrease methadone levels, but opiate withdrawal rarely occurs. Monitor and titrate dose if needed. May require methadone dose.	Methadone AUC ↓ 53%. Opiate withdrawal may occur. Monitor and titrate dose if needed. May require ↑ methadone dose.

Erectile dysfunction agents					
Sildenafil	Sildenafil AUC ↑ 3 fold. Use cautiously. Start with reduced dose of 25 mg every 48 hours and monitor for adverse effects.	Sildenafil AUC ↑ 11 fold. Use cautiously. Start with reduced dose of 25 mg every 48 hours and monitor for adverse effects	Sildenafil AUC ↑ 2 fold. Use a 25 mg starting dose of sildenafil.	Sildenafil AUC ↑ 2-11 fold. Use cautiously. Start with reduced dose of 25 mg every 48 hours and monitor for adverse effects.	Sildenafil AUC ↑ 11-fold in combination with RTV. Do not exceed 25 mg every 48 hours.
Miscellaneous	<p>Grapefruit juice ↓ IDV levels by 26%. Vitamin C ≥ 1 gram/day ↓ IDV AUC by 14% and C_{min} by 32%.</p> <p>Amlodipine: Amlodipine AUC ↑ 90% when co-administered with IDV/RTV. No change in IDV/RTV levels. Monitor closely.</p>	<p>Many possible interactions</p> <p>Desipramine ↑ 145%, reduce dose.</p> <p>Trazodone AUC ↑ 2.4 fold when given with 200 mg BID or RTV. Use lowest dose of trazodone and monitor for CNS and CV adverse effects.</p> <p>Theophylline ↓ 47%, monitor theophylline levels.</p> <p>RTV 100 mg bid significantly increase systemic exposure of inhaled (oral or nasal fluticasone, may predispose patients to systemic corticosteroid effects. Co-administration not recommended unless benefit of fluticasone outweighs the risk.</p>	<p>Grapefruit juice ↑ SQV levels.</p> <p>Dexamethasone ↓ SQV levels.</p>		

Table 20.10 Use of ARVs in Paediatric Therapy

Drug	Formulation	Adverse Events	Comments
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)			
Zidovudine (AZT,ZDV)	Suspension 10mg/ml Capsules 100mg, Tablets 300mg	Neutropenia, anaemia, headache; Myopathy, lactic acidosis (rare)	Can be given with food store at room temperature
Lamivudine (3TC)	Available as FDC with 3TC and 3TC/NVP Suspension 10mg/ml Tablets 150mg Available as FDC with ABC , AZT and AZT/NVP	Headache ,abdominal pain, fatigue, pancreatitis, peripheral neuropathy; neutropenia, ↑ LFTs, lactic acidosis (rare)	Can be given with food store at room temperature
Stavudine (d4T)	Suspension 1mg/ml Capsules 15 mg, 20mg,30mg,	Headache, GI upset, rash, peripheral neuropathy, ↑ LFTs, pancreatitis, lactic acidosis	Can be given with food Keep suspension refrigerated
Didanosine (ddI)	Suspension 10mg/ml Tablets 25mg,50mg,100mg,150mg	Diarrhoea, abdominal pain, nausea; peripheral neuropathy, pancreatitis, lactic acidosis ↑ LFTs	Give on empty stomach Keep suspension refrigerated
Abacavir (ABC)	Suspension 20mg/ml Tablets 300mg Available as FDC with 3TC	Hypersensitivity rash (5%),fever, malaise, mucositis, pancreatitis, lactic acidosis	Can be given with food store at room temperature Do not re-challenge after hypersensitivity
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)			
Nevirapine (NVP)	Suspension 10mg/ml Tablets 200mg Available as FDC with AZT/ 3TC	Rashes, Stevens-Johnson syndrome, ↑ LFTs; hypersensitivity and hepatitis	Can be given with food store at room temperature Watch for liver toxicity
Efavirenz (EFV)	200mg and 600 mg tablets	Rash(mild),somnolence, abnormal dreams,insomnia,confusion,hallucinations,euphoria,amnesia,agitation,abnormal thinking	Can be given with food Administer at night Store at room temperature No pharmacokinetic data <10kg and <3years of age
Protease Inhibitors (PIs)			
Ritonavir (RTV)	Suspension 80mg/ml Capsules 100mg Available as FDC with LPV	GI intolerance, Headache, anorexia, ↑ LFTs; Abnormal lipids (rare)	give with food palatability improved by mixing with milk, honey, ice cream, yogurt or chocolate milkshake store in refrigerator or room temperature
Nelfinavir	Suspension 50mg/ml/1gm spoon tablets 250mg	Diarrhoea, vomiting, rash, abnormal lipids, exacerbation of chronic liver disease(rare)	Administer with food. Suspension may be mixed with water, milk, pudding, ice cream, formula
Lopinavir/ritonavir LPV/RTV, Kaletra	Suspension 80mg LPV and 20mg RTV per ml Heat stable 200mg LPV/ 50mg RTV	GI intolerance, rash; headache, abnormal lipids, hyperglycaemia, pancreatitis (rare)	Give with food store. A high fat meal increases absorption Refrigerate suspension or keep at room temperature for 2months

NB: For dosages refer to table 20.15: Antiretroviral Drug dose Chart for children

Table 20.11 Renal dosing of agents used in the management of HIV and AIDS in adults – NRTIs

Agent	Dose for normal renal function	Estimated creatinine clearance (CrCL) in ml/min 10 – 50	Estimated creatinine clearance (CrCL) in ml/min <10
Abacavir/ABC	300 mg po bid	No adjustment recommended	
Didanosine/ddI	Weight <60kg: 125mg bid	125mg OD	62.5mg OD
	Weight > 60kg: 200mg bid	200mg OD	100mg OD
Lamivudine/3TC	150mg bid	100%	150mg OD
Stavudine/d4T	30mg bid	30mg bid or 30 mg OD	15mg OD
Zidovudine/AZT	300mg bid	300mg bid	300mg OD

Table 20.12 Renal dosing of agents used in the management of HIV and AIDS in adults – NNRTIs

Agent	Dose for normal renal function	Estimated creatinine clearance (CrCL) in ml/min >50	Estimated creatinine clearance (CrCL) in ml/min 10 – 50	Estimated creatinine clearance (CrCL) in ml/min <10
Efavirenz/EFV	600mg po OD	No adjustment recommended	No adjustment recommended	
Nevirapine/NVP	200mg OD x 14 days, then 200mg po bid	No adjustment recommended	No adjustment recommended	

Table 20.13 Renal Dosing of Agents used in the Management of HIV and AIDS in Adults – PIs and INSTIs

Agent	Dose for normal renal function	Estimated creatinine clearance (CrCL) in ml/min > 50	Estimated creatinine clearance (CrCL) in ml/min 10 – 50	Estimated creatinine clearance (CrCL) in ml/min <10
Lopinavir/ ritonavir LPV/r	As indicated in table 20.3 for adults	No adjustment recommended	No adjustment recommended	
Indinavir				
Azatanavir				
Darunavir				
Fosamprenavir				
Nelfinavir/NFV				
Raltegravir		No adjustment required		

Table 20.14 Renal dosing of agents used in the management of HIV and AIDS in adults – FDCs

Agent	Dose for normal renal function	Estimated creatinine clearance (CrCL) in ml/min > 50	Estimated creatinine clearance (CrCL) in ml/min 10 – 50	Estimated creatinine clearance (CrCL) in ml/min <10
Zidovudine/Lamivudine AZT/3TC	300/150mg bid	300/150mg bid	Use individual drugs at doses listed above	
Nevirapine/Lamivudine/Stavudine NVP/3TC/d4T	200/150/30mg bid	200/150/30mg bid	Use individual drugs at doses listed above	

12 – 13.9	2 tab	2 tab	2 tab	0.5 tab BD	0.5 tab BD	12 ml	200 mg tab	10 ml	0.5 tab	10 ml	0.5 tab twice daily	2 ml	1 tab twice daily
14 – 16.9	2.5 tab	2.5 tab	2.5 tab	0.5 tab BD	0.5 tab BD		0.5 tab BD 1.5 tablet of 200 mg	15 ml			1 tab in am 0.5 tab in pm	2.5 ml	1 tab twice daily
17 – 19.9	2.5 tab	2.5 tab	2.5 tab	0.5 tab BD	0.5 tab BD		0.5 tab BD 1.5 tablet of 200 mg	15 ml			1 tab in am 0.5 tab in pm	2.5 ml	1 tab twice daily
20 – 24.9	3 tab	3 tab	3 tab	1 tab in am 0.5 tab in pm	1 tab in am 0.5 tab in pm		1 tab in am 0.5 tab in pm 1.5 tablet of 200 mg	15 ml			1 tab in am 0.5 tab in pm	3 ml	1 tab twice daily
25 – 29.9	Treat as Adult	Treat as Adult	Treat as Adult	1 tab BD	1 tab BD		1 tab BD 2 tablets of 200 mg		1 tab		1 tab twice daily	3.5 ml	2 tab in am 1 tab in pm
30 – 34.9	Treat as Adult	Treat as Adult	Treat as Adult	1 tab BD	1 tab BD		1 tab BD 2 tablets of 200 mg		1 tab		1 tab twice daily	4 ml	2 tab in am 1 tab in pm
35 – 39.9	Treat as Adult	Treat as Adult	Treat as Adult	1 tab BD	1 tab BD		1 tab BD 2 tablets of 200 mg		1 tab		1 tab twice daily	5 ml	2 tab in am 2 tab in pm

Paediatric fixed dose combinations (FDCs) are available as ABC/3TC, AZT/3TC and AZT/3TC/NVP. All young children requiring ART should be put on appropriate FDCs based on their weight.

ABC/3TC tablet is crushable. They can be chewed or crushed and dispersed in water (5–15 ml) or onto a small amount of food and immediately ingested
AZT/3TC and AZT/3TC/NVP tablets are water dispersible and should be given in 5–15 ml of water.

Single formulations: These formulations should only be used where appropriate paediatric or adult FDCs cannot be used. Single formulations increase the pill burden in adolescent thus affecting the adherence.

Abacavir (ABC) – tablets may be swallowed whole or crushed.

Lamivudine – tablets may be swallowed whole or crushed

Zidovudine – tablets may be swallowed whole or crushed. For children requiring triple nucleosides (AZT+3TC+ABC), they should be given ABC/3TC FDC along with AZT tablet or liquid

Nevirapine – Nevirapine induction dose is once daily for 14 days and if no rash develops is followed by a maintenance dose of twice daily. Nevirapine syrup should mainly be used for prophylaxis in HIV-exposed infants using the dosing as indicated in table 16.6.

Efavirenz 200mg – tablet is scored and may be divided into equal parts. Tablet may be crushed and dispersed in water (5–15 ml) or onto a small amount of food and immediately ingested.

Lopinavir/Ritonavir – dose is calculated based on lopinavir component. Oral solution should be taken with food. Oral solution must be refrigerated until dispensed. After removing from refrigeration oral solution is only stable for 60 days at room temperature (up to 25°C). Where temperatures are expected to exceed 25°C, the feasibility of dispensing smaller amounts and giving more frequent refills should be considered (for instance, no more than monthly supplies dispensed at one time). The amount of solution has been rounded up to nearest ½ ml for easier measurement as per the manufacturer's recommendation.

Table 20.16 Normal developmental milestones

Age	Milestones	Red FLAGS
3 months	<ul style="list-style-type: none"> • Turns head toward sound • Smiles • Raises head when on stomach • Brings hand to mouth • Watches faces intently • Recognises familiar people • Follows moving objects with eyes • Vocalizes 	<ul style="list-style-type: none"> • Does not seem to respond to loud noises • Floppy or excessively stiff • Poor sucking or swallowing • No visual fixation or following • Asymmetry of tone or movement • Excessive head lag • Does not smile
6 months	<ul style="list-style-type: none"> • Sits unsupported or with minimal support • Babbles • Turns to caregiver's voice • Reaches for familiar persons • Reaches for objects • Shows likes and dislikes • Plays with feet when prone • Rolls over 	<ul style="list-style-type: none"> • Floppiness or excessive stiffness • Failure to use both hands • No response to sound • Squinting or inability to move both eyes • Does not roll over
9 months	<ul style="list-style-type: none"> • Sits without support • Rolls over • Babbles and imitates sounds • Understands a few words, e.g. "bye-bye" or "no" • Able to drink from a cup and hold a bottle • Points at objects or people • Pulls to stand 	<ul style="list-style-type: none"> • Floppiness or excessive stiffness • Unable to sit • No response to sound • Squinting or inability to move both eyes, follow object or face • Persistence of primitive reflexes
12 months	<ul style="list-style-type: none"> • May walk alone or "creep" around furniture • Imitates actions • Looks for toys or objects that are out of sight • Responds to own name • Understands simple commands, e.g. "Close the door" • Feeds self finger foods 	<ul style="list-style-type: none"> • Unable to bear weight on legs • No single words • Does not point to objects • Does not use gestures, such as waving or shaking head • No response to sound • Unable to grasp objects

¹ Adapted from Guidelines for Paediatric PITC for Zambia available at: <http://cumc.columbia.edu/dept/icap/resources/peds/V6%20PITC%20Guidelines%20Appendices.pdf>

18 months	<ul style="list-style-type: none"> • Runs • Scribbles • Throws a ball • Climbs onto chair • Obvious hand preference • Can say 6–20 words • Spoon feeds • Imitates actions • Walks backward 	<ul style="list-style-type: none"> • Failure to walk • Unable to understand simple commands • Cannot say any words • Unable to grasp small objects
2 years	<ul style="list-style-type: none"> • Combines words • Asks for food, drink, and toilet • Handles spoon well; spoon feeds without mess • Pretend play • Looks at pictures 	<ul style="list-style-type: none"> • Does not develop mature heel-toe walking pattern after several months of walking, or walks only on toes • Does not use a 2-word sentence • Does not understand simple instruction • Poor coordination
3 years	<ul style="list-style-type: none"> • Climbs • Goes up and down stairs • Knows name and sex • Balances on one foot • Puts on a shirt • Speech is understandable 	<ul style="list-style-type: none"> • Unstable walk • Few words, no sentences • No involvement in “pretend” play • No interest in other children
4 years	<ul style="list-style-type: none"> • Hops • Knows full name and age • Recognizes colours • Dresses and undresses • Make-believe play 	<ul style="list-style-type: none"> • Speech difficult to understand because of poor articulation, omission, or substitutions of consonants • No interest in interactive games • No interest in other children • Does not use sentences

Regression of milestones between assessments should be considered a red flag

Table 20.17 HSS building blocks in the context of HIV care and treatment

HSS building block	Activities
Service delivery	Integration of comprehensive care services within the normal functions of the facility systems and improvement of quality and accessibility of lab services for both HIV and larger health systems needs
Human resources for health	Embracing task-shifting of health care workers duties, allowing a broader pool of trained individuals to assume tasks formerly provided by doctors, through continuous professional development targeted at improving the skills of mid-level health care providers
Medical products, vaccines and technologies	Through training health care providers on comprehensive injection safety programmes to reduce the medical transmission of HIV and other blood-borne pathogens. Health workers have been equipped with skills to appropriately order, forecast and store medical products
Information	Public private partnerships have enhanced the electronic medical records systems which supports appropriate reporting to the national programme.
Governance and leadership	The National AIDS and STI Control Programme has been supported by development partners to develop enabling ART policies. And in turn the national programme has supported provinces, districts and communities to scale up ART
Financing	National, provincial and district level personnel identifying opportunities to improve resource flows and understanding the contribution of all sources of HIV programming and the larger health system

Table 20.18 Summary of the levels of health service delivery in Kenya (Source: MOH 2006)

Level	Population served (Max)	Function
Level 1 – community health unit	5000	Community health units consisting of households, communities, and villages. This level of care was specified under NHSSP II and is in the process of being rolled out. Activities encourage healthy behaviours and assist community members to identify symptoms of conditions that need to be managed at other levels of care. (See section 9.6 on community participation in health for more information on level 1 roll-out.)
Level 2 – dispensaries/ clinics	10 000 (rural) –15 000 (urban)	Interface between the community and health system facilities. This level is responsible for engaging the community and its structures through curative, promotive, preventive, and rehabilitative care at the most basic levels, as well as participating in the census, keeping health records, and micro-planning to contribute to the AOP and ensure that all communities are receiving care.
Level 3 – health centres, maternities, nursing homes	30 000 – 40 000	Level 3 provides the services specified under level 2 for its immediate catchment population (10 000–15 000) and also provides additional services to support the level 2 facilities in its area, including: higher level health activities; recognizing and facilitating referral services; providing logistical support to level 2 facilities (e.g. cold chain support for KEPI); and coordinating information flow. Additional health activities added at this level include: additional outpatient care, largely limited to minor surgery on outpatient basis; limited emergency inpatient services (emergency inpatients, awaiting referral, 12-hour observation, etc.); limited oral health services; individual health education; maternal care for normal deliveries; specific laboratory tests (routine lab, including malaria; smear test for TB; HIV testing).
Level 4 – primary hospitals	100 000 (rural) – 200 000 (urban)	Level 4 is the principal referral level for all KEPH interventions from levels 1–3 and includes management functions supported by the DMOH and district partners. Its focus is appropriate curative care through primary hospitals. Hospitals at this level provide the level 2 and 3 functions for their surrounding areas but also provide: clinical supportive supervision to levels 2–3, higher level health activities, recognizing and facilitating referrals, providing logistical support, and coordinating information flow from facilities in the catchment. Additional health activities added at this level include: referral level outpatient care, inpatient services, emergency obstetric care, oral health services, surgery on inpatient basis, client health education, more specialized laboratory tests, and radiology services.
Level 5 – secondary hospitals	1 000 000	Consists of secondary hospitals and management functions supported by the PMOH and province partners. These facilities offer a broader spectrum of curative services and they serve as training facilities for nursing staff and clinical officers.
Level 6 – tertiary hospitals		Consists of national referral hospitals and management functions supported by MOMS. This level provides all the remaining specialized services at the national level, provides training for specialized cadres of health workers, and serves as a centre for research.

Table 20.19 List of review meetings participants

The revision of these guidelines took place through a consultative process spanning a period of over one and a half years. The process incorporated a broad range of participation including health policy experts, front-line healthcare professionals, researchers, patient representatives among other stakeholders. Below is a list of participants who attended and contributed to various meetings convened to develop the recommendations contained in this document:

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