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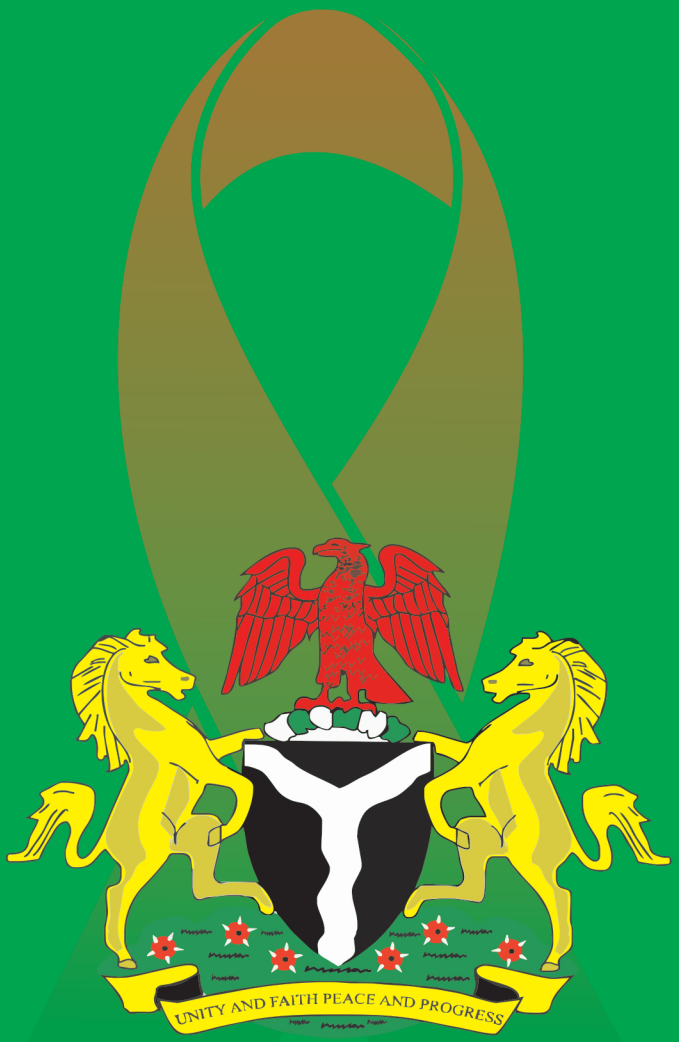
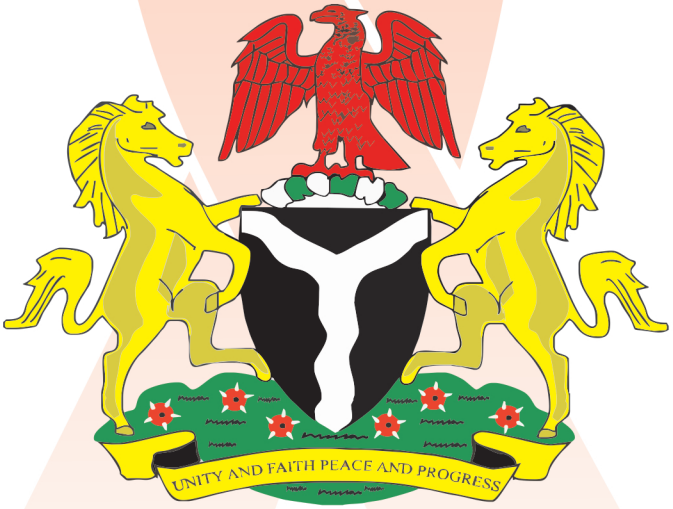


INTEGRATED NATIONAL GUIDELINES FOR HIV PREVENTION TREATMENT AND CARE

NATIONAL AIDS/STIs CONTROL PROGRAMME
FEDERAL MINISTRY OF HEALTH

2014



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The Federal Ministry of Health wishes to acknowledge the contributions of everyone who participated in the development of 2014 National Guidelines for HIV Prevention, Treatment and Care.

We wish to express special appreciation to the World Health Organization for providing the 2013 WHO Consolidated Guidelines on the use of ARV drugs for treating and preventing HIV infection, which served as an important resource material for the development of these guidelines.

We wish to express sincere appreciation to UNICEF, the Center for Integrated Health Programs and the Clinton Health Access Initiative for providing financial support for the development of these Guidelines

We also acknowledge the technical contributions of PEPFAR Nigeria and the local USG HIV Implementing Partners to the process of guidelines development.

Similarly, We extend special thanks to the members of the academia, the civil society and the body of PLHIV in Nigeria for their invaluable contributions to the process.

Finally, we wish to commend the staff of the National HIV/AIDS Division for the professionalism by which they coordinated the entire process leading to the development of these guidelines

Dr. Bridget Okoeguale
Director Public Health

FOREWORD

The 2014 Integrated National Guidelines for HIV Prevention, Treatment and Care provides general and specific guidance for the prevention and treatment of HIV infection in the country. The development of these guidelines underscores Government's commitment to ensuring that all PLHIV in the country have access to high quality HIV prevention and treatment services.

The 2014 Integrated National Guidelines for Prevention and Treatment of HIV Infection is the product of the review and integration of three existing guidelines; the National Guidelines for HIV/AIDS Treatment and Care in Adults and Adolescents, National Guidelines for Paediatric HIV/AIDS Treatment and Care and the National Guidelines for Prevention of Mother to Child Prevention of HIV Infection.

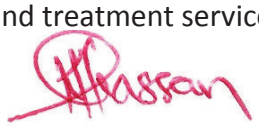
The process leading to the development of these guidelines was inclusive and painstaking with relevant stakeholders in the national HIV/AIDS partnership making necessary inputs to the process. Prominent stakeholders involved in the process included representatives of Federal Ministry Health, WHO, UNAIDS, UNICEF, USG supported agencies, PLHIV groups, CSOs, medical and pharmaceutical regulatory agencies, State Ministries of Health and facility level service providers.

These guidelines for the prevention and treatment of HIV infection reflect a reasonable balance between expectations of science and the realities of public health with extra care taken to ensure that quality is not compromised for convenience. In developing this document the Guidelines Review Working Groups deferred to the expertise of the World Health Organization and adopted many of the recommendations contained in the 2013 WHO Consolidated Guidelines on the use of ARVs for Preventing and Treating HIV Infection.

The 2014 integrated national guidelines for prevention and treatment of HIV infection is different from 2010 guidelines in many respects; it has integrated three separate guidelines into one document for ease of application and has adopted new eligibility criteria for initiation of ART in HIV positive adults and children. The new recommendations require that all HIV+ adults with CD4+ cell counts ≤500 cells/mm3 receive ART irrespective of clinical stage of the disease with priority consideration for persons with CD4 cell count ≤350 cells/mm3. In the case of HIV+ children initiation of ART is now indicated for children less 59 months of age up from 24 months of age recommended in the 2010 guidelines. For PMTCT the new guidelines align with 2013 WHO recommendations prescribing ARV prophylaxis for all HIV positive pregnant women for the duration of pregnancy and breastfeeding.

This document serves the purpose of ensuring that the prevention and treatment of HIV infection is of uniformly high standard across the country and that in exercising their mandates stakeholders are not in breach of Government's aspirations for the wellbeing of its people living with HIV including the key affected populations.

I recommend these guidelines for all persons and organizations involved in the delivery of HIV prevention and treatment services in Nigeria.



Dr. Khaliru Alhassan
Honourable Minister of State for Health

EXECUTIVE SUMMARY

The 2014 Integrated National Guidelines for HIV Prevention, Treatment and Care is an integration of the 2010 guidelines for HIV treatment and care in adults and children and prevention of mother –to-child transmission of HIV (PMTCT).

The 2014 Integrated National Guidelines for HIV Prevention, Treatment and Care is a twelve-chapter document that provides general guidance for the implementation of key interventions for the prevention, treatment and care of PLHIV. The Guidelines document is presented as Chapter 1- Introduction; Chapter 2 -Diagnosis of HIV Infection; Chapter 3 -Antiretroviral Therapy; Chapter 4-Monitoring and Follow-Up; Chapter 5 and 6-PMTCT; Chapter 7- Management of Adverse Drug Reactions and Complications of ART; Chapter 8 Preventive Management of HIV/AIDS; Chapter 9-Adherence to ART; Chapter 10-Management of Common Opportunistic Infections; Chapter11- Care and Support and Chapter 12-Programmatic Management of HIV/AIDS.

Key recommendations contained in these Guidelines include the new eligibility criteria for ART in adults and children and recommendation for use ARVs in the prevention of mother to child transmission of HIV. HIV positive individuals with CD4+cell count ≤500cells/mm3 are eligible for ART irrespective of clinical staging with priority consideration for persons with CD4+cell count ≤350cells/mm3. HIV+ children under 59 months are eligible for ART. The recommendation for PMTCT is that all HIV+ pregnant women receive ARV prophylaxis for the duration of pregnancy and breastfeeding and thereafter be referred to a comprehensive ART centre for assessment of eligibility for ART for her own health.

The 2014 Integrated Guidelines for HIV Prevention, Treatment and Care provides unambiguous recommendations for PMTCT and HIV treatment and care in adults, adolescents and children and it is expected that faithful application of these recommendations will lead to significant improvements in the quality of HIV services offered to our population of persons living with HIV.

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ABBREVIATIONS AND ACRONYMS

3TC	-	Lamivudine
ABC	-	Abacavir
ADR	-	Adverse Drug Reaction
AIDS	-	Acquired Immunodeficiency Syndrome
ANC	-	Antenatal Care
ALP	-	Alkaline Phosphatase
ALT	-	Alanine Transaminase
ARM	-	Artificial Rupture of Membrane
ART	-	Antiretroviral Therapy
ARV	-	Antiretroviral drugs
AST	-	Aspartase Transaminase
ATV/r	-	ritonavir boosted Atazanavir
AZT	-	Zidovudine
CD4+	-	Cluster of Differentiation 4
CDC	-	Centres for Disease Control
CKD	-	Chronic Kidney Disease
CMS	-	Central Medical Stores Oshodi
CMV	-	Cytomegalovirus
CNS	-	Central Nervous System
CPK	-	Creatinine Phospokinase Test
CPT	-	Cotrimoxazole preventive Therapy
CrCl	-	Creatinine Clearance
CRRIRF	-	Combined Report Requisition Issue and Receipt Form
CSF	-	Cerebrospinal Fluid
CSO	-	Civil Society Organization
CT	-	Computed Tomography
CTX	-	Cotrimoxazole
CXR	-	Chest X-Ray
D4T	-	Stavudine
DBS	-	Dried Blood Spot
Ddl	-	Didanosine
DLV	-	Delavirine
DNA	-	Deoxyribonucleic Acid
DOTS	-	Direct Observed Treatment Short Course
DRV/r	-	ritonavir boosted Darunavir
DTG	-	Dolutegravir
EFV	-	Efavirenz
ELISA	-	Enzyme Linked Immunosorbent Assay
ESRD	-	End Stage Renal Disease
EVG	-	Elvitegravir
FBS	-	Fasting Blood Sugar
FDC	-	Fixed Dose Combination
FMOH	-	Federal Ministry of Health
FP	-	Family Planning
FPV	-	Fosamprenavir
GFR	-	Glomerular Filtration Rate
HAART	-	Highly Active Antiretroviral Therapy
Hb	-	Haemoglobin
HbsAg	-	Hepatitis B surface Antigen
HBV	-	Hepatitis B Virus
HCV	-	Hepatitis C Virus
HIV	-	Human Immunodeficiency Virus
IDV	-	Indinavir
IGA	-	Income Generating Activity
INH	-	Isoniazid
IPT	-	Isoniazid Preventive Therapy
LIP	-	Lymphoid Interstisial Pneumonia
LMIS	-	Logistic Management Information System
LPV/r	-	Lopinavir/ritonavir
MARPs	-	Most at Risk Populations
M&E	-	Monitoring and Evaluation
MOH	-	Ministry of Health
MTCT	-	Mother to Child Transmission
MTB	-	Multidrug Resistance TB
MUAC	-	Mid Upper Arm Circumfrence
NACA	-	National Agency for the Control of AIDS
NARHS	-	National AIDS and Reproductive Health Survey
NASCP	-	National AIDS and STIs Control Programme
NFV	-	Nelfinavir
NEPWHAN	-	Network of People Living with HIV in Nigeria
NNRTI	-	Non-Nucleoside Transcriptase Inhibitors
NRTI	-	Nucleoside Reverse Transcriptase Inhibitors
NSAIDS	-	Non Steroidal Anti-Inflammatory Drugs
NVP	-	Nevirapine
OIs	-	Opportunistic infections
Pap	-	Papanikolaou Test for cervical cancer screening
PCP	-	Pneumocystis jirovecii Pneumonia
PCR	-	Polymerase Chain Reaction
PCV	-	Packed Cell Volume
PEP	-	Post Exposure Prophylaxis
PEPFAR	-	US President Emergency Plan For AIDS Relief
PHC	-	Primary Health Care
PHDP	-	Positive Health Dignity and Prevention
PI	-	Protease Inhibitor
PI/r	-	Ritonavir boosted Protease Inhibitor
PITC	-	Provider Initiated HIV Testing and Counselling
PJP	-	Pneumocystis jirovecii Pneumonia
PLHIV	-	People Living with HIV
PME	-	Programme Monitoring and Evaluation
PMM	-	Patient Management and Monitoring
PMTCT	-	Prevention of Mother to Child Transmission
PrEP	-	Pre-Exposure Prophylaxis
RAL	-	Raltegravir
RCT	-	Randomized Controlled Trials
RNA	-	Ribonucleic Acid
RVP	-	Rilpivirine
sdNVP	-	Single dose Nevirapine
SQV	-	Saquinavir
STI	-	Sexually Transmitted Infection
tARVp	-	Triple Antiretroviral Drug Prophylaxis
TB	-	Tuberculosis
TDF	-	Tenoforvir
TPV	-	Tipranavir
TT	-	Tetanus Toxoid
UNAIDS	-	Joint United Nations Programme on HIV/AIDS
UNICEF	-	United Nations Children's Fund
USAID	-	United State Agency for International Development
VIA	-	Visual Inspection Acetic Acid for cervical cancer screening
VL	-	Viral Load
WBC	-	White Blood Cell
WHO	-	World Health Organization

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CHAPTER ONE

INTRODUCTION

Background and context

The first draft of the National Guidelines on the use of ARV drugs was developed in 2003. This provided the template for the development of National Guidelines for HIV and AIDS Treatment and Care in Adults and Children, and National Guidelines for Prevention of Mother-to-Child Transmission of HIV in 2005. However, the 2005 edition of the guidelines on treatment and care was considered inadequate for management of HIV in children which prompted the creation of separate documents for children and adults in 2007. Following new developments in the management of HIV, these documents became obsolete and were updated in 2010. The new recommendations from the recently released World Health Organization (WHO) consolidated guidelines in 2013 stimulated the review and harmonization of the three guidelines into a set of consolidated guidelines based on current scientific evidence and practices with the primary aim of providing guidance on the use of ARV for HIV treatment and prevention across all age groups and key affected populations, based on the broad continuum of HIV care.

1.1.1 Guiding Principles

These guidelines are founded on the basic principles of equality and justice and they align strongly with the universal declarations of human rights. They strive to ensure universal access to comprehensive services for HIV/AIDS prevention, treatment and care for all persons in Nigeria who are exposed to the risk of HIV infection and disease. The recommendations of these guidelines are the product of pragmatic balancing of dictates of science and the many factors that limit access to public health in developing countries.

The core principles that inform these guidelines align with the basic principles of equality, freedom of choice and natural justice and they include:

PROMOTION OF HUMAN RIGHTS AND HEALTH EQUITY: Access to quality health care services including HIV prevention, treatment, care and support is a basic human right all people are entitled to regardless of nationality, sex, ethnicity, race, religion, language, or other status. This right should be recognized as fundamental to realizing the universal right to health. These guidelines will ensure equitable provision of quality HIV services including ART and related interventions to the people who need them; including pregnant women, children and key populations. The services will be provided in an environment that minimizes stigma and discrimination.

Basic rights and freedom of all clients will be respected in the implementation of the guidelines. For example, informed consent (for HIV testing and initiating ART) and adequate health information safeguards will be in place to ensure consent and confidentiality. Priority will be given to people who are most ill and those already receiving treatment, while also striving to implement expanded eligibility criteria to ensure fairness and equity.

CONTRIBUTION TO NATIONAL AND GLOBAL HEALTH GOALS: These guidelines have taken into consideration the letter of the 2011 Political Declaration on HIV and seek to facilitate the attainment of Global Health Sector Strategy on HIV/AIDS (2011–2015). In addition, this document will contribute to achieving the goals and targets articulated in the National Health Strategic Development Plan (2010-2015), National HIV/AIDS Strategic Plan (2010-2015).

PUBLIC HEALTH APPROACH: In line with the national scale-up strategy of decentralization and integration of health services, these guidelines are based on a public health approach to scale up the use of ARV drugs for HIV treatment and prevention. The public health approach will ensure access to high-quality services at all levels of the health care system for all peoples including the community and primary health care settings with a focus on best practices that are commensurate with available resources.

IMPLEMENTATION GUIDED BY IN-COUNTRY PECULIARITIES: Implementation of the recommendations in these guidelines will be informed by local context, including HIV epidemiology, availability of resources, the organization and capacity of the health system. While aiming to achieve attainment of the global milestones, best practices within the country will be promoted and expanded.

STRENGTHENING HEALTH SYSTEMS THROUGH INNOVATION AND LEARNING: New ways of service delivery recommended and described in these guidelines will be implemented in a manner that strengthens health systems and enhances local capacity to keep pace with rapidly evolving science of HIV medicine.

INCREASING THE EFFECTIVENESS AND EFFICIENCY OF PROGRAMMES: As the country scales-up access to ART in the face of competing national priorities, efforts will be made to optimize the effectiveness and efficiency of National HIV programmes. This involves:

- Giving priority to provision of ART to people living with HIV who are eligible for treatment and most in need;
- Implementing strategies and recommendations that are sustainable and less dependent on foreign aid

1.1.2 Rationale for Integration of Prevention and Treatment Guidelines

The 2010 national guidelines for Paediatric ART, Adult ART and PMTCT were separate and distinct documents that encouraged the creation of parallel management structures for the management of HIV/AIDS in adults, children and pregnant women. In this form the guidelines failed to emphasis synergies and complementarities and as such encouraged the existence of different systems for capacity development and logistical pathways for delivery of commodities and hardware.

The integration of guidelines will improve coordination of programmes, greater integration of services and efficiency in the management of patients. With the increasing decentralization of HIV services to peripheral level facilities with limited number of health workers and dependence on a single health worker to provide multiple services, efficiency requires that guidance for efficient service delivery is contained in a single document.

The integration helps to facilitate linkages and promotes consistency of approaches across the various settings where ART and related services are provided, including specialized HIV care, primary care, community-based care, maternal and child health services, and TB/HIV services.

Prior to the development of the integrated guidelines we had three separate documents for PMTCT, adult and paediatric ART and this had serious implications for funding and assimilation of the contents of the documents.

With integration of the guidelines less funding is expended on guidelines development and the training of health workers on the use of the guidelines. The health workers have to contend with a single document containing harmonized recommendations for PMTCT and HIV treatment and care in adults and children. This approach will ensure that health workers address the needs of the PLHIV holistically in one all-encompassing continuum of care.

1.1.3 Objectives of the Integrated Guidelines

THE OBJECTIVES OF THESE INTEGRATED GUIDELINES ARE:

- To provide updated and evidence-based clinical recommendations based on a public health approach to provision of HIV prevention, treatment, care and support services.
- To provide programmatic guidance for decision-makers at all levels of government on clinical and operational recommendations as well on monitoring implementation and impact.
- To provide guidance on key operational and service delivery issues that need to be addressed to increase access to HIV services, strengthen the continuum of HIV care and integrate the different components HIV/AIDS services.

1.1.4 Process of Guidelines Review

The development of the 2014 National guidelines on HIV prevention, treatment, and care commenced following the official release of the WHO 2013 consolidated guidelines on the use of ARV drugs for preventing and treating HIV infection. The National HIV/AIDS Division of the Federal Ministry of Health convened a total of three critical stakeholders meetings which reviewed the three existing guidelines; National Guidelines for HIV/AIDS Treatment and Care in Adults and Adolescents, National Guidelines for Paediatric HIV/AIDS Treatment and Care and the National Guidelines for PMTCT and adapted and adopted recommendations from the newly released 2013 WHO Consolidated Guidelines on the use of ARVs for preventing and treating HIV infection.

Stakeholders involved in the development of the guidelines include representatives of the Federal Ministry of Health, State Ministries of Health, National Primary Health Care Development Agency, NACA, WHO, UNICEF, PEPFAR, CDC, USAID, CHAI, HIV Implementing Partners, NEPWHAN, CSOs, National Task Teams for ART, PMTCT and HCT, facility level HIV service providers and the private health sector.

Guidelines recommendations are the product of majority stakeholder consensus, taking into account the national health systems capacity and availability of resources. These include guidance on HIV diagnosis, general HIV care and the strategic use of ARV drugs for treating and preventing HIV infection.

1.1.5 Target audience

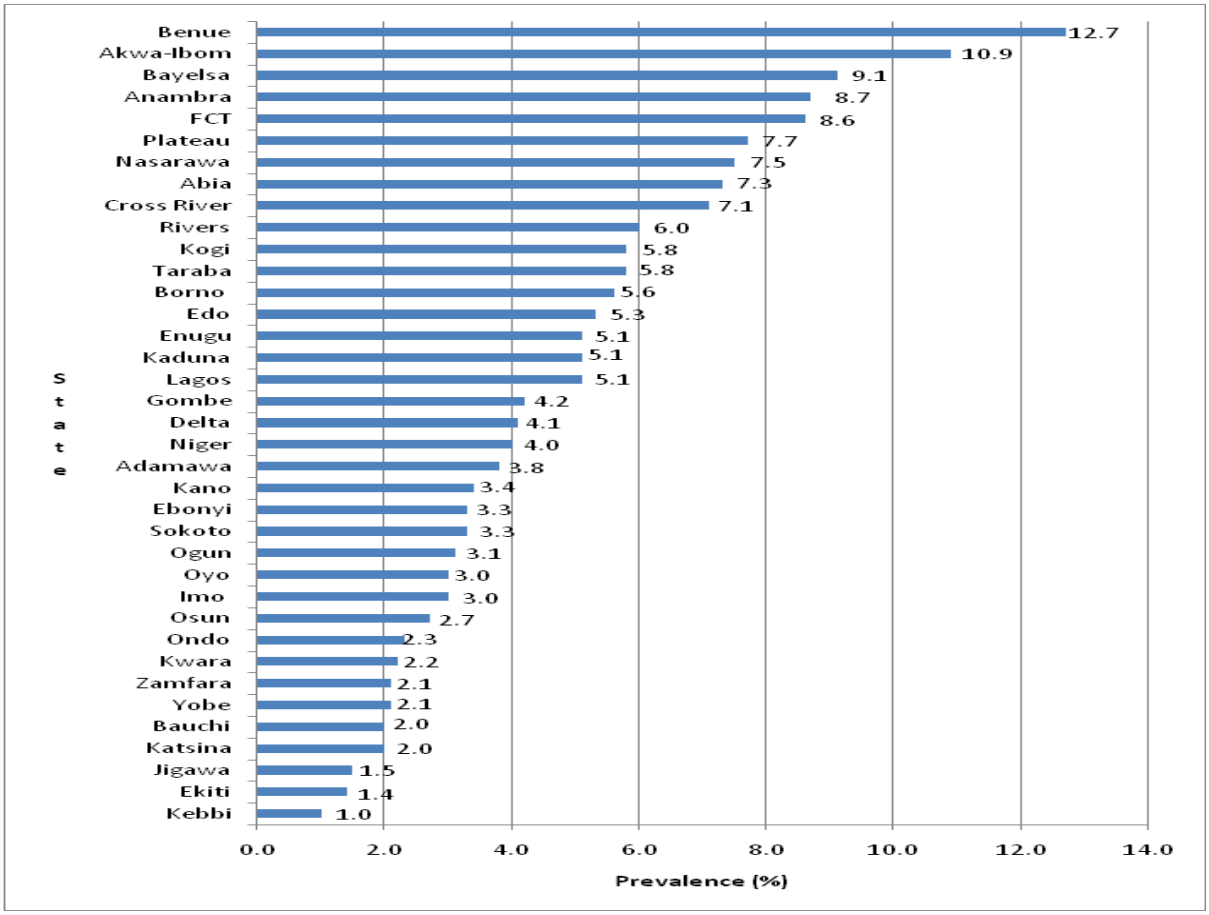
The 2014 Integrated National Guidelines for HIV Prevention, Treatment and Care is intended primarily for use by HIV programme managers and service providers at all levels of HIV service delivery. The critical audience for the guidelines include:

- National HIV Programme Managers
- Health facility level service providers
- National HIV treatment and prevention technical working groups;
- National TB programme managers
- Managers of maternal, new born and child health and reproductive health programmes;
- Clinicians and other health service providers;
- Managers of national laboratory services;
- Community-based organizations including People living with HIV
- International and bilateral agencies and organizations that provide financial and technical support to HIV programmes in Nigeria

1.2 Epidemiology of HIV in Nigeria

The first case of AIDS in Nigeria was reported in 1986. Since then, HIV prevalence increased exponentially until it peaked at 5.8% in 2001 before progressively declining over the years down to 4.1% in 2010 (ANC Survey Report). According to 2010 ANC Survey Report, HIV prevalence variations across states remain considerable; ranging from 1% to 12.7% (see figure 1.1).

Figure 1.1: HIV Prevalence by State (source: ANC Survey Report, 2010)



The stabilizing of HIV prevalence is probably due to the massive scaling up of ART services, which has resulted in improved quality of life and reduced mortality among PLHIV. However, Nigeria has an estimated 3.4 million people living with HIV, second only to that in South Africa and approximately 54% of these individuals within the 15-64 years age range. In 2012, 388,864 new HIV infections were reported with approximately 217,148 AIDS related deaths in the same year. In this regard, Nigeria bears nearly 10% of the global burden of HIV/AIDS.

As the government's operational plan stresses a balanced approach that includes treatment and broad ranges of care and support activities for PLHIV- making full use of increasing access to ART and care interventions, Nigeria has made progress in increasing the number of people on ART from 51,000 in 2005 to 636,000 in 2013.

1.2.1 HIV Transmission

Heterosexual transmission accounts for the majority of HIV transmissions in Nigeria. The 2010 Mode of Transmission Study[1] reported that 34.6% of new HIV infections occur among couples considered as engaging in 'low-risk' sex, while 23% occur among most at risk populations (MARPs). More than a third of all new infections were linked to female sex workers, their clients and partners.

Most children less than 15 years living with HIV acquire the infection through mother-to-child transmission (MTCT). This can occur during pregnancy, labour and delivery or during breast-feeding. In the absence of interventions, the risk of such transmission is 15-45%.

1.2.2 Natural History of HIV

Adults and Children older than 5 years

The course of HIV infection varies within a population. Nonetheless, a typical infection can be divided into three stages: primary infection, asymptomatic infection, and symptomatic infection including AIDS. Following primary HIV infection, the CD4+ cell count decreases and the HIV RNA rises significantly. With sufficient exposure to viral antigens, cytotoxic T-lymphocyte responses are generated and the HIV viral load typically declines to an equilibrium known as a virologic "set-point," within 6 to 12 months of infection. Once this viral set-point is reached, the CD4+ cell count may rebound again marginally, although it does not often return to baseline values. Concurrent with these events are clinical manifestations of acute HIV infection in 30% to 60% of individuals. About half of newly infected people experience flu-like symptoms; the remainder are asymptomatic. Once infected, adults experience an asymptomatic clinical latency that lasts 2 to 10 years, during which HIV is produced and removed by the immune system and CD4+ T cells are killed and replaced. This latency period is considerably shorter in children. During this asymptomatic period, the number of infected circulating CD4+ cells and free virions is relatively low. Moreover, the hematopoietic system is able to replace most T cells that are destroyed, thus keeping the CD4+ cell counts in the normal range for adults and children >6 years (636-977 cells/µl).

A number of opportunistic infections, including recurrent oral candidiasis and tuberculosis are common during the early symptomatic phase of AIDS. As the CD4+ cell count declines to an even lower level, additional life-threatening opportunistic infections such as herpes zoster, amoebiasis, and dermatomycoses may occur with increasing frequency and severity. In the later stages of symptomatic HIV infection, the viral load levels rise again. Quantitative PCR methods (viral load assays), demonstrate:

- Continuous replication of HIV occurs in nearly all infected individuals, although the rates of virus production vary by as much as 70-fold in different individuals;
- The average half-life of an HIV infected cell in vivo is 2.1 days. Recent reports have suggested an even faster turnover of plasma virus of 28 to 110 per minute
- Up to 10^9–10^{10} HIV particles are produced each day; and averages of 2 x 10^9 CD4+ cells are produced each day.

HIV in Pregnancy

In pregnancy, immune function is suppressed in both HIV-infected and uninfected women. There is a decrease in immunoglobulin, reduced complement levels in early pregnancy and a more significant decrease in cell-mediated immunity. Studies have shown that pregnancy may however have no effect on the progression of HIV or on the rate of death. On the other hand, HIV infected women with pregnancies were more likely to develop early pregnancy complications such as bacterial pneumonia, urinary tract infections and other infections.

HIV infection has also been reported to have varying effect on pregnancy outcome or complications in Africans, and may reflect the extent of the epidemic and the nature of the HIV-related disease in different communities. These complications in early pregnancy include a higher rate of spontaneous abortion, higher rates of ectopic pregnancy and increased stillbirth rates, especially from areas where the epidemic has been present for a long time. The risk appears to be lower in asymptomatic HIV positive pregnant women.

On the whole, African women do not appear to experience more rapid progression of HIV disease during their pregnancies, despite the additional factors of multiple pregnancies, other infections and poor nutrition.

HIV infection in children under 5 years

There are critical differences between the disease progression in children and in adults. Stemming largely from the lower efficiency of a child's immature (but developing) immune system, these differences usually result in much more rapid disease progression and a much shorter duration for each stage.

At birth, viral load is usually very low but within the first 2 months of life it increases rapidly to values well above 100,000 copies/ml. Thereafter the viral load remains high until the age of 2 or 3 years after which it declines gradually to reach the viral load set point. These viral dynamics are significantly different from the rapid increase and decrease of the viral load seen in horizontally infected older children and adults.

In children, the higher viral load is associated with the somatic growth of the lymphatic system and the inability of their immature immune system to mount an HIV-specific response. When assessing the immune system in infants and children, it is very important to compare the child's CD4+ T-cell count with the age-appropriate values. Lymphocyte counts are very high in infancy and decline to adult levels around 6 years of age.

A higher mortality in HIV-infected children may result from inter-current infections, malnutrition, and lack of access to primary HIV care including delayed definitive diagnosis. With no interventions, the majority of children who acquired HIV perinatally develop HIV-related symptoms by 6 months of age.

Perinatally infected children fit into one of three categories:

- ***Category 1:*** Rapid progressors develop signs and symptoms of HIV and AIDS and die by age 1 year. These children are likely to have acquired the infection in utero or during the early perinatal period (about 25–30%)
- ***Category 2:*** Children develop symptoms early in life, followed by rapid deterioration and death by age 3 to 5 years (about 50–60%)
- ***Category 3:*** Long-term survivors live beyond age 8 years (about 5–25%)

Quantifying CD4+ cell is currently the most direct measurement of the HIV disease process. It is used to assess the risk of disease progression and viral load indicates response to antiretroviral therapy (ART). As the disease progresses, CD4+ cell count declines but may rebound if therapy is efficacious; this parameter alone is an incomplete marker for clinical assessment of a patient. Nevertheless, in resource poor settings, the CD4+ cell count is a more affordable and hence more widely available for monitoring disease progression and ART efficacy. Viral load is increasingly being recommended for monitoring ART efficacy.

CHAPTER TWO

DIAGNOSIS OF HIV INFECTION

2.1 HIV Counselling and Testing

Introduction

HIV Counselling and Testing (HCT) is universally acknowledged as the entry point to HIV prevention, treatment and care services, and also as a vital component of the strategy for expansion of access to comprehensive care for PLHIV.

The benefits of HCT are numerous. It is a strong weapon against stigma and discrimination, provides accurate information on HIV prevention, offers psycho-social support for the infected and affected, and links the infected to other care and support services. The benefits of HCT are dependent on the quality of service provided, it is therefore imperative that all persons and organizations that provide HCT services operate within acceptable standards.

Definitions

HIV COUNSELLING: Counselling, in relation to HIV and AIDS, is a confidential dialogue between a person and a caregiver aimed at enabling the person cope with stress, and make informed personal decisions relating to HIV and AIDS. It is an intervention that empowers an individual to make informed decision to take an HIV test to know his/her HIV status. The entire process must be voluntary and confidential.

HIV counselling and testing involves the following:

- Pre-test counselling/information
- HIV testing
- Post-test counselling
- Follow up counselling and referral for care and support

All forms of HIV counselling and testing should be voluntary and adhere to the five C's: consent, confidentiality, counselling, correct test results and connections to care, treatment and prevention services. Quality assurance of HIV counselling and testing is essential in all approaches to HIV counselling and testing.

HCT Service Delivery Models

The HCT service delivery models already in practice in the country incorporate both client-initiated and provider-initiated approaches:

Client-initiated approach is the traditional Voluntary Counselling and Testing (VCT) in which an individual voluntarily seeks counselling and testing services. This approach will continue to be offered in all HCT settings.

Provider-initiated Testing and Counselling (PITC) approach allows the health care provider to recommend HCT routinely to clients/patients as a standard component of medical care in the facility.

Two strategies commonly used in the Provider-initiated HCT approach are:

- **"Opt-out":** HIV test is routinely recommended to every patient and the patient is informed of his/her right to refuse the test
- **"Opt-in":** HIV test is recommended and offered to each patient and the patient explicitly consents to receive the HIV test.

Nigeria has adopted the opt-out strategy to boost access to HCT within selected clinical settings. The opt-out strategy is used as part of basic care for antenatal clinic clients, all patients with tuberculosis (TB), sexually transmitted infections (STIs) and HIV-related diseases.

HIV Counselling and Testing can be offered in many different settings, it can be offered as a stand-alone service in a facility, which does not necessarily have to be a health facility in which case persons who tests positive is referred to an ART offering facility. It can also be offered in a health facility as part of an integrated system for HIV service delivery and this is the most common setting for accessing HCT services. Finally HCT can be offered in mobile/outreach programmes as community based HCT services.

Community – based HIV counselling and testing

Community- based HCT approach complements the facility based HCT approach in the sense that it provides the opportunity to diagnose HIV and link people living with HIV to care in the early course of the infection. It can be provided in different settings including homes, transport stations, schools, workplace and venues frequented by key populations and as a result improves access to hard-to-reach populations that may not normally utilize health services. Hard to reach populations includes groups such as fishermen, nomads, women in purdah and residents of remote areas, highly mobile populations, long distance truck drivers, Intravenous Drug Users (IDU), Sex workers (SW), factory shift workers, displaced and confined people.

Community- based HCT uses different approaches such as stand-alone, mobile, door-to- door, special testing events and multi disease campaigns, workplace and school based HCT. Locations/premises at which outreach services are provided should meet the required national standards for quality HCT services.

2.1.1 HIV Testing and Counselling for PMTCT

An important entry-point for PMTCT services is HIV testing of pregnant women at the earliest opportunity; during antenatal care, labour and delivery. In all settings, HIV testing and counselling (HTC) should be offered to all pregnant women seeking antenatal care, and service providers should promote strategies to mobilize pregnant women and other women of reproductive age for testing and counselling wherever these services are available, including family planning clinics, community and home-based testing.

Approach to HIV Testing in Pregnant Women

HIV testing of pregnant women should be accompanied by culturally acceptable counselling that covers the benefits of knowing ones HIV status and its implications for the health of the mother, the pregnancy and the unborn child. The elements of effective counselling are confidentiality, timeliness, acceptance, accessibility, consistency and accuracy.

The recommended approach to testing and counselling is the routine approach (also referred to as the PITC "opt-out" approach) where HIV testing is offered as part of routine tests in antenatal clinics, the woman has the right to refuse taking the test. Mandatory testing is not recommended.

Essential Components of Testing and Counselling for PMTCT
These include:

- Pre-test information
- HIV testing with same day result
- Post-test counselling
- Follow-up counselling.

Women should be encouraged to start antenatal care early (from 14 weeks of pregnancy) and HIV testing and counselling should be conducted during the first ANC visit

HIV testing and counselling for women in labour

HIV testing in labour should be recommended for all women of unknown HIV status including those who tested negative during pregnancy. This is because some women might not have registered in the antenatal clinic and are presenting for the first time in labour. Such women should be offered the opt-out approach and given appropriate post-test counselling in the post-partum period or pre-test counselling if she had declined the test. The following steps should be taken:

- Determine HIV test history
- Discuss the benefits of testing and ARV prophylaxis
- Explain the testing process
- Offer the test.

If the above is not feasible at the time the woman presents, steps should be taken to offer the test as soon as possible after delivery.

Other Components of HIV Counselling in PMTCT

• Couple counselling and partner notification

Couple HIV counselling and testing has emerged as an important intervention aimed at preventing the transmission of HIV among sex partners in sub-Saharan Africa. Counsellors should assist couples by:

- Providing clear and accurate prevention messages;
- Mitigating tension and diffusing blame
- Dispelling myths
- Providing tailored HIV prevention messages based on the couple's life style.

All pregnant women should be encouraged to come along with their partners for ANC visits. Couple counselling should always be offered in ANC clinic to couples who attend the clinic together and have unknown HIV status. Partner invitation slips/letters can be used to invite partners to next ANC visit or HIV testing services elsewhere. Couple counselling and testing helps:

- To address the challenges associated with disclosure
- To reduce HIV transmission from one partner to the other
- Take appropriate decisions about sexual behaviour and act on those decisions.
- Create supportive environment for children in the home that may require HCT

Where couples are reluctant to be tested together or men are reluctant to test with their partners, provisions can be made for them to be counselled and given their results separately and then encouraged to disclose results to each other. Partner testing should be adapted to existing services in the facility and can take place either in the ANC or the HCT centre.

Partner notification helps:

- To make choices around infant feeding practices easier and provide family support for care of exposed infants, including administration of infant prophylaxis
- The infected partner access health care earlier
- Offers the partner opportunity to provide other psychosocial support necessary for adherence to therapy, clinic appointments, family planning etc.

Significant others refer to other family members or relatives that some women may wish to involve for important supportive roles.

- **Sharing HIV Status with health care providers**

For a pregnant woman to benefit from MTCT interventions, it is important that other health care providers are aware of her HIV status on a 'need to know basis'. The patient should be counselled on the benefits of such shared confidentiality and be assured that it would not result in stigma and discrimination against her.

Benefits of HCT for the individual include:

- Improved health through educational and nutritional advice;
- Early access to care (including ART) and prevention of HIV-related illnesses
- Emotional support and improved ability to cope with HIV-related anxiety
- Awareness of safer options for reproduction and infant-feeding, need for infant testing and prophylaxis
- Motivation to initiate or maintain reduced risky behaviours

All seropositive individuals from stand-alone, mobile, and primary facilities should be referred to appropriate health facilities for enrolment into care and assessment for ART.

2.1.2 HIV Testing and Counselling in Children

HIV counselling and Testing in children presents special challenges for counsellors for obvious reasons and depending on the age of the child considerable reliance on care givers including parents and non-parental care givers to achieve the primary objectives of HCT.

These steps taken in providing HCT vary depending on HIV status and age of patient:

In the Child with unknown HIV status presenting with clinical signs suggestive of HIV infection and/or has risk factors such as mother/sibling with HIV/AIDS

- Ascertain child's and/or mother's or caregiver's understanding of HIV infection in general and, more specifically, MTCT
- Discuss presumptive diagnosis of HIV in light of existing signs, symptoms, and risk factors
- Explain the benefits of early awareness of HIV infection in the child's life and for the family
- Counsel and test child/parents to determine their HIV infection status
- If parents decline testing or decide to postpone the test, accept their decision and reassure them that while their refusal will not compromise the management of the child's current illness, they and the health workers may be missing the opportunity to plan for the child's optimum care if the child is HIV infected.

In Child known to be HIV positive and responding poorly to treatment

- Ascertain child's and/or mother's or caregiver's understanding of HIV infection
- Discuss the management of current problems and the reasons for poor response to treatment
- Ascertain adherence to ARV therapy
- Refer child to a higher level of care for further investigations
- Discuss psychological implications of HIV for child, mother, father, and other family members
- Provide on-going psychosocial support on coping with a chronic illness such as HIV.

In Child known to be HIV infected and responding well to treatment

- Discuss follow-up, care, and risk factors for future illness.
- Discuss shared confidentiality and the social well being of the child and the family.

2.2 Laboratory Diagnosis of HIV Infection

Laboratory diagnosis of HIV infection is based on the demonstration of antibodies in plasma or serum (indirect testing) or of virus in the blood (direct testing). With the technology that is available at present, HIV antibodies are detectable within four to six weeks of infection, and within 24 weeks in virtually all infected individuals. The virus can be demonstrated in the blood with nucleic acid-based tests (PCR for proviral DNA and RTPCR for plasma viral RNA), culture and p24 antigen assay.

Antibody Assays

The antibody assays that are used for HIV diagnosis consist of screening tests: rapid tests or ELISA, and confirmatory tests: Western blot and Indirect immunofluorescent assay. Routine antibody testing is performed with the serial or parallel testing algorithms using rapid or ELISA test kits.

HIV Rapid Testing Algorithm

There are two HIV testing algorithms that have been used by government in recent times and they are the serial and the parallel testing algorithms. However, the recommended algorithm for routine use is the serial HIV testing algorithm. Rapid HIV test kits currently recommended for use in Nigeria include: Determine, Unigold, Stat Pak and Double-check gold.

Serial testing

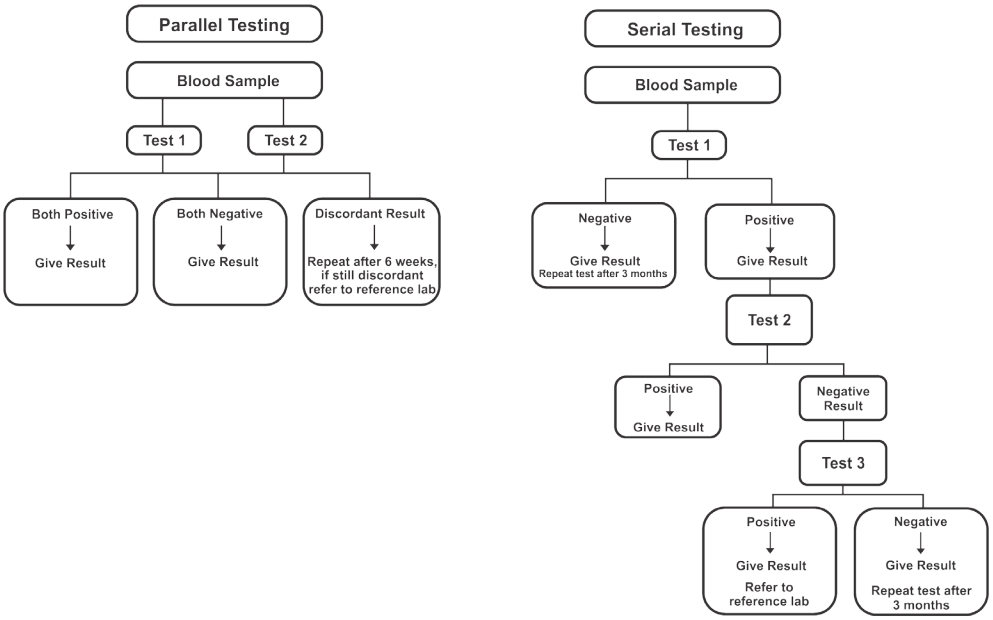
This refers to the use of 2 screening tests employed sequentially to test for HIV antibody. If the initial screening is negative, no further testing is required. If the initial test is positive, it is followed by one more test. The first test should be the most sensitive test and the second test should be very specific, and be based on an antigen source different from that of the first test.

Samples that produce discordant results in the two tests are subjected to further testing.

Parallel testing

This involves the use of two screening tests performed simultaneously. Samples reactive to both tests are regarded as positive. However, those with discordant results require further testing. Main advantage of parallel testing over serial testing is that it minimises overall testing time and the incidence of false negative results. The serial and parallel testing algorithms are illustrated below:

Figure 2.1 Parallel vs. Serial Testing Algorithms



Nucleic acidbased tests

These consist of DNA Polymerase Chain Reaction (DNA PCR) and Reverse Transcriptase Polymerase Chain Reaction (RT-PCR). These tests are not routinely used for laboratory diagnosis of HIV infection in adults and adolescents.

- **HIV DNA Polymerase Chain Reaction**

The DNA PCR involves the amplification of specific DNA sequences in the proviral DNA that has been integrated in the host cell. This test is the preferred procedure for diagnosing or confirming HIV infection in infants less than 18 months of age. Because of the high sensitivity of the test, false positive results may occur as a result of contamination or due to improper specimen handling. There is need therefore to always conduct confirmatory testing using a separate specimen.

- **Reverse Transcriptase Polymerase Chain Reaction (RT PCR)**

RTPCR is used to detect and quantify the amount of HIV RNA in plasma. The assay requires the conversion of viral RNA to DNA and amplification of specific sequences in the DNA produced by a process known as reverse transcriptase polymerase chain reaction (RTPCR).

2.2.1 Laboratory Diagnosis of HIV Infection in Children by Age Group

Age < 18 months (Infants)

- Children <18 months old may have circulating maternal antibodies. A positive antibody test may be the result of HIV antibodies from the child and/or the mother; in this case, DNA or RNA PCR is the test of choice as this provides a definitive diagnosis of HIV infection.
- Rapid test can be used to screen any infant for HIV exposure. However a positive result in an infant <18 months does not confirm infection and should be confirmed using DNA PCR.
- All HIV–exposed infants should have initial DNA PCR testing at 4-6 weeks of age (or earliest opportunity thereafter) and 6 weeks after complete cessation of breastfeeding.
- Infant DNA PCR test results should be returned to the clinic and caregiver as soon as possible; latest within four weeks of specimen collection.
- Infants between 9 and 18 months, should first have a rapid test and if positive, DNA PCR done as confirmation.
- If a screening Ab test is negative, HIV-infection is ruled out if the test has been conducted at least 6 weeks after complete cessation of breastfeeding
- For sick infants <18 months in whom HIV infection is being considered, in the absence of virological tests, HIV serological testing (rapid HIV tests) and use of the algorithm for presumptive clinical diagnosis is recommended.

Age ≥18 months

Antibody detection is useful and reliable for children ≥18 months. The exception is during the window period (4-6 weeks post-exposure) where antibodies may not be present at a detectable level.

- For children testing negative, repeat antibody testing 3 months later is recommended if window period is suspected.
- From 18 months of life, an antibody test should be performed irrespective of whether a child received breast milk or replacement feeds.
- If the child is receiving breast milk after 18 months of age, repeat the test 6 weeks after complete cessation.
- Methods such as DNA/RNA PCR could be used to resolve suspected false negative results.

2.3 Clinical Diagnosis and Staging of HIV Infection

The WHO clinical staging of HIV for adults and adolescents that are HIV positive is as shown in Tables 2.2 and 2.3. Staging is based on the patient's clinical presentation at the time of initial assessment with the healthcare provider. The most advanced symptoms at the time of evaluation represent the initial clinical stage of HIV infection. Clinical staging guides the decision on when to start ART or cotrimoxazole prophylaxis.

Table 2.1 WHO Clinical Classification of Established HIV Infection

HIV-Associated Symptomatology	WHO Clinical Stage
Asymptomatic	1
Mild Symptoms	2
Advanced Symptoms	3
Severe Symptoms	4

Table 2.2: WHO Clinical Staging of HIV/AIDS for Adults, adolescents and children

Adults and Adolescents	Children
Clinical Stage 1	
• Asymptomatic • Persistent generalized lymphadenopathy • Performance scale 1: asymptomatic, normal activity	• Asymptomatic • Persistent generalized lymphadenopathy • Performance scale 1: asymptomatic, normal activity
Clinical Stage 2	
• Weight loss, <10% of body weight • Minor mucocutaneous manifestations (seborrhoeic dermatitis, fungal nail infections, recurrent oral ulcerations and angular chelitis) • Herpes zoster within the last five years • Recurrent upper respiratory tract infection (i.e. bacterial sinusitis) • And/or performance scale 2: symptomatic, normal activity	• Unexplained persistent hepatosplenomegaly • Papular pruritic eruptions • Extensive wart virus infection • Extensive molluscum contagiosum • Recurrent oral ulcerations • Unexplained persistent parotid enlargement • Linear gingival erythema • Herpes zoster • Recurrent/chronic upper respiratory tract infection (otitis media, otorrhoea, sinusitis, tonsillitis) • Fungal nail infections • And/or performance scale 2: symptomatic, normal activity

Adults and Adolescents	Children
Clinical Stage 3	
• Weight loss > 10% of body weight • Unexplained chronic diarrhoea> 1 month • Unexplained persistent fever (Continuous or intermittent for longer than 1 month) • Oral candidiasis (thrush) • Oral hairy leukoplakia • Pulmonary tuberculosis within the past year • Severe bacterial infections (i.e. pneumonia, pyomyositis) And/or performance scale 3: bedridden <50% of the day during last month • Acute necrotizing ulcerative stomatitis, gingivitis, or periodontitis • Unexplained anaemia (below 8 g per dl), neutropaenia and chronic thrombocytopaenia.	• Unexplained moderate malnutrition[a], no response to therapy • Unexplained persistent diarrhoea (14 days or more) • Unexplained persistent fever (>37.5° C, intermittent/ constant, >1 month) • Persistent oral candidiasis (after 1st 6 weeks of life) • Oral hairy leukoplakia • Acute necrotizing ulcerative gingivitis/periodontitis • Lymph node TB • Pulmonary TB • Severe recurrent bacterial pneumonia • Symptomatic lymphoid interstitial pneumonitis • Chronic HIV-associated lung disease including bronchiectasis • Unexplained anaemia (Hb <8.0 g/dl), neutropenia: (neutrophils <0.5 x 109/l3) • Chronic thrombocytopenia (platelet count <50 x 109/l3)
Clinical Stage 4	
• HIV wasting syndrome • Pneumocystis Jirovecii Pneumonia (PCP) • Toxoplasmosis of the Central Nervous System • Cryptococcus, extrapulmonary • Cytomegalovirus disease of an organ other than liver, spleen or lymph node e.g retinitis • Herpes simplex virus infection, mucocutaneous (>1 month) or visceral • Progressive multifocal leucoencephalopathy • Any disseminated endemic mycosis • Candidiasis of esophagus, trachea and bronchi • Lymphoma • Kaposi's sarcoma • HIV encephalopathy • Extrapulmonary tuberculosis and/or perfomance scale 4: bedridden>50% of the day during last month • Atypical disseminated leishmaniasis • Disseminated non-tuberculous mycobacterial infection • Chronic cryptosporidiosis • Chronic isosporiasis • Recurrent septicaemia • Invasive cervical carcinoma.	• Unexplained severe wasting, stunting[b] or severe malnutrition not responding to standard therapy • Pneumocystis pneumonia • Recurrent severe bacterial infections (e.g. empyema, pyomyositis, bone or joint infection but excluding pneumonia) • Chronic Herpes simplex infection (oro-labial or cutaneous of >1 month, or visceral at any site) • Extra-pulmonary TB • Kaposi's sarcoma • Oesophageal candidiasis (or candida of trachea, bronchi or lungs) • Central nervous system toxoplasmosis (after the neonatal period) • HIV encephalopathy • CMV infection; retinitis or infection affecting another organ with onset >1 month) • Extra-pulmonary cryptococcosis (including meningitis) • Disseminated endemic mycosis (extra-pulmonary • histoplasmosis, coccidiomycosis) • Chronic cryptosporidiosis (with diarrhoea) • Chronic isosporidiasis • Disseminated non-tuberculous mycobacterial infection • Cerebral or B-cell non-Hodgkin lymphoma • Progressive multifocal leukoencephalopathy • HIV-associated cardiomyopathy or nephropathy • HIV-associated recto-vaginal fistula.

Adults and Adolescents	Children
*Assessment of body weight in pregnant women need to consider expected weight gain of pregnancy *Unexpected refer to those conditions whose presence is not explained by other conditions	[a] For children younger than 5 years, moderate malnutrition is defined as weight-for-height <–2 z-score or mid-upper arm circumference ≥115 mm to <125 mm. [b.] For children younger than 5 years of age, severe wasting is defined as weight-for-height <–3 z-score; stunting is defined as length-for-age/height-for-age <–2 z-score; and severe acute malnutrition is defined as either weight for height <–3 z-score or mid-upper arm circumference <115 mm or the presence of oedema.

CHAPTER THREE

ANTIRETROVIRAL THERAPY

3.1 Goals of Antiretroviral Therapy

Antiretroviral Therapy (ART) is the gold standard for the management of HIV infection and all persons who are eligible should be commenced on ART as soon as possible. ART should be offered in a comprehensive manner, which means that HIV positive should have access to on-going adherence counselling, baseline and routine/periodic laboratory investigation, prevention and management of OIs, routine treatment monitoring and follow-up.

When properly administered, ART should achieve the following goals;

- **Reduce morbidity (includes morbidity from OIs) and Prolong life of HIV infected individuals**

Optimal ART leads to rapid improvement of clinical indices, pre-existing OIs are more amenable to antimicrobial agents and patients become less susceptible to new infections. Prior to the advent of ARVs, mortality rates due to advanced HIV disease was unacceptably high nearing 100% in most cases. However, following the introduction of HAART, many more people live long and productive lives.

- **Improve quality of life of infected persons**

The absence of symptomatic HIV and HIV-related illness means that persons infected with HIV are able to carry on a normal existence and fend for themselves and their families unlike in the past when they were largely bedridden and dependent on others for support.

- **Achieve rapid and sustained suppression of viral load**

Under optimal conditions, administration of ART should lead to rapid and sustained suppression of viral load. Usually by week 24 following initiation of treatment, patient's viral load should be at the least < 400 copies /ml. Rapid and sustained viral load suppression is necessary to prevent or delay the development of ARV drug resistance and allow for restoration of CD4 cells. The ideal is sustained viral suppression at 50cells/ml for as long as possible to halt, prevent or delay disease progression.

- **Enhance immunity by increasing CD4+ cell count**

Potent and effective ART leads to an increase in CD4 cells and recovery of immune functions. Under optimal conditions patients should be able to achieve a CD4 cell count increase of 50 to 100 cells/ml / year.

- **Reduce risk of transmission of HIV to infants (mother to child transmission) and sexual partners**

ART is effective in reducing transmission of HIV from a positive person to an uninfected person. When used as prophylaxis in an infected pregnant woman, it leads to a markedly significant reduction in mother to child transmission of the virus.

3.2 Antiretroviral Drugs

There are 6 classes of ARV drugs currently available for treatment based on the site and mechanism of drug action. Pharmaceutical research has enabled the development of various Fixed Dose Combinations (FDCs) of ARV drugs for adult and dispersible FDCs for paediatrics. These formulations are generally more convenient to use and have significantly enhanced the adherence to ART.

Strength and dosing of ARV drugs in Children

Doses of most paediatric drugs are expressed per kilogram or per square meter of body surface area. However for simplification and ease of implementation, a simplified dosing schedule whereby doses are expressed per weight-band has been adopted. When the simplified weight-band dosing was developed, careful consideration was given to the usual body surface area of children from low and middle-income countries in that weight band. Dispersible tablets (or tablets for oral solution) are the preferred solid oral dosage forms, since each dispersible tablet can be made into liquid at the point of use.

3.3 Initiation of ART in Adults and Adolescents

Early initiation of ART is associated with significant benefits for the patient and the community and this has been linked to improved survival and reduction of the incidence of HIV infection at the community level.

3.3.1 Evaluation for ART in Adults and Adolescents

Baseline Assessment

The baseline assessment and preparation of patients for ART should include:

- Capturing documented evidence of a positive HIV test result
- Completing history and physical examination (assessment of weight, height, renal diseases, cardiovascular diseases, pregnancy, anaemia, STI, prior ART use - including single dose nevirapine and drug misuse – e.g. heroine, alcohol, etc. should be documented). Social and sexual history should also be considered especially for adolescents
- Screening for symptoms of TB and Hepatitis (B and C) should be done in addition to diagnostic testing for persons with symptoms. For TB, Gene Xpert MTB/Rif should be used where available for symptomatic cases.
- Determination of nutritional, psychosocial, growth and immunization status of clients (including determination of BMI for adults)
- Sundry physical examinations including rectal and vaginal examination (including Inspection with Acetic Acid- VIA or/and PAP smear where possible)
- Determination of WHO clinical stage of disease in both adults and adolescents
- Conducting baseline laboratory assessments (See Table 4.1).
- Assessment of patient's readiness for therapy
- Development of patient-specific adherence strategy

3.3.2 Pre-ART Care for Adults and Adolescents

HIV positive adolescents and adults who are not yet eligible for ART initiation should be enrolled for pre-ART care. Pre-ART care should include:

- On-going counselling and education of clients to promote retention in care and positive health dignity and prevention (PHDP)
- Periodic clinical and laboratory evaluation that include:
- Six monthly CD4+ cell estimation (see Chapter Four)
- WHO staging, TB screening and overall co-morbidities/opportunistic infection screening at each visit
- Pregnancy assessment and family planning counselling and services, where required
- Provision of Cotrimoxazole and Isoniazid prophylaxis for eligible individuals

3.3.3 Criteria for Initiating ART in Adults and Adolescents

All HIV+ individuals with a CD4+ cell count less than 500cells/mm³ are eligible for ART and should receive ART irrespective of clinical symptoms. Such persons should be commenced on treatment as soon as necessary laboratory and clinical assessments have been carried out and the person is deemed ready to receive ART. While CD4+ cell count <500/mm³ is the critical set point for initiating ART, priority consideration should be given to clients with CD4+ cell count <350 cells/mm³.

All HIV+ individuals with WHO HIV clinical stage 3 and 4 are eligible for ART irrespective of the CD4+ cell count and should commence ART with minimum delay.

ART is indicated in persons with certain co-infection and co-morbidities irrespective of CD4+ cell count and clinical staging and these include persons co-infected with TB, HBV or HCV and persons with HIV-related nephropathy. The use of ART in discordant couples is not recommended routinely but may be considered only in very special situations.

Table 3.1 When to Start ART in adults and adolescents (including pregnant women)

Target population	Recommendation
Severe/advanced HIV infection (WHO clinical stage 3 or 4)	Initiate ART in all individuals regardless of CD4+ cell count
HIV infection (WHO clinical stage 1 or 2)	Initiate ART if CD4 ≤500 cells/mm³
TB disease	Initiate ART in all individuals with active TB disease regardless of CD4 cell count*
Hepatitis B co-infection	Initiate ART in all individuals regardless of CD4 cell count in the presence of severe chronic liver disease**
HIV-associated nephropathy	Initiate ART if CD4 ≤500 cells/ mm³. Consider ART in persons with CD4+ >500 cell/mm³
HIV-sero-discordant couples	Consider ART in sero-discordant couples

** In patients with dual TB/HIV disease TB treatment should be initiated first, followed by ART as soon as possible thereafter (and within the first eight weeks of initiating TB treatment). For those with a CD4 count less than 500 cells/mm3, ART should be provided within two weeks of starting TB treatment.*

***Severe chronic liver disease includes cirrhosis and end-stage liver disease and is categorized into compensated and decompensated stages.*

Decompensated cirrhosis is defined by the development of clinically evident complications of portal hypertension (ascites, variceal haemorrhage and hepatic encephalopathy) or liver insufficiency (jaundice).

3.3.4 Criteria for Initiation of ART in children

Early initiation of ART in HIV infected infants and children, reduces morbidity and mortality associated with the rapid disease progression in this age group and helps maintain normal growth and development. Treatment of children infected with HIV in the perinatal period should anticipate prior exposure to ARV drugs through the mother either as a result of ARV prophylaxis for PMTCT or ART for her own health. It is important to identify a primary or secondary caregiver who understands the disease and importance of adherence to ART to provide support in the care of the child.

Table 3.2: Criteria for initiating ART in children and non-pregnant adolescents up to 15 Years Old

Population	Recommendation
Adolescents (10-15 years) Children (5-10 years)	Initiate ART if CD4 cell count ≤500 cells/mm^3 or WHO clinical stage 3 or 4
	Initiate ART regardless of WHO clinical stage and CD4 cell count for those with: • Active TB • HBV co-infection + severe chronic liver disease • WHO clinical stage 3 or 4
Children (<5 years old)	Initiate ART in all regardless of WHO clinical stage and/or CD4 cell count

3.4 Recommended First Line ART Regimen for Adolescents and Adults

It is recommended that combinations of three drugs from at least two different classes of ARV be used to act on at least two different points or mechanisms in the HIV life cycle.

Typically, a backbone of an NNRTI or a PI can be combined with 2 NRTIs. The recommendations are based on availability, accessibility, affordability, efficacy and ease of administration of antiretroviral drugs. Monotherapy or dual therapy is not recommended for treatment because of the increased risks of development of drug resistance.

Patients should fulfill the criteria for readiness to commence ART before commencing treatment and this includes willingness to adhere fully to treatment.

Table 3.3 Recommended first line ARV regimens for ART naive adults

First-Line ART	Preferred first-line Regimens	Alternative first-line regimens
Adults (including pregnant and breastfeeding women and adults with TB disease and HBV co-infection)	TDF + 3TC + EFV	AZT + 3TC + NVP AZT + 3TC +EFV ABC + 3TC + EFV
Adolescents (10 to 19 years) ≥35 kg		AZT + 3TC + NVP AZT + 3TC + EFV ABC + AZT + 3TC

TDF based regimen should be used with extreme caution in individuals with hypertension, diabetes, existing or evidence of chronic kidney disease. AZT should be avoided in individuals with severe anaemia (<8g/dl). Where TDF and AZT are contraindicated as in chronic kidney disease the use of ABC based regimen is recommended. However provision should be made for dose adjustment of 3TC in cases of renal impairment. In very special situations, triple nucleoside regimens (AZT+3TC+ABC) may be considered.

- All women receiving NVP containing ART regimens should be closely monitored for symptoms and signs of hepatic toxicity such as skin rash and elevations in serum transaminases.
- Efavirenz (EFV) is recommended as the preferred option for a non-nucleoside reverse transcriptase inhibitor in optimized first-line antiretroviral regimens. Review of the available data and programmatic experience provides reassurance that exposure to EFV in early pregnancy has not resulted in increased birth defects or other significant toxicities as previously suspected.
- This guideline recommends the phasing out of stavudine (d4t) regimen. However, it is permissible to continue use of stavudine in the occasional client for whom no safe alternative drug can be found.
- In suspected cases of renal impairment dosage modifications are recommended for many ARV drugs:
  - If Creatinine Clearance (CrCl) is elevated at baseline
  - If at any time CrCl is above baseline,
- Patients with elevations in CrCl should:
  - Undergo an evaluation for potential causes of decreased renal function.
  - Have serum creatinine monitored more frequently until resolution of renal insufficiency or failure.

The administration of ART in the presence of renal failure should be done in consultation with a qualified physician.

Table 3.4. First Line ARV Regimens for Children

Age Group	Considerations	Preferred 1st line regimen	Alternative 1st line regimens (in order of preference)
0 to 36 months (0-3 years)	With no prior exposure to NNRTIs	AZT + 3TC + NVP	ABC + 3TC + NVP AZT+ 3TC+ ABC ++
	With prior exposure to NNRTIs (through PMTCT)	AZT + 3TC + LPV/r**	ABC + 3TC + LPV/r
	With unknown exposure to NNRTIs	AZT + 3TC + NVP NB: Closely monitor for treatment failure	AZT + 3TC + EFV ABC + AZT + 3TC D4T + 3TC + EFV
3 to 10 years	Regardless of NNRTI exposure	AZT+3TC+EFV***	AZT + 3TC + NVP ABC + AZT + 3TC D4T + 3TC + EFV
Special Circumstances	Severe Anaemia/ Neutropenia	AZT should not be used in persons with Hb <8g/dl	
	HBV in children >3 years	TDF+ 3TC + EFV*** (or NVP)	
	TB in children	See TB treatment	

**** EFV is only indicated for use in children >3 years of age and >10kg.*

++ In case of ABC hypersensitivity reactions, do not ever re-use in patient

Triple NRTI therapy (i.e. ABC + AZT + 3TC) is suboptimal and should only be used if there is absolutely no alternative

Table 3.5 Recommendations for ART in HIV+ Children with active TB

Considerations	Time of initiation of ART[a]	Preferred ART regimen
Active TB diagnosed, not yet on HAART	Start anti-TB treatment* Start ART 2 to 8 weeks after commencing anti-TB treatment	Children <3 years and PMTCT exposure to NNRTI Use Triple NRTI (AZT + 3TC + ABC) Children < 3 years and no PMTCT exposure to NNRTI Initiate NVP-based regimen and increase NVP dose to 200 mg/m^2 per day, OR Triple NRTI (AZT + 3TC + ABC) Children >3 years: Standard 1st line AZT + 3TC + EFV[e] is preferred. Consider 1st line alternatives if preferred regimen not applicable.
Active TB diagnosed, already on HAART	If <3 years and on NVP-based regimen	Continue regimen but increase NVP to maximum dose (200mg/m^2/day)
	If >3 years and on NVP-based regimen	Substitute: Replace NVP with EFV
	If on LPV/r based regimen	Increase dose of Ritonavir to make 1:1 ratio with LPV

[a] *Administration of CPT is important in children with TB/HIV co-infection.*

** Regimen assumed to contain Rifampin*

[c] *Careful clinical monitoring with lab support, is recommended where NVP is used with rifampicin. This combination should only be used if there are no other options*

[e] *EFV is not currently recommended for children <3 years of age.*

3.5 Management of HIV Treatment Failure

Definition of Treatment Failure

ARV treatment failure may be defined as sub-optimal treatment outcomes following initiation of ART. It can be classified as;

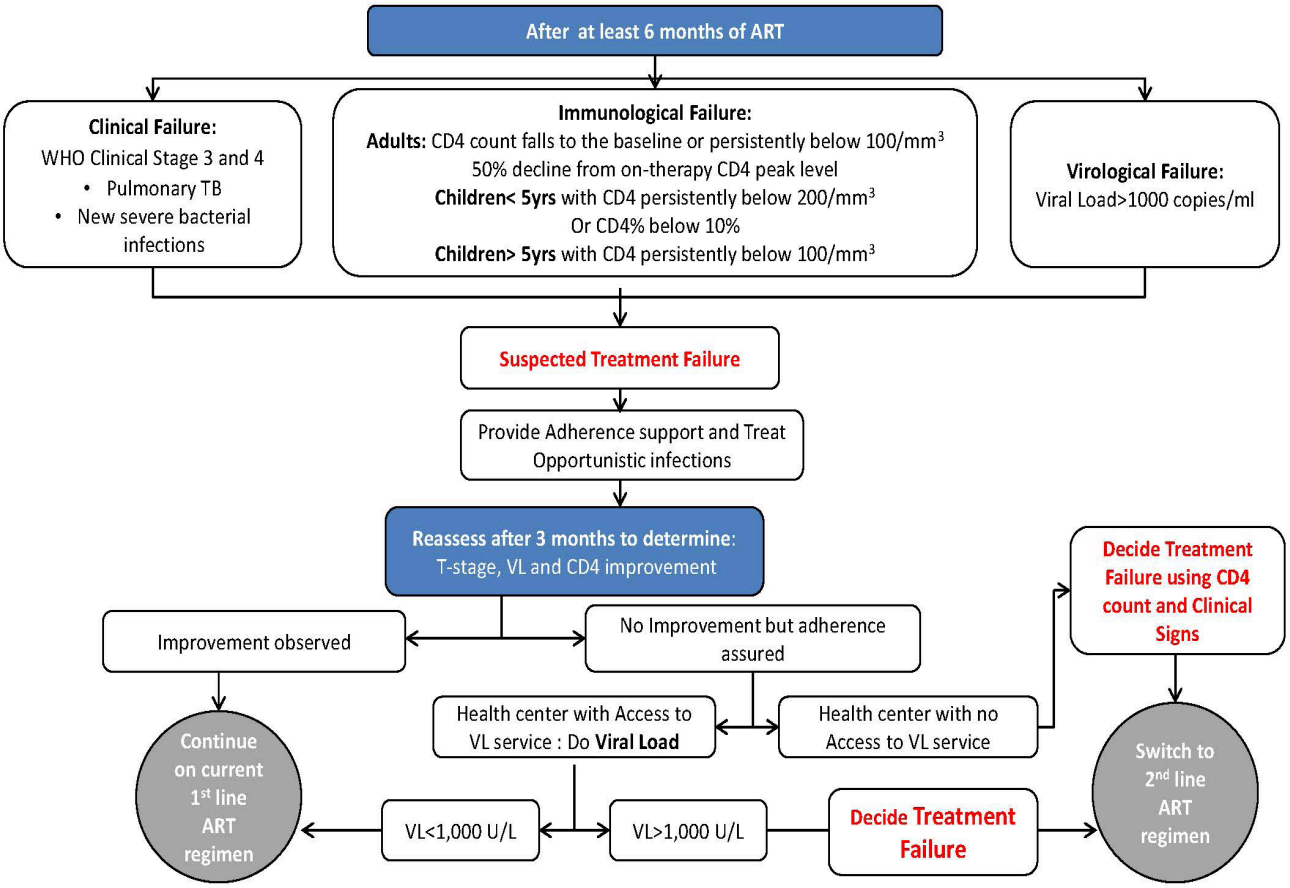
- Virologic failure
- Immunologic failure
- Clinical failure

Table 3.6: Definition of Clinical Failure

Failure	Definition	Comments
Clinical Failure	**Adults and adolescents** New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 condition) after 6 months of effective treatment. **Children** New or recurrent clinical event indicating advanced or severe immunodeficiency (WHO clinical stage 3 and 4 clinical condition with exception of TB) after 6 months of effective treatment	The condition must be differentiated from Immune Reconstitution Inflammatory Syndrome occurring after initiating ART For adults, certain WHO clinical stage 3 conditions (pulmonary TB and severe bacterial infections) may also indicate treatment failure
Immunological failure	**Adults and adolescents** CD4 count falls to the baseline (or below) Or Persistent CD4 levels below 100 cells/mm^3 50% decline from on-therapy CD4 cell peak level **Children** **Younger than 5 years** Persistent CD4 levels below 200 cells/mm^3 or <10% **Older than 5 years** Persistent CD4 levels below 100 cells/mm^3	Without concomitant or recent infection to cause a transient decline in the CD4 cell count A systematic review found that current WHO clinical and immunological criteria have low sensitivity and positive predictive value for identifying individuals with virological failure. The predictive value would be expected to be even lower with earlier ART initiation and treatment failure at higher CD4 cell counts.
Virological Failure	Plasma viral load above 1000 copies/ml based on two consecutive viral load measurements after 3 months, with adherence support	The optimal threshold for defining virological failure and the need for switching ART regimen has not been determined. An individual must be taking ART for at least 6 months before it can be determined that a regimen has failed Assessment of viral load using DBS and point-of-care technologies should use a higher threshold* Blips are a transient increase in viral load between 50 and 1,000 copies/ml and can occur during periods of inter-current infections.

**There is currently no global consensus on threshold to define treatment failure; on-going validation studies to establish an acceptable threshold.*

Figure 3.1: Algorithm for Treatment Failure Evaluation in Adults, Adolescents and Children



3.5.2 Causes of Treatment Failure

Viral factors

- Acquired drug resistance. Patients may develop drug resistance mutations while on ART if maximal adherence (>95%) is not maintained.
- Transmitted drug resistance. Patients may be infected with drug resistance virus during their initial exposure or be re-infected with drug resistant virus from risky exposures while on ART.

Non-viral Factors

Treatment failure may result when ARV drug levels do not reach therapeutic concentration.

This may be due to:

- Host factors -poor adherence, malnutrition and malabsorption,
- Choice of initial ART regimen – poor potency or improper dosing
- Drug-drug Interactions

3.5.3 Substitution and switch of ARV drugs

Substitution is the replacement of one or two ARV drugs in a regimen with another drug within the same class usually because of the following;

- Toxicity/ adverse drug reactions
- Co-morbidity
- Pregnancy
- Drug interaction

Switching is the replacement of two or more ARV drugs in a regimen with other drugs, including drugs of a different class due to treatment failure. Switching can also be referred to as changing a patient from a first line regimen to a second line regimen or from a second line regimen to third line or salvage regimen.

3.6 Second line ART regimen

Second-line ART regimens refer to combination of antiretroviral drugs reserved for persons on who have failed treatment on a first line regimen. Second line regimens recommended by these guidelines consist of nucleoside reverse transcriptase inhibitors and a ritonavir-boosted protease inhibitor (PI).

The protease inhibitors recommended are Atazanavir and Lopinavir and the choice of NRTI will depend on the combination of NRTI utilized in the failing first line regimen.

Table 3.7: Preferred Second line ART regimen

Target Population		Preferred Options
Adults and adolescents (including pregnant women)	If TDF used in first-line therapy	AZT + 3TC + ATV/r or AZT + 3TC + LPV/r
	If AZT is used in first-line therapy	TDF + 3TC + ATV/r or TDF + 3TC + LPV/r
TB/HIV coinfection	*Rifabutin should replace Rifampicin.	Same regimens as recommended above for adults and adolescents, where rifabutin is not available, double-dose LPV/r (that is, LPV/r 800 mg/200 mg twice daily)
Hepatitis B coinfection		AZT + TDF + 3TC + ATV/r or LPVr
Paediatric**		ABC+3TC+LPV/r AZT+3TC+LPR/r TDF+3TC+ATV/r (for patients >6 years)

**When used with ATV/r or LPVr, Rifabutin should be dosed at 150mg qod or 3x/week*

***Choice of second line also depends on first line NRTI backbone (as in adults)*

3.7 Third line Therapy

Third line therapy refers to the ART offered to PLHIV in response to failure of second line treatment. The choice of third line therapy is more difficult if genotype or phenotype resistance testing is not readily available. In the event of treatment failure on 2nd line ART, a comprehensive evaluation (including adherence assessment) to ascertain the cause of failure should be conducted.

It is important to note that patients failing a PI/r based regimen may have no PI resistance mutations in which case failure can be secondary to non-adherence. Effort must be made to assess and optimize adherence and rule out any significant drug interactions. When this has been done and there is still evidence of failure, patients would benefit from specialist care.

The recommendation is that the switch to third line therapy be left in the hands of highly qualified HIV specialists with experience and expertise in the management of advanced and complicated HIV disease.

Consideration for third line

Targeted literature review of relevant studies provides limited evidence to guide third-line strategies in resource-limited settings, with few studies of newer agents in these settings. Data from randomized controlled trials (RCTs), predominantly in developed countries, are available for boosted darunavir (DRV/r), etravirine and raltegravir. Third-line regimens should include new drugs with minimal risk of cross-resistance to previously used regimens, such as integrase inhibitors and second-generation NNRTIs and PIs. The following combination should be considered for third line therapy:

- Raltegravir/boosted Darunavir/Etravirine, adjusted according to scoring chart.
- Plus Optimized NRTI (dependent on genotype findings)

CHAPTER FOUR

ART MONITORING AND FOLLOW-UP

ART Monitoring and Follow-Up in Adults

Adequate monitoring of individuals receiving ART is critical in ensuring successful treatment, optimal retention of patients on ART, identification of adherence problems and determining when the patient becomes eligible for regimen switch. To achieve optimal treatment outcomes the clinician and patient must be actively involved in developing the schedule for monitoring the disease progression and options available for care prior to starting ART (baseline assessment) and during ART. Patients who are not yet eligible for ART should undergo baseline assessments, routine clinical assessments and routine CD4+ cell counts evaluation every six months.

Follow-up of patients on antiretroviral therapy continues throughout the patient's lifetime. These visits should be scheduled at a minimum interval of 2-3 months or earlier if clinically indicated. At treatment initiation or in the event of any treatment change, monitoring should be more frequent.

Baseline assessment

(See Section 3.3.1)

4.1.1 Assessment during follow-up

Once therapy has begun, assessment should look out for:

- Any persisting or new signs/symptoms of HIV related conditions
- Potential drug toxicities.
- Optimal Adherence
- Response to therapy.
- Weight changes, growth and development including height in children
- Abnormal in laboratory findings

Table 4.1: Recommended Schedule for Monitoring Patients on HAART: Clinical Assessments

	Pre-Treatment (Baseline)	Week 2	Week 4	Week 8	Week 12	Every 12 Weeks	Every 24 Weeks	Every Clinic Visit
Physical Exam	X	‡	X	X	X	X		X
Adherence Counselling	X	X	X	X	X			X
Clinical Screening for TB	X	X	X	X	X	X	X	X
Clinical Screening for Chronic Care & PHDP Services	X	X	X	X	X	X	X	X

Table 4.2: Recommended Schedule for Monitoring Patients on HAART: Laboratory Tests

	Pre-Treatment (Baseline)	Month 1	Month 3	Month 6	Month 12	Every 6 Months	Every 12 Months (Annual)
HIV-1 RNA (viral load estimation)				X‡	X‡		X
CD4+*	X			X	X	X	
Hb/PCV	X	X[1]	X			X	
WBC, Platelets	As clinically indicated						
ALT	As clinically indicated						
Creatinine (Calc CrCl)	X					X	
HbsAg and HCV	X						
Urinalysis	X		X[3]			X[3]	
Syphilis test	X						
VIA/Pap Smear	X	Annual thereafter					
AST, ALP, FBS, Amylase, Preg test, Lipid profile, U/E, Sputum AFB, Chest X-Ray	As clinically indicated						

X Essential

[1] For patients on AZT; [2] Patients on NVP;[3] patients on TDF

** Patients that are not yet eligible for ART will have a baseline CD4+ cell count done and subsequently at 6 monthly intervals, or more frequently as desirable, in addition to other symptomatically indicated investigations.*

X‡. We recommend that all clients initiating ART should have viral load determined at 6 and 12 months following initiation of therapy and 12 monthly thereafter to determine the efficacy and suitability of the regimen for the individual client. In suspected cases of virologic failure, viral load testing should be repeated 3 months after an intense regime of reinforced adherence counselling and support. A viral load test result of >1000cp/ml following reinforced adherence counselling and support is indicative of virologic failure. Clients with persistent virologic failure despite adherence interventions should have their drug regimen switched to second line ART regimen.

4.2 ART Monitoring and Follow-Up in Children

Clinical and laboratory monitoring are essential parts of HIV and AIDS care in children. These are required:

- At baseline (i.e. at entry into HIV care)
- Every 6 months for the care of patients who are not yet eligible for ART
- Prior to initiating ART
- On-going investigations while on ART.

4.2.1 Baseline Clinical and Laboratory Assessment

All infants and children who are diagnosed with HIV infection should undergo a baseline clinical and laboratory assessment in order to determine:

- Weight, height, head circumference and other measurements of growth
- Developmental status
- Nutritional status, including assessment of quality and quantity of intake.
- Immunization status
- History of previous ARV exposure, including PMTCT interventions
- The clinical stage of HIV disease
- Laboratory tests as indicated in Table 4.2; however, baseline laboratory tests should not delay ART initiation in children less than five years of age. Treatment should be initiated as results are being awaited.
- Screening for TB and other active opportunistic infections and co-infections
- Eligibility for ART and other interventions such as Cotrimoxazole prophylaxis (CPT) and INH preventive therapy (IPT)

4.2.2 Follow-Up Visits for Children on ART

The following should be conducted during follow-up visits:

Clinical assessment

- Growth monitoring using growth charts
- Physical examinations
- Systematic screening for TB symptoms at every clinical encounter
- Age appropriate disclosure counselling
- Developmental assessment and monitoring
- Check Immunization status
- Nutritional assessment
- Psychosocial assessment
- Check for occurrence adverse drug events
- Review ARV dosages for changes in body weight.
- Provide adherence support and monitoring

Monitoring Schedule for Children on HAART

Clinical assessment and laboratory monitoring schedule for children on HAART is as provided for in Tables 4.1 and 4.2. Chest x-ray or use of GeneXpert should be considered where clinically indicated as part of TB diagnosis. Clinical visits reflected in these tables are for scheduled appointments only. Follow-up schedule may be more intensive based on patient's status and progress.

It is recommended that drug pickup visits be monthly for the first 6 months as adherence is being reinforced. Thereafter, drug pick up visits can be up to 3 monthly or other appropriately determined timeframes if adherence is considered optimal. Viral load testing is recommended at 6 and 12 month following initiation of therapy and every 12 months thereafter. Baseline viral load can be performed especially for those with prior exposure to ARVs but is not routinely recommended.

CHAPTER FIVE

PREVENTION OF MOTHER TO CHILD TRANSMISSION OF HIV INFECTION (PMTCT)

5.1. Mother-to-Child Transmission of HIV

Most children less than 15 years living with HIV acquire the infection through mother-to-child transmission (MTCT). This can occur during pregnancy, labour and delivery or breast-feeding. In the absence of interventions, the risk of MTCT is 25-40%.

The high burden of mother-to-child transmission of HIV in sub-Saharan Africa including Nigeria is due to high rates of heterosexual transmission, high prevalence of HIV in women of reproductive age, high total fertility rate, characteristically prolonged breastfeeding culture, sub-optimal infection prevention measures during labour and delivery and limited access to general HIV prevention interventions. Transmission of HIV in children has become a critical health challenge that threatens to undermine the gains of child survival strategies in the African continent.

Risk factors for MTCT

The rate of mother to child transmission of HIV is affected by many factors. These have been grouped into viral, maternal, obstetric, foetal and breastfeeding factors (see Table 5.1. below)

Table 5.1: Factors associated with increased risk of MTCT

Factors	Strong Evidence	Limited Evidence
• Viral	• High maternal viral load • Viral characteristics	• Viral resistance
• Maternal	• Advanced disease • Immune deficiency • HIV infection acquired during pregnancy or breastfeeding • Sexually transmitted infections • Malaria	• Vitamin A deficiency • Anaemia • Chorioamnionitis • Frequent unprotected sex • Multiple sexual partners • Smoking • Alcohol • Intravenous drug abuse • Genetic (HLA subtypes, mutations of surface CD4 receptor)
• Obstetric	• Vaginal delivery • Rupture of membranes for more than 4 hours • Prolonged labour	• Invasive or traumatic procedures • Instrumental deliveries • Amniocentesis • Episiotomy/genital lacerations • External cephalic version • Ante-partum/intra-partum haemorrhage
• Foetal/Infant	• Prematurity • First of multiple deliveries	• Lesions of the skin and/or mucus membrane (e.g. oral thrush) • Genetic
• Breastfeeding	• Mixed feeding • Breast disease (abscess/ mastitis/cracked nipples) • Prolonged breastfeeding	

5.2 Comprehensive approach to primary prevention of MTCT

The prevention of mother- to-child transmission of HIV involves all persons of reproductive age group. It is based on the globally accepted four-pronged approach:

- *Primary prevention of HIV infection in women of reproductive age and their partners*
- *Prevention of unintended pregnancies among HIV positive women*
- *Prevention of HIV transmission from infected mothers to their infants*
- Provision of appropriate treatment, care and support to HIV-infected mothers, their infants and family

Primary prevention of HIV infection in women of reproductive age and their partners using a Combination approach which includes the following:

- Targeted information and education including the use of the "ABC" approach to enhance safer and responsible sexual behaviour and practices which covers:
  - **Delaying the onset of sexual activity until marriage**
  - **Practicing abstinence**
  - **Reducing the number of sexual partners**
  - **Consistent and correct use of condoms.**
- Provision of early diagnosis and treatment of STIs: The early diagnosis and treatment of STIs can reduce the incidence of HIV in the general population by about 40%. Comprehensive STI treatment services present an opportunity to provide information on HIV infection, MTCT and referral for testing and counselling.
- Making HIV testing and counselling widely available: HIV testing and counselling services need to be made available to all women of child-bearing age because PMTCT interventions depend on the woman knowing her HIV status.
- Provision of appropriate counselling for women who are HIV negative: Counselling provides an opportunity for a woman who is HIV negative to better understand how to protect herself and her infant from HIV infection. It can also serve as powerful motivation to adopt safer sex practices, encourage partner testing and discuss family planning. School based sex education and counselling also plays an important role.

These measures should be specifically promoted for all women who test HIV negative during antenatal, labour, delivery and postnatal care.

Prevention of unintended pregnancies among HIV positive women

The responsibility of the government and health services is to provide HIV positive women and their partners with comprehensive information and education about the risks associated with child bearing as part of routine public information about HIV and AIDS. This is to ensure that HIV positive women and their partners have informed choices of action, and to respect and support the decisions they reach. This implies:

- Providing good quality, user-friendly, and easily accessible family planning services so that HIV positive women can avoid pregnancy if they choose
- Promoting condom (male/female) use combined with a more effective method of contraception (dual method) for dual protection from HIV and other STIs and from unplanned pregnancies as an effective strategy to prevent HIV transmission
- Integrating dual protection messages into family planning counselling services

- Offering contraception to all HIV positive mothers in the immediate postpartum period to prevent unintended pregnancy because lactational amenorrhoea does not guarantee adequate contraception even in women who exclusively breastfeed.

Prevention of HIV transmission from infected mothers to their infants

- HIV testing and counselling
- HIV and Infant feeding counselling
- Modification of obstetric practices
- Administration of ART to eligible women
- Administration of ARV prophylaxis to mother-child pair for women not eligible for HAART

Provision of appropriate treatment, care and support to HIV-infected mothers, their infants and family

- Package of services for mothers
  - ART for women eligible for treatment
  - Cotrimoxazole prophylaxis
  - TB screening, prophylaxis and treatment
  - Continued infant feeding counselling and support
  - Nutritional counselling and support
  - Sexual and reproductive health services including FP
  - Cervical cancer Screening (PAP smear)
  - Psychosocial support.
  - Partner counselling and testing
- Package of services for HIV exposed children
  - ARV prophylaxis
  - Routine immunization and growth monitoring and support
  - Cotrimoxazole prophylaxis starting at 6 weeks
  - HIV diagnostic testing (EID) at 6 to 8 weeks of age and 6 weeks after breastfeeding has ended. Virologic test to be used where available, HIV antibody test can be used for HIV diagnosis for children older than 9 months where virologic test is not available. HIV antibody test is the recommended diagnostic testing strategy for children older than 18 months.
  - HIV antibody tests should primarily be used for screening of infants and children less than 18 months, so as to establish exposure status where the mother has not herself been tested for HIV or is not willing to be tested
  - Ongoing infant feeding counselling and support
  - Screening and management of tuberculosis
  - Prevention and treatment of malaria
  - Nutritional care and support
  - Psychosocial care and support
  - Antiretroviral therapy for eligible HIV infected children(see Chapter 4)
  - Symptom management and palliative care if needed.
  - The success of the interventions depend on strategies that will address stigma and discrimination as well as those that will strengthen referral, adherence, retention and community mobilization.

5.3 Antenatal Care for Hiv Positive Women

When a woman is known to be HIV positive or is diagnosed as HIV positive during pregnancy, her obstetric and medical care will need to be strengthened and modified. Post-test counselling for HIV positive pregnant women should include information on the following:

- Disclosure, partner notification and testing
- Benefits of PMTCT intervention
- ART
- Nutrition
- Delivery
- Infant feeding and infant testing
- Importance of testing other children and benefits of paediatric ART
- The need for follow-up and adherence.

All HIV positive women should be given optimal health care to ensure their safe delivery. In a situation where the life of the woman is being threatened by the continuation of the pregnancy, termination of pregnancy should be in accordance with the provisions of the law.

All pregnant HIV positive women must be screened for TB at ANC. TB screening should include the following:

- Ask the patients about cough, weight loss, fever and night sweats.
- Check for lymph node enlargement

5.3.1 Initial Examination

An HIV-infected pregnant woman should have a full physical examination. This should focus on HIV related illnesses including symptoms and signs of OIs (especially tuberculosis). Special attention should be paid to the following:

- Anaemia
- Persistent diarrhoea
- Respiratory infections: TB is a common OI and other bacterial respiratory infections are common in HIV-positive women
- Oral and vaginal candidiasis
- Lymphadenopathy
- Herpes zoster (chronic/re-current) is a common presenting sign of HIV infection, occurring early in the disease, often before there is much immune suppression
- Other skin conditions such as candidiasis, vaginal wart, etc
- Other sexually transmitted infections
- Weight gain or loss.

5.3.2 Laboratory Investigations

HIV positive pregnant women should be tested for syphilis (VDRL) and have haemoglobin or haematocrit estimation and urinalysis done. $CD4^+$ cell count should be ordered prior to commencement of ARVs for baseline assessment and ARVs initiated once the sample has been taken. $CD4^+$ cell count should also be repeated before exit from PMTCT services. The table below summarises the recommended laboratory investigations:

Table 5.2: Recommended Laboratory Investigations for HIV Positive Pregnant Women

Lab Test	At Booking/First Presentation (Baseline)	Second Visit	Third Visit	Fourth Visit	Fifth Visit
Routine for all pregnant women					
PCV or FBC where available	X	X	X	X	X
HBsAg and HCV	X				
Syphilis test	X				
Urinalysis	X	X	X	X	X
MP	As clinically indicated				
Specific for HIV positive					
CD4+	X				X
Viral load	As recommended by ART guideline (Table 4.2)				
LFT	As clinically indicated				
E/U/Cr	As recommended by ART guideline (Table 4.2)				
Lipid Profile	As clinically indicated				

5.4 Management of HIV Positive Women in Labour

Labour management should follow usual obstetric guidelines. Analgesia should be given in labour if required and epidural analgesia is not contraindicated *(See Table 5.3 Interventions for safe vaginal delivery)*

HIV positive women should not be isolated or treated differently from other women in labour. Supportive measures, empathy and caring attitudes by the health care provider are important for all women, particularly for the HIV-infected woman concerned about her condition and risks of HIV transmission to the child. There should be no room for stigmatization and discrimination by medical staff including for those who may not have disclosed their status to their partner or family members.

Whenever possible, during labour, HIV positive women should have the option to have a companion of their choice who knows their HIV status and can provide supportive companionship. Where this is not possible labour ward staff must be sensitive to the fears and concerns of the HIV positive mother about her infection, and how much she had told any of her companions.

Induction of Labour

As prolonged rupture of membranes is associated with increased risk of MTCT, careful assessment of the desirability of Ceasarean Section (CS) rather than induction of labour is necessary. Where induction is chosen, membranes should be left intact for as long as possible. Oxytocin should not be used with intact membranes. The use of prostaglandins or its analogues can be considered.

Conduct of Delivery

Delivery should be conducted using standard practices and aseptic techniques while avoiding unnecessary trauma or prolongation of the second stage.

Vaginal Delivery

HIV positive women who are on HAART or ARV prophylaxis should be allowed to deliver vaginally where there is no obstetric contraindication. Vaginal delivery remains the primary delivery mode of choice even where it is not possible to initiate any ARV prophylaxis due to the high mortality/morbidity risks of emergency caesarean section.

Caesarean Section (CS)

HIV infection on its own is not an indication for CS. Available evidence shows that elective CS for women on ART who have achieved viral suppression has no added advantage over vaginal delivery.

Elective CS can be considered for HIV positive women before the onset of labour or rupture of membranes in cases when the woman is not on ART and/or where the maternal viral load is known to be high. Indeed, available evidence shows that when elective CS is performed before the onset of labour or rupture of membranes, it reduces the risk of MTCT by greater than 50% as compared to vaginal delivery among women not on ART or with high viral load[1]. These guidelines however, do not recommend routine offer of elective CS for any group of HIV positive pregnant women.

Where CS is performed (elective or emergency) in HIV positive women, they should receive prophylactic antibiotics. If CS is performed after prolonged labour or prolonged rupture of membranes, longer courses of antibiotics should be provided.

5.5 Specific Modification of Obstetric Care for HIV Positive Women

- Avoid invasive procedures such as chorionic villous sampling, amniocentesis or cordocentesis
- External cephalic version (ECV) may carry a risk of HIV transmission to the foetus and should therefore be avoided
- Care should be individualized in special circumstances such as premature rupture of membranes (preterm and term) and ante-partum haemorrhage
- Use of the partograph: proper and consistent use of the partograph in monitoring the progress of labour will improve the management and reduce the risk of prolonged labour in all women
- Artificial rupture of membranes (ARM) is practiced routinely in many settings although it should be reserved for women with abnormal progress of labour. Rupture of membranes of more than four (4) hours duration is associated with an increased risk of HIV transmission. Therefore early ARM should be reserved for those with foetal distress or abnormal progress. ARM can be done if cervical dilatation is 7 cm or more
- Instrumental delivery: forceps and vacuum delivery should be avoided as they have been shown to be associated with increased risk of MTCT. If it has to be done,
- vacuum with silastic cup is preferred
- Vaginal cleansing with chlorhexidine (0.25% solution) is believed to reduce the risk of puerperal and neonatal sepsis. It may also have some effect on HIV transmission where membranes are ruptured for more than 4 hours. After every vaginal examination, the birth canal is wiped with gauze or cotton wool, soaked in chlorhexidine solution. The number of vaginal examinations should be kept to a minimum

1 *Jennifer S. Read; Preventing mother to child transmission of HIV: the role of caesarean section Sex Transm Infect 2000;76:231-232 doi:10.1136/sti.76.4.231*

- Routine episiotomy has been shown to have no obstetric benefit; it should be used only for specific obstetric indications.

Best Obstetric Practices

There should be capacity to:

- Train and retrain health care providers in safe delivery techniques and life-saving skills for mothers and infants
- Provide safe delivery kits and essential obstetric drugs
- Provide a safe delivery infrastructure with a safe water source, good drainage, electricity, delivery beds covered with waterproof material, antiseptics, gloves, and other materials required for a hygienic delivery environment
- Ensure a safe blood supply
- Provide community education about the importance of antenatal care and hospital delivery.

Table 5.3: Procedure for Safe Delivery

Interventions during labour/delivery	Care of the baby at delivery
• Perform vaginal cleansing with warm (0.25%) chlorhexidine solution to prevent genital infections • Avoid the following: • Frequent vaginal examinations • Episiotomies (unless absolutely necessary) • Instrumental delivery (unless when necessary) • Avoid milking the cord before clamping. • Clamp cord immediately after baby is delivered and cut, under cover of wrapped gauze swab to avoid blood spurting.	• Wipe baby's mouth and nostrils with gauze at delivery of the head. • Handle all babies with gloves regardless of mother's HIV status until blood and secretions are washed off • Keep all babies warm soon after delivery • Where suctioning is indicated, a mechanical suction unit (at a pressure below 100mmHg) or bulb suction should be used; mouth operated suction should be avoided • Place the baby on the mother's body for skin-to-skin contact soon after delivery.

5.6 Benefits of PMTCT

In settings where there are no PMTCT or paediatric ART services, most children acquiring HIV through MTCT will die early in life (50% by their second year). The increasing number of AIDS-related deaths in under-fives across sub-Saharan Africa and in Nigeria in particular is threatening to reverse the gains made by child survival programmes. The cost of care and support for HIV infected children places heavy financial burden on families, communities and the health care system. PMTCT benefits the mother, infant, family, community and the health system in the following ways.

Benefits to the Mother

- Identifies HIV positive mothers for targeted interventions to reduce risk of transmission of infection to their babies and to access treatment, care and support services
- Promotes positive behaviour change and reduces risk of HIV transmission
- Increases use of dual protection methods of family planning and STI prevention
- Helps clients plan for the future
- Promotes infant feeding support
- Promotes access to early preventive and medical care
- Helps personal and financial decision-making.

Benefits to the Infant

- Prevents HIV transmission to infants
- Promotes early diagnosis and intervention for the HIV exposed infants
- Improves child health and survival.

Benefits to the Family

- Promotes communication between couples and testing of both partners
- Reduces the risk of sexual transmission to sero-discordant partners
- Provides opportunity for testing other family members
- Contributes to reduction of stigma and discrimination
- Provides infant feeding support.

Benefits to the community

- Promotes the understanding of the HIV and AIDS epidemic among those living with HIV and AIDS within the community
- Promotes uptake of risk reduction practices
- Promotes acceptance and uptake of HIV testing and counselling
- Contributes to reduction of stigma and discrimination
- Provides infant feeding support.

Benefits to the health system

- Decreases the disease burden on the health system
- Gives an opportunity to strengthen the health system.

CHAPTER SIX

USE OF ANTIRETROVIRAL DRUGS FOR PMTCT

6.1 Overview

There is a significant amount of evidence available on the effectiveness of ARV prophylaxis for the prevention of mother to child transmission of HIV. The evidence indicates the benefits of starting ARV prophylaxis during early pregnancy and its extended use for mothers or infants to prevent post-partum transmission through breastfeeding. Pregnancy constitutes an indication for the use of triple ARVs for therapy or prophylaxis.

Antiretroviral drug (ARV) use in the Nigerian PMTCT programme has evolved from single dose Nevirapine (sdNVP) in labour in 2003[2] to triple ARV prophylaxis (tARVp) in 2010[3]. These Guidelines recommend breastfeeding with tARVp coverage, which is stopped when the risk of MTCT ceases at the end of breastfeeding.

6.2 Eligibility for HAART in pregnant and lactating women

Women who are eligible should be put on HAART at any time they come into contact with the health system during antenatal, labour, delivery, postnatal care and during the breast feeding period.

6.3 Eligibility criteria for ARV prophylaxis

Pregnancy or breastfeeding in the HIV positive woman is an indication for triple ARV prophylaxis (tARVp) irrespective of CD4, VL or clinical stage. ARV drugs should be provided as soon as possible irrespective of gestational age. For positive pregnant women with CD4+cell count ≤500, ART should be provided for life (see section 3.3.3 for eligibility in Adults).

6.3.1 ARV prophylaxis for PMTCT and duration of therapy

All pregnant and breastfeeding women with HIV should receive triple ARV drugs, which should be maintained for the duration of risk of mother-to-child transmission of HIV. All HIV positive pregnant women should continue ARV prophylaxis until one week after complete cessation of breastfeeding. Thereafter the mother-baby pair should be referred immediately to a competent ART centre for proper evaluation for comprehensive HIV treatment and care for mother and child. Women that meet treatment eligibility criteria (CD4+cell count <500) should be enrolled for ART while those not eligible should be enrolled for pre-ART care.

A once-daily fixed-dose combination of TDF + 3TC + EFV is recommended as first-line ARV regimen for pregnant and breastfeeding women, including pregnant women in the first trimester of pregnancy. Available evidence indicates that EFV is safe in pregnancy. However, as is indicated in use of medicines in pregnancy caution should be exercised in the use of ARVs in early pregnancy.

2 *National PMTCT Guidelines, 2003*
3 *National PMTCT Guidelines, 2010*

Table 6.1: Recommended First Line ARV Regimen for use in PMTCT

Definition	Preferred first-line Regimen	Alternative first-line Regimens
Adults (including pregnant and breastfeeding women and adults with TB and HBV co-infection)	TDF+3TC + EFV	(AZT + 3TC + EFV)[a] (AZT + 3TC + NVP)[b] (TDF + 3TC + NVP)[c]

a AZT is the recommended alternative to TDF for pregnant and breastfeeding women

b For pregnant women who cannot tolerate EFV

c For pregnant women who cannot tolerate AZT and EFV

6.4 Infant Feeding in the Context of HIV

Nutrition is essential for child survival. Optimizing infant and child nutrition is necessary to ensure good health and normal growth/development. Malnutrition is a common condition in HIV infected children, and is a major contributor to morbidity and mortality in this population. HIV infection can result in nutritional deficiencies, growth failure and developmental delay. Malnutrition itself results in decreased immune function and greater susceptibility to infections, thus accelerating disease progression. Malnutrition makes HIV infection worse and HIV infection worsens malnutrition.

Goals of Nutritional Management for HIV Exposed and Infected Children

- Provide nutritional counselling to caregivers
- Encouraging exclusive breastfeeding for infants less than 6 months
- Introduction of complementary foods in infants beginning at 6 months
- Stopping breastfeeding at the age of 12 months or soon after as appropriate
- Maintaining adequate nutritional support during periods of illness.

Breastfeeding and HIV Infection

Breastfeeding is one of the most important child survival strategies. However, HIV can be transmitted through breast milk. Exclusive breastfeeding from birth in the presence of maternal ART contributes to HIV-free survival in exposed infants. This avoids the risks and complexities associated with replacement feeding.

It is recommended that health care providers counsel and support the HIV positive mother to breastfeed her infant for 12 months (breastfeeding exclusively for the first six months), however, both mother and baby must however receive ARV drugs for prophylaxis or treatment as appropriate. This strategy will give Nigerian infants the greatest chance of HIV-free survival. However, women who choose not to breastfeed and those with medical contraindications to breastfeeding should be counselled and supported in their decision.

Complementary feeding

After 6 months of age, breast milk alone is not adequate for nutritional support of the infant. Complementary food should therefore be introduced for additional caloric requirements. The use of locally available foods is encouraged, as it is both cheap and sustainable.

Examples of locally available complementary feeds;

- Fruits e.g. bananas, plantains and cooked carrots
- Soft prepared foods e.g. bean cakes (akara /kose), fortified pap (with palm oil, crayfish, groundnut), “Acha”, “Tom Brown”
- High-protein foods e.g. beans, eggs, moin-moin, fish and liver
- Green leafy foods, e.g. vegetable soup

When to stop breastfeeding

HIV-infected women who decide to stop breastfeeding should gradually wean over one month. Mothers or infants on ARV prophylaxis should continue prophylaxis for one week after complete cessation of breastfeeding. At this time, infants should be provided with safe and adequate complementary foods to enable normal growth and development.

Growth Monitoring and Nutritional Assessment

Regular and careful assessment of a child's growth helps monitor HIV disease progression, identify complications early and offer the opportunity to intervene. Growth faltering may occur even before the emergence of opportunistic infections or other symptoms.

Growth monitoring includes:

History:

- Feeding history (types and amounts of food taken, frequency of meals, problems with feeding)
- Potential causes of malnutrition (food insecurity, change of caregivers, illness)
- Assess for any major changes in the child's circumstances.
- Checking mother's health (need for ART) and her care of other children.

Anthropometry:

- Measuring the weight, height or length at every encounter with child and comparing with the age and sex-appropriate WHO Z Score Card.
- Measurement of mid-upper arm circumference (MUAC) and head (Occipito-frontal circumferences as indicated
- Using the Modified Wellcome Classification chart or other growth charts.

Complete physical examination and appropriate laboratory assessments should be performed.

Micronutrient Supplements

All HIV infected children should receive micronutrients as follows:

Single dose vitamin A supplementation every 6 months between 6 and 59 months of age, as per the guidelines for uninfected children:

- <6 months – 50,000 IU
- 6–12 months – 100,000 IU
- 12 months – 5 years – 200,000 IU

Zinc supplements

- < 2 years 10 mg b.d x 14 days
- >2 years 20 mg b.d x 14 days

Iron supplements:

- 3-6mg/kg/day as required

Folate supplements:

- < 4 months 2.5 mg/day
- > 4 months 5 mg/day

Multivitamins, B6, B12, C, E

Note:

De-worming: Albendazole oral, 400 mg single dose every 6 months after the first year of life.

6.5 ARV Prophylaxis for HIV exposed Infants

All babies born to HIV positive mothers are exposed to infection and should receive post exposure prophylaxis as shown in Table 6.2.

Table 6.2 NVP Dosing for Infant HIV Prophylaxis

Infant Age	Daily Dosing
Birth to 6 weeks: Birthweight <2,500 grammes Birthweight ≥2,500 grammes	 10 mg (1 ml) once daily 15 mg (1.5 ml) once daily
>6 weeks to 6 months*	20 mg (2 ml) once daily
>6 months to 9 months*	30 mg (3 ml) once daily
>9 months to 12 months*	40 mg (4 ml) once daily

**Dosing beyond 6 weeks of age should be considered in special situations.*

6.5.1 Special situations for Extended Infant NVP Prophylaxis

Mother is breastfeeding but not on HAART:

Give daily NVP to infants from birth until one week after cessation of all exposure to breast milk.

Mother is breastfeeding and eventually commenced on HAART:

Give daily NVP to infants from birth and continue until 12 weeks after maternal commencement of HAART.

Table 6.3: Summary of Maternal & Infant Prophylaxis for different Clinical Scenarios

Scenario	Maternal ARV Recommendation	Infant ARV prophylaxis	Duration of infant ARV prophylaxis
Mother diagnosed with HIV during pregnancy	Initiate maternal ARV	Daily NVP	6 weeks
Mother diagnosed with HIV during labour or immediately postpartum and plans to breastfeed	Initiate maternal ARV prophylaxis	Daily NVP	Give daily NVP to infants from birth and continue until 12 weeks after maternal commencement of ART
Mother diagnosed with HIV during labour or immediately postpartum and plans replacement feeding	Evaluate for maternal ART eligibility	Daily NVP	6 weeks
Infant identified as HIV exposed after birth (through infant or maternal HIV antibody testing) and is breastfeeding	Initiate maternal ARV prophylaxis	Daily NVP	Perform infant PCR early infant diagnosis test and then immediately initiate 6 or 12 weeks of NVP depending on maternal timing of ART initiation. Initiate infant immediately on treatment if PCR result is positive
Infant identified as HIV exposed after birth (through infant or maternal HIV antibody testing) and is not breastfeeding	Evaluate for maternal ART	No drug	Perform infant PCR test at 6 weeks; no infant ARV prophylaxis; initiate treatment if infant is infected
Mother receiving ART but interrupts ART regimen while breastfeeding (such as toxicity, stock-outs or refusal to continue)	Determine an alternative ART regimen or solution; counsel regarding continuing ART without interruption. Seek expert consultation	Daily NVP	Until 6 weeks after maternal ART is restarted or until 1 week after breastfeeding has ceased,

6.6 Opportunistic Infection Prophylaxis for Children

HIV–exposed infants should be offered cotrimoxazole (CTX) from age 6 weeks until HIV status is determined. If the HIV status is positive, CTX should continue but if negative, it should be stopped. CTX is given once daily. The recommended doses are shown in Table 6.4

Table 6.4 Dosing for Cotrimoxazole Prophylaxis in HIV-Exposed Infants and HIV-InfectedChildren

Recommended dosage: Sulfadoxine/Trimetoprim	Suspension (200/40 mg /5ml)	Paediatric Tab (100/20mg)	Single Strength Adult Tab (400/80mg)
<6 months 100mg/20mg	25mls	1 tab	1/4 tab (possibly mix with feeding)
6months - 5years 200mg/40mg	5mls	2 tab	1/2 tab
6 - 14years 400mg/80mg	10mls	4 tab	1 tab

CHAPTER SEVEN

MANAGEMENT OF ADVERSE DRUG REACTIONS AND COMPLICATIONS OF ART

The therapeutic benefits of ARV use far outweigh the risk, thus despite the ADRs and toxicities encountered with ARV use, they are still essential in patient management.

7.1 Adverse drug reaction (ADR) and Pharmacovigilance

Adverse drug reaction (ADR) is defined by World Health Organization as "a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function." Pharmacovigilance is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.

There are two methods of pharmacovigilance namely: active and passive pharmacovigilance methods. The active method involves the routine screening of all patients on treatment at every visit for signs and symptoms indicating possible adverse reactions, follow-up and documentation of all suspected adverse reactions observed after commencement of treatment. The passive method involves an unplanned voluntary communication of adverse reactions/ events in a patient on therapy with one or more drug products and depends on the discretion of the health care provider.

Monitoring and reporting of drug therapy problems (including ADRs and medication errors) should be an integral part of clinical practice for ensuring patient safety and optimal treatment outcomes. This becomes more important due to the scale up of antiretroviral therapy with limited experience of the toxicity profile of the drugs used. Therefore, an intensive monitoring system for drug therapy problems should be supported in all hospitals. All healthcare providers (doctors, pharmacists, nurses and counsellors etc.) at various service delivery points should assess patients for adverse drug reaction at every encounter and report all suspected adverse events using the National Individual Case Safety Report Form.

7.2 Classification of Adverse Drug Reactions

The World Health Organization classifies ADRs into four categories based on the severity grades. Severity is a subjective assessment made by the healthcare provider and/or the patients. Despite being subjective, it is useful in identifying adverse reactions that may affect adherence or that needs prompt intervention. The following guide can be used to estimate the severity grade of ADRs:

Table 7.1: WHO Severity Grading of ADR

Grade 1 – Mild ADR	Transient or mild discomfort (<48 hours) No limitation of activity No medical intervention or therapy required
Grade 2 – Moderate ADR	Mild to moderate limitation of activity Some assistance may be needed No or minimal medical intervention required

Grade 3 – Severe ADR	Marked limitation of activity Some assistance usually required Medical intervention or therapy required Hospitalization possible
Grade 4 – Life Threatening ADR	Extreme limitation of activity Significant assistance required Significant medical intervention or therapy required Hospitalization or hospice care probable.

7.3 Drug toxicity

This is the unwanted effect of drugs resulting from administration in excess of the required therapeutic dose, or accumulation of drug in the body due to inefficient absorption, distribution, metabolism or excretion. Drug toxicity can be detected clinically (history and clinical examination) and/or through laboratory testing.

In the event of drug toxicity and adverse drug reactions, the offending drug(s) must be discontinued and changed to another drug from within its class.

Laboratory Toxicity Monitoring

Laboratory monitoring of patients receiving drugs for HIV treatment or prophylaxis is very important for early detection and prevention of some ADRs. The abnormal laboratory values (laboratory test abnormalities) may be early warning signals preceding the clinical manifestations of some ADRs in patients receiving antiretroviral drugs (ARVs). The following laboratory tests are desirable for laboratory toxicity monitoring of patients receiving ARVs for treatment or prophylaxis:

Table 7.2: Common laboratory and clinical abnormalities associated with ARV drugs

Drug class	Drug	Abnormality	Laboratory Tests
NRTI	Zidovudine	Anaemia, leucopenia, neutropenia, Myopathy	Full haematology CPK
	Tenofovir	Nephropathy	E/U and creatinine
	Stavudine	Hepatotoxicity Pancreatitis	Liver enzymes Amylase
	Abacavir	Hepatotoxicity Hypersensitivity	Liver enzymes CPK, creatinine, Haematology
NNRTI	Nevirapine	Hepatotoxicity	Liver enzymes
	Efavirenz	Hepatotoxicity Hypercholesterolaemia	Liver enzymes Serum cholesterol
PI	Ritonavir	Hepatotoxicity Hyperglycaemia Hyperlipidaemia Elevated CPK, Uric acid	Liver enzymes Urinalysis, BSL Serum lipids CPK, Uric acid

The severity grading of laboratory test abnormalities may guide prompt intervention and prevent the negative consequences of ADR. The following guide (Table 7.3) can be used to estimate the severity grade of laboratory adverse events:

Table 7.3: Severity Grading of Laboratory Adverse Events in Adults and Adolescents

Item	Reference Range	LABORATORY TEST ABNORMALITIES			
		Grade 1 Toxicity	Grade II Toxicity	Grade III Toxicity	Grade IV Toxicity
HAEMATOLOGY					
Hemoglobin	10.5 - 18.0g/dl	8.0 – 9.4 g/dl	7.0 - 7.9 g/dl	6.5 - 6.9 g/dl	< 6.5 g/dl
Absolute neutrophil count or Granulocyte count	2.0 – 7.5 x109/L	1 - 1.5x109/L	0.75 – 0.99x109/L	0.5 - 0.749 x109/L	<0.5 x 109 /L
Platelet count	100–450 x 109/L	70–99x 109/L	50 – 69 x 109/L	30 – 49 x109/L	< 29 x 109/L
Total WBC	4.0 – 11.0x109/L	2.0-3.9x109/l	1.0 – 1.9 x 109/L	< 1.0 x 109/L	-
CHEMISTRY					
ALT	5.0 – 38U/L	1.25 - 2.5 x ULN	>2.5 - 5xULN	>5.0 -10 x ULN	>10 x ULN
Triglycerides	<1.69 mmol/l	1.69- 2.25 mmol/l	2.26-5.63mmol/l	5.64- 13.5mmol/L	>13.56 mmol/L
Cholesterol		>1.0 - 1.3 x ULN	4.52- 8.48mmol/L	8.49-13.56mmol/l	>13.56mmol/L
Lactate	< 2 mmol/l	-	2 – 5 mmol/l	5 – 10 mmol/l	>10mmol/l
Glucose (hyperglycemia)	4 – 6 mmol/l	6–8.9 mmol/l	8.91-13.88mmol/l	13.89-27.76mmol/l	> 27.76mmol/l
Glucose (hypoglycemia)	4 – 6 mmol/l	3.01-3.55mmol/l	2.19-3.00 mmol/l	1.67-2.18 mmol/l	<1.67 mmol/l
Amylase	28 - 100U/L	> 1.0 – 1.5 x ULN	> 1.5 – 2.0 x ULN	> 2.0 – 5.0 x ULN	> 5.0 x ULN
Bilirubin	2 – 21µmol/L	1.1 – 1.5 x ULN	1.6 – 2.5 x ULN	2.6 – 5.0 x ULN	> 5.0 x ULN
Lipase	< 1.5 U/mL	> 1.0 – 1.5 x ULN	> 1.5 – 2.0 x ULN	> 2.0 – 5.0 x ULN	> 5.0 x ULN
Creatinine	0.7 –1.5mg/dl or 62-133µmol/L	> 1.0 -1.5x ULN	> 1.5-3.0 x ULN	> 3.0 -6.0 x ULN	> 6.0 x ULN
Sodium Hyponatraemia	136-145 mmol/l	130 - 135mmol/l	123-129mmol/l	116-122mmol/l	<116mmol/l
Sodium Hypernatraemia	136-145mmol/l	146 - 150mmol/l	151-157mmol/l	158 -165mmol/l	>165mmol/l
Potassium Hyperkalaemia	3.5 – 5.0 mmol/l	5.1 – 6.0 mmol/l	6.1– 6.5 mmol/l	6.6 - 7.0 mmol/l	>7.0mmol/l
Potassium Hypokalaemia	3.5 -5.0 mmol/l	3.5 –3.0 mmol/l	3.0 –2.5 mmol/l	2.5 –2.0 mmol/l	<2.0mmol/L
Management		Continue ART, and consult expert		Continue ART, and consult expert	Consider stopping ART, Consult
		Lipid imbalances could be managed with exercise, diet and pharmacologically using fibrates and/or statins			

7.4 Steps to Recognize ADRs

- Take a proper history and do a proper examination of patient
- Establish time relationships, as the time from the start of therapy to the time of onset of the suspected reaction must be logical
- Carry out a thorough physical examination with appropriate laboratory investigations (if necessary)
- Check the known pharmacology of the medicine

What Should Be Reported About ADRs?

- All serious or unexpected (unusual) ADRs that one suspects for established or well-known drugs
- All suspected reactions, including minor ones for new drugs
- If an increased frequency of a given reaction is observed
- All suspected ADRs associated with drug-drug, drug-food or drug-food supplement interactions
- ADRs in special fields of interest such as drug abuse
- ADRs related to failure of contraceptives
- Drug use in pregnancy and during lactation
- ADRs occurring from overdose or medication error
- Lack of efficacy of a medication, or when suspected pharmaceutical defects are observed
- Reactions suspected of causing death, danger to life, admission to hospital, prolongation of hospitalization, or birth defects.
- When in doubt whether the suspected adverse event/reaction is an ADR or not, you must report to the National Pharmacovigilance Centre.

All ADRs should be reported to the National Pharmacovigilance Centre using the National Individual Case Safety Report Form.

7.5 Principles of management of Adverse Drug Reactions

- **Ensure routine screening of all patients receiving antiretroviral drugs for signs/ symptoms indicating possible adverse reactions using ADR Screening Form (see Appendix I).**
  - If there are no new signs and/or symptoms indicating possible adverse drug reactions, continue case management of patients.
  - If there are any new signs and/or symptoms indicating possible adverse drug reactions:
    - Determine the severity of the adverse event(s) using WHO Severity Grading of ADRs
    - If the suspected adverse event(s) is mild (ADR severity grade 1), counsel patients on how to manage the adverse event(s), document intervention and then manage patients as appropriate.
    - If the suspected adverse event(s) is moderate, severe or life-threatening (ADR severity grade II – IV), manage the patients' ADRs as appropriate and then document intervention, report the adverse events using the National Individual Case Safety Report Form (Yellow Form – see Appendix II).

- **Antiretroviral drugs (ARVs) regimen may be continued in cases of the grade I or II adverse event**
- **If the adverse drug reaction is severe (grade III), consider stopping antiretroviral drugs regimen or implement the following:**
  - De-challenge the patient of the suspected drug(s). For non-ARVs, discontinue the least critical drug(s) to the patient's health one at a time; but for ARVs institute appropriate substitute drugs/regimen for the patient and observe response to the change.
  - Monitor the patient closely as much as possible on the new medications
  - Continue the usual case management of the patient

Follow up and document the suspected adverse reactions, intervention and outcome of the intervention.

- **Antiretroviral drugs regimen must be stopped immediately if there is suspected life threatening adverse drug reaction (grade IV) following the provisions of the national guidelines.**
  - Never discontinue only one antiretroviral drug. Any suspected drugs can also be substituted as appropriate.
  - If there is need to stop ARV drugs, all drugs must be stopped (tail off NNRTI where applicable).
- **Dealing with multiple drugs suspected to be associated with an ADR:**
  - Consider the possibility of a drug-drug interaction; do a label and literature search (consult the pharmacovigilance and drug information focal person as necessary).
  - Consider discontinuing only one drug at a time to observe de-challenge.
  - Discontinue the drug least critical to short-term health, e.g. can the individual tolerate a period off drug to evaluate change in event (in the case of non-ARVs)? Institute appropriate substitute drugs/regimen for the patient (in the case of ARV drugs) and observe response to the change.
  - Follow up and document the observed adverse reactions, intervention and outcome of the intervention.
- **After the de-challenge; If the symptoms (and signs) are abated:**
  - ADR is probably due to the initially suspected drug(s)
  - Follow up and document the observed adverse reactions, intervention and outcome of the intervention
- **After the de-challenge; If the symptoms (and signs) are not abated***:*
  - Re-evaluate the patient for the severity of the adverse drug reaction
  - Consider stopping all medications and/or switch to an entirely new ARVs regimen using approved guidelines.
  - Stabilize and manage the patient as appropriate.
  - Continue to monitor the patient condition
  - Follow up and document properly the observed adverse reactions, intervention and outcome of the intervention.

- **If there are no new ADR(s)**
  - Continue case management of the patient

- **Ensure strict adherence to the above standard procedures for detecting, evaluating and reporting ADRs in ART/PMTCT Clinical Settings**

- **Establish a functional hospital – based pharmacovigilance committee (with a term of reference) in all ART/PMTCT centers to coordinate ARV clinical pharmacovigilance. This committee is very vital to the success of pharmacovigilance and management of ADRs in a clinical setting.**

7.5.1 Management of Specific Adverse ARV Drug Reactions

Adverse reactions associated with ARV drugs usually have a class similarity; however certain drugs in each of the classes present more severe forms of adverse reactions than others. In the management of adverse events, special attention should therefore be paid to drug specific adverse reactions. For example zidovudine is implicated in ARV-induced anaemia more than any other ARV in the same class, just as Nevirapine is more likely to cause liver toxicity than the other ARV drugs in the same class.

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

All NRTIs are capable of inhibiting mitochondria DNA [(mtDNA) polymerase gamma] polymerase enzyme resulting in mitochondrial toxicity. As NRTIs inhibit DNA polymerase, all tissues that have DNA can be affected. Depending on the organ involved, there can be myopathy presenting with muscle weakness, bone disorders causing depression of haemopoiesis leading to anaemia, leucopoenia and thrombocytopenia; lipolysis resulting in fat atrophy (lipoatrophy). It can cause myelotoxicity and neuropathy when it affects peripheral neurones, thus precipitating peripheral neuropathy. Though rare, prolonged usage of NRTIs may also affect myocardial cells resulting in cardiomyopathy. Others include hepatitis, pancreatitis and lactic acidosis.

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

They increase the incidence of severe hepatotoxicity in women with CD4 count > 250cells/mm^3 and men with CD4 count > 400cells/mm^3. Other common reactions include skin rash, and CNS disorders.

Protease Inhibitors (PIs)

PIs are potent CYP3A4 inhibitor hence many drug-drug interactions can occur on co-administration with other drugs. ADRs due to PIs can be severe. These include acute effects of diarrhoea, vomiting and hepatotoxicity; and long term toxicity which includes peripheral loss of subcutaneous fat (lipoatrophy), fat accumulation within the abdominal cavity (protease paunch or crix-belly), fat accumulation in the upper back (dorsocervical pad or buffalo hump), gynaecomastia in males, fat accumulation in the breast in females and fat accumulation in subcutaneous tissue (peripheral lipomastosis). Management of acute ADRs includes reassurance and symptomatic treatment as it clears within 4-6 weeks of therapy.

Table 7.4 Adverse drug reactions associated with the use of specific ARV drugs and their management.

Antiretroviral Drug	Primary toxicities	Minor toxicities	Monitoring/Management
Zidovudine (AZT)	Anaemia, neutropaenia, myopathy, lipoatrophy or lipodystrophy [Risk factors include - Baseline anaemia or neutropaenia; CD4 count ≤200 cells/mm^3] Lactic acidosis or severe hepatomegaly with steatosis [Risk factors include - BMI >25 (or body weight >75 kg); Prolonged exposure to nucleoside analogues]	Blue to black discoloration of nails, nausea and headache	For anaemia: Change to TDF and/or transfuse Do not use AZT if Hb < 8.0 g/dl (PCV <24%) For myopathy, discontinue if CPK rises If AZT is being used in first-line ART, substitute with TDF or ABC. If AZT is being used in second-line ART, substitute with ABC
Lamivudine (3TC)	Pancreatitis, Liver toxicity Mild peripheral neuropathy	Skin rash, headache	Discontinue if serum amylase elevated. Restart when resolved or change to ABC
Stavudine (d4T)	Peripheral neuropathy presenting with painful and peripheral sensations in the lower more than in the upper limb; lipoatrophy or lipodystrophy [Risk factors: Older age; CD4 count ≤200 cells/mm^3; Concomitant use of isoniazid or ddI] Lactic acidosis or severe hepatomegaly with steatosis, acute pancreatitis. This is worse when d4T is used in combination with ddI. [Risk factors: BMI >25 (or body weight >75 kg); Prolonged exposure to nucleoside analogues]	Insomnia, anxiety, panic attacks	Periodic serum triglycerides should be monitored. Suspicion of lactic acidosis – measure serum lactate and/or anion gap and serum bicarbonate. At first signs of mitochondrial toxicity Stavudine should be substituted If d4T is used in first-line ART, substitute with TDF or AZT or ABC. If d4T is being used in second-line ART (after TDF or ABC are used in first-line ART), substitute with AZT
Emitricitabine (FTC)	Similar to lamivudine	Occasional hyperpigmentation	

Table 7.4 CONTD... Adverse drug reactions associated with the use of specific ARV drugs and their management.

Antiretroviral Drug	Primary toxicities	Minor toxicities	Monitoring/Management
Tenofovir (TDF)	Tubular renal dysfunction, Fanconi syndrome [Risk factors: Underlying renal disease; Older age; BMI <18.5 (or body weight <50 kg); Untreated diabetes mellitus; Untreated hypertension; Concomitant use of nephrotoxic drugs or a boosted PI] Decreases in bone mineral Density [Risk factors: History of osteomalacia and pathological fracture; risk factors for osteoporosis or bone loss] Lactic acidosis or severe hepatomegaly with steatosis [Risk factors: Prolonged exposure to nucleoside analogues; Obesity] Exacerbation of hepatitis B (hepatic flares) [Risk factors: Discontinuation of TDF due to toxicity]	Occasional GI intolerance	If creatinine clearance declines, substitute with a non-nephrotoxic drugs such as ABC or adjust dosage. (See section on co-morbidities) If TDF is being used in first-line ART, substitute with AZT or d4T or ABC. If TDF is being used in second-line ART (after d4T + AZT use in first-line ART), substitute with ABC or ddI. Use alternative drug for hepatitis B treatment.
Abacavir (ABC)	Life-threatening hypersensitivity reaction may occur in 3-9% of patients [Risk factors - presence of HLA-B*5701 Gene] Lactic acidosis may also occur with/ without hepatic steatosis		Discontinue therapy if hypersensitivity develops. Abacavir should never be used in that individual again. If ABC is being used in first-line ART, substitute with TDF or AZT or d4T. If ABC is being used in second-line ART, substitute with TDF
Nevirapine (NVP)	Life-threatening skin rash and hypersensitivity reaction (Stevens-Johnson syndrome) which occurs in less than 5% of patients and usually within 8 weeks of treatment DRESS syndrome (drug rash, eosinophilia and systemic symptoms) manifesting as fever, arthralgia, etc. Hepatotoxicity [Risk factors: Underlying hepatic disease; HBV and HCV co-infection; Concomitant use of hepatotoxic drugs; CD4 >250 cells/mm^3 in women; CD4 >400 cells/mm^3 for men; First month of therapy (if lead-in dose is not used)		Low-dose over first 2 weeks minimizes rash occurrence. If mild or moderate (Grade 1/2) continue cautiously or substitute with EFV. If severe discontinue NVP and permanently if hepatitis confirmed. Change to EFV. If the person cannot tolerate either NNRTI, use boosted PIs

Table 7.4 CONTD... Adverse drug reactions associated with the use of specific ARV drugs and their management.

Antiretroviral Drug	Primary toxicities	Minor toxicities	Monitoring/Management
Efavirenz (EFV)	Persistent central nervous system toxicity (such as abnormal dreams, hallucination, insomnia, amnesia, depression or mental confusion). CNS side effects occur in about 50% of patients (usually self-limiting) [Risk factors: Depression or other mental disorder (previous or at baseline); Daytime dosing] Hepatotoxicity [Risk factors: Underlying hepatic disease – HBV and HCV co-infection Concomitant use of hepatotoxic drug] Convulsions [Risk factor: History of seizure] Hypersensitivity reaction, Stevens-Johnson syndrome. Mobiliform rash may appear but usually not life-threatening Potential risk of neural tube birth defects (very low risk in humans) Male gynaecomastia.	Dizziness,	Rash in 10% but rarely severe in <1%; CNS symptoms often resolve 2-4 weeks. EFV is contraindicated in patients who already have psychiatric manifestations. Change to NVP. If the person cannot tolerate either NNRTI, use boosted PIs
Etravirine	Severe skin rash; hypersensitivity reactions (Stevens-Johnson syndrome), Erythema multiforme, hepatotoxicity, lipid abnormality and psychiatric disorders	GI Intolerance, rash	Monitor liver enzymes and lipids. Rarely discontinue (<2%) due to adverse reaction. Limited options are available
Atazanavir/ ritonavir (ATV/r)	Electrocardiographic abnormalities (PR interval prolongation) [Risk factors: Pre-existing conduction disease; Concomitant use of other drugs that may prolong the PR interval] Indirect hyperbilirubinaemia (clinical jaundice) [Risk factors: Underlying hepatic disease HBV and HCV co-infection; Concomitant use of hepatotoxic drugs] Nephrolithiasis and risk of prematurity [Risk factor unknown]	Nausea and diarrhoea, skin rash	Unconjugated hyperbilirubinemia is cosmetic and not related to hepatitis or liver damage. Monitor liver enzymes Change to LPV/r or DRV/r. If boosted PIs are contraindicated and NNRTIs have failed in first-line ART, consider integrase inhibitors

Table 7.4 CONTD... Adverse drug reactions associated with the use of specific ARV drugs and their management.

Antiretroviral Drug	Primary toxicities	Minor toxicities	Monitoring/Management
Lopinavir/ritonavir (LPV/r)	Electrocardiographic abnormalities (PR and QT interval prolongation, torsades de pointes) [Risk factors: People with pre-existing conduction system disease; Concomitant use of other drugs that may prolong the PR interval] QT interval prolongation [Risk factors: Congenital long QT syndrome; Hypokalaemia; Concomitant use of drugs that may prolong the QT interval] Hepatotoxicity [Risk factors: Underlying hepatic disease; HBV and HCV co-infection; Concomitant use of hepatotoxic drugs] Pancreatitis [Risk factors: Advanced HIV disease] Risk of prematurity, lipoatrophy or metabolic syndrome, dyslipidaemia or severe diarrhoea [Risk factors unknown]	Headache, weakness, nausea, vomiting and skin rash	Diarrhoea rarely severe should be managed with antispasmodics – usually resolves after weeks to months of therapy. If LPV/r is used in first-line ART for children, use an age-appropriate NNRTI (NVP for children younger than 3 years and EFV for children 3 years and older). ATV can be used for children older than 6 years If LPV/r is used in second-line ART for adults, use ATV/r or DRV/r. If boosted PIs are contraindicated and the person has failed on treatment with NNRTI in first-line ART, consider integrase inhibitors
Darunavir/ritonavir (DRV/r)	Hepatotoxicity [Risk factors: Underlying hepatic disease HBV and HCV co-infection Concomitant use of hepatotoxic drugs] Severe skin and hypersensitivity reactions [Risk factors: Sulfonamide allergy]		If DRV/r is being used in second-line ART, substituting with ATV/r or LPV/r can be considered. When it is used in third-line ART, limited options are available
Raltegravir (RAL)	Rare	Myopathy, myalgia	Limited options are available

7.6 ARV Drug Interactions

Drug interaction is the modification of the action of one drug by another. Drug interactions can be useful, of no consequence, or harmful. Multiple drug use ('polypharmacy') is extremely common in ART/PMTCT settings, so the potential for drug interaction is enormous. Adverse interactions may be catastrophic, but are often avoidable. Patients receiving care for HIV infection have the likelihood of experiencing various drug interactions because of several drugs in ART combinations, co-administered drugs for opportunistic infections and co-administered drugs for other concurrent ailments.

There are two major groups of ARV drug interactions:

- Non-ARV vs. ARV Drug Interactions
- ARV vs. ARV Drug Interactions

As a rule of thumb, most ARV drugs are metabolized by the Cytochrome P450 3A4 isoenzyme in the liver. Many other drugs are also metabolized by this enzyme and ARV drugs will either raise or lower these other drug levels and either be increased or decreased themselves by these interactions. All PIs as well as all current clinically used NNRTIs are metabolized by CYP 450 enzyme cascade (in particular CYP 3A4) which can be induced and/or inhibited by several drugs thus the possibilities of a large number of drug/drug interactions.

Table 7.5 Non-ARV vs. ARV Drug Interactions

Drug	Interaction	Action
Rifampicin	Decreases plasma level of all PIs by at least 75% (except ritonavir, which it decreases by 35%). Rifampicin also decreases plasma levels of EFV (25%), and NVP (20%–58%) and DLV (96%).	Contraindicated with all PIs in general. Rifampicin can be used with EFV. Maintain EFV dose at 600 mg once daily and monitor for virologic response. It is not recommended that Rifampicin be used with NVP.
Rifabutin .	It reduces levels of all PIs and NNRTIs by 15 to 35%, except DLV that is reduced by 80% LPV/r increases Rifabutin level by 300%; ATV increases Rifabutin level by 250% EFV reduces Rifabutin level by 38%.	It should not be used with DLV Rifabutin dosage should be reduced to 150 mg od or 3x/week when used with LPV/r, ATV or ATV/r Rifabutin dose should be increased to 450–600 mg once daily or 600 mg three times a week if EFV is not co-administered with a PI.
Clarithromycin	Clarithromycin AUC: increased 94%; Cmax: increased 50%; Cmin: decreased 62% by ATV/r, ATV. Increased clarithromycin effects through the inhibition of CYP450 3A4 by ATV. DRV/r: increase clarithromycin AUC by 57%; LPV/r : increase clarithromycin level expected; EFV and NVP decrease clarithromycin levels by 39% and 31% respectively	Monitor for clarithromycin-related toxicities or consider alternative macrolide (e.g., azithromycin). Reduce clarithromycin dose by 50% with CrCl 30-60 mL/min. Reduce clarithromycin dose by 75% in patients with CrCl <30 mL/min. Monitor for effectiveness or use alternative agent, such as azithromycin, for MAC prophylaxis and treatment with EFV, NVP.

Table 7.5 CONTD... Non-ARV vs. ARV Drug Interactions

Drug	Interaction	Action
Simvastatin, Lovastatin	Boosted PI (ATV/r, LPV/r): Significant increase in levels of statins EFV decrease level of simvastatin by 68%; NVP, ETR decrease levels of simvastatin and lovastatin possible	Contraindicated. Do not co-administer. Use pravastatin or low dose atorvastatin during concurrent PI therapy Adjust lovastatin or simvastatin dose according to lipid responses, not to exceed the maximum recommended dose. If EFV, ETR or NVP used with RTV-boosted PI, simvastatin and lovastatin should be avoided.
Methadone	LPV/r decrease methadone AUC by 26%–53%; ATV/r, DRV/r, decrease methadone AUC by 16%-18%; Methadone plasma levels decreases by EFV (52%), NVP (37%–51%) and ETR (no significant effect). Methadone increases level of AZT by 29%–43%	Opioid withdrawal unlikely but may occur. Dosage adjustment of methadone is not usually required, but monitor for opioid withdrawal and increase methadone dose as clinically indicated. Opioid withdrawal common; increased methadone dose often necessary. Monitor for AZT-related adverse effects.
H2 Receptor Antagonists e.g. Cimetidine	It decreases atazanavir effects by reducing its GI absorption No significant effect on LPV/r and DRV/r	For treatment-naive patients, atazanavir 400 mg QD can be used if dosed 2 hours before or 10 hours after the H2-blocker or atazanavir 300 mg with ritonavir 100 mg QD can be used. For treatment-experienced patients, atazanavir 300 mg with ritonavir 100 mg QD can be used if dosed at least 2 hours before and at least 10 hours after the H2-blocker.
Erectile dysfunction (ED) drugs (Sildenafil, tadalafil, etc)	Levels of ED drugs increased 4 folds by Protease Inhibitors (PIs)	Encourage use of lower dose of ED drugs and adverse effects of ED drugs or avoid if patient can tolerate the decision
Antacids	ATV, ATV/r: when given simultaneously, it decreases ATV effects	Give ATV at least 2 hours before or 1 hour after antacids or buffered medications.
Proton Pump Inhibitors (PPIs) e.g. Omeprazole	ATV/r: decreases ATV level DRV/r, LPV/r: no significant effect on these PIs	PPIs should be administered at least 12 hours before ATV/r. PPIs are not recommended in PI-experienced patients.
Budesonide, Fluticasone, Prednisone	Decrease PI levels possible; and increase levels of glucocorticoids	Use with caution. Co-administration can result in adrenal insufficiency, including Cushing's syndrome. Do not co-administer unless potential benefits of using the drug outweigh the risks of systemic corticosteroid adverse effects
Ketoconazole	LPV/r increase the level of Ketoconazole by 204%; increased ketoconazole effects; decreased lopinavir/ritonavir effects NVP decreased the AUC and maximum concentration (Cmax) of ketoconazole by 63% and 40% respectively through the induction of CYP450 3A4. Decreased ketoconazole effects while NVP levels increased by 15-30%. Similar effects with EFV	Dose of Ketoconazole must not exceed 200 mg daily if it must be used or use alternative agent (Fluconazole) Do not co-administer NVP, EFV and Ketoconazole.

Table 7.5 CONTD... Non-ARV vs. ARV Drug Interactions

Drug	Interaction	Action
Fluconazole can be used with PIs and NNRTIs without dose adjustments unlike Ketoconazole).	NVP levels increased by 110% EFV: No significant effect	Increased risk of hepatotoxicity possible with this combination. Monitor NVP toxicity or use alternative ARV agent.
Estrogen-based hormonal Contraception	Boosted PI (ATV/r, LPV/r); EFV, NVP: Plasma ethinyl-oestradiol and norethindrone concentrations are decreased significantly by these ARVs (causing failure of contraception) thus necessitating alternative contraceptive methods.	Use alternative or additional contraceptive methods
Carbamazepine Phenobarbital Phenytoin	EFV, NVP: decrease levels of anticonvulsant, EFV and NVP possible	Monitor anticonvulsant and NVP, EFV levels and virologic responses or consider alternative anticonvulsant.
Metronidazole	LPV/r oral solution (contains alcohol): Disulfiram reaction (hypotension, headache, nausea, vomiting) through inhibition of alcohol and aldehyde dehydrogenase by metronidazole.	Do not coadminister; may consider lopinavir/ritonavir capsules
Tenofovir (TDF)	High fat meal increase AUC (total drug exposure over time) by 40%, Cmax (maximum concentration that a drug achieves after administration) by 14%	Take with meals
Efavirenz (EFV)	High fat meals increases absorption by 50% Taking with food may increase central nervous system toxicity	Avoid high fat meals with EFV Take on an empty stomach
Lopinavir/ ritonavir (LPV/r)	Food increases AUC by 48%, Cmax by 23%	Take with food
Garlic, St John's wort	Significant decrease in PI levels, potentially leading to virologic failure St John's wort decreases levels of NNRTI (NVP, EFV, ETR)	Avoid concurrent use during PI therapy Do not co-administer.

Table 7.6 Important ARV vs. ARV drug interactions

Drug	Interaction	Action
Zidovudine (AZT)	Concurrent use of AZT and Stavudine (d4T) has been shown to be antagonistic. They compete for same enzyme that phosphorylates them to their active form	Avoid concomitant use of AZT and d4T
EFV; NVP	Decreased level of Atazanavir and LPV/r significantly occur when used concomitantly with EFV or NVP	Avoid the combination or consider increase LPV/r dose to 533mg/133mg twice daily in PI-experienced patients.
TDF	Concomittant use with ATV: TDF level is increased by 24%–37% and Atazanavir level is decreased by 25%	Dose: ATV/r 300/100 mg daily co-administered with TDF 300 mg daily. Avoid concomitant use without RTV. If using TDF and H2 receptor antagonist in ART-experienced patients, use ATV/r 400 mg/100 mg daily.Monitor for TDF-associated toxicity.

Note: Abacavir (ABC) is not currently associated with any clinically significant pharmacokinetic drug interactions. However, a large dose of ethanol (>0.7g/kg body weight) increases ABC plasma AUC by 41% as well as prolongs ABC elimination half-life by 26%. Patients must therefore be cautioned on alcohol use during ABC therapy.

7.7 Prevention of Adverse Drug Reactions

Applying the principles of rational use of medicines can prevent most ADRs:

- Use of few drugs, whenever possible
- Use drugs that you are familiar with
- Do not change therapy from known drugs to unfamiliar ones without good reason
- All patients commencing ARV should be properly counselled on the ADRs related to the medications and what to do when it occurs or is suspected. The healthcare provider should be very knowledgeable on this
- Be vigilant (look for) to these adverse effects when initiating therapy and during follow-up.

CHAPTER EIGHT

PREVENTIVE MANAGEMENT OF HIV/AIDS

8.1 Introduction

There are six major strategies for preventive management of HIV/AIDS, one of which is PMTCT (discussed in Chapters 5 and 6). The other five include; Post-Exposure Prophylaxis (PEP), Isoniazid Preventive Therapy (IPT), Cotrimoxazole Preventive Therapy (CPT), Pre-Exposure Prophylaxis (PrEP) and management of STIs.

8.2 Post-Exposure Prophylaxis

Post Exposure Prophylaxis (PEP) refers to the short-term use of ARV drugs to reduce the likelihood of HIV infection in persons exposed to potential risk of acquiring HIV infection. This applies usually to accidental exposure to HIV either in the course of legitimate work as could occur among health workers who are vulnerable to needle stick injuries or contact with infectious body fluids. It also applies to sexual assault victims especially in cases where the HIV status of the perpetrator cannot be readily determined.

Animal models show that after initial exposure, HIV replicates within dendritic cells of the skin and mucosa before spreading through lymphatic vessels and developing into a systemic infection. This delay in systemic spread leaves a "window of opportunity" for PEP using antiretroviral drugs designed to block replication of HIV. PEP aims to inhibit the replication of the initial inoculums of virus and thereby prevent establishment of chronic HIV infection.

8.2.1 Post Exposure Prophylaxis for Occupational HIV exposure

There is evidence that, in the occupational setting, HIV transmission is significantly associated needle stick injury especially where there is deep injury, visible blood on the sharp instrument, procedures involving a needle placed in the source patient's blood vessel, and terminal illness in the source patient.

The following types of exposures may pose the risk of HIV transmission for health workers and should be considered for PEP:

- Needle-stick injury or injury with a sharp object that has been used on a HIV positive patient
- Mucosal exposure of the mouth, eye or nose by splashing infectious body fluids
- Broken skin exposed to blood, blood stained body fluids or other infectious body fluids

Actions recommended following a needle-stick injury or mucosal exposure

In the event of an injury with a sharp object such as a needle or scalpel that has been used on a patient or in the event of a mucous surface being contaminated with blood or secretions from a patient the following steps should be followed:

- Do not squeeze or rub the injury site
- Allow blood or secretion to flow freely
- Wash exposed area immediately with soap and running water or antiseptic solutions such as 2% polyhexidine or 70% glutaryladehyde.

- After a splash to the eye or any other mucous surface, irrigate/rinse the exposed area immediately with water (preferably running water) or normal saline
- Report the exposure to a senior member of staff, supervisor or the PEP officer
- If eligible, give antiretroviral drugs recommended for postexposure prophylaxis immediately possibly within 1 hour and at the latest within 72 hours of the exposure (persons presenting after 72 hours of the exposure should also be considered for PEP).

Evaluation for PostExposure Prophylaxis

Evaluating exposed person's eligibility for HIV postexposure prophylaxis involves assessing the following:

- Timing of the potential exposure
- HIV status of exposed person
- The nature and risk of the exposure
- HIV status of the source of the potential exposure

Determination of Risk and ARV drugs for PEP

The exposure should be classified as "low risk" or "high risk" for HIV infection as below:

Low Risk:

- Solid needle or superficial exposure on intact skin
- Small volume (drops of blood) on mucous membrane or non-intact skin exposures
- Source is asymptomatic or viral load <1500 copies/ml

High Risk:

- Large bore needle, deep injury, visible blood on device, needle in patient artery/vein
- Large volume (major blood splash on mucous membrane or non-intact skin exposures)
- Source patient is symptomatic, in acute seroconversion and has high viral load

Immediately after exposure all exposed individuals should take PEP according to the assumed risk. Those of low risk should take 2-drug combination and those with high risk should take a 3drug combination. Where the risk cannot be ascertained, a 2-drug combination should be used. If the preferred regimen is not available, it is better to administer an alternative regimen than to wait.

Actions following HIV testing in PEP

If the source person is HIV negative:

- No PEP is necessary for the exposed health worker unless there is suspicion that the source is newly infected, and in the 'window period' of sero-negativity.

If the exposed health worker is HIV positive

- No PEP is necessary
- The health worker should be referred for further counselling and long-term management.

If the health worker is HIV negative and the source patient is HIV positive.

- Give ARV drugs for a period of four weeks;
- Repeat health worker's HIV test at 3 and 6 months after the initial test.
- Should the health worker seroconvert during this period, provide appropriate care and counselling, refer for expert opinion and long term management.

If it is not possible to determine the HIV status of the source patient

- Assume that the source patient is positive and proceed according to guidelines above.

Table 8.1 Recommended Drug Combinations for PEP

Recommended 2-Drug Combinations	Recommended 3-Drug Combinations
TDF/3TC (300/300mg) o.d. or AZT/3TC (300mg/150mg) b.d.	TDF/3TC/EFV (300/300/600mg) o.d. or AZT/3TC (300/150mg) b.d. + EFV (600mg) o.d. Nevirapine should never be used for PEP as the risk of fatal hepatotoxicity outweighs the risk of HIV infection. Where Efavirenz is contraindicated, either of the 2drug combinations may be combined with ATV/r or LPV/r

The chosen regimen should be continued for 28 days or until the result of HIV test for the source patient is known to be negative. In areas of high HIV incidence, a significant number of HIV positive individuals may be in the 'window period' of acute infection and test antibody negative. A high level of suspicion for acute HIV infection should therefore be maintained and PEP continued if the source patient is suspected to have been recently infected with HIV.

Guidance should be given on risk reduction measures until the exposed person is known to be HIV negative. It is important to consider the risk of exposure to viral hepatitis when evaluating persons for post exposure management.

Table 8.2: Recommended Schedules of Investigations following Exposure

Period	Recommended Investigations
Baseline	HIV screening, Full blood count, Liver function test, Renal function test
Two weeks	Full blood count, Liver function test, Renal function test
Six weeks	HIV screening
3 months	HIV screening
6 months	HIV screening

8.2.2 Post-Sexual Assault Exposure Prophylaxis

The possibility of HIV exposure from sexual assault should be assessed at the time of the post-assault examination. The benefit of PEP in the prevention of HIV infection should be discussed with the assault victim if risk of HIV exposure exists. The likelihood of the assailant being HIV infected, the time that elapsed after the event and any exposure characteristics that might increase the risk for HIV transmission will impact the medical recommendation for PEP and assault victim's acceptance of the recommendation. When an assailant's HIV status is unknown, the following factors should be considered in evaluating the level of risk:

- Occurrence of vaginal or anal penetration
- Occurrence of ejaculation on mucous membranes
- Involvement of multiple assailants
- Presence of mucosal lesions on the assailant or victim
- Other characteristics of the assault, victim, or assailant that might increase risk for HIV transmission

If PEP is offered, the following information should be discussed with the patient:

- Proven benefits and known toxicities of ARV;
- Close follow-up that will be necessary
- Benefit of adherence to recommended dosing
- Necessity of early initiation of PEP to optimize potential benefits (as soon as possible after and up to 72 hours after the assault)

In post sexual assault PEP, ARV drugs should be administered as in the case of occupational exposure to HIV (see table 8.1); in this circumstance, a three-drug regimen should be used. As with all cases of sexual assault, it is important to arrange for continuous counselling and support for the victim. Emergency contraception should also be considered.

8.3 Isoniazid Preventive Treatment (IPT)

Isoniazid Preventive Therapy (IPT) is the use of isoniazid to prevent the development of active TB disease in HIV positive individuals. Available evidence shows that TB is the most common opportunistic infection and a leading cause of death among PLHIVs and that IPT is effective in preventing it. IPT is not the treatment for active TB. It is therefore necessary to exclude active TB before commencing a patient on IPT.

For a patient to benefit from IPT, he must:

- Be HIV positive.
- Not have active TB.
- Be motivated to adhere to treatment.

8.3.1 Steps to Initiating IPT

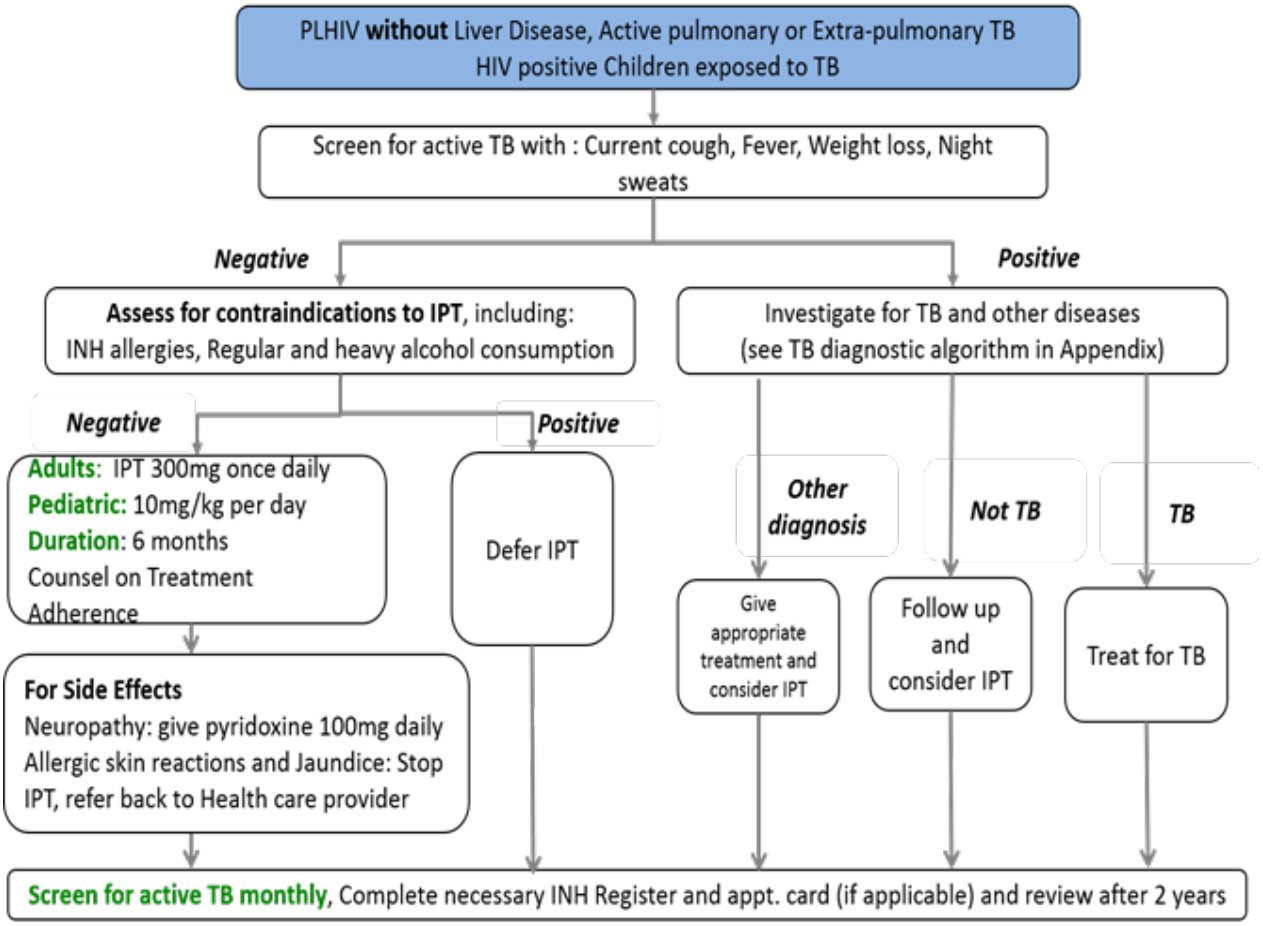
- Verify/Confirm HIV Status.
- Counsel on TB/HIV interactions.
- Exclude active TB:
  - Ask the patients about cough, weight loss, fever and night sweats.
  - Check for lymph node enlargement
  - For patients who do not have cough, weight loss, fever, night sweats or lymph node enlargement, assess for contraindications to IPT, counsel on adherence, and commence IPT.
- For patients with the above symptoms/signs:
- Do sputum examination (Where available, the new molecular test for TB (Xpert MTB/Rif) should be used as the test of choice)
- If smear positive refer/commence short course chemotherapy for TB (DOTS, preferably).
- Those with negative sputum results should be referred to medical officers for confirmation of diagnosis.
- If signs and symptoms absent, do chest x-ray
- If no active TB confirmed, assess for contraindications to IPT, counsel on adherence, and commence IPT.

Dosage of INH for IPT in adults is 300mg/day for 6 months. Harmonize dispensing schedule with that of ARVs and emphasize the importance of adherence at each visit.

8.3.2 IPT in Children

- All HIV-infected infants and children exposed to TB through household contacts, but with no evidence of active disease, should begin Isoniazid Preventive therapy (IPT).
- HIV-infected children >12 months of age should receive 6 months of IPT as part of a comprehensive package of HIV care irrespective of TB exposure; active TB disease must be ruled out.
- 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.
- The recommended dose of INH for preventive therapy in HIV co-infection is 10 mg/kg/day for 6 months (maximum 300 mg/day)

Figure 8.1. Algorithm for TB screening among adults and adolescents living with HIV



Counsel patient/caregiver on:

- Treatment adherence
- Side effects of INH: peripheral neuropathy, jaundice, rash
- Immediate recognition and reporting of signs and symptoms of active TB

If patient develops active TB during the course of IPT, discontinue IPT and refer/commence antiTB treatment (DOTS).

During the monthly visit, monitor the patients for:

- Signs and symptoms of active TB.
- Side effects. The most common side effect is peripheral neuropathy (numbness/tingling sensation of extremities). In addition allergic skin eruptions and jaundice can occur.

If numbness/tingling/burning sensation is present give Pyridoxine 100mg daily.

If jaundice develops, discontinue IPT and refer to Medical Doctor for assessment.

Complete necessary INH prophylaxis register and INH appointment card, review after 2 years.

8.4 Cotrimoxazole Preventive Therapy

Cotrimoxazole preventive therapy (CPT) is use of cotrimoxazole for the prevention of several secondary bacterial and parasitic infections in HIV infected individuals. It is particularly useful as prophylaxis against malaria especially in malaria endemic countries. CPT is therefore useful for improving quality of life and reduce the rate of death among HIV infected patients.

Criteria for initiating CPT in a person living with HIV:

- Symptomatic HIV, irrespective of CD4 count.
- Asymptomatic with CD4 count <500 cells/mm^3
- Be motivated to adhere to treatment.
- Active TB at any CD4 count.
- Pregnancy (after the first trimester).
- HIV-exposed infants from 6 weeks of age.
- HIV positive child in the first year of life.
- HIV positive children aged 1-5 years with WHO clinical stages 2, 3 and 4 regardless of CD4 % or any WHO stage and CD4 <25%.

Steps in initiating CPT.

- Verify HIV status.
- Take medical history
- Conduct physical examination.
- Counsel on OIs in HIV infection.
- Treat pre existing OIs. (Refer to appendix on management of opportunistic infections)
- Screen for contraindications for CPT: e.g known allergy to sulphur-containing drugs (which includes cotrimoxazole and sulphadoxine-pyrimethamine), first trimester pregnancy, kidney or liver disease, seriously ill patients (refer for specialized medical care).

Counsel patient on:

- Drug adherence,
- Side effects of Cotrimoxazole include:
  - Skin eruptions, which may be severe (Stevens Johnson syndrome)
  - Nephritis
  - Hepatitis.
  - Anaemia and other signs of bone-marrow suppression
  - Hyperkalaemia

Commence CPT

Dose of cotrimoxazole (CPT) in the Adult: cotrimoxazole 960mg daily (two single strength or one double strength tablet) until CD4 cell count >500cells/mm^3 is achieved and maintained for 12 months.

For infants below 6 months or < 5 kg (cotrimoxazole 120mg daily)

For children 6 months–5 years or 5-15 kg (cotrimoxazole 240 mg daily)

For children 6–14 years old or 15–30 kg (cotrimoxazole 480 mg daily)

For anyone over 14 years or >30 kgs (cotrimoxazole 960 mg)

Monitoring and follow-up

- Adults should be reviewed monthly initially, and then three monthly thereafter if the medications are tolerated.
- Laboratory monitoring of adults should take place every six months or when clinically indicated. This should include haemoglobin and white cell count.
- Replenish patient's drug review and Assess for ART

When to discontinue CPT:

- CPT should be continued in all patients until the person has achieved a CD4+ cell count+ >500 cells/mm^3 and remained clinically stable thereafter for one year. Then CPT can be discontinued.
- Discontinue if there is an occurrence of side effects to cotrimoxazole

8.5 Sexually Transmitted Infections (STIs)

HIV and other sexually transmitted infections and non-sexually transmitted infections of the reproductive tract frequently coexist. Most of these infections are asymptomatic, especially among women. However, even asymptomatic sexually transmitted infections can cause complications, be transmitted to sexual partners and enhance HIV transmission. Further, HIV infection alters the natural history of sexually transmitted infections. The objectives of diagnosing and managing sexually transmitted infections include identifying the infection and providing appropriate treatment and preventing transmission. Screening, diagnosis and treatment of sexually transmitted infections should be offered routinely as part of comprehensive HIV care among adults and adolescents.

CHAPTER NINE

ADHERENCE TO ANTIRETROVIRAL THERAPY

9.1 Definitions

Adherence is a term used to describe the patients' behaviour of taking drugs correctly based on mutual agreement between the patient and health care provider; it involves:

- Taking the right drugs
- The right dose
- The right frequency
- The right time

Adherence also means a patient attending all scheduled clinic visits. Adherence to ART is an essential component of individual and programmatic treatment success. Adherence rates exceeding 95% are necessary for improved and sustained virologic, immunologic and clinical outcomes. Adherence is crucial for delaying or preventing the development of drug resistance, reducing the risk of transmitting HIV, and ensuring maximum durability of the first-line ARV regimen. The measures to ensure optimal adherence should be undertaken at initiation and during therapy.

9.2 Adherence Preparation for ART

The success of any adherence strategy depends on the education of patients before the initiation of ART, an assessment of their understanding of and readiness for treatment. Adherence counselling includes giving basic information on HIV, its manifestations, and the benefits and side effects of ARV medications. It also includes how the medications should be taken and the importance of not missing any dose. Peer counsellors and visual materials can be particularly useful in this process. Consideration should be given to minimizing the number of pills, frequency of dosing, food restrictions, adjusting ARV drugs to the patient's lifestyle when possible, and involving relatives, friends and/or community members as agreed with the patient.

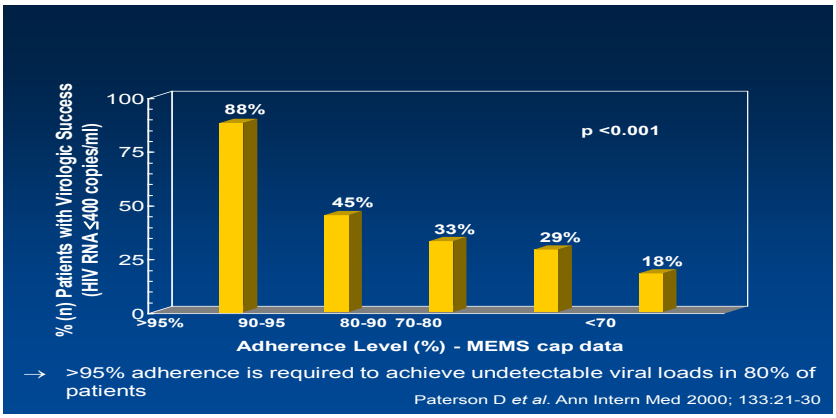
9.3 On-going adherence for clients on ART

It is essential to continue with adherence counselling. This should involve adherence assessments during every visit, emphasis on importance of adherence and continuous involvement of relatives, friends, peers and/or community support personnel.

9.4 Measurement of Adherence

Virologic success of therapy is strongly dependent on adherence to ARVs (Figure 9.1). Adherence in many studies is measured by expressing the number of doses taken as a percentage of the number of doses prescribed. For example if 20 doses are prescribed and 19 doses are taken adherence is 95%. This translates to missing one dose in ten days on a twice-daily regimen. Other measurement methods include; patient self-report, pharmacy drug pick-up and electronic methods (e.g. the MEMS cap).

Figure 9.1 Correlations between Adherence and Virologic Success



9.4.1. Factors known to improve Adherence

The following factors have been associated with high adherence rates:

- Increased access to free ART.
- Individual patients, family, peers and friends, community members, or treatment-supporter engagement in adherence education.
- Family-based care if more than one family member is infected with HIV
- Continuous and effective adherence counselling, including on knowledge and understanding of HIV infection, course of treatment, and expected adverse reactions and what to do if happens.
- Drug regimen simplicity e.g. Fixed Drug Combination (low pill burden)
- When possible use drugs with less adverse effects

9.4.2 Factors Associated With Poor Adherence

- Poor patient-caregiver relationship
- High pill burden
- Forgetfulness
- AIDS Dementia Complex
- Depression
- Lack of patient education
- Inability of patients to identify their medications
- Drug toxicity
- Severe illness
- Pregnancy related conditions
- Incarceration
- Long duration of treatment
- Complexity of the treatment
- Perceived benefits versus barriers e.g. discrimination and stigmatisation
- Lack of social support
- Substance abuse

- Self-efficacy regarding adherence
- Cost of treatment
- Distance to facility

9.4.3. Strategies for Improving Adherence

- Treatment education for patients and treatment partners
- Treatment-supporter involvement.
- Peer health education.
- Routine assessment and reinforcement of adherence during follow up
- Directly Observed Therapy –where possible
- Fixed dose combination
- Reminders and patient engagement tools (e.g. a cell phone, SMS text messages , alarm clock)
- Convenient monthly packs (Using pill storage boxes.)
- Follow up before supplies are exhausted
- Positive feedback on health improvements
- Address adverse events
- Address life-style factors e.g. alcohol abuse
- Adapting therapy to the client's lifestyle
- Avoiding imposing out-of-pocket payments at the point of care
- Support groups
- Improved social support

CHAPTER 10

MANAGEMENT OF COMMON OPPORTUNISTIC INFECTIONS

Persons living with HIV are more prone to develop infections than persons not infected with the virus largely because of the immune system damage associated with HIV infection. The bulk of infections that occur in PLHIV are called opportunistic infections because they thrive on compromised immune states. The appearance of opportunistic infections in HIV infected persons is directly related to the extent of immune deficiency and depletion of CD4+cells. The lower the CD4+cell count, the higher the likelihood of the appearance of opportunistic infections. With the exception of TB most opportunistic infections in PLHIV begin to appear at CD4+cell counts of <350cells/mm3 and several of them are useful for staging the severity of HIV disease.

Opportunistic infections associated with HIV fall into four broad categories namely bacterial, viral, fungal and protozoal infections. The infections affect all major systems of the body including the nervous, gastrointestinal, respiratory, skin, musculoskeletal, eyes, ear nose and throat etc. When opportunistic infections occur in persons living with HIV/AIDS they should be treated immediately since they can cause considerable damage to the immune system and lead to rapid increase in viral replication.

Table 10.1 contains details of the symptoms and signs of the more opportunistic infections and suitable treatment for each of them.

Effective use of antiretroviral therapy and cotrimoxazole reduces the incidence of HIV related opportunistic infections.

Table 10.1: Common HIV related Opportunistic Infections: Clinical Features, Treatment, and Prophylaxis

Infection/ Conditions	Causative organisms	Symptoms and signs	Diagnosis	Treatment and Prophylaxis	Comments
Tinea corporis Tinea capitis	Malassaezia furfur Trichophyton rubrum	Itchy circular lesions with raised edges, fine scaly area in the centre, loss of hair	Clinical Laboratory: skin scrapings stained with KOH	Topical application: Whitfield's ointment applied b.d. for 3-5 weeks 2% Miconazole cream bid to skin for 3-5 weeks Oral therapy: Paediatric dose Griseofulvin 10mg/kg/day x 8weeks Oral Ketoconazole 3.3-6.6 mg/kg o.d. x 2-4 weeks Adult dose - Griseofulvin: 500mg daily x 30 days -Oral ketoconazole: 200 – 400mg daily	Extra caution for possible NVP interactions with ketoconazole (see section on drug interactions)
Seborrhoeic dermatitis	Allergic reaction to yeast infection (Pityrosporum)	Greasy scales over scalp and redness of cheek and flexural aspects	Clinical	Selenium sulphide shampoo, or Tar shampoo followed by sulphur salicylic acid cream or 1% hydrocortisone , or Ketoconazole cream.	Secondary bacterial infection may be common.
Candidiasis: Oral thrush	Candida albicans	White painless plaques on the buccal and or pharyngeal mucosa or surface of the tongue that is not easily scraped off	Clinical Laboratory: Wet mount microscopy using KOH preparation.	Adult: Nystatin 100,000-200,000 IU gargled or delivered to the cheeks in children 4-5 times/day for 14 days, Or Pastiles (mucosal adhesive capsule MAC) 4-5x/day for 7 – 10 days, Or 1% aqueous solution of gentian violet, local application 2 x daily x 7 days, Or Fluconazole - oral 6mg/kg stat day 1, then 3mg/kg/ day for 14 days Paediatric: Nystatin 400,000-600,000 units 4 – 5 times/day, swish in mouth several minutes and then swallow Fluconazole 200 mg PO on Day 1, then 100 mg daily	Side effects of antifungal drugs: Mild - Nausea, vomiting, diarrhoea, abdominal pain Severe - Hepatotoxicity agranulocytosis, seizures
B. Oesophagitis	Candida albicans	White patches, in mouth, retro-sternal pain on swallowing, food refusal, excessive salivation	Suspected presence of oro-pharyngeal thrush, odynophagia Oesophagoscopy	Adult: Fluconazole – oral, 6mg/kg stat day 1 then 3mg/kg/ day for 14-21 days Ketoconazole 3.3-6.6mg/kg/day x 14-21 days Paediatric: Fluconazole – oral 200mg day 1, THEN 100 mg daily; doses up to 400 mg/day may be used based on patient's response. Treat for a minimum of 3 weeks and for at least 2 weeks following resolution of symptoms Oral ketoconazole: 200 – 400mg daily	With fluconazole, hepatotoxicity, nausea, vomiting abdominal pain, pancytopaenia may occur Avoid use of ketoconazole with NVP

Table 10.1.....cont.... Common HIV related Opportunistic Infections: Clinical Features, Treatment, and Prophylaxis

Infection/ Conditions	Causative Organisms	Symptoms and Signs	Diagnosis	Treatment	Comments
Cryptococcal meningitis	Cryptococcus neoformans	Headache, fever, delirium, neck pain, convulsion, photophobia	Clinical Lab: CSF Serology/India Ink stain	Initially, administer amphotericin B at 0.7-1 mg/kg/d for 2 weeks, with or without 2 weeks of flucytosine at 100 mg/kg/d in 4 divided doses, followed by fluconazole at 400 mg/d for a minimum of 8-10 weeks.	Refer to infectious disease specialist
Pneumocystis pneumonia	Pneumocystis jirovecii (carinii) PJP	Acute/sub-acute non productive cough, difficulty in breathing	Clinical: CXR: focal interstitial infiltrates and mediastinal lymphadenopathy, ground glass appearance, Laboratory: induced sputum or bronchio-alveolar lavage for cytology.	Acute: Trimethoprim 20mg/kg PO or iv x 21 days (in divided doses, q.i.d), or Dapsone 2mg/kg o.d. max. 100mg/ day x 21 days, or Pentamidine 4mg/kg/o.d.iv x 21 days, or Clindamycin 10-30mg/kg/day i.v. tid x 14-21 days (oral clindamycin may be considered in adults) For severe disease: (PO2 <90mmHg: add prednisolone 2mg/kg/day x 7-14 days Prophylaxis: Paediatrics: CTX 6-8mg/kg/day PO daily Adult: CTX tablets 960mg daily	Complications of drug treatment - Severe reactions: Stevens-Johnson syndrome Toxic epidermal necrolysis Anaemia, hepatitis, haemolysis in G6PD deficient patients
Stomatitis, Aphthous ulcers	Herpes simplex virus 1 and 2	Recurrent, painful, oral vesicular lesions, shallow ulcers Oesophagitis: odynophagia	Clinical; Laboratory: Tzanck smear Rising serum HSV antibody titres	Adult: Mild-moderate lesions: IV acyclovir 5 mg/ kg 8hourly for 7 days or PO 400 mg 5 times daily for 7 days Paediatrics: Mild-moderate lesions: 8 mg/kg/ dose t.i.d orally; If severe: Acyclovir 40-80mg/kg/day tid x 5-10 days Topical antiseptics to avoid bacterial superinfection Analgesics.	
Herpes virus encephalitis	Herpes simplex virus 1 and 2	Fever, altered consciousness, convulsions ± focal neurological signs	Increased CSF: serum HSV antibody ratio Viral isolation	IV Acyclovir Paediatrics: 20mg/kg tid x 21days Adult: 10-15 mg/kg IV q8hr for 14-21 days	Nausea, vomiting, diarrhoea, headache, malaise, rash, seizures, renal dysfunction

Table 10.1.....cont.... Common HIV related Opportunistic Infections: Clinical Features, Treatment, and Prophylaxis

Infection/ Conditions	Causative Organisms	Symptoms and Signs	Diagnosis	Treatment	Comments
Herpes zoster (Shingles)	Varicella zoster virus	Painful vesicular lesions in a dermatomal distribution, on face and trunk	Clinical	IV Acyclovir Paediatrics: 30mg/kg/day tds x 7 days Adult: 10 mg/kg IV q8hr for 7 days Analgesics – NSAIDS, carbamazepine, amitriptyline Local appl of calamine lotion; Topical application of Acyclovir cream	Refer intractable cases for specialist care.
Cytomegalovirus: Enteritis Colitis CNS involvement	Cytomegalovirus (CMV)	Enterocolitis: Fever, cramps, dysphagia, odynophagia, diarrhoea ± blood; CNS: Delirium, lethargy, headache, malaise disorientation, neck stiffness, photophobia, cranial nerve palsy, blurred vision or "floaters"	Clinical Laboratory: Biopsy (intracellular inclusions) Serology Skull X ray CT Scan CMV in CSF	Ganciclovir 5mg/kg IV bid x 2-3 weeks; Foscarnet IV 40-60mg/kg 8 hrly x 2-3 weeks Retinitis – Opthamological examination; same drug therapy as above.	
Measles	Measles virus	Fever, cough, red eyes, kerato-conjunctivitis, coryza , maculo-papular rash; Complications: Pneumonia, diarrhoeal disease, malnutrition.	Clinical	Supportive therapy Anti-pyretics Vitamin A, antibiotics as indicated, adequate hydration	Highly contagious; Refer Complications; Nutrition support
Chicken pox	Varicella virus	Fever, centrifugal (starts from trunk to extremities) umbilicated rash in crops	Clinical	Supportive therapy Reduce fever; Antibiotics for bacterial infections	
Anal/Genital warts Cutaneous warts (Verruca plana)	Human papilloma virus	Anal/Genital: Crops of papules or nodules with a rough surface Verruca planar: Widespread flat hypo/hyper-pigmented rash on face, trunk and limbs, not itchy, dry, often scaly	Clinical	Apply Salicylic acid preparation, or Liquid nitrogen, Cryotherapy or Electrocautery	

Table 10.1.....cont.... Common HIV related Opportunistic Infections: Clinical Features, Treatment, and Prophylaxis

Infection/ Conditions	Causative Organisms	Symptoms and Signs	Diagnosis	Treatment	Comments
Molluscum contagiosum	Pox virus	Light-coloured nodules with central umbilication commonly seen on face and trunk.	Clinical	Leave alone unless super-infected, OR Use Electro-cautery, OR Use of Liquid nitrogen application.	Antibiotics for bacterial super-infection.
Toxoplasmosis	Toxoplasma gondii	Fever, reduced alertness, headache, focal neurological deficits, seizures, chorio-retinitis	Clinical: Response to empiric therapy. Serology: rising IgG titre CT scan	Non Pregnant Adult: Pyrimethamine (100mg loading dose orally followed by 25 - 50 mg/day) plus sulfadiazine (2 - 4 g/day divided 4 times daily) OR Pyrimethamine (100 mg loading dose orally followed by 25-50 mg/day) + clindamycin (300 mg orally 4 times daily) Folinic acid (leucovorin) (10 - 25 mg/day) should be given to all patients to prevent hematologic toxicity of pyrimethamine Trimethoprim (10 mg/kg/day) sulfamethoxazole (50 mg/kg/day) for 4 weeks Pregnant Adult: Spiramycin 1 g orally every 8 hours If the amniotic fluid test result for T gondii is positive: 3 weeks of pyrimethamine (50 mg/day orally) and sulfadiazine (3 g/day orally in 2-3 divided doses) alternating with a 3-week course of spiramycin 1 g 3 times daily for maternal treatment OR Pyrimethamine (25 mg/day orally) and sulfadiazine (4 g/day orally) divided 2 or 4 times daily until delivery (this agent may be associated with marrow suppression and pancytopenia) and Leucovorin 10-25 mg/day orally to prevent bone marrow suppression Paediatrics: Pyrimethamine 2mg/kg/dose/day max 50mg x 2 days then maintenance 1mg/kg/day max 25mg + Sulphadiazine 50mg/kg/every 12 hours then treat 4 weeks beyond resolution of symptoms Pyrimethamine + Folinic acid 5-20 mg 3 times weekly + Clindamycin 10-30mg/ kg/ day tds x 6wks Corticosteroids to reduce oedema/mass effect. Prophylaxis: CTX	Complications of treatment - Nausea, vomiting, abdominal pain; Megaloblastic anaemia, pancytopaenia, rash, Stevens Johnson Syndrome, photosensitivity Folinic acid 5-20 mg given as prevention
Pneumonia	Respiratory viruses Bacteria: S. pneumoniae H. influenza S. aureus M. catarhalis Kl. pneumonia P. aeruginosa	Fever, chills, cough and pleuritic chest pain, difficulty/ fast breathing. Crepitations, bronchial breath sounds	Clinical Laboratory: blood culture. Chest x ray	Viral pneumonia is self-limiting – requires only supportive care Bacterial: Out-patient therapy with CTX or Ampiclox, amoxicillin or Amoxicillin/ clauvullic acid. For in-patient therapy: Crystalline Penicillin & Gentamicin. 2nd generation cephalosporins as 2nd line.	For severe pneumonia in children <12 months old treat PJP presumptively with CTX. If facilities to exclude PJP infections are not available or if child on CPT develops bacterial pneumonia do not treat with CTX but refer.

Table 10.1.....cont.... Common HIV related Opportunistic Infections: Clinical Features, Treatment, and Prophylaxis

Conditions/ Infections	Causative Organisms		Symptoms and Signs	Diagnosis	Treatment	Comments
Acute Pharyngo–tonsillitis	Respiratory viruses Bacteria: Strep. pneumoniae H. influenza Moxerella Catarhalis Klebs. pneumoniae		Fever, cough, vomiting, refusal of feeds, drooling of saliva, inflamed tonsils/ pharynx.	Clinical Laboratory: Throat swab for m/c/s	Amoxicillin or Amoxicillin/ clauvullinic acid. 2nd generation cephalosporins	
Acute otitis media	Respiratory viruses Bacteria: Strep. pneumoniae H. influenza Staph. Aureus Moraxella catarhalis Klebs. pneumoniae		Fever, vomiting, cough, ear-tugging; Hyperaemic tympanic membrane, purulent ear discharge	Clinical Laboratory: Ear swab for m/c/s	Amoxicillin or Amoxicillin/ clauvullinic acid 2nd generation cephalosporins Ear wicking	
Chronic suppurative otitis media	S. pneumoniae H. influenza S. Aureus	M. Catarhalis Kl. pneumoniae P. aeruginosa	Ear discharge lasting >14 days	Clinical Laboratory: Ear swab for m/c/s X ray of mastoid	Refer to ENT specialist	Hearing loss is a complication
Acute watery Diarrhoea	Viruses: Rotavirus Enteroviruses Other viruses	Bacteria: Enterobacteriae E. Coli C. jejuni	Frequent watery stools	Clinical Laboratory: Stool m/c/s Serology	Rehydrate (SSS,ORS or Resomal as required)	Provide and maintain adequate nutrition
Dysentery	E. hystolitica G. Lamblia Isospora belli Cryptosporidia Salmonella spp. Shigella	C. Pylori C. jejuni Cyclospora Microsporidia C. albicans M. avium complex S. Stercoralis	Frequent watery stools, abdominal cramps bloody stools, fever, nausea and vomiting, dehydration	Clinical Laboratory: Stool m/c/s Serology, e.g. Widal test	Oral rehydration If antibiotics required: Ciprofloxacin Metronidazole and CTX For Strongyloidiasis: Albendazole Oral Zinc therapy	Provide and maintain adequate nutrition

Table 10.1.....cont.... Common HIV related Opportunistic Infections: Clinical Features, Treatment, and Prophylaxis

Infections/ Conditions	Causative Organisms		Symptoms and Signs	Diagnosis	Treatment	Comments
Malaria	Mainly P. falciparum		Fever, chills and rigor, headache, nausea and vomiting	Clinical Laboratory: malaria parasite in blood	Uncomplicated: Artemisinin-based Combination Therapy Complicated: Injectable Artesunate	Refer to higher level facility if complicated
Sepsis	S. pneumoniae H. influenzae Salmonella N. meningitides	Staph aureus Gram negatives (e.g. E. coli) Anaerobes	Fever Shock	Clinical assessment Laboratory: FBC Blood culture Urine culture	While awaiting m/c/s results, either: Penicillin + Chloramphenicol Penicillin + Gentamycin Ampiclox + Gentamycin Amoxicillin/clauvullinate + genticin Metronidazole for anaerobes 2nd or 3rd generation Cephalosporins used as 2nd line	Refer to tertiary facility if necessary If in shock, provide supportive therapy
Impetigo contagiosum	Streptococcus spp, Staph. Aureus		Skin pustules crusts Fever, rarely	Clinical	Clean sore with antiseptics Drain pus if fluctuant Ampicillin/cloxacillin	
Meningitis	S. pneumonia H. influenzae Salmonella N. meningitides Staph aureus		Fever, headache, vomits, irritability, altered sensorium, convulsions Nuchal rigidity, bulging fontanelle	Cinical assessment Laboratory: FBC Blood culture CSF analysis	Penicillin & Chloramphenicol Or 3rd generation cephalosporin + Gentamycin Supportive treatment	Refer to tertiary facility if necessary
Scabies	Sarcoptes scabei		Intense itchy lesions most prominent in inter-digital webs, cleft; Papular rashes or generalised (Norwegian)	Clinical, Laboratory: Microscopy on KOH prep. of skin scrapings	20% Benzyl benzoate applied whole body, neck down nocte for 3 days OR Permethrin cream 5% applied whole body, neck down and washed off after 8–14 hours. Repeat after 1–2 weeks.	Treat super-imposed bacterial infection with oral antibiotics Treat all household members even if asymptomatic

Table 10.1.....cont.... Common HIV related Opportunistic Infections: Clinical Features, Treatment, and Prophylaxis

Infections/ Conditions	Causative Organisms	Symptoms and Signs	Diagnosis	Treatment	Comments
Mycobacterium Avium Complex	M. avium spp.	Disseminated form – recurrent fever, chronic diarrhoea, lymph-adenopathy, weight loss/failure to thrive, abdominal pain, Respiratory symptoms rare	Clinical Laboratory: Multiple blood cultures; Lymph node biopsy for intracellular inclusions	Adult: Clarithromycin 500 mg b.d. + ethambutol 15 mg/kg daily with or without rifabutin (300 mg daily). Azithromycin (500-600 mg daily) can be substituted for clarithromycin. Paediatrics: Clarithromycin 7.5mg/kg/dose b.d or azithromycin 5-20mg/kg/dose once daily plus Ethambutol 15mg/kg/day for 6 months. Prophylaxis: guided by CD4+ count	Nausea and vomiting Optic neuritis
Lymphoid interstitial pneumonitis (LIP)	Unknown, but associated with co-infection with Epstein Barr Virus	May initially be asymptomatic. Recurrent Cough, respiratory distress, parotid enlargement, generalized lymphadenopathy, hepatosplenomegaly, digital clubbing, and poor response to TB therapy.	Clinical Chest X Ray: reticulo-nodular infiltrates, bilateral hilar/mediastinal lymphadenopathy; Diagnosis of exclusion.	Steroids (prednisolone 2mg/kg/day x 6 weeks, taper off) Oxygen Bronchodilators (salbutamol) Chest physiotherapy Referral to specialist (paediatric pulmonologist)	Complications of therapy with prednisolone include Hypertension, gastritis, adrenal insufficiency, seizures, pseudo-tumor cerebri, hypokalaemia, fluid retention, glucose intolerance.

CHAPTER ELEVEN

CARE AND SUPPORT

11.1 Definition

Care and Support, in the context of HIV, means catering to the needs of people living with HIV and providing appropriate support for persons affected by it. HIV/AIDS Care and Support is the holistic and comprehensive client-focused, community centred care of the PLHIV and their families a multidisciplinary team at all stages of the HIV infection.

11.2. Care and Support for People Living with HIV

11.2.1 Nutritional Support

People living with HIV will thrive best on a healthy diet and may need nutritional support to achieve this. HIV positive clients should be advised on the following:

- The need for adequate intake of energy and protein rich foods, fruits and vegetables
- The need for micronutrient supplementation, which should include: iodine, zinc, calcium, magnesium, iron, folic acid, selenium and vitamins A, C, B6, B12 and D.

These micronutrients may enhance the immune status of the client. They may be found in dark green leafy vegetables, yellow and orange fruits, sweet potatoes, pumpkins, carrots, avocado and tomatoes. In cases where clients are unable to maintain normal food intake, small but frequent meals should be encouraged to increase food absorption.

11.2.2 Lifestyle and Behavioural Change

Behavioural changes that should be encouraged to reduce risk of HIV transmission include:

- Smoking, alcohol and recreational drug use should be discouraged
- PLHIV should be counselled on how to deal with stress and on a healthy lifestyle.

11.2.3 Treatment of Common Infections

- HIV positive clients may have other sexually transmitted infections that will require treatment, e.g. syphilis and gonorrhoea
- Urinary tract infection and respiratory infections are more common in HIV positive women and may require antibiotic therapy
- Vaginal candidiasis may be recurrent and may be treated with local antifungal compounds.

11.2.4 Prophylaxis for Common Infections

- ***Pneumocystis jirovecii pneumonia (PCP) prophylaxis:*** PCP prophylaxis (cotrimoxazole 960mg once daily) should be given to all clients with CD4 cell counts below 500 cells/µl)

Specific Considerations to HIV Positive Pregnant Women

- Investigate and treat for vaginal candidiasis, syphilis and gonorrhea.
- Give Iron and Folate supplements: AZT in addition to Pregnancy predisposes HIV Positive women to anaemia.
- Intermittent Preventive Therapy (IPT) with Sulfadoxine-pyrimethamine (SP) for malaria prophylaxis. Three (3) doses of SP are recommended for all HIV Positive Pregnant Women, avoiding the first trimester and the last 4 weeks of pregnancy. Do not give Malarial prophylaxis if the woman is already on cotrimoxazole prophylaxis.
- Tetanus Toxoid Immunization

Unprotected sex during pregnancy and breastfeeding may be associated with an increased risk of HIV transmission to the baby. Women should be encouraged to use condoms, even with their spouse or trusted partner, to protect against HIV and other STIs. Couple counselling and testing is encouraged so that both partners know if they are at risk for HIV infection with unprotected sex.

11.3 Care and Support for HIV Infected and Exposed Child

A family focused model of care is effective for engaging children and their families in the long-term management of HIV. Care and support for HIV infected and exposed children:

- Enhances the quality of life, and may also positively influence management outcomes
- Is applicable early in management, and includes investigations needed to better understand and manage clinical complications.

11.3.1 Retention in Care, Treatment and Support

Patient retention refers to the proportion of people who continue ART among those who ever started. This is critical to the overall success and impact of HIV programme. While ART can dramatically improve outcomes for children infected with HIV, excellent adherence is required for treatment success.

Retention applies to HIV-exposed infants and HIV-positive children pre-ART and on ART. It is noteworthy that children who are in pre-ART have poorer retention than children on ART and special efforts should be made to retain pre-ART children and regularly assess eligibility for ART.

11.3.2 Disclosure of HIV Status to Children

Disclosing HIV status to children is a sensitive issue, which must consider the needs, feelings, age, beliefs and understanding of the child and caregiver. It must however be done to improve outcomes in the treatment and care of children.

Importance of Disclosure to Children

- Reduction of developing myths about their illness
- Improvement of access to care and support services
- Enhancement of adherence to treatment and coping strategies
- Reduction of negative psychosocial impact

Counselling for disclosure in children

This involves counselling the caregivers to support age-appropriate HIV status disclosure to the child with minimal negative impact. Parents who decline or fail to disclose to their children should be counselled on the importance of the child knowing his/her status, and assisted to do so.

Steps for Counselling HIV-Infected/Affected Children and their Families

- Evaluate the child and family for readiness-including child's age and maturity. Five to seven years are earliest recommended ages for disclosure, and all should be disclosed by age 12.
- Ascertain a child's and caregiver's understanding of HIV infection
- Explain the benefits of early awareness of HIV infection to the child and care giver/family
- Provide ongoing psychosocial support.

11.4 Nutrition

Good nutrition contributes to the wellbeing of the person living with HIV at all stages of the disease and may even prolong life. It is important to have nutritional counselling as soon as the diagnosis of HIV is made and at subsequent contacts with care providers.

Nutritional Guide for People Living With HIV

- Eat a variety of foods
- Make carbohydrates which are high in energy the basis for each meal
- Eat a lot of fresh fruits and vegetables to supply vitamins
- Daily protein intake e.g. eggs, meat, fish, milk, beans, groundnuts and soya beans
- Include fats and oils in meals to provide energy
- Use salt sparingly
- Drink lots of water
- Do not drink alcohol
- Food, drinking water and beverages should be hygienically prepared

Strategies for improving and monitoring nutritional status

- Weight monitoring
- Nutrition education and counselling
- Prompt treatment of OIs that interfere with nutrition (mouth disorders, diarrhoea etc)
- Nutritional Support (macro- and micronutrients)
- Economic empowerment

Indications for therapeutic nutritional support

- Patients with malnutrition (body mass index <18m^3, micronutrient deficiency etc)
- Inability to eat

11.5 Immunization

Immunization is an effective way of preventing diseases. Patients with HIV infection are at increased risk for a variety of infections that can be prevented by using available vaccine preparations. Immunizations should be given according to the national immunization schedule. Patients with relatively well-preserved immune function are more likely to have a favourable response to vaccine challenge than those who are significantly immuno-compromised.

- Initiation of combination ART in patients with advanced HIV infection may improve the immunologic response to vaccine preparations.
- HIV exposed infants and HIV positive children should receive routine immunization according to the national immunization schedule however live attenuated vaccines, such as yellow fever and varicella-zoster virus are avoided in HIV-infected adults and children with advanced disease (CD4 < 200 cells/mm^3 or < 14%, or Stage 3/4 disease).
- The risk, morbidity and mortality of having wild type measles infection in our setting is considered much higher than that associated with the vaccine, therefore it is recommended for all HIV clients (especially children) regardless of immune function. Severely ill or hospitalized clients may be excluded.
- Killed or inactivated vaccines such as OPV, IPV, Measles, Yellow fever, and BCG are generally considered safe in all patients regardless of immune status.
- BCG is a live vaccine but is given at birth or very early in life, before the opportunity to assess HIV status or immune function in children. Therefore BCG vaccine often cannot be avoided.
- Hepatitis B, Pneumococcal Conjugate Vaccine (PCV), Pentavalent vaccine (DPT-HepB-Hib), Tetanus toxoid (TT) vaccines are all safe and recommended for all HIV clients especially those with CD4 count > 200 cells/mm^3
- Human Papilloma Virus (HPV) to be given in females age 9-26 is not recommended during pregnancy
- Some live vaccine preparations; anthrax, smallpox are not recommended for HIV positive adults

11.6 Universal Safety Precautions

All health facilities in the private and public sector should adopt a policy for the prevention of accidental occupational exposure to blood borne pathogens.

Minimum Standards of Universal Safety Precautions to be observed by health workers include:

- Routine hand washing with soap and water before and after contact with any patient
- Use of barrier precautions
- Safe handling and disposal of sharp instruments and equipment, including needles and syringes

Health facilities owe their employees the responsibility of providing materials for universal precautions. The minimum materials/equipment to be provided includes:

- Liquid soap from a dispenser or container

- Running water or a bucket with tap kept full with clean water or a ladle for dipping, if running water is not available
- Single-use towels (paper towels, or cloth towels that will be used once and laundered). If not available, hands should be air-dried.
- Materials to educate personnel on susceptibility to HIV infection and means of preventing

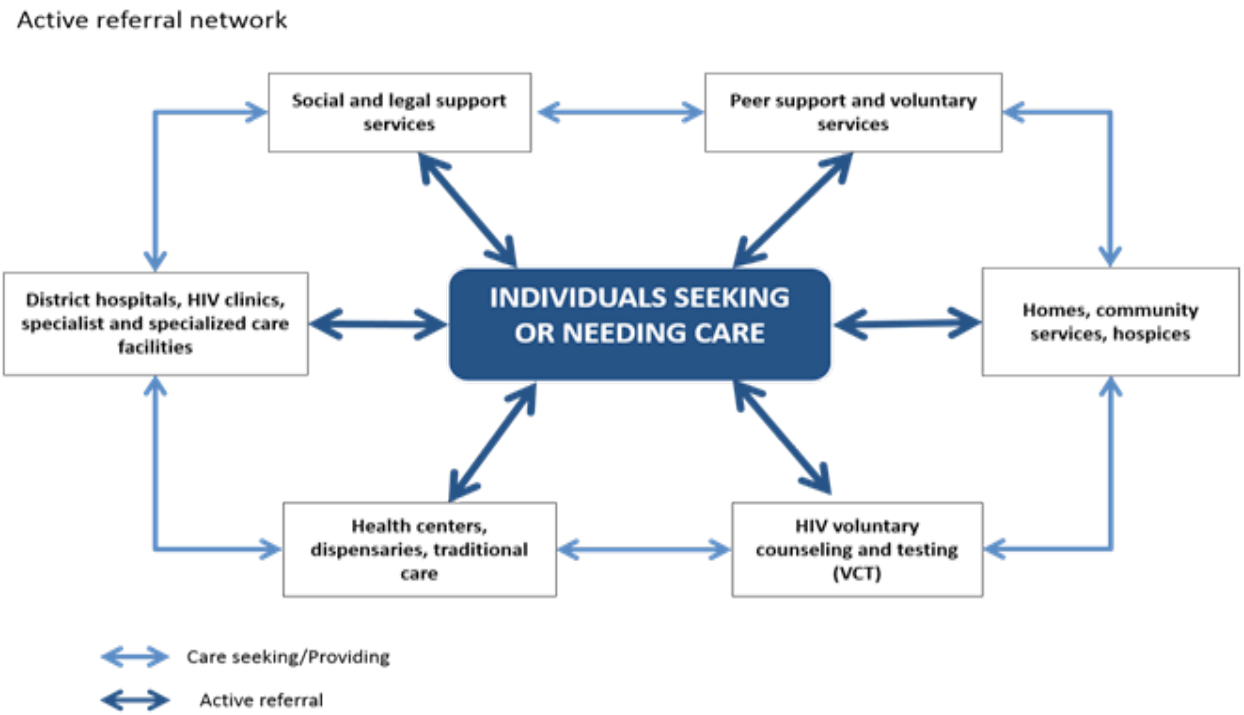
11.7 Linkages, Networks and Referral Services

Referral is the process by which client needs for treatment, care and support services are assessed and prioritized, and clients are provided with assistance in accessing such services. Referral should also include proactive actions necessary to facilitate initial contact with treatment, care and support service providers. PLHIV should have unfettered access to medical and non-medical services that are necessary to reduce the burden of HIV and mechanisms to ensure that this is possible should be established. Patients who are receiving care and treatment in primary health centres should be able to access secondary and tertiary level facilities for more advanced services, as the situation requires. Patients in health facilities should also be access non-medical support services that exist outside the facilities such as legal aid, IGAs etc.

Linkages to support services within and outside of the health care setting

The following diagram depicts the variety of services that should be available to the PLHIV and their families. It is premised on the availability of functional referral systems facility and community level support services for the PLHIV, requiring that the care providers have a working knowledge of the availability and locations of these services.

Figure 11.1 The Continuum of Care for PLHIV



Source: National Guideline on Palliative Care, Federal Ministry of Health (2006)

Reasons for referral

Clinical services.

These include clinical evaluation and management, prevention and treatment for opportunistic infections and HIV related conditions, early identification of communicable disease e.g. TB, STIs and hepatitis.

Reproductive health services

Pregnant and women of childbearing age should receive or be referred for reproductive health services. Reproductive health services will include prevention and treatment of STIs, family planning services, and cancer screening services among others. A major benefit is the prevention of unintended pregnancies, which is prong 2 of PMTCT.

Prevention and treatment of drug or alcohol abuse

Clients who abuse drugs or alcohol should receive or be referred to substance or alcohol abuse prevention and treatment services.

Mental health services

Clients with mental illness, developmental disability, or difficulty coping with HIV diagnosis or HIV-related conditions should receive or be referred to appropriate mental health services.

Social/Legal support services

Clients who test positive may require legal and/or social services for counselling on how to prevent or deal with discrimination in employment, housing and public accommodation.

Additional HIV prevention and support services

Additional client needs may be addressed through other HIV prevention and support services such as education materials, support with housing, food, employment, transportation, child care, domestic violence and legal services. Peer support and voluntary services are essential in this regard.

Positive Health Dignity and Prevention (PHDP)

This provides prevention counselling, follow up and subsequent referral where necessary for clients with needs that affect their ability to adopt and sustain positive behavioural change with a view to reducing their risk for acquiring and/or transmitting HIV infection. PHDP activities include short term and ongoing behavioural counselling to reduce high-risk behaviours, provision of condoms, attention to risks imposed by alcoholism and use of other drugs, and screening and treatment of sexually transmitted infections at every contact with the care provider.

Table 11.1 Minimum Package of Care by Health Facility

This summarizes the minimum package of care services that should be available at the various levels of care

Primary level	Secondary level	Tertiary level
• HCT • Routine ARV-re-fill • ARV Prophylaxis for PMTCT • Haemoglobin (Hb) /PCV • Prevention and treatment of OIs • Prevention and treatment of malaria • DOTS • Adherence counselling • Psycho-social counselling • Home-based care services • Nutritional support • Palliative care • HIV care (pre-ART) • M & E • Linkage to secondary level facility	• HCT • Hb/PCV • E & U, Creatinine, LFT • Hepatitis screening • CD4+ count estimation • X-ray, • ART • Prevention and treatment of OIs including TB • Prevention and treatment of malaria • Nutritional management • Adherence counselling • M & E • Linkage to tertiary level facility	• HCT • Hb/PCV • E & U, Creatinine,LFT • Hepatitis screening • CD 4+ count estimation • X-ray • LFT • ART • Prevention and treatment of OIs including TB • Prevention and treatment of malaria • Nutritional management • Adherence counselling • M & E • Viral load

CHAPTER TWELVE

PROGRAMMATIC MANAGEMENT OF HIV

Essential operational and service delivery issues will be addressed on an ongoing basis to ensure long-term effectiveness and sustainability of the national programme. This will be achieved by making the best use of available human and financial resources, ensuring appropriate linkages between care settings and services, supporting adherence to lifelong treatment and maximizing retention of patients across the continuum of care. Specifically, efforts will be made to promote task shifting, improve laboratory and diagnostic services; and strengthen procurement and supply management systems.

12.1 Decentralization and Integration of services

HIV treatment and care services providers should implement recommendations of the National Guidelines for the decentralization of ART services. Decentralization and integration of ART services will contribute to improvement in the quality and integrity of services and at the same time take the services to the doorstep of the PLHIV by involving PHCs in the management of HIV/AIDS. Decentralization involves the devolution of part responsibility for the offer of HIV treatment and care from the tertiary and secondary level ART centres to the primary level health facilities. Under the arrangement PHCs can now offer additional ART services such as initiation of ART and routine ARV refills. The offer of PMTCT in the PHCs is an excellent example of decentralization and integration of ART services.

12.2 Human Resource Development

The non-availability of the right numbers and mix of health workers to deliver quality ART services is a major obstacle to the achievement of universal access to HIV prevention, treatment and care. At all levels of service provision, whether health facility to the community-based there should be adequate human resource to cater to the needs of PLHIV unfortunately this is not the case and as such several interventions should implemented to boost human resource for HIV/AIDS.

Training of Health Workers

- All health workers and lay providers involved in the provision of HIV treatment and care must have received training prior to offering services and periodic re-training thereafter.
- Training of health workers and lay providers must conform with globally accepted standards for high quality training
- Training of health workers and lay provides should be conducted using nationally approved HIV training curriculum and manuals

Staff Recruitment and Retention

- Responsible Governments and agencies should ensure that adequate numbers of health workers are deployed to all facilities providing HIV/AIDS prevention and treatment services
- Government and all responsible organizations should provide suitable non-monetary incentives to health workers to encourage motivation and retention in service
- Responsible Government and agencies of government should adopt staffing and staff depolyment policies that enhance retention of personnel in HIV service.

Task Shifting and Task Sharing

Task shifting involves the rational redistribution of tasks among health workforce teams. It involves health workers undertaking tasks that are not listed in their professional schedule of duties. Task shifting reduces the burden of work on a particular cadre of health worker and is particularly useful in health facilities with large volumes of patient. Task shifting applies to the different services that are offered to the PLHIV including ART services, PMTCT services, paediatric ART services and laboratory services.

Tasks to be considered for shifting or sharing include the following:

- Assessment for ART eligibility;
- Initiation of ART (based on clinical and/or immunological criteria);
- Assessment for opportunistic infections (OIs);
- Treatment of opportunistic infection
- Refill of prescriptions
- Prescription and initiation of ARV prophylaxis for PMTCT
- Adherence counselling;
- Adherence monitoring and support; and,
- Dispensing medication to patients who are already on ART between regular clinic visits
- HIV Testing

12.3 Procurement and Supply Management Systems

This includes processes necessary to ensure that HIV commodities including ARV drugs are available in sufficient quantities at all times when they are needed. It depends on adequate financing, planning, forecasting, procurement, distribution and tracking of commodities. The successful administration of this system requires multi-team collaboration including pharmacists, medical officers, medical records personnel, finance officer, procurement officers, distribution agents, customs and excise officers, shipping agents, manufacturers of the commodities and administrators of health facilities. The very first step however is in determining what should be procured and in what quantity.

Common HIV commodities required:

- ARV drugs
- Drugs for Treatment of OIs
- Rapid test kits and consumables
- PCR reagents and Dried Blood Spot (DBS) collection kits
- Viral load reagents, sample collection kits, and consumables
- CD4 reagents and consumables
- Equipment, reagents and consumables for haematology and chemistry laboratory tests and molecular diagnostic facilities
- Nutritional supplements (Ready to use therapeutic foods).

HIV/AIDS Commodities Storage and Distribution

The commodities distribution process begins when the commodities are sent from the manufacturers or suppliers and ends when the commodity consumption information is sent to the Central Medical Store, with a feedback mechanism to the health facilities. An effective distribution system is the pillar of HIV/AIDS commodity logistics management system. Such a system should not only maintain a constant supply of the commodities but also keep the commodities in good conditions throughout the distribution process, minimise losses due to spoilage and expiry, maintain accurate records, reduce theft and fraud and provide information for forecasting future commodity needs.

Flexibility should be introduced in the supply system such as procedures for reporting and redistribution of excess ARV drug supplies, more frequent ordering and filling of non-routine orders to minimize expiries and stock outs.

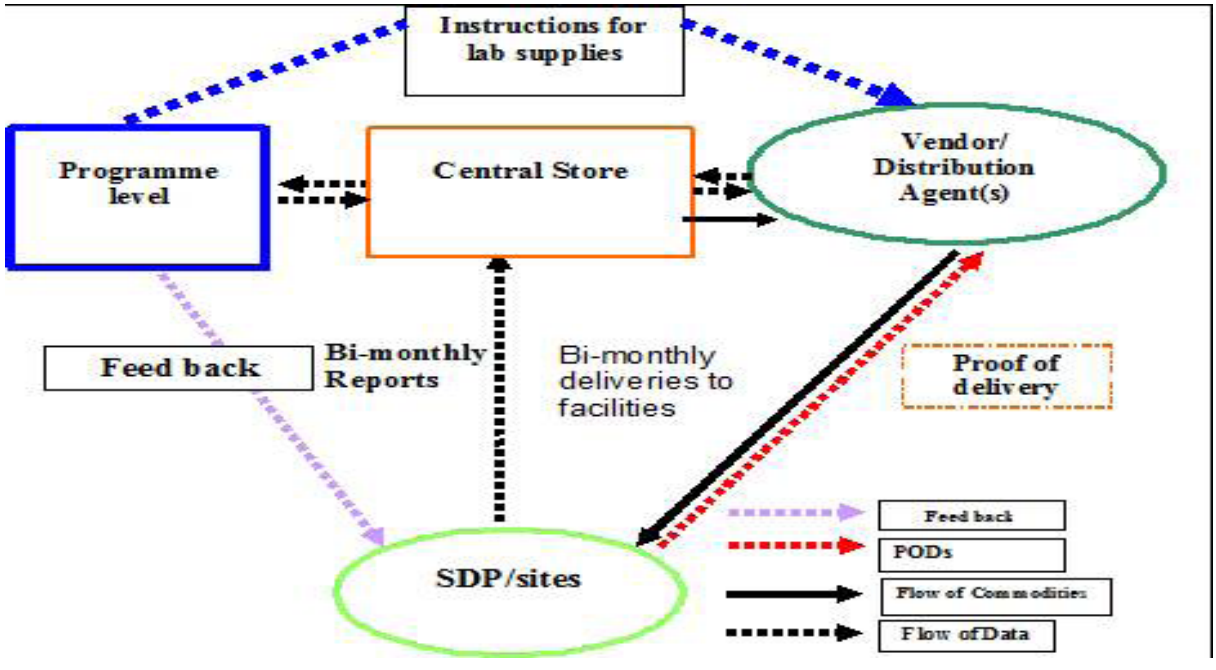
Flow of Commodities and Information for HIV and AIDS

The logistic pipeline is the entire chain of storage facilities and transportation links through which supplies move from the manufacturer to the patient, including the port facilities, central warehouse, regional warehouses, state warehouses, all service delivery points and transport vehicles.

The Nigerian HIV/AIDS logistics system is designed to operate as a two-tier system – central and facility. It is a 'forced ordering maximum-minimum inventory control system' i.e. orders are placed at a fixed time interval (2 months) and the order quantities are determined by the responsible person at the facility level using consumption data. This 'pull' system ensures that the quantities of commodities at the system remain within a defined maximum-minimum level.

In implementing this system, commodities will move from the stores down to the health facility and then specifically to the point at which the customer or user receives and/or uses the products. At the same time, information will move up the system to inform re-supply and program monitoring activities. The timely submission of reports containing accurate logistic data is critical to the timely re-supply of products, ensuring that products are always available to meet the clients' and users' needs. The diagram below outlines the flow of commodities and information for HIV and AIDS services.

Figure 12.1: Flow of commodities and information for HIV/AIDS



The responsibility for maintaining appropriate stock levels rests on the facility logistic team. Facility's replenishment for consumed stock comes up bi-monthly in response to submission of copies of the ordering Combined Report and Request forms. The reports are directly transmitted to the Central Medical Stores and then to the Logistics Unit in the National Programme where they are analyzed for various decisions – ranging from routine re-supply to strategic decisions such as quantification and forecasting. Feedback on reports from the facilities is processed by the Logistics Unit of NASCP and communicated to the facilities. When orders are ready for pick-up, distribution agents are notified and the commodities are transported and delivered directly to the service delivery points.

Table 12.1 National Reporting schedule:

Bimonthly Review Period	Report sent to the central
January – February Report	1st – 7th March
March – April Report	1st – 7th May
May – June Report	1st – 7th july
July – August Report	1st – 7th September
September – October Report	1st – 7th November
November – December Report	1st – 7th January

Key features of Nigerian HIV/AIDS commodities' logistics system

Inventory control system

- The forced ordering ("Pull" system) has two-levels (Central and Facility) and is based on maximum-minimum thresholds. Service delivery points are "forced" to order at the end of the review period (2 months in FMOH program)
- The quantity of commodities in the logistics system is tracked as a stock status (i.e. how long stocks will last).
- The maximum stock level (4 months of stock in FMOH program) is set high enough to guarantee adequate supply at all times during the ordering cycle, but low enough to prevent overstock and waste
- The minimum stock level (2 months of stock in FMOH program) is set as low as possible but includes a safety margin to prevent stock-outs
- The stock level in the facility has to be assessed frequently as this will alert the storekeeper in case of the need to place emergency order. The emergency order is done when stock levels drop to 2 weeks of stock; it disregards the review period. The quantity to order is calculated to top up the stock on hand to maximum level.

12.3.1 Logistics Management Information system (LMIS)

One of the primary components of any logistics system is a functional Logistics Management Information System (LMIS) that ensures availability of timely and accurate data for decision-making. These essential data must always be collected for products at all levels.

The three essential data elements include:

Stock on Hand: Describes the quantities of usable stock of commodities available at a particular point in time. Stock-on-hand information guides us when to place an order and how much of each item is in stock. It also guides redistribution decisions.

Consumption: Describes the quantity of commodities used during the report and order cycle. The rate of consumption is the link between the customer and the supply chain.

Losses and Adjustments: Losses include the quantity of commodities removed from the distribution system for any reason other than usage (e.g. losses, expiry, and damage). Adjustments may include receipt or issue of supplies to or from one facility to another that is not their usual supplier (e.g., a transfer) or a correction to account for a difference between what was counted during a physical inventory and what was recorded on the inventory control card. Losses/adjustments may therefore be a negative or positive number.

In order to collect and report the above mentioned data items, a number of forms described below were designed for the management of these commodities.

The LMIS Forms /Tools

- **Inventory Control Card**

This tracks the quantity of ARV drugs in a facility's storage area. This record collects two essential data items: stock on hand and the losses & adjustment data. The Inventory Control Card should always be kept in a facility's storage area.

- **Daily Consumption Record for ARV drugs and Daily Usage Record or Register for Test Kits and Reagents**

These collect the number of commodities that have been used in the facility daily over a defined period of time. This information is called Consumption data and is one of the essential data items. The Daily Consumption Record for ARV drugs should be kept with the person(s) who dispenses. The Daily Usage Record should be kept with the person(s) who runs the lab tests.

- **Record for Returning/Transferring Commodities**

This is a transactional form that is used in the event that commodities may be required to be returned to the CMS or transferred to another facility at the same level for various reasons ranging from expiry, damage, change in the treatment guidelines, or over-stocking.

- **Combined Report Requisition Issue and Receipt Form (CRRIRF)**

This form summarizes the information that is collected on the Inventory Control Card, Daily Consumption Record, and Daily Usage Record and is sent to the central store on a regular basis. The CRRIRF uses this reported data to calculate the facility order quantities and monitor whether stock is maintained according to plan (no overstock, shortages, or stock outs). Information from this report is critical to a well-functioning logistics system.

Roles and Responsibilities of Logistics personnel

- **Central Store Pharmacist**
  - Receives commodities
  - Fulfils orders (re-supply)
  - Updates inventory control card when commodities are issued or received
  - Ensures the storage of commodities according to the storage standards
  - Helps to manage commodities in the warehouse
  - Generates national-level reports

- **Central Store Officer**
  - Ensures the storage of commodities according to the storage standards
  - Updates inventory control cards.

- **Facility Pharmacists/Laboratory Scientist**
  - Completes the daily consumption record and usage record for commodities Documents all transactions in the inventory control cards maintained in the unit
  - Orders commodities and issue commodities to the various point of service in the facility
  - Completes the CRRIRF at the end of review period
  - Collects the daily consumption and usage registers / reports from other locations where commodities are dispensed e.g. PMTCT units and feeder sites
  - Sends back unusable commodities that must be returned to the CMS after filling out the record for returning commodities
  - Aggregates all usage data from the daily usage register for commodities and enter in the Combined Reports Requisition Issue and Issue Forms and send to the Central Warehouse
  - Monitors the management of commodities in the store.

- **Facility ART Team Leader**
  - Endorses CRRIRF to be sent to the central store
  - Facilitates meetings with all the focal team leaders (Paediatrics, PMTCT, HCT, Pharmacists and Laboratory scientists).

12.4 Programme Monitoring and Evaluation

The ART Programme in the country aims to achieve a number of objectives and targets which are detailed in various national plans including the national strategic framework, the health sector Strategic plan for HIV and AIDS and the scale-up plan for HIV and AIDS, the decentralization and the Presidents' Comprehensive Response Plan for HIV. These documents also contain a number of targets set to be achieved within specific time periods.

The Monitoring and Evaluation component of the ART programme enables the country to measure the level of success in achieving targets in coverage and quality of service by the programme. It also provides information that can be used to measure the performance of the programme, provide basis for future decision making on the programme, inform future allocation of resources, and enable us compare the programme with other health programmes both within and outside the country.

Monitoring and evaluation for the ART programme will be in line with the National Strategic Work plan; therefore some details below may vary as the National M&E strategy is updated.

ART Management Information System (MIS)

The ART Management Information Systems is used to monitor patient and programme implementation utilizing a set of indicators that measure coverage, quality of service, quantum of service and outcomes. The indicators include the internationally recognized indicators, which the country is obligated to report internationally and others designed to track service coverage in the country.

This ART Management Information System is made up of 2 integrated parts:

- Patient Management and Monitoring (PMM)
- Programme Monitoring and Evaluation (PME)

PMM provides information on individual patients. It should help in improving diagnosis and management of individual patients. The information may be monitored over time and enable clinicians to determine reasons for the success or failure of treatment in their patients and on the long run help to improve care provided to individual patients.

PME provides information on the delivery of care to HIV positive patients as a group. This system provides data that can be used to routinely monitor and evaluate the effectiveness, efficiency and acceptability of HIV service provision at health centres, sub-national and national levels.

The MIS is used to monitor and evaluate HIV care service delivery at the sites, Local Government Area, State, and National levels. The data will be used to identify programme areas that need to be strengthened for effective and efficient programme implementation.

Special studies may be required for specific issues but in general, the emphasis will be on using the PMM/PME system for providing information for the ART programme planning. Process and outcome evaluations will be periodically conducted to assess current programme success and inform future revisions and strategic plans.

Data Collection Instruments

The following are current tools used for M&E.

PMM Tools:

- Care/ART card
- Initial Clinical Evaluation form (Adult and Paediatric)
- Medication Adherence Assessment
- Immunology/Virology Order & Results form
- Pharmacy Order form

The PME tools include:

- Care/ART card
- Pre-ART Register
- ART Register
- ART monthly summary form
- ART MIS guidelines including guidelines for filling the monthly summary form
- Cohort analysis report

Other tools that will be required in an ART site include the registers required for HIV counselling and testing. These include HCT register, and the HCT laboratory register/worksheet.

Data Security

Handling of PMM/PME tools including the care/ART card and the registers will require confidentiality and efficiency. This will give the clients a sense of security. A filing system for HIV care records should be developed and followed within each institution. All records must be kept confidential and stored in a secure room with lockable cabinets. Backup records should be secured from damage or loss.

M&E Data Flow

At each ART site, the ART monthly summary form should be completed and forwarded to the Local Government, where the data are collated and in turn forwarded to the state Ministry of Health. At the state level, all HIV data should be collated, analyzed and forwarded to the National HIV/AIDS Division of FMOH

The respective health authorities at the various levels will have responsibility for reporting to the HIV and AIDS coordinating authorities at the level (i.e. health facility to LGA to State MOH to FMOH).

Logistics for M&E for the ART Programme

The FMOH will provide registers and summary forms for all sites delivering HIV care and ART. PMTCT registers shall be made available to all facilities (public and private) to ensure that all women, their partners, children, and their family members receive all the necessary services. They also facilitate the reporting of routine data which help track progress and identify challenges in the implementation of the PMTCT services within the facilities and nationally. Guidelines and training materials for proper completion of the registers and forms will also be made available. The FMOH in collaboration with partners and other stakeholders will support training on data collection and reporting.

APPENDIX I

ADVERSE DRUG REACTIONS SCREENING FORM

State: _____ **L.G.A.:** _____ **Facility Name:** _____

Patient ID: _____ **Patient Name:** _____ **Age:** _____ **Sex:** _____

	Insert Visit Date →	_/__/_	_/__/_	_/__/_	_/__/_	_/__/_	_/__/_	_/__/_	_/__/_	_/__/_
Any signs/symptoms indicating NEW adverse drug reactions (ADRs) at this visit? *Mark x as applicable*	No/Yes									
	ADR Start Date	_/__/_	_/__/_	_/__/_	_/__/_	_/__/_	_/__/_	_/__/_	_/__/_	_/__/_
If yes, enter severity code, 1 – 4 in the corresponding box (see key below). NB: *To be completed by healthcare professional at every visit*	ADR Screening done by *(enter name):*									
Skin and Appendages										
Pruritus										
Skin rash										
Steven-Johnson Syndrome										
Musculoskeletal System										
Athralgia										
Myalgia										
Myopathy										
Cardiovascular System / Respiratory System										
Chest pain / Chest discomfort										
Cough										
Dyspnoea / Shortness of breath										
Palpitation										
Tachycardia										
Tachypnea										
Wheezing										
Central and Peripheral Nervous										
Anorexia										
Anxiety										
Blurred vision										
Depression										
Dizziness										
Headache										
Insomnia										
Nightmares										
Pain / Tingling / Numbness										
Gastrointestinal / Hepato-biliary / Renal System										
Abdominal pain										
Constipation										
Diarrhea										
Dyspepsia										
Hepatomegaly										
Jaundice										
Nausea / Vomiting										
Metabolic / Endocrine System										
Lipodystrophy										
Polydipsia (excessive thirst)										
Polyuria (Increased micturition)										
Systemic Signs /symptoms – General										
Anemia										
Fatigue / Weakness										
Fever										
Malaise										
Rigors / Chills										
Sweating / Diaphoresis										
Others										
Intervention										
Hospitalization										
Referral to other facility										
Drugs initiated										
Others:										
Signature of Healthcare Proessional										

KEY TO GRADING OF ADVERSE DRUG REACTIONS

Grade 1: Mild	Transient or mild discomfort, no limitation of activity, no medical intervention / therapy required
Grade 2: Moderate	Mild to moderate limitation in activity, some assistance may be needed, no or minimal medical intervention therapy required
Grade 3: Severe	Marked limitation in activity, some assistance usually required, medical intervention / therapy required, hospitalization possible
Grade 4: Life-threatening	Extreme limitation in activity, significant assistance required, significant medical intervention / therapy required, hospitalization and hospice care

APPENDIX II

NATIONAL PHARMACOVIGILANCE CENTRE (NPC) NIGERIA

National Agency for Food and Drug Administration & Control (NAFDAC), Headquarters Office
Plot 2032 Olusegun Obasanjo Way
Wuse Zone 7 Abuja

Tel: 08086899571 or Fax: 09-5241108

FORM FOR REPORTING OF SUSPECTED ADVERSE DRUG REACTIONS

IN STRICT CONFIDENCE

1. * PATIENT'S DETAILS

Full Name or Initials: _____ Patient Record No: _____

AGE/DATE OF BIRTH: _____ SEX: M ☐ F ☐ WEIGHT (kg): _____

HOSPITAL/Treatment Centre: _____

2. * ADVERSE DRUG REACTION (ADR)

A. DESCRIPTION

DATE Reaction Started	DATE Reaction Stopped

C. OUTCOME OF REACTION
TICK AS APPROPRIATE

☐ Recovered fully
☐ Recovered with disability (Specify) _____
☐ Congenital Abnormality (Specify) _____
☐ Life Threatening (Specify) _____
☐ Death
☐ Others (specify) _____

B. Was Patient Admitted Due to ADR Yes ☐ No ☐

If Already Hospitalized, Was it Prolonged Due to ADR Yes ☐ No ☐

Duration of Admission (days) _____

Treatment of Reaction: _____

3. * SUSPECTED DRUG (Including Biologicals Traditional/Herbal Medicines & Cosmetics)

A. DRUG DETAILS (State name and other details if available / Attach product label / Sample (if available)

Brand Name: _____ Generic Name: _____ Batch No: _____

NAFDAC No: _____ Expiry Date: _____

Name & Address of Manufacturer: _____

B. Indications for Use	Dosage	Route of Administration	Date Started	Date Stopped

4. * CONCOMITANT MEDICINES (All medicines taken within the last 3months including herbal and self medication)

Brand or Generic Name	Dosage	Route	Date Started	Date Stopped	Reason for Use

5. * SOURCE OF REPORT:

Name of Reporter: _____

Address: _____

Profession: _____

Signature: _____ Tel No/E-mail: _____

*: **MANDATORY FIELDS**

APPENDIX III

Classes and Mechanisms of action of ARV drugs

Class	Mechanism of Action	Molecules	
Nucleoside / Nucleotide Reverse Transcriptase Inhibitors (NRTIs/ NtRTIs)	NRTIs stop HIV production by binding directly onto the reverse transcriptase enzyme thus preventing the transcription of viral RNA to DNA	Tenofovir (TDF) Zidovudine (AZT) Abacavir (ABC) Lamivudine (3TC)	Emtricitabine (FTC) Didanosine (ddI) Stavudine (d4T) Tenofovir Alafenamide Fumarate (TAF)
Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	NNRTIs incorporate themselves into the DNA of the virus, thereby stopping the building process. The resulting DNA is incomplete and cannot create a new virus.	Efavirenz (EFV) Nevirapine (NVP)	Etravirine (ETR) Rilpivirine (RVP)
Protease Inhibitors (PIs)	PIs prevent HIV from being successfully assembled from long chain amino acids and released from the infected CD4+ cell	Atazanavir-ritonavir (ATV/r) Lopinavir-ritonavir (LPV/r) Ritonavir (RTV)1 Darunavir (DRV)	Saquinavir (SQV) Indinavir (IDV) Nelfinavir (NFV) Amprenavir (APV) Tipranavir Fosamprenavir (FPV)
Integrase Inhibitors	Integrase inhibitors prevent the integration of viral DNA into the T-cell DNA and as such permanent infection of the cell is aborted and reproduction of viral RNA genome cannot occur neither can transcription of viral mRNA	Raltegravir (RAL) Dolutegravir (DTG)	Elvitegravir (EVG)
Fusion Inhibitors	Fusion inhibitors bind to viral gp41 and prevent the virus from penetrating the T-cell membrane	Enfuvirtide (T-20)	
Chemokine Receptors Antagonists (CCR5) Inhibitors	CCR5 inhibitors bind to CCR5 or CXCR4 on the T cell surface thereby preventing viral attachment to these co-receptors	Maraviroc Vicriviroc	

APPENDIX IV

Strength and dosing of ARV drugs in Adults

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

Drug	Adult dosing	Comments
Zidovudine (AZT)	300 mg b.d.	Use with caution in patients with anaemia. Increased toxicity possible when used with other drugs that are associated with bone marrow suppression. Should not be administered in combination with d4T. Also available in FDC with 3TC (AZT/3TC); with 3TC and NVP (AZT/3TC/NVP)
Abacavir (ABC)	300 mg b.d. or 600mg o.d.	Causes hypersensitivity reaction (HSR), which can be fatal; never re-challenge the patient. Educate patient on HSR Also available in FDC with 3TC (ABC/3TC); with 3TC and AZT (AZT/3TC/ABC)*
Tenofovir (TDF)	300mg o.d.	Caution should be taken in renal impairment and renal function (in particular estimated GFR) should be monitored. Also available in FDC with 3TC (TDF/3TC); with 3TC and EFV (TDF/3TC/EFV); with FTC (TDF/FTC); with FTC and EFV (TDF/FTC/EFV);
Lamivudine (3TC)	150 mg b.d. or 300mg o.d.	May be taken 300mg o.d. as prescribed by physician. Also available in FDC with TDF and EFV (TDF/3TC/EFV); with TDF (TDF/3TC); with AZT (AZT/3TC) and with ABC (ABC/3TC)
Emtricitabine (FTC)	200mg o.d.	Closely related to 3TC and should not be co-administered with it. Also available in FDC with TDF and EFV (TDF/FTC/EFV); with TDF (TDF/FTC)
Didanosine (ddI)**	400mg o.d. if weight is >60kg, 250mg o.d. for weight <60kg	EC capsules must be swallowed whole and taken on an empty stomach (at least 1 hour before or 2 hours after a meal). Co-administration with Ribavirin and allopurinol is contraindicated
Stavudine (d4T)	30 mg b.d.	Not to be used with ZDV. No longer recommended in adults and adolescents.

**Not available in Nigeria*

***Didanosine use is being phased out in Nigeria*

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Drug	Adult dosing	Comments
Efavirenz (EFV)	600mg o.d. at bedtime	No longer required to increase dose when co-administered with Rifampicin in patients weighing >60 kg.
Nevirapine (NVP)	200mg b.d.	Increased incidence of severe hepatotoxicity in women with CD4+ cell count > 250cells/mm3 and men with CD4+ cell count > 400cells/mm3. Other common reactions include skin rash. A 14-day lead-in period with 200 mg once daily (o.d.) dosing must be strictly followed; it has been demonstrated to reduce the frequency of rash. If rash persists beyond the 14-day lead-in period, do not change dose to 200 mg twice daily (b.d.). The 200 mg o.d. dosing regimen should not be continued beyond 28 days, at which point an alternative regimen should be considered.
Etravirine	Adult 200mg b.d. following meals	Used in treatment experienced patients who retain sensitivity to it
Rilpivirine	Adults; 25mg o.d. with meals	It is not known whether Rilpivirine is secreted in human milk. Because of both the potential for HIV transmission and the potential for adverse reactions in nursing infants, mothers should be instructed not to breastfeed if they are receiving Rilpivirine. Safety and effectiveness in paediatric patients have not been established; it is not recommended for use in children

Protease Inhibitors*

Drug	Adult dosing	Comments
Atazanavir/ritonavir (ATV/r)	300mg boosted with 100mg ritonavir o.d.	Asymptomatic hyperbilirubinaemia is common. May present with mild jaundice or scleral icterus but is not considered a true toxicity. Should not be administered with rifampicin containing TB treatment.
Lopinavir/ritonavir (LPV/r)	400mg/100mg b.d.	Lopinavir/ritonavir is extensively metabolized by hepatic cytochrome P450 3A. There are potential multiple drug interactions including with rifampicin containing TB treatment
Ritonavir (r, RTV) (with other PIs)	100mg b.d. in most cases	Used only to boost other PIs except NFV.
Saquinavir (SQV)	1000mg + RTV 100mg b.d.	Administer with or after food. No longer widely in use.
Darunavir (DRV)	600mg + 100mg ritonavir b.d.	Administer with or after food. A newer PI effective against many PI resistant mutants
Tipranavir (TPV)	500mg +200mg ritonavir b.d.	Active against PI resistant HIV and has established efficacy in salvage regimen.

**PIs should not be used with Rifampicin containing anti-TB drugs in TB/HIV co-infected patient*

Integrase Inhibitors

Drug	Adult dosing	Comments
Raltegravir	400mg film coated tablets b.d.	Co-administration of Raltegravir with drugs that are strong inducers of UGT1A1 may result in reduced plasma concentrations of Raltegravir .
Dolutegravir	50mg o.d. in treatment naïve patients.	Twice daily when co-administered with the following potent UGT1A/CYP3A inducers: Efavirenz, Fosamprenavir/ritonavir, Tipranavir/ritonavir, or Rifampicin.
Elvitegravir Only available in a FDC tablet with cobicistat, tenofovir, and emtricitabine (Stribild)	150mg o.d.	The fixed-dose combination elvitegravir/cobicistat/tenofovir/ emtricitabine should not be initiated in patients with CrCl <70 mL/min and should be discontinued in those with CrCl <50 mL/min. Dosage adjustment for mild or moderate hepatic impairment is not required. No data are available to guide use in persons with severe liver disease.

Commonly used Adult ARV drug formulations

Drug	Strength of tablet (mg)	Number of tablets per day
TDF / 3TC / EFV	Tablets 300mg / 300mg / 60mg	1 tablet o.d.
TDF / 3TC	Tablets 300mg / 300mg	1 tablet o.d.
AZT / 3TC / NVP	Tablets 300mg / 150mg / 200mg	1 tablet b.d.
AZT / 3TC	Tablets 300mg / 150mg	1 tablet b.d.
ABC / 3TC	Tablets 600mg / 300mg	1 tablet o.d.
EFV	Tablets 600mg	1 tablet o.d.
NVP	Tablets 200mg	1 tablet b.d.*
LPV/r	Tablets 200mg / 50mg	2 tablets b.d.
ATV/r	Tablets 300mg / 100mg	1 tablet o.d.
AZT	Tablets 300mg	1 tablet b.d.
ABC	Tablets 300mg	1 tablet b.d. or 2 tablets o.d.
3TC	Tablets 150mg	1 tablet b.d or 2 tablets o.d.

APPENDIX V

Strength and dosing of ARV drugs in Pediatrics

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

ARV Drug	Dosing	Information for parents/caregivers
Zidovudine (AZT)	180-240 mg/m^2/dose b.d. to a maximum of 300 mg/dose	Use with caution in patients with anaemia - avoid if Hb < 8mg/dl Toxicity possible if used with other drugs associated with marrow suppression Should not be administered in combination with d4T Use the higher dose with nervous system involvement Available in dispersible FDC with 3TC (AZT/3TC); with 3TC and NVP (AZT/3TC/NVP).
Lamivudine (3TC)	4 mg/kg/dose b.d. to a max. of 150 mg/dose	Low toxicity and no food restrictions Available in dispersible FDC with AZT and NVP (AZT/3TC/NVP) with AZT (AZT/3TC) and with ABC (ABC/3TC)
Tenofovir (TDF)*	8mg/kg/dose o.d. to a maximum of 300mg/dose	Not recommended for use in patients <2 years Requires baseline and routine renal function assessments. Pediatric TDF containing FDC's are currently not available
Abacavir (ABC)	8 mg/kg/dose b.d. to a maximum of 300 mg/dose	Potential for hypersensitivity in genetically predisposed individuals (fever, rash, dyspnoea, abdominal pain) Parents/caregivers to return to hospital in case of hypersensitivity Should not be re-introduced if hypersensitivity occurs No food restriction: tablet can be crushed, mixed with small amounts of water/food and ingested immediately Also available as dispersible FDC with 3TC (ABC/3TC)
Stavudine (d4T)	1 mg/kg/dose b.d. to a max. of 30mg/dose	Not to be used with ZDV. Available in dispersible FDC with 3TC (d4T/3TC); with 3TC and NVP (d4T/3TC/NVP).

**300mg TDF tablets only recommended for children 30kg and above*

Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Drug	Dosing	Information for parents/caregivers
Nevirapine (NVP)	<8 years: 200mg/m^2 b.d. >8 years: 120-200mg/m2 b.d. Maximum dose: 200 mg b.d. Initiate at half dose (o.d.) for 2 weeks then increase to b.d. dosing. May consider omitting lead in dosing in children <2 years	Patients should be warned about the potential for severe life threatening rash. Solution stable for 2 months once opened Ketoconazole should not be co-administered with NVP. No food restriction needed Oral suspension must be well shaken.
Efavirenz (EFV)	10 to <15 kg: 200 mg o.d. at bedtime 15 to <20 kg: 250 mg o.d. at bedtime 20 to <25 kg: 300 mg o.d. at bedtime 25 to <32.5 kg: 350 mg o.d. at bedtime 32.5 to <40 kg: 400 mg o.d. at bedtime> 40 kg: 600 mg	Not recommended for use in children under the age of 3 years and weighing less than 10kg. Best given at bedtime to decrease the risk of side effects. Can be taken with food, however when taken with a high fat meal absorption is increased by 50%.
Etravirine	Pediatric (6 to less than 18 years): 16 - < 20kg: 100mg b.d. 20 - < 25kg: 125mg b.d. 25 - < 30kg: 150mg b.d. >30kg: 200mg b.d.	Not approved for use in children <6 years Used in treatment experienced patients who retain sensitivity to it Should be administered with food

Protease Inhibitors (PIs)

Drug	Dosing	Information for parents/caregivers
Lopinavir/r (LPV/r)	300mg (LPV)/75mg RTV)/m2 b.d. Maximum dose 400mg/100 mg b.d.	Oral solution should be refrigerated, but can be kept at room temperature (up to 25°C) if used within 2 months. Tabs to be swallowed whole & must not be crushed or chewed No food restrictions
Atazanavir (ATV)	Not approved in < 6 years 15-<20kg: 150mgATV+100mg RTV o.d. 20-<32kg: 200mg ATV + 100mg RTV o.d. 32-40kg: 250mg ATV + 100mg RTV o.d.	Should be administered with food Must be taken with separate RTV booster (no coformulated pediatric FDC available of Atazanavir and Ritonavir)
Ritonavir (RTV)	Major use is to boost PIs; dose varies with PI.	Not used alone, but to boost other PI's Only coformulation available is LPV/r, when using ATV or DRV separate RTV must be administered as a booster
Darunavir (DRV)	10 - <20kg – 240mg DRV + 40mg RTV b.d. 20 - <30kg – 375mg DRV + 50mg RTV b.d. 30 - < 40kg – 450mg DRV + 60mg RTV b.d.	Not approved <3 years Should be taken with food

Fusion, Integrase and CCR5 Inhibitors

Drug	Dos	Information for parents/caregivers
Raltegravir (RAL)	10-<14mg: 75mg b.d. 14-<20mg: 100mg b.d. 20-28mg: 150mg b.d. 28-<40mg: 200mg b.d.	Higher doses required for patients taking hepatic enzyme inducing drugs

Ritonavir is used as a pharmacoenhancer

Simplified dosing of child-friendly formulations for twice-daily (b.d.) dosing among children

Drug	Strength of tablets (mg)	Number of tablets by weight band morning and evening										Strength of adult tablet (mg)	Number of tablets by weight band	
		3–5.9 kg		6–9.9 kg		10–13.9 kg		14–19.9 kg		20–24.9 kg			25–34.9 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM
AZT / 3TC	Tablet (dispersible) 60 mg/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300/150	1	1
AZT / 3TC / NVP	Tablet (dispersible) 60 mg/30 mg/50 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300/150/200	1	1
ABC / AZT / 3TC[2]	Tablet (dispersible) 60 mg/60 mg/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300/300/150	1	1
ABC / 3TC	Tablet (dispersible) 60 mg/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	600/300	0.5	0.5
LPV/r[3]	Tablet (heat stable) 100 mg/25 mg	–	–	–	–	2	1	2	2	2	2	100/25	3	3
LPV/r[4]	80/20 mg/ml	1 ml	1 ml	1.5ml	1.5ml	2 ml	2 ml	2.5ml	2.5 ml	3 ml	3 ml	–	–	–
NVP[5]	Tablet (dispersible) 50 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	200	1	1
d4T / 3TC	Tablet (dispersible) 6 mg/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	30/150	1	1
d4T / 3TC / NVP	Tablet (dispersible) 6 mg/30 mg/50 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	–	4	4
ABC	Tablet (dispersible) 60 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300	1	1

[2] *FDC not available in Nigeria, ABC 60mg + AZT/3TC 60mg/30mg to be used*

[3] *The LPV/r heat-stable tablet formulation must be swallowed whole and should not be split or crushed.*

[4] *LPV/r liquid requires a cold chain during transport and storage.*

[5] *NVP dose escalation with half dose for 2 weeks when initiating ART is still recommended to avoid toxicity from high initial NVP levels. However, secondary analysis from the (CHAPAS) -1 trial recently suggested that younger children have a lower risk of toxicity, and consideration can be given to starting with a full dose (Fillekes Q et al. Is nevirapine dose escalation appropriate in young African HIV+ children? 20th Annual Conference on Retroviruses and Opportunistic Infections, Atlanta, GA, USA, 3–6 March 2013 (http://retroconference.org/2013b/Abstracts/46904.htm, accessed 15 May 2013). More definitive evidence is expected from an ongoing trial.*

Simplified dosing of child-friendly solid formulations for once-daily (o.d.) dosing in children

Drug	Strength of tablets (mg)	Number of tablets by weight band morning and evening					Strength of tablet (mg)	Number of tablets by weight band
		3–5.9 kg	6–9.9 kg	10–13.9 kg	14–19.9 kg	20–24.9 kg		25–34.9 kg
EFV[6]	Tablet (scored) 200 mg	-	-	1	1.5	1.5	200	2
ABC/3TC	Tablet (dispersible) 60/30 mg	2	3	4	5	6	60 + 30	1

[6.] *EFV is not recommended for children younger than 3 years and weighing less than 10 kg. FDA approval for use in children less than 3 years weighing more than 3.5 kg was granted during the finalisation of these guidelines (3.5-5 kg two 50 mg capsules; 5-7.5 kg three 50 mg capsules; 7.5-15 kg one 200 mg capsule), however more data are urgently needed to inform recommendations for use of EFV in this age group.*

APPENDIX VI

DOSING OF ANTIRETROVIRAL DRUGS FOR HIV-INFECTED ADULTS WITH CHRONIC KIDNEY DISEASE (CKD) OR END-STAGE RENAL DISEASE (ESRD)

Antiretroviral drug, dosing category	Dosage
Nucleoside reverse-transcriptase inhibitors	
Zidovudine	
Usual dosage	300 mg po b.i.d.
Dosage for patients with CKD or ESRD	
Creatinine clearance ≥15 mL/min	No adjustment
Creatinine clearance <15 mL/min	100 mg po q6—8h
Receiving hemodialysis	100 mg po q6—8hc
Receiving peritoneal dialysis	100 mg po q6—8h
Lamivudine	
Usual dosage	150 mg po b.i.d./300 mg po q.d.
Dosage for patients with CKD or ESRD	
Creatinine clearance ≥50 mL/min	No adjustment
Creatinine clearance 30—49 mL/min	150 mg po q.d.
Creatinine clearance 15—29 mL/min	150 mg po first dose, then 100 mg po q.d.
Creatinine clearance 5—14 mL/min	150 mg po first dose, then 50 mg po q.d.
Creatinine clearance <5mL/min	50 mg po first dose, then 25 mg po q.d.
Receiving hemodialysis	50 mg po first dose, then 25 mg po q.d.
Receiving peritoneal dialysis	50 mg po first dose, then 25 mg po q.d.
Tenofovir	
Usual dosage	300 mg po q.d.
Dosage for patients with CKD or ESRD	
Creatinine clearance ≥50 mL/min	No adjustment
Creatinine clearance 30—49 mL/min	300 mg po q48h
Creatinine clearance 10—29 mL/min	300 mg po q72h
Receiving hemodialysis	300 mg po every 7 daysc
Receiving peritoneal dialysis	Unknown, use with caution

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