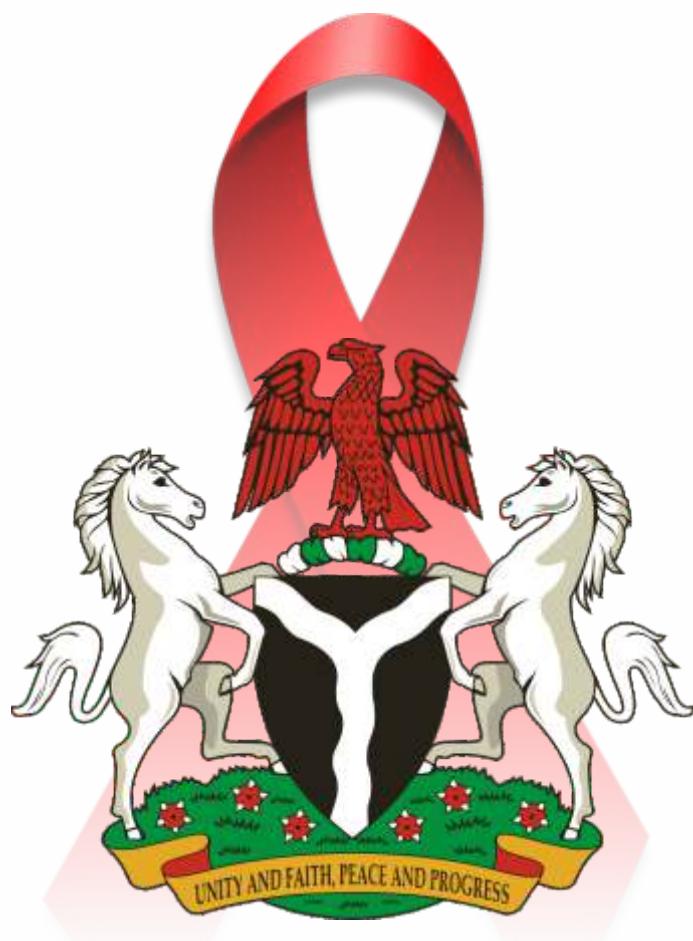




# **NATIONAL GUIDELINES FOR HIV PREVENTION TREATMENT AND CARE**

**NATIONAL AIDS AND STIs CONTROL PROGRAMME  
FEDERAL MINISTRY OF HEALTH  
NIGERIA**

**2016**



# NATIONAL GUIDELINES FOR HIV PREVENTION TREATMENT AND CARE

NATIONAL AIDS AND STIs CONTROL PROGRAMME

FEDERAL MINISTRY OF HEALTH

NIGERIA

2016

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## ACKNOWLEDGMENTS

We would like to acknowledge all the individuals and organizations that contributed time, energy and professional expertise to the development of this document. We attribute the timely completion of the guidelines review to the extraordinary cooperation we received from them.

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We are grateful to the networks of people who participated in the guidelines review for their very enlightened contribution to process and for insisting that recommendations are considerate of the welfare and safety of the PLHIVs.

We reserve special thanks for the facility level service providers for the hands on experience they brought to bear on the process.

We thank everybody who contributed one way or the other to the successful development of these guidelines.



Dr. Evelyn Ngige  
Director Public Health



## FOREWORD

The Federal Ministry of Health is deeply committed to the provision of high quality health care for all citizens of this country, especially the vulnerable and those in most need. In this regard the Ministry is taking every step necessary to reduce the burden of disease and untimely deaths from all preventable causes.

Government's commitment to safeguarding the health of Nigerians assumes greater urgency in the case of HIV because unlike most other disease conditions it is complicated by psychological, emotional, social and economic consequences.

These guidelines for the prevention, treatment and care of HIV infection provide the guidance that health workers require to deliver a comprehensive package of high quality HIV prevention, treatment and care interventions that cater to the needs of persons living with HIV and of individuals exposed to a high risk of acquiring HIV infection. Beyond the individual patient, these guidelines will serve as launch pad for the attainment of the UNAIDS 90-90-90 targets.

The key recommendations of these guidelines include initiation of ART in all persons testing positive for HIV including children, adolescents, adults, pregnant and breastfeeding women, regardless of clinical and immunological stages of the disease. Other recommendations cover the retesting of patients prior to initiation of ART, adoption of pre-exposure prophylaxis for individuals at high risk of acquiring the infection and addition of Dolutegravir, Efavirenz 400 mg and Darunavir/ritonavir to the pool of approved antiretroviral drugs.

The guidelines are the product of extensive cross-sectoral collaboration involving government, bilateral and multilateral organizations, civil society and the academia. I am optimistic that proper deployment and application of its recommendations will bring about a marked improvement in the way HIV infection is managed in this country.

I endorse and recommend the 2016 National Guidelines for HIV Prevention, Treatment and Care for use in Nigeria especially by persons and organizations engaged in the work of providing HIV/AIDS services.



Prof. Isaac F. Adewole FAS, FRCOG, FSPSP, DSc (Hons)  
Honourable Minister of Health, Nigeria



## EXECUTIVE SUMMARY

The National Guidelines for HIV Prevention Treatment and Care is a ten-chapter document that provides general and specific guidance for the prevention and treatment of HIV Infection using a broad range of interventions:

Chapter one is the introduction of the guidelines and its focus is on the guiding principles for the guidelines, the process of guidelines review and the epidemiology of HIV/AIDS in Nigeria, while chapter two provides guidance on HIV testing services and laboratory and clinical diagnosis of HIV infection.

Chapter three deals with the use of ART in treatment of HIV disease with emphasis on the characteristics and mechanism of action of ARVs, criteria for initiation of ART in different age groups, the approved regimens for ART and management of treatment failure. Chapter four recognizes the need to track and manage adverse drug reactions and provides guidance for effective pharmacovigilance in ART.

In chapter five the focus is on adherence to antiretroviral therapy and the factors that limit or enhance its achievement while chapter six is dedicated to the prevention of mother to child transmission of HIV using ART and non-ART interventions including prophylaxis for the HIV exposed infant.

Chapter Seven is the preventive management of HIV/AIDS providing detailed guidance for offer of PrEP and PEP. Chapter Eight is focused on the management of opportunistic infections and comorbidities and provides guidance on a broad range of subjects such as Cotrimoxazole Preventive Therapy, IPT and TB co-infection and the management of common opportunistic infections.

The focus of Chapter Nine is on improving efficiency of service delivery through innovative models such as differentiated care, decentralization of services, logistics management and linkage to care among other recommendations.

Chapter Ten deals with monitoring of services and provides basic information on the strategies for monitoring implementation of HIV/AIDS services under these guidelines



**Dr. Sunday Aboje**  
National Coordinator NASCP



## EDITORIAL TEAM

---

Dr. Emeka Asadu	Head Treatment, Care and Support NASCP - <i>Coordinating Editor</i>
Dr. Chukwuma Anyaike	Head Prevention NASCP
Dr. Isaac Elon	WHO Consultant for the Guidelines Review
Dr. Ikechukwu Amamilo	Programme Officer CHAI
Dr. Justus Jiboye	Senior Programme Manager CHAI
Dr. Solomon Odafe	Senior Programme Specialist CDC
Dr. Daniel Adeyinka	Focal Person Paediatric ART NASCP
Dr. Dorothy Mbori-Ngacha	Chief of Section HIV UNICEF
Dr. Obinna Ogbanufe	Senior Care and Treatment Advisor CDC
Dr. Olanrewaju Olayiwola	Senior Clinical Specialist CCFN
Dr. Eugene Onu	Deputy Director Training CCCRN

## CONTRIBUTORS

---

### FEDERAL MINISTRY OF HEALTH

Dr. Evelyn Ngige	Director Public Health
Dr. Sunday Aboje	National Coordinator NASCP
Pharm. Yeeken Oloyede	Director Programme Development & Logistics NASCP
Dr. Bolanle Alonge	Consultant Special Grade 1 DHOS
Dr. Chukwuma Anyaike	Consultant Special Grade 11 NASCP
Dr. Emeka Asadu	Head, Treatment, Care and Support NASCP
Mr. Samson Banjo	Assistant Director Laboratory NASCP
Mr. Obadiah Ombugadu	Assistant Director Programme Development NASCP
Mrs. Ima John-Dada	Assistant Director HCT NASCP
Mrs. Helen Izoigbe	ACNO MNCH FMOH
Dr. Uba Sabo	Senior Medical Officer TB/HIV NASCP
Dr. Chioma Ukanwa	Senior Medical Officer PD NASCP
Dr. Fintirimam Sambo-Donga	Senior Medical Officer PMTCT NASCP
Dr. Emperor Ubochioma	Senior Medical Officer TB/HIV NTBLCP
Dr. Adeyinka Daniel	Medical Officer NASCP
Mrs. Caroline Osahon	Chief Clerical Officer NASCP
Mrs. Leticia Nwafor	Assistant Chief NASCP
Dr. Chamberline Ozigbu	Medical Officer NASCP
Dr. Bodunde Onifade	Medical Officer NASCP
Ms. Bridget Onyebuchi	Senior Scientific Officer NASCP
Mrs. Isichei Patience	Principal Community Dev. Inspector NASCP



Mrs. Mercy Tende	Senior Medical Lab Scientist NASCP
Mrs. Etubi Eruona	Principal Medical Lab Scientist NASCP
Mrs. Uche Okorie	Senior Medical Lab Scientist NASCP
Mrs. Ukamaka Okeke	Scientific Officer NASCP
Ms. Sabina Aiki	Scientific Officer NASCP
Mr. Zeni Franklin	Principal Community Development Inspector NASCP
Mr. Turaki Abdul	Pharmacy Technician NASCP
Mr. Donatus Ibeku	Principal Executive Officer FMOH
Mrs. Adenike Okunade	Senior Clerical Officer NASCP
Mrs. Julian Ogwariri	Senior Clerical Officer NASCP
Mr. Gabriel Ikechukwu	Senior Executive Officer NASCP
Mr. Emmanuel Ibeku	Senior Executive Officer NASCP

## STATE MINISTRY OF HEALTH

Dr. Afam Anaeme	States AIDS Programme Coordinator Anambra
Dr. Benson Udu	States AIDS Programme Coordinator FCT
Mr. Jafar Dalhatu	States AIDS Programme Coordinator Kano
Dr. Bashar Kangiwa	States AIDS Programme Cordintor Kebbi
Dr. Olubunmi Ayinde	States AIDS Programme Coordinator Oyo
Mrs. Maria Pawa	States AIDS Programme Coordinator Plateau
Mr. Mairiga Shehu	States AIDS Programme Coordinator Niger
Dr. Golden Owhonda	States AIDS Programme Coordinator Rivers

## NACA / SACA

Dr. Emmanuel Agogo	Assistant Director NACA
Dr. Tolu Oladele	Chief Programme Officer NACA
Dr. Gideon Dura	Executive Director BENSACA

## HIV/AIDS IMPLEMENTING PARTNERS

Dr. Rex Mpazanje	Acting WHO Representative WHO
Dr. Meg Doherty	Coordinator WHO Guidelines Development Group
Dr. Dorothy Mbori-Ngacha	Chief of Section HIV UNICEF
Dr. Oluwafunke Ilesanmi	National Professional Officer WHO
Dr. Modupe Oduwole	Senior Programme Specialist UNAIDS
Tseday Alemseged	Strategic Intervention Advisor UNAIDS
Dr. Anslem Audu	HIV Specialist UNICEF
Dr. Amos Omoniyi	NPO TB/HIV WHO
Dr. Abiola Davies	HIV Specialist UNICEF
Mr. Omotayo Hamza	NPO EDM WHO
Dr. Jerry Gwamna	Chief, Prevention Branch CDC
Dr. Dennis Onotu	Chief, Care and Treatment Branch CDC
Dr. Obinna Ogbanufe	Senior Care and Treatment Advisor CDC
Dr. Solomon Odafe	Senior Care and Treatment Advisor CDC



Dr. Tim Efuntoye	Senior Programme Specialist CDC
Dr. Odume Bethrand	Senior Programme Specialist CDC
Dr. Ezekiel James	Advisor Treatment and Care USAID
Dr. Emeka Okechukwu	Treatment Manager USAID
Pharm. Tunji Odelola	Pharmacy Logistics Manager USAID
Mrs. Pamela Gado	Programme Manager HTS USAID
Ms. Folu Lufadeju	Director Access Program CHAI
Dr. Justus Jiboye	Senior Program Manager CHAI
Mr. Ademola Osigbesan	Senior Associate CHAI
Dr. Ikechukwu Amamilo	Programme Officer CHAI
Ms. Juliet Odogwu	Senior Analyst CHAI
Dr. N. Kumarasamy	Consultant CHAI
Ms. Vivienne Mulema	Country Support Manager CHAI
Mr. Jibrin Kama	Associate CHAI
Dr. Kinanga Magambo	Clinical Advisor CHAI
Dr. Dotun Olutola	Chief of Party CCCRN
Dr. Patrick Akande	Director Clinical Services APIN
Dr. Ladi-Akinyemi	Associate Director APIN
Dr. Abutu Inedu	Associate Director Clinical CIHP
Mrs. Oluwakemi Akagwu	CSO CIHP
Dr. Ernest Ekong	Director Clinical Services IHVN
Dr. Anthony Okwuosah	Director Community Medicine IHVN
Mrs. Helen Omuh	Associate Director IHVN
Dr. Hadiza Khamofu	Deputy Chief of Party-Technical FHI 360
Dr. Edward Oladele	DPCT FHI 360
Dr. Chris Obanubi	Senior Technical Officer FHI 360
Dr. Seun Asala	Senior Technical Officer FHI 360
Dr. Adewale Adefila	Senior Technical Officer FHI 360
Dr. Kenneth Agu	Assistant Director Howard University Pace Centre
Dr. Seun Asieba	Deputy Project Director HUPACE SIDHAS
Dr. Wilfred Ugwuochukwu	Senior Programme Officer Hygeia Foundation
Dr. Olagoke Ewedairo	Medical Advisor GSK
Mr. Ola Omolasey	Regional Manager GSK
Mr. Tunji Awomolo	Enterprise Manager Abbott
Mr. Joseph Raji	Project Officer JSI/SCMS
Dr. Kema Onu	State Coordinator AHF
Dr. Amana Effiong	Project Director Pro-Health International
Pharm Constance Nnadozie	Country Representative ABBVIE SA
Dr. Adebola Bashorun	HIV Advisor
Dr. Adamu Maikano	Technical Officer Clinical Services APIN
Dr. Olarewaju Jonathan	Senior Clinical Advisor CCCRN
Mrs. Victoria Archibong	Senior Technical Officer FSW-SFH
Dr. Eugene Onu	Deputy Director Training and TB
Mrs. Chika Obiora-Okafo	Technical Officer M&E FHI 360
Dr. Joseph Enegele	Senior Technical Officer Pro Health International
Mrs. Elizabeth Duile	PPM AIDS Heath Care Foundation



Dr. Adetayo Towolawi	Programme Manager AIDS Health Care Foundation
Dr. Vincent Ojoh	Project Officer ANECCA
Mrs. Oluwakemi Akagwu	CSO CIHP
Mr. Joseph Okeme	Programme Manager Africa Health Project
Dr. Okezie Onyedinachi	Deputy Program Manager ECEWS
Dr. Prince Anyanwu	Senior Technical Officer ECEWS
Dr. Emmanuel Nwabueze	STA Management Sciences for Health
Mr. Chike Anyachor	Product Manager GSK
Dr. Saidu Ishaq	DCS Friends for Global Health
Dr. Olanrewaju Olaiya	Clinical Advisor /STL Pro Health International
Mr. Innocent Ibegbunam	Director JSI/SCMS
Dr. Adeyemi-Doro	Country Manager Mylan
Dr. Olanrewaju Olayiwola	Senior Clinical Specialist CCFN
Dr. Wale Fadare	Senior Clinical Specialist CCFN
Dr. Ali Onoja	CEO Africa Health Project

## FACULTIES

Prof. Sulaimon Akanmu	Chairman NTTA / Haematologist LUTH Lagos
Prof. Oladapo Shittu	Chairman NTTPMTCT /OB/GYN ABUTH Zaria
Prof. Ifeoma Emodi	Vice-Chairman NTTA /Paediatrician UNTH Enugu
Prof. Charles Uwakwe	Chairman NTTHCT UCH Ibadan
Prof. William Ogala	Paediatrician ABUTH Zaria
Prof. Austin Omoigberale	Paediatrician UBTH Benin
Prof. Ebun Adejuwigbe	Paediatrician OAUTH Ile-Ife
Prof. Edna Iroha	Vice Chairman NTTPMTCT Paediatrician LUTH
Prof. Joseph Onakewhor	OB/GYN UBTH Benin
Prof. Stephen Oguche	Paediatrician JUTH Jos
Prof. Musa Babashani	Physician AKTH Kano
Prof. Anene Moneke	Microbiologist UNN Nsukka
Prof. Douglas Nwagbo	Statistician /Demographer UNTH Enugu
Prof. Jesse Otegbayo	Gastroenterologist UCH Ibadan
Dr. Oche Agbaji	Physician JUTH Jos
Dr. Isaac Elon	Paediatrician FTH/Gombe State University
Dr. Jonah Abah	Family Physician FMC Makurdi
Dr. Sunday Ochigbo	Paediatrician UCTH Calabar
Dr. Eugenia Ofondu	Dermatologist FMC Owerri
Dr. Dominic Umoru	Paediatrician FCTA Abuja
Dr. Olufunke Bolaji	Paediatrician FMC Ido-Ekiti
Dr. Oliver Ezechи	OB/GYN NIMR Lagos
Dr. Olutosin Awolude	OB/GYN UCH Ibadan
Dr. Chinelo Madubuike	Paediatrician NAUTH Nnewi
Pharm. Muhammed Garba	Pharmacist AUTH Gwagwalada FCT
Dr. Cajetan Onyedum	Physician UNTH Enugu
Dr. Ann Ogbenna	Physician LUTH Lagos
Dr. Philip Oshun	Microbiologist LUTH Lagos



Dr. Mathew Uzoanya	Resident FMC Umuahia
Dr. Peter Nkwo	OB/GYN UNTH Enugu
Dr. Michael Nyemenim	ART Coordinator BMSH Port Harcourt
Dr. Joseph Ugwu	Physician Niger Foundation Specialist Hospital Enugu
Dr. Athanasius Eze	Medical Director Miracle Seed Hospital and Maternity Abuja
Dr. Ejike Asadu	Secretary State Education Board Enugu
Mrs. Uche Ezenwaka	Research Associate Policy Research Group UNTH Enugu
Mr. Olusoji Adeyemi	Secretary MLSCN Lagos
Mr. Gerald Teleh	CEO Y.E Langtang Management Consult

## CIVIL SOCIETY / NEPWHAN

Mr. Walter Ugwuocha	Executive Secretary CiSHAN
Mrs. Helen Aphan	M&E Specialist ASWHAN
Mr. Hart Kingsley	HCT Specialist 82 DMSH Enugu
Mrs. Eunice Peters	Member NEPWHAN
Dr. Benjamin Aiwonodagbon	HIV TA Heartland Alliance International Nigeria
Barr. Jennifer Beko	AIDS Rights Alliance Lagos



## ABBREVIATIONS AND ACRONYMS

3TC	Lamivudine
ABC	Abacavir
ACT	Artemisin-based Combination Therapy
ADR	Adverse Drug Reaction
AIDS	Acquired Immunodeficiency Syndrome
AKTH	Aminu Kano University Teaching Hospital
ALP	Alkaline Phosphatase
ALT	Alanine Transaminase
ANC	Antenatal Care
ANECCA	Africa Network for Care of Children affected by AIDS.
APIN	AIDS Prevention Initiative in Nigeria
ARM	Artificial Rupture of Membrane
ART	Antiretroviral Therapy
ARV	Antiretroviral drugs
AST	Aspartate Transaminase
ASWHAN	Association of Women Living with HIV/AIDS in Nigeria
ATV/r	ritonavir boosted Atazanavir
AUC	Area under the curve
AUTH	Abuja University Teaching Hospital
AZT	Zidovudine
BBFSW	Brothel based Female Sex Worker
BMSH	Braithwaite Memorial Specialist Hospital
c-ART	Combination ART
CCCRN	Centres for Clinical Care and Research Nigeria
CD4+	Cluster of Differentiation Antigen 4
CDC	Centres for Disease Control
CFCC	Client and Family Centred Care
CHAI	Clinton Health Access Initiative
CHEW	Community Health Extension Worker
CIHP	Centres for Integrated Health Programs
CiSHAN	Civil Society for HIV/AIDS in Nigeria
CKD	Chronic Kidney Disease
Cmax	Maximum Concentration
CMS	Central Medical Stores Oshodi
CMV	Cytomegalovirus
CNS	Central Nervous System
COBI	Cobicistat
COPD	Chronic Obstructive Pulmonary Disease
CPK	Creatinine Phosphokinase
CPT	Cotrimoxazole preventive Therapy



CrAg	Cryptococcal Antigen
CrCl	Creatinine Clearance
CRRIIF	Combined Report Requisition and Receipt Issue Form
CS	Cesarean Section
CSF	Cerebrospinal Fluid
CSO	Civil Society Organization
CT	Computed Tomography
CTX	Cotrimoxazole
CXR	Chest X-Ray
D4T	Stavudine
DAA	Directly Acting Antiviral
DBS	Dried Blood Spot
Ddl	Didanosine
DHOS	Department of Hospital Services
DLV	Delavirine
DNA	Deoxyribonucleic Acid
DOTS	Direct Observed Treatment Short Course
DRESS	Drug Reaction, Eosinophilia, Systemic Symptoms
DRV/r	Ritonavir boosted Darunavir
DRTB	Drug Resistant Tuberculosis
DTG	Dolutegravir
ED	Erectile Dysfunction
EFV	Efavirenz
EID	Early Infant Diagnosis
ELISA	Enzyme Linked Immunosorbent Assay
eMTCT	Elimination of Mother to child transmission of HIV
ENT	Ear Nose Throat.
EPTB	Extra Pulmonary Tuberculosis
EQA	External Quality Assurance
ESRD	End Stage Renal Disease
ETR	Etravirine
ECV	External Cephalic Version
EVG	Elvitegravir
FBO	Faith based Organization
FBS	Fasting Blood Sugar
FCT	Federal Capital Territory
FCTA	Federal Capital Territory Administration
FDC	Fixed Dose Combination
FETH	Federal Teaching Hospital
FMC	Federal Medical Centre
FMOH	Federal Ministry of Health
FP	Family Planning
FPV	Fosamprenavir
FTC	Emtricitabine
GFR	Glomerular Filtration Rate
HAART	Highly Active Antiretroviral Therapy



Hb	Haemoglobin
HbsAg	Hepatitis B surface Antigen
HBV	Hepatitis B Virus
HCT	HIV Counselling and Testing
HCV	Hepatitis C Virus
HCW	Health Care Worker
HIV	Human Immunodeficiency Virus
HLA	Human Leucocyte Antigen
HPV	Human Papilloma Virus
HSR	Hypersensitivity Reaction
HSV	Herpes Simplex Virus
HTS	HIV Testing Services
HUPACE	Howard University Pharmacy Continuing Education
IBBSS	Integrated Biological Behavioural Sentinel Survey
IDV	Indinavir
IGA	Income Generating Activity
IHVN	Institute of Human Virology Nigeria
INH	Isoniazid
INSTI	Integrase Strand Transfer inhibitor
IPT	Isoniazid Preventive Therapy
IPV	Intramuscular Polio Vaccine
IRIS	Immune Reconstitution inflammatory Syndrome
JUTH	Jos University Teaching Hospital
LGBTI	Lesbian, Gay Bisexual Transgender and Intersex
LIP	Lymphoid Interstitial Pneumonia
LMCU	Logistic Management Coordinating Units
LMIS	Logistic Management Information System
LPV/r	Lopinavir/ritonavir
LUTH	Lagos University Teaching Hospital
M&E	Monitoring and Evaluation
MAC	Mycobacterium Avium Complex
MARPs	Most at Risk Populations
MCH	Maternal and Child Health
MLSCN	Medical Laboratory Science Council of Nigeria
MNCH	Maternal, Newborn and Child Health.
MOH	Ministry of Health
MP	Malaria Parasites
MTB	Multidrug Resistance TB
MTCT	Mother to Child Transmission
MUAC	Mid Upper Arm Circumference
NACA	National Agency for the Control of AIDS
NACS	Nutrition Assessment Counselling and Support
NARH	National AIDS and Reproductive Health Survey
NASCP	National AIDS and STIs Control Programme
NAUTH	Nnamdi Azikiwe University Teaching Hospital
NBBFSW	Non Brothel Based Female Sex Worker



NEPWHAN	Network of People Living with HIV in Nigeria
NFV	Nelfinavir
NIMR	Nigeria Institute of Medical Research
NNRTI	Non-Nucleoside Transcriptase Inhibitors
NPHCDA	National Primary Health Care Development Agency
NRTI	Nucleoside Reverse Transcriptase Inhibitors
NSAIDS	Non Steroidal Anti-Inflammatory Drugs
NTTA	National Task Team on ART
NTTPMTCT	National Task Team on PMTCT
NVP	Nevirapine
OIs	Opportunistic infections
Pap	Papanicolaou Test for cervical cancer screening
PCR	Polymerase Chain Reaction
PCV	Packed Cell Volume
PCV	Pneumococcal Conjugate Vaccine
PDSA cycle	Plan, Do, Study, Act
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 Jiroveci 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
QA	Quality Assurance
QI	Quality Improvement
RAL	Raltegravir
RNA	Ribonucleic Acid
RVP	Rilpivirine
SACA	State Agency for the Control of AIDS
SQV	Saquinavir
STI	Sexually Transmitted Infection
tARVp	Triple Antiretroviral Drug Prophylaxis
TB	Tuberculosis
TDF	Tenofovir
TPV	Tipranavir
TT	Tetanus Toxoid
UBTH	University of Benin Teaching Hospital
UCH	University College Hospital Ibadan
UCTH	University of Calabar Teaching Hospital
UNAIDS	Joint United Nations Programme on HIV/AIDS



UNICEF	United Nations Children Emergency Fund
UNN	University of Nigeria
UNTH	University of Nigeria Teaching Hospital
USAID	United States Agency for International Development
VIA	Visual Inspection Acetic Acid for cervical cancer screening
VL	Viral Load
WBC	White Blood Cell
WHO	World Health Organization



## DEFINITION OF TERMS

**HIV Re-testing:** This is a second HIV test conducted after a positive first test result. Re-testing is recommended before initiation of ART.

**Sero-discordance:** Sexual relationship in which one partner is HIV positive and the other HIV negative.

**Key populations:** These are groups of individuals who bear a high burden of HIV and are exposed to higher risk of acquiring the infection.

**ARVs:** These are medicines used to treat HIV

**ART:** This is the use of a combination of three or more ARVs to treat HIV in order to achieve better viral suppression. Highly active anti-retroviral therapy (HAART) or combination Anti-Retroviral Therapy (cART) is used interchangeably.

**Viral load:** It is the number of HIV RNA copies in a milliliter of plasma.

**Sustained viral suppression:** This is optimal response to ART such that the viral load remains below the detection threshold usually at less than 20 copies of HIV RNA/ml.

**Stable on ART:** These are PLHIV who have received ART for at least one year and have no adverse drug reactions that require regular monitoring, no current illnesses, have good understanding of lifelong adherence with evidence of treatment success (i.e. two consecutive viral load measurements below 1000 copies/mL)

**Clinical failure in adults and adolescents:** It is the presence of new or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 condition) following 6 months of effective treatment.

**Clinical failure in Children:** It is the presence new or recurrent clinical event indicating advanced or severe immunodeficiency (WHO clinical stage 3 and 4 clinical condition with the exception of TB) after 6 months of effective treatment.

**Immunological failure in adults and adolescents:** It represents is CD4+ cell count fall to or below pre-treatment baseline value or persistent CD4 levels below 100 cells/mm<sup>3</sup> or 50% decline from on-therapy CD4+ cell count peak level

**Immunological failure in Children younger than 5 years:** It is persistent CD4 levels below 200 cells/mm<sup>3</sup> or <10%.

**Immunological failure in Children older than 5 years:** It is persistent CD4 levels below 100 cells/mm<sup>3</sup>.

**Virologic failure:** It is a persistently detectable viral load exceeding 1000 copies/ml (that is, 2 consecutive viral load measurements within a 3-month interval, with adherence support between measurements) after at least six months of using ARV drugs.



**Pharmacovigilance in HIV:** This is also known as drug safety. It is the collection, detection, assessment, monitoring, and prevention of adverse effects in patients on antiretroviral drugs and other medicines associated with the management of HIV/AIDS.

**Adherence to ART:** It is the extent to which a PLHIV behaviour coincides with the ART regimen as agreed through a mutual decision-making between the PLHIV and the adherence counsellor.

**MTCT of HIV:** This is mother to child transmission of HIV, which can occur in pregnancy, labour and delivery, or through breastfeeding.

**PMTCT:** Prevention of mother to child transmission of HIV is the strategy for ensuring that HIV infection is not transmitted to an infant during pregnancy and lactation period

**HIV-exposed infants:** These are infants delivered to HIV positive women.

**High-risk infants:** These are infants delivered to HIV positive women. These women may not have had ARVs, or have had less than 4 weeks of ARV or have a viral load of greater than 1000copies/ml in the last month prior to delivery.

**Infant ARV prophylaxis:** These are ARVs administered to all HIV exposed infants to prevent them acquiring HIV infection.

**EID:** Early infant diagnosis of HIV is the testing of all HIV exposed babies to determine their HIV infection status by detecting the presence of HIV DNA using PCR.

**DBS:** Dried blood spot testing (DBS) is a form of biosampling where blood samples are blotted and dried on filter paper. The dried samples can easily be shipped to an analytical laboratory and analysed using various methods such as DNA amplification.

**PCR DNA:** Polymerase chain reaction is the use of an enzyme to multiply both HIV DNA and RNA in blood sample.

**PrEP:** It is the use of oral ARVs (TDF and FTC) to prevent HIV infection in individuals exposed to high risk of acquiring HIV.

**PEP:** It is the use of oral ARVs by individuals exposed to HIV in order to block the acquisition of HIV.

**IPT:** Isoniazid preventive therapy is the administration of isoniazid to all HIV positive individuals to prevent the development of tuberculosis. Active TB has to be excluded before isoniazid therapy.

**CPT:** Cotrimoxazole preventive therapy is the routine administration of cotrimoxazole in all HIV positive individuals to prevent the development of variety of infections.

**Co-infection:** Co-infection is the spontaneous existence of two or more infections in an individual.

**Co-morbidity:** Co-morbidity is the occurrence of one or more illnesses in an individual with a primary disease.



**Opportunistic infection:** Opportunistic infections (OIs) are infections that occur more frequently and can become severe in individuals with HIV when their immune system becomes weakened.

**Differentiated care:** Differentiated care is the delivery of a minimum package of HIV/AIDS treatment care and support services according to the diversity of the care needs for people living with HIV.

**Decentralization in the context of HIV:** Decentralization is 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.

**Retention in HIV care:** It is the number of individuals on ART who are retained in same facility or are transferred out to another facility offering ART services over a period of time.

**Linkage to HIV prevention, care, treatment and support:** Proportion/number of individuals who complete a medical visit within 3 months of the diagnosis of HIV

**Task shifting/sharing:** It is a rational redistribution of tasks among health workforce teams, allowing a wider range of cadres to offer certain services, safely and effectively as a means of rapidly expanding access and improving health care.

**Continuum of care:** it is an integrated system of care that guides and tracks clients over time, through a comprehensive range of health services starting from screening for HIV, through to initiation of ART, retention in care and psychosocial support

**Monitoring in HIV:** Monitoring in HIV is the regular observation, recording and process of routinely gathering information of activities taking place in HIV programme.

**Evaluation:** Evaluation in HIV is a systematic assessment which focuses on expected and achieved accomplishments in HIV programmes.

**HIV Data flow:** Data flow is the transmission of HIV data from source (health facilities) through local governments and states data platforms to the Federal ministry of health as the final data repository.

**HIV Data validation:** Data validation is defined as the checking of all collected HIV data for completeness, thoroughness and reasonableness, and the elimination of errors.

**Data Quality Assurance:** Data Quality Assurance is a routine measure to ensure quality of data through a process of validation, reliability, precision, integrity and timeliness



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# CHAPTER ONE

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# INTRODUCTION

The 2016 Guidelines are informed by the basic principles of equality, equity and social justice and they align strongly with the universal declarations of human rights. They promote universal access to comprehensive HIV/AIDS prevention, treatment and care for all persons in Nigeria. The recommendations of these guidelines are the product of careful balancing of science and public health. The core principles of these guidelines include:

1. **Public Health Approach:** These guidelines reinforce the objectives of the national strategy for decentralization of HIV/AIDS services in Nigeria. They seek to make HIV prevention, treatment and care services universally available to all Nigerians irrespective of socioeconomic class and creed. This approach uses simplified drug formularies, fixed dose combinations, task shifting and sharing, and simplified systems for clinical mentoring.
2. **Promotion of human rights and equity:** Access to quality health care services including HIV prevention, treatment, care and support is a basic human right which is the entitlement of all people regardless of nationality, sex, ethnicity, race, religion or other status. These rights should be recognized as fundamental to realizing the universal right to health. These guidelines will support equitable provision of quality HIV services including ART and related interventions to all the people who need them; especially pregnant women, children and high risk populations. These services should 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 initiation of ART) and adequate health information safeguards should be put in place to ensure consent and confidentiality. Priority should be given to people who are most ill and those who are already on treatment.
3. **Implementation guided by in-country peculiarities:** Implementation of the recommendations of these guidelines will be informed by local context including; HIV epidemiology, availability of resources, the organization and capacity of the health systems. Indigenous best practices will be promoted alongside global standard practices.
4. **Strengthening health systems through innovation and learning:** Service delivery approaches recommended in these guidelines will be implemented in a manner that strengthens health systems and enhances local capacity to keep pace with the rapidly evolving science of HIV medicine.
5. **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 through provision of ART to people living with HIV and implementing strategies and recommendations that are sustainable and less dependent on foreign aid.



6. **Decentralization and Integration of Services:** With the new UNAIDS 90-90-90 targets, scale up of HIV and AIDS care, treatment and support services and decentralizing ART treatment become imperatives for expanding access to treatment and care. Strengthening linkage and referral are at the core of decentralization. The integration and linkage of HIV services with TB, sexual and reproductive health, maternal newborn and child health services offers opportunity for providing ART, increasing adherence and reducing attrition in care.
7. **The HIV Continuum of Care.** This integrated guideline is predicated on HIV continuum of care. The diagnosis of HIV requires, timely initiation of ART with retention in care and improved health outcomes and quality of life. As many more PLHIV live longer, stable and healthier, HIV has become a chronic health condition. This requires that health systems and community interventions would need modifications to optimize this chronic care model.
8. **Contribution to National and Global Health Goals:** These guidelines have taken into consideration the letter of the 2016 UNGASS Political Declaration on HIV which affirms the 2030 agenda for sustainable development including the resolve of member states to end the AIDS epidemic by 2030, and 2014 UNAIDS 90-90-90 targets seek to facilitate the attainment of Global Health Sector Strategy on HIV/AIDS (2015-2020). In addition, this document will contribute to achieving the goals and targets articulated in the National strategic framework.

## 1.1 Objectives of the Guidelines

- To provide updated and evidence-based clinical recommendations for provision of HIV prevention, treatment, care and support services.
- To provide guidance on key service delivery and operational issues needed to increase effectiveness and efficiency of HIV service delivery and strengthen the continuum of HIV care through linkage and integration.
- To provide programmatic guidance for the effective delivery of HIV/AIDS prevention, treatment, care and support services at all levels of the health care system.

These guidelines will support;

- Early HIV diagnosis, timely initiation of lifelong combination ART regardless of clinical stage or CD4+ cell count
- Use of viral load testing for monitoring ART treatment success and diagnosis of treatment failure
- Offer of ARV prophylaxis to HIV exposed infants, timely DNA PCR testing and early linkage of HIV positive infants to treatment and care.
- Prevention of new HIV infections among adults, adolescents, pregnant and breastfeeding women and children.
- Strengthened adherence to ART and retention in care
- Improved quality ART service delivery all over the country

## What is new in the National Guidelines for HIV Prevention, Treatment and Care?

ART should be initiated in all adults, adolescents, pregnant and breast feeding women, and children with a diagnosis of HIV regardless of WHO clinical stage and regardless of CD4+ cell



count. This recommendation envisages that many more people who test HIV positive will be initiated on ART once they are willing and ready to start ART for life. However as a priority, health care workers should initiate ART in the following;

- All Adults and adolescents with severe or advanced HIV clinical disease (WHO stage 3 or 4)
- All adults and adolescents with HIV and CD4+ cell count of less than 350 cells/mm<sup>3</sup>
- All HIV positive pregnant and breastfeeding women
- All HIV positive children older than 5 years of age with severe or advanced disease(WHO stage 3 or 4)
- All HIV positive children older than 5 years of age with CD4+ cell count less than 350 cells/mm<sup>3</sup>
- All HIV positive children less than 2 years of age
- All HIV positive children less than 5 years of age with CD4+ cell count of less than 750 cells/mm<sup>3</sup> or CD4 percentage less than 25%

**Table 1.1: List of new recommendations**

What is new for HIV positive adults and adolescents	<ul style="list-style-type: none"> <li>• Initiate ART in all adults and adolescents with a diagnosis of HIV. This is regardless of the clinical stage of the disease and also regardless of CD4+ cell count.</li> <li>• Dolutegravir (DTG) and Efavirenz (EFV) 400mg are new alternative options in first line ART regimens.</li> </ul>
What is new for HIV positive pregnant and breast feeding women.	<ul style="list-style-type: none"> <li>• Initiation of ART for all HIV-positive and pregnant, post-partum and breast-feeding women, regardless of CD4+ cell count</li> <li>• Use of maternal ART throughout pregnancy and breastfeeding to reduce MTCT. This ART treatment is for life</li> <li>• Repeat HIV testing for HIV-negative pregnant women in the last trimester</li> <li>• Viral load testing for pregnant women in the last trimester of pregnancy</li> </ul>
What is new for HIV exposed infants	<ul style="list-style-type: none"> <li>• Infants born to mothers with HIV who are at high risk of acquiring HIV should receive dual prophylaxis with AZT (twice daily) and NVP (once daily) for the first 6 weeks of life, whether they are breastfed or formula fed</li> <li>• Breastfed infants who are at high risk of acquiring HIV, should continue infant prophylaxis for an additional 6 weeks (total of 12 weeks of infant prophylaxis)</li> </ul>
What is new in prevention	<ul style="list-style-type: none"> <li>• Pre-exposure prophylaxis is recommended for most at risk persons with special emphasis on serodiscordant couples and key populations</li> </ul>



## Process of Guideline Review

The review and development of the 2016 National Guidelines on HIV prevention, treatment, and care, commenced after the official release of WHO 2016 Consolidated Guidelines on the use of ARV drugs for preventing and treating HIV infection. The process involved several stakeholders meetings convened by NASCP-FMOH that reviewed and adopted recommendations of WHO 2016 Consolidated Guidelines on the use of ARVs for preventing and treating HIV infection and the 2014 Integrated National Guidelines for HIV Prevention Treatment and Care.

Recommendations contained in this document are the product of stakeholder consensus, and the principal consideration guiding choice of recommendations is the wellbeing of the patients. The recommendations are essentially guidance on HIV diagnosis, general HIV care and support and the rational use of ARV drugs for treating and preventing HIV infection.

Stakeholders involved in the review and development of the 2016 national guidelines included representatives of the Federal Ministry of Health, State Ministries of Health, National Primary Health Care Development Agency, NACA, CHAI, UNAIDS, WHO, UNICEF, PEPFAR, CDC, USAID, HIV Implementing Partners, NEPWHAN, CSOs, National Task Teams for ART, PMTCT and HCT, facility level HIV service providers and the private health sector. The process was coordinated by the NASCP.

## Target Audience

The 2016 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 audiences for the guidelines include:

- National and State level 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

## 1.2 Epidemiology of HIV in Nigeria

The first case of AIDS in Nigeria was reported in 1986. Since then, national HIV prevalence has increased exponentially from 1.8% in 1991 peaking at 5.8% in 2001 and progressively declining since then to the current figure of 3.1% in 2014 (ANC Survey Report). Nigeria has the second highest burden of HIV globally with 3.4 million PLHIV as at 2014. There is a considerable regional and state to state variation in HIV prevalence in the country; ranging from 1% in Kebbi State to 12.7% in Benue State.

### 1.2.1 HIV Transmission

Heterosexual transmission accounts for the majority of HIV transmissions in Nigeria. Over 90% of HIV transmission is via unprotected sexual intercourse between heterosexual individuals. Homosexual sex contributes to HIV transmission and prevalence of HIV among this group of persons is high, nearing 35%.



Another prominent mode of transmission of HIV is from the HIV positive mother to her child. 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%.

Other modes of transmission of HIV, whose incidence rate is not well documented include, transmission from transfusion with infected blood and blood products, contact with sharp piercing object used for scarifications, tattoos, and surgical procedures.

## 1.3 Natural History of HIV

### 1.3.1 Adults and Children older than 5 years

A typical HIV 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 remainders 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/ $\mu$ l).

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  $2 \times 10^9$  CD4+ cells are produced each day.

### 1.3.2 HIV in Pregnancy

In pregnancy, immune function is suppressed in both HIV-infected and uninfected women. There is a decrease in immunoglobulin and 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 of 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.

### 1.3.3 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 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 level of 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%)



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## CHAPTER TWO

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# DIAGNOSIS OF HIV INFECTION

## 2.0 INTRODUCTION

Diagnosis of HIV infection is simply proof of the presence of HIV infection in an individual and this can be achieved by demonstrating the presence of HIV antibodies in plasma or serum (indirect test) or the virus in blood (direct test). Available test for diagnosis of HIV include antibody test, antigen tests and nucleic acid tests. The antibody detection test is suitable for diagnosis of HIV infection in adults and children 18 months and above, while the nucleic acid tests is used mainly for diagnosis of HIV infection in children under 18 months. On no account should a diagnosis of HIV infection be made without first obtaining a positive result from either of the test methods highlighted above.

It is highly recommended that prior to commencing ART all persons who have tested positive should be retested. Retesting is usually done to verify the diagnosis of HIV infection and rule out possible technical and clerical errors, including specimen mix-up as well as random error either by the provider or faulty test device. Retesting of a new specimen for each newly diagnosed individual should best be conducted by a different provider using the same algorithm, and better still at a different site preferably the site where the decision on starting ART is made.

It is not advisable to retest persons who are already on ART.

## 2.1 HIV Testing Services

HIV Testing Services (HTS) provide a gateway to HIV prevention, treatment and care services. HTS consists of a range of services that include diagnosis of HIV using HIV testing methods, counselling (pre-test information and post-test counselling), linkage to HIV prevention, treatment and care and other clinical services; and coordination with laboratory services for quality assurance and the delivery of accurate results.

All forms of HIV testing services should be voluntary and should adhere to WHO's five C's: consent, confidentiality, counselling, correct test results and connections to care, treatment and prevention services. The WHO five C's are principles that apply to all models of HTS and in all circumstances.

The five C's are:

**Consent:** People receiving HTS must give informed consent to be tested and counseled. Verbal consent is sufficient; written consent is not required. They should be informed of the process for HIV testing and counselling and of their right to decline testing.

**Confidentiality:** HTS must be confidential, meaning that what the HTS provider and the client



discuss will not be disclosed to anyone else without the expressed consent of the person being tested. Confidentiality should be respected, but it should not reinforce secrecy, stigma or shame. Shared confidentiality with a partner, family members, trusted other and a health-care provider is often highly beneficial.

**Counselling:** Pre-test information can be provided in a group setting, but people should have the opportunity to ask questions in a private setting if they request it. All HIV testing must be accompanied by appropriate and high-quality post-test counselling, based on the HIV test result and HIV status reported. Quality Assurance (QA) mechanisms as well as supportive supervision and mentoring systems should be in place to ensure the provision of high quality counselling.

**Correct test results:** Providers of HIV testing should strive to provide high-quality testing services. Quality management systems (including QA) should be in place for all HTS, regardless of where testing takes place, to ensure that people receive a correct diagnosis. QA should include both internal and external measures, and should receive support from the national reference laboratory. All people who receive a positive HIV diagnosis should be retested to verify their diagnosis before initiation of HIV care or treatment.

**Connection:** Linkage to prevention, treatment and care services should include effective and appropriate follow-up, including long-term prevention and treatment support. Quality assurance is essential in all approaches used for HIV testing services  
All HTS should be provided using the national testing algorithm.

## Pre-test services

Pre-test information may be provided through individual or group information sessions and through media such as posters, brochures, and short video clips shown in waiting rooms. When children and adolescents are receiving HTS, information should be presented to them in an age appropriate manner and in a manner their guardians can understand. Pre-test information sessions for people receiving HIV testing should include clear information about:

- The benefits of HIV testing;
- The meaning of an HIV-positive and an HIV-negative test;
- The services available in the case of an HIV-positive diagnosis, including location of ART centres.
- A brief description of prevention options and encouragement of partner testing;
- Assurances that the test result and any information shared by the client are confidential;
- The fact that the client has the right to refuse to be tested;
- The potential risks to the client, especially for those whose sexual or other behavior is stigmatized;
- Exploration of personal HIV risk behaviour and options for reducing risk including dual protection
- Assessment of clients' readiness for HIV testing
- Exploration of support systems and discussion of disclosure mechanism
- An opportunity to ask the provider additional questions;
- Provision of informed consent for testing.



## Post Test services

Post-test information and counselling for people who test HIV negative should include the following:

- An explanation of the test result
- Information on methods to prevent HIV acquisition and provision of male and/or female condoms, lubricant and guidance on their use
- Emphasis on the importance of knowing the status of sexual partners and information about the availability of sexual partner testing services
- Referral and linkage to other relevant HIV prevention services, such as pre-exposure prophylaxis and post-exposure prophylaxis
- Advice to people who test negative but report recent risky behavior to return in 4 weeks for repeat testing; if they again test HIV negative after 4 weeks, people with ongoing risk should be advised to return for testing every 6–12 months
- No requirement for repeat testing (window period) for people who report no recent risk.
- Provision of partner testing when pregnant women test HIV negative, as incident HIV in pregnancy and during the postpartum period is associated with a high risk of mother-to-child transmission

Post-test information and counselling for people who test HIV positive should include the following:

- An explanation of the test result and diagnosis, giving the client time to consider the result and helping the client to cope with emotions arising from the diagnosis
- Discussion of immediate concerns and help for the client to decide who in his or her social network may be available to provide immediate support
- Assessment of the risk of intimate partner violence and discussion of possible steps to ensure the client's physical safety
- Assessment of the risk of suicide, depression and other mental health consequences of an HIV-positive diagnosis and referral to relevant services
- Clear information on ART and its benefits for maintaining health and reducing the risk of HIV transmission, as well as where and how to access ART;
- Arranging a specific date and time for active referral and follow-up of clients who are unable to enroll in HIV care on the day of diagnosis;
- Information on how to prevent transmission of HIV, including information on the reduced transmission risks when virally suppressed on ART;
- Provision of male or female condoms and lubricants and guidance on their use;
- Discussion of the risks and benefits of disclosure, particularly among sexual partners, and provision of partner testing services
- Provision of HIV testing for, children and other family members
- Provision of or referral to prevention, counselling, support and other services as appropriate, including screening and treatment for tuberculosis (TB) and sexually transmitted infections (STIs), prophylaxis for opportunistic infections, contraception and antenatal care.
- Offering time for the client to ask additional questions.



## 2.1.1 Partner Testing Services

### Partner Testing Services

HIV partner testing services offers HIV Testing Services (HTS) to the sexual partners of individuals newly diagnosed with HIV (i.e., index cases). Such services are a key strategy to increase HIV case finding.

Partner testing services should be implemented across all HTS models in Nigeria for the following benefits;

- Presents an opportunity to provide HTS to the sexual partner(s) and children of the index patient
- Offers the partner(s) of the index patient the opportunity to provide other psychosocial support necessary for adherence to therapy, clinic appointments, and family planning
- Increases HIV case finding efficiency
- Supports achievement of epidemic control and the UNAIDS 90-90-90 in the shortest time possible

## 2.1.2 HIV Testing Service Delivery Models

HIV Testing services can be offered either in the facility or in the community.

**Facility based HTS** are those that are routinely offered in a health facility. Facility based HTS 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 case an individual voluntarily seeks counselling and testing services.

**Provider-initiated Testing and Counselling (PITC)** approach allows the health care provider to recommend HTS routinely to clients/patients as a standard component of medical care in the facility. PITC should be offered for all clients and in all services (including services for sexually transmitted infections (STI), viral hepatitis, tuberculosis (TB), children under the age of 5 years, immunization, malnutrition, antenatal care and all services for key populations) as an efficient and effective way to identify people with HIV.

In TB Settings, routine HIV testing should be offered to all clients with presumptive or confirmed TB; partners of known HIV-positive TB patients should be offered voluntary HTS with support for mutual disclosure.

Two strategies commonly used in the provision of PITC are:

- “Opt-out” approach: HIV test is routinely provided to every patient and the patient is informed of his/her right to refuse the test
- “Opt-in” approach: HIV test is recommended to each patient and the patient explicitly consents to receive the HIV test.

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.



**Community based HIV testing services** may be offered in places such as schools, work places, churches and mosques, and community-based organizations. Community based HIV testing can provide mobile services in vehicles or tents on market days and festivities and in places like bars and clubs. Close linkage and collaboration with health facilities is necessary to ensure that all individuals are linked to treatment care and support services.

## 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 the viral nucleic acid in the blood (direct testing). With the technology that is available at present, HIV antibodies are usually 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 RT-PCR 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 Enzyme-linked Immunosorbent Assay (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 commonly used HIV testing algorithms: serial and the parallel testing algorithms. The algorithm recommended for routine HIV testing is the serial HIV testing algorithm. Rapid Test Kits recommended for use under this algorithm are Determine, Unigold, Stat-Pak, Double-check Gold and Sure-Check. HIV serological assays adopted for use should have a minimum sensitivity of 99% and specificity of 98% under quality-assured laboratory conditions. It is recommended that all groups and organizations wishing to procure test kits for use in the country adhere to the kits in this algorithm. Similarly all newly procured batches of HIV test kits should undergo post-market validation duly endorsed by the national HIV Program.

#### Serial testing

This refers to the use of 2 different 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 a second test. The first test should be the most sensitive test and the second test should be very specific, and based on an antigen source different from that of the first test.

Samples that produce discordant results in the two tests are subjected to a third test called a tiebreaker. The main advantage of the serial over the parallel testing is the cost-savings in testing.

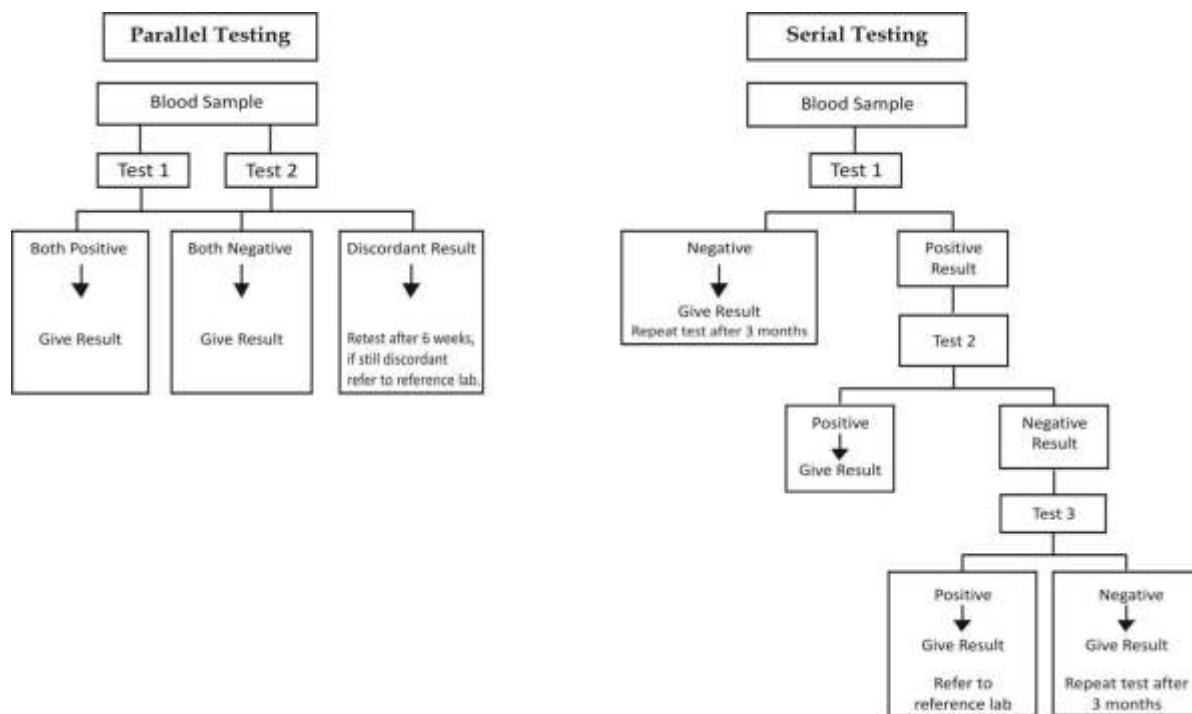
#### Parallel testing

This involves the use of two different screening tests performed simultaneously. Samples reactive to both tests are regarded as positive. However, those with discordant results require a third test as a tie-breaker. The main advantage of parallel testing over serial testing is that it minimizes



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 Algorithm**



## Nucleic acid based 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. Nucleic acid tests are virological assays because they detect the presence of viral particles, confirming the presence of the virus, and for measuring the amount of viral particles in the blood. It is recommended that virological assays used for the purpose of clinical diagnostic testing (usually at 6 weeks of age and below 18 months of age) should have a sensitivity of  $\geq 95$  and a specificity of  $\geq 98\%$  under quality-assured, standardized and validated laboratory conditions.

### A. HIV DNA Polymerase Chain Reaction

The DNA PCR test 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.



## B. Reverse Transcriptase Polymerase Chain Reaction (RT-PCR)

RT-PCR test 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 (RT-PCR).

### 2.2.1 Laboratory Diagnosis of HIV Infection in Children by Age Group

#### Children aged < 18 months

- Children < 18 months old may have circulating maternal antibodies. A positive antibody test may be from the child and/or the mother; in this case, DNA or RNA PCR is the test of choice and provides a definitive diagnosis of HIV infection.
- Rapid test can be used to screen a child less than 18 months for HIV exposure. However, a positive result in a child <18 months does not confirm infection and should be confirmed using DNA PCR.
- All HIV-exposed infants should have initial DNA PCR testing at 6 weeks of age (or earliest opportunity thereafter) and 12 weeks after complete cessation of breastfeeding. DNA PCR test results should be provided to the clinic and caregiver as soon as possible; latest within four weeks of specimen collection.
- Children aged between 9 and 18 months, should first have a rapid test and if positive, DNA PCR done to confirm diagnosis.
- If a screening antibody test is negative, HIV-infection is ruled out if the test has been conducted at least 12 weeks after complete cessation of breastfeeding
- For sick children <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 (WHO clinical staging) for presumptive clinical diagnosis are recommended.
- In a child less than 18 months with an initial positive virological test result, it is recommended that ART should be started immediately, while a second specimen is collected to confirm the result. It is not advised to defer ART until confirmation result is received.
- HIV-exposed infants who are well should undergo HIV serological testing at 9 months of age (or at the time of last immunization visit). Infants who have reactive serological assays at 9 months should have a virological test to confirm HIV infection and the need for ART.
- It is strongly recommended that children less than 18 months of age, with signs and symptoms suggestive of HIV infection should undergo HIV serological testing and if positive (reactive), do a virological test.
- Nucleic acid testing (NAT) technologies that are developed and validated for use at or near to the point of care can be used for early infant HIV testing.

#### Children aged ≥18 months

- Antibody detection is reliable and recommended 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, a 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 12 weeks after complete cessation of breastfeeding.
- Methods such as DNA/RNA PCR could be used to resolve suspected false negative results.

## 2.2.2 HIV Diagnosis in Pregnancy

The entry-point for PMTCT services is through HIV testing of pregnant women at the earliest opportunity; during antenatal care, labour and delivery including post-partum. In all settings, HIV testing services (HTS) should be offered to all pregnant women seeking antenatal care. Retesting for HIV in late pregnancy is recommended for pregnant women who tested negative in early pregnancy.

### Approach to HIV Testing Services in Pregnant Women

HIV testing of pregnant women should be accompanied by culturally acceptable counselling that highlights the benefits of knowing ones HIV status and its implications for the woman's health, 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 pregnant woman reserves the right to refuse the test.

### Essential Components of HIV Testing service 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 services should be provided during the first ANC visit.

### HIV testing service for women in labour

HIV testing in labour should be provided for all women of unknown HIV status and 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 HIV testing and ART
- Explain the HIV 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.



## 2.2.3 HIV Testing Services in PMTCT

### Couple HTS and partner notification

Couple HTS has emerged as an important intervention aimed at preventing the transmission of HIV between individuals who are sex partners. 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 HTS 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 HTS 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 HTS

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 tested and given their results separately and then encouraged to disclose results to each other. Partner testing should be adapted to the services in the facility and can take place either in the ANC or the HTS centre or laboratory.

The counsellor should not disclose the result(s) of one partner to the other without his or her consent, but should instead attempt to resolve issues around disclosure of an HIV result to a partner and significant others. 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
- To offer the partner(s) of the index patient the opportunity to provide other psychosocial support necessary for adherence to therapy, clinic appointments, family planning and other services
- Present an opportunity to provide HTS to the sexual partner(s) and children of the index patient

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

### Sharing HIV Status with health care providers

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



## 2.2.4 HIV Testing Services in Adolescents.

Adolescents are at high risk of HIV infection because of a number of reasons related to biological and psychosocial factors. This age group is characterised typically by risk taking, experimentation and vulnerability. Adolescents may experiment with injecting drugs, sexuality and sexual orientation and some may be sexually exploited. Worldwide the rate of HIV infection is highest among people aged 15 and 24. HIV infected adolescents face considerable psychosocial and health facility centred challenges that impact significantly on their health outcomes. HIV prevention among adolescents therefore should be listed as a priority item on the HIV/AIDS agenda. HIV testing services, especially in community settings, for adolescents should be strengthened and linked to health facilities for treatment and care.

## 2.2.5 HIV Testing Services in Key Populations.

Key populations have disproportionately high HIV prevalence because of a higher risk of contracting and transmitting HIV. They include:

- People in prisons and closed settings
- Injecting drug users
- Commercial sex workers
- Men who have sex with men
- Transgender people

The 2014 Integrated biological and behavioural surveillance survey (IBBSS) showed a high prevalence of HIV among men who have sex with men (MSM), brothel-based female sex workers (BBFSW), non-brothel based female sex workers (NBBFSW), and people who inject drugs (PWID), as 22.9%, 19.4%, 8.6%, and 3.4%, respectively.

These key populations need tailored HTS approaches and health care providers need appropriate skills and knowledge to provide high quality services for key populations. In addition health workers should be non-judgmental, ensure confidentiality and respect the rights of key populations to prevention, treatment, care and support services. HTS for key populations could be provided at both health facility and community settings. HIV negative individuals should undergo retesting at regular intervals (every 3-6 months). As much as possible, care and treatment services should be provided at the same location (one-stop shop) with prevention services for this population

## 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 2.1 and 2.2. 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



***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

The revised staging systems include:

- Presumptive clinical diagnoses that can be made in the absence of sophisticated laboratory tests.
- Definitive clinical criteria that require confirmatory laboratory tests



**Table 2.2: WHO Clinical Staging of HIV/AIDS for Adults and Adolescents with confirmed HIV Infection**

<b>Clinical Stage 1</b>
<ul style="list-style-type: none"> <li>- Asymptomatic</li> <li>- Persistent generalized lymphadenopathy</li> </ul>
<b>Clinical Stage 2</b>
<ul style="list-style-type: none"> <li>- Moderate unexplained weight loss (&lt;10% of presumed or measured body weight)</li> <li>- Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis)</li> <li>- Herpes zoster</li> <li>- Angular cheilitis</li> <li>- Recurrent oral ulceration</li> <li>- Papular pruritic eruption</li> <li>- Fungal nail infections</li> <li>- Seborrhoeic dermatitis</li> </ul>
<b>Clinical Stage 3</b>
<ul style="list-style-type: none"> <li>- Unexplained severe weight loss (&gt;10% of presumed or measured body weight)</li> <li>- Unexplained chronic diarrhoea for longer than 1 month</li> <li>- Unexplained persistent fever (intermittent or constant for longer than 1 month)</li> <li>- Persistent oral candidiasis</li> <li>- Oral hairy leukoplakia</li> <li>- Pulmonary tuberculosis</li> <li>- Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia)</li> <li>- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis,</li> <li>- Unexplained anaemia (&lt;8 g/dl), neutropaenia (&lt;0.5 × 10<sup>9</sup>/L) and/or chronic thrombocytopaenia (&lt;50 × 10<sup>9</sup>/L)</li> </ul>
<b>Clinical Stage 4</b>
<ul style="list-style-type: none"> <li>- HIV wasting syndrome</li> <li>- Pneumocystis (jirovecii) pneumonia</li> <li>- Recurrent severe bacterial pneumonia</li> <li>- Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month in duration or visceral at any site)</li> <li>- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)</li> <li>- Extrapulmonary tuberculosis</li> <li>- Kaposi sarcoma</li> <li>- Cytomegalovirus infection (retinitis or infection of other organs)</li> <li>- Central nervous system toxoplasmosis</li> <li>- HIV encephalopathy</li> <li>- Extrapulmonary cryptococcosis, including meningitis</li> <li>- Disseminated nontuberculous mycobacterial infection</li> <li>- Progressive multifocal leukoencephalopathy</li> <li>- Chronic cryptosporidiosis</li> <li>- Chronic isosporiasis</li> <li>- Disseminated mycosis (extrapulmonary histoplasmosis, coccidioidomycosis)</li> <li>• Lymphoma (cerebral or B-cell non-Hodgkin)</li> <li>• Symptomatic HIV-associated nephropathy or cardiomyopathy</li> <li>• Recurrent septicaemia (including nontyphoidal Salmonella)</li> <li>• Invasive cervical carcinoma</li> <li>• Atypical disseminated leishmaniasis</li> </ul>



**Table 2.3: WHO Clinical Staging of HIV/AIDS for Children with confirmed HIV Infection**

Clinical Stage 1
<ul style="list-style-type: none"> <li>- Asymptomatic</li> <li>- Persistent generalized lymphadenopathy</li> </ul>
Clinical Stage 2
<ul style="list-style-type: none"> <li>- Unexplained persistent hepatosplenomegaly</li> <li>- Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis)</li> <li>- Herpes zoster</li> <li>- Lineal gingival erythema</li> <li>- Recurrent oral ulceration</li> <li>- Papular pruritic eruption</li> <li>- Fungal nail infections</li> <li>- Extensive wart virus infection</li> <li>- Extensive molluscum contagiosum</li> <li>- Unexplained persistent parotid enlargement</li> </ul>
Clinical Stage 3
<ul style="list-style-type: none"> <li>- Unexplained moderate malnutrition not adequately responding to standard therapy</li> <li>- Unexplained persistent diarrhoea (14 days or more)</li> <li>- Unexplained persistent fever (above 37.5°C, intermittent or constant, for longer than one month)</li> <li>- Persistent oral candidiasis (after first six weeks of life)</li> <li>- Oral hairy leukoplakia</li> <li>- Lymph node tuberculosis; pulmonary tuberculosis</li> <li>- Severe recurrent bacterial pneumonia</li> <li>- Acute necrotizing ulcerative gingivitis or periodontitis</li> <li>- Unexplained anaemia (&lt;8 g/dL), neutropaenia (&lt;0.5 × 10<sup>9</sup>/L) or chronic thrombocytopaenia (&lt;50 × 10<sup>9</sup>/L)</li> <li>- Symptomatic lymphoid interstitial pneumonitis</li> <li>- Chronic HIV-associated lung disease, including bronchiectasis</li> </ul>
Clinical Stage 4
<ul style="list-style-type: none"> <li>- Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy</li> <li>- Pneumocystis (jirovecii) pneumonia</li> <li>- Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)</li> <li>- Chronic herpes simplex infection (orolabial or cutaneous of more than 1 month's duration or visceral at any site)</li> <li>- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)</li> <li>- Extrapulmonary tuberculosis</li> <li>- Kaposi sarcoma</li> <li>- Cytomegalovirus infection (retinitis or infection of other organs with onset at age older than one month)</li> <li>- Central nervous system toxoplasmosis (after the neonatal period)</li> <li>- HIV encephalopathy</li> <li>- Extra pulmonary cryptococcosis, including meningitis</li> </ul>



**Clinical Stage 4 (*continued*)**

- Disseminated nontuberculous mycobacterial infection
- Progressive multifocal leukoencephalopathy
- Chronic cryptosporidiosis (with diarrhoea)
- Chronic isosporiasis
- Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidioidomycosis, penicilliosis)
- Cerebral or B-cell non-Hodgkin lymphoma
- HIV-associated nephropathy or cardiomyopathy

**2.4 Linkage of HTS to care and ART**

Following an HIV diagnosis, a package of support interventions should be offered to ensure timely linkage to care for all people living with HIV. The following interventions should be used in improving linkage to care:

- Enhanced linkage with case management
- Support for HIV disclosure
- Patient tracking for those who failed to engage in care
- Training staff to provide multiple services
- Streamlined services to accelerate time to initiation
- Peer support and navigation approaches for linkage and
- Quality improvement approaches using data to improve linkage

**2.5 HIV Retesting**

It is recommended that people newly and previously diagnosed with HIV should be re-tested before initiation of ART in order to verify their serostatus.

Procedures for re-testing are as follows;

- Retesting of a new specimen for each newly diagnosed individual. This should preferably be done by a different provider using the national testing algorithm and using a different batch of test kit
- Retesting should be done at the site where the decision about ART initiation will be made.

**2.6 Improving quality and efficiency of HTS**

HTS remains the critical gateway to prevention, treatment, care and support services in Nigeria. The need for improved and sustainable high quality HTS must be underscored. Quality management systems, retraining and supervision of non-laboratory personnel in providing HTS services remain important considerations for program managers and should be put in place. Integration of HTS with other health services especially in the era of increasing decentralization of HIV/AIDS services is a priority in Nigeria. Health programming practices that can also improve the quality and proficiency of HTS in clinical and community settings include:



- Decentralization of HTS to primary health-care facilities and outside the health system
- Task-sharing of HTS responsibilities to increase the role of trained lay providers.

The laboratory needs to demonstrate quality as measured through documentation, standard operating protocols (SOPs), quality control (QC) and external quality assurance (EQA) such as proficiency testing.



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## CHAPTER THREE

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# ANTIRETROVIRAL THERAPY

## 3.1 INTRODUCTION

Antiretroviral therapy (ART) is the treatment of HIV infection using a combination of antiretroviral drugs (ARVs). All HIV infected persons should be initiated on ART as soon as possible following diagnosis. ART should be offered in a comprehensive manner that includes access to on-going adherence counselling, baseline and routine/periodic laboratory investigations, prevention and management of opportunistic infection (OIs), treatment monitoring and follow-up.

The objectives of ART include achievement of sustained virologic, immunologic, clinical, and epidemiologic control of HIV. Under optimal conditions, administration of ART should lead to rapid and sustained suppression of viral load down to  $\leq 400$  copies /ml after 24 weeks and  $<50$  copies/ml after 48 weeks of initiation of therapy. Sustained viral suppression is necessary to prevent or delay the development of ARV drug resistance.

Effective ART results in recovery of the immune functions with a progressive increase in CD4+ cell count at a rate of 50 to 100 cells/ $\mu\text{l}$  /year. In addition, there is significant improvement in clinical outcomes with reduced occurrence of morbid conditions and improved clinical indices with patients becoming less susceptible to infections. ART reduces morbidity from opportunistic infections and improves the quality of life of HIV infected individuals. In children ART will promote and restore normal growth and development.

ART is effective in reducing transmission of HIV from an infected person to an uninfected person. Widespread and sustained use of ART may lead to reduction of transmission of HIV in communities, which is the epidemiologic objective of ART.

ART should be initiated in all adults, all including pregnant and breastfeeding women, adolescents and children living with HIV, regardless of WHO clinical stage and at any CD4+ cell count. As a priority, ART should be initiated in all adults and adolescents with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) with CD4+ cell count  $\leq 350$  cells/ $\text{mm}^3$ . As a priority, ART should be initiated in all children  $\leq 2$  years of age or children younger than 5 years of age with WHO clinical stage 3 or 4 disease or CD4+ cell count  $\leq 750$  cells/ $\text{mm}^3$  or CD4 percentage  $<25\%$ , and children 5 years of age and older with WHO HIV clinical stage 3 or 4 disease or CD4+ cell count  $\leq 350$  cells/ $\text{mm}^3$ .

## 3.2 Classification of antiretroviral drugs

Antiretroviral drugs are classified according to their modes of antiviral action. Each class targets a different step in the viral life cycle. The classes of antiretroviral drugs are:



**Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs):** These compete with host nucleotides to serve as the substrate for reverse transcriptase chain elongation. Absence of 3'OH group on sugar moiety prevents the addition of another nucleotide, resulting in chain termination, abortion of viral DNA chain elongation and cessation of viral replication. Examples include:

- Abacavir (abacavir sulfate, ABC)
- Didanosine (ddI)\*
- Emtricitabine (FTC)
- Lamivudine (3TC)
- Stavudine (d4T)\*
- Tenofovir Disoproxil fumarate (TDF)
- Tenofovir Alafenamide (TAF)
- Zidovudine (AZT, ZDV)

**Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs):** They inhibit HIV reverse transcriptase by binding a hydrophobic pocket close to the active site thereby locking the site in an inactive conformation. Examples include:

- Efavirenz(EFV)
- Etravirine (ETR)
- Nevirapine (NVP)
- Rilpivirine (RPV)

**Protease Inhibitors (PI):** They inhibit HIV protease by binding to its active site, preventing the cleavage of gag and gag-pol precursor. Virions are produced but they are incomplete and non-infectious. Examples include:

- Atazanavir (ATV)
- Darunavir (DRV)
- Fosamprenavir (FPV)
- Indinavir (IDV)\*
- Nelfinavir (NFV)\*
- Ritonavir (RTV)
- Saquinavir (SQV)\*
- Tipranavir (TPV)
- Lopinavir (LPV)

**Entry Inhibitors:** They are designed to block the mechanisms by which HIV gains access into the cytoplasm of CD4 molecule bearing cell. These inhibitors are traditionally classified into 3 types:

- a) **Attachment inhibitors:** These agents complex with glycoprotein 120 and prevent it from interacting with the CD4+ molecule. Thus attachment of the virus to the cell is blocked. Examples include:
  - Fostemsavir
  - Ibalizumab
  - Anti CD4 adnectin
- b) **Fusion inhibitors:** These are agents designed to complex with the viral GP41. GP41 is the viral protein that is capable of fusing with cellular membrane molecules called chemokine receptors. The interaction of fusion inhibitors with GP41 blocks the fusion of viral membrane with cellular membrane. Examples include



- Enfuvirtide
- Anti-GP41 Adnectin
- Combinectin

c) **Chemokine Receptor Antagonists:** These are agents that complex with cell membrane receptors that serve as fusion proteins i.e. CXCR4, CCR5. Examples are:

- Maraviroc
- Vicriviroc
- Cenicriviroc<sup>1</sup>

<sup>1</sup>These products are currently at different stages of development

\*These products are no longer used for routine ART treatment

**HIV Integrase Inhibitors:** Also known as Integrase Strand Transfer Inhibitors (INSTI). These inhibit DNA strand transfer into host-cell genome and thus prevent viral integration. Integrase Inhibitors do not confer resistance to other ART classes. Examples include:

- Dolutegravir (DTG)
- Elvitegravir(EVG)
- Raltegravir (RAL)

**Pharmacokinetic enhancers:** These are drugs used in HIV treatment to increase the effectiveness of certain classes of ARV drugs. Protease inhibitors (PIs), an important component of the antiretroviral armada, were historically associated with poor oral bioavailability and high pill burden. However, because the PIs are metabolized by cytochrome P450 (CYP) 3A enzymes, intentional inhibition of these enzymes leads to higher drug exposure, lower pill burden, and simplified dosing schedules with this class of drug. This is the basis of pharmacokinetic enhancement. In HIV therapy, two pharmacokinetic enhancers or boosting agents are used: ritonavir and cobicistat. Both agents inhibit CYP3A4, with cobicistat being a more specific CYP inhibitor than ritonavir. Unlike ritonavir, cobicistat does not have antiretroviral activity.

It is recommended that combinations of a minimum of three drugs from at least two different classes of ARVs be used for ART. These ARVs are expected to act at different points of the HIV life cycle.

Typically, a backbone of 2 NRTIs combined with an NNRTI or a PI is used. Monotherapy or dual ARV therapy for HIV infection is not recommended for treatment because of the increased risk of development of drug resistance.

### 3.3 Initiation of ART in adults, adolescents and children

Early initiation of ART is associated with improved survival for patients and reduction of the incidence of HIV infection in the community. These guidelines recommend initiation of ART as soon as possible preferably within two weeks of diagnosis of HIV infection. However, patient's informed consent should be established before starting ART.

In conditions such as pregnancy, labour and serious ill health, treatment should be initiated with an increased sense of urgency as delay in these circumstances may lead to poor clinical outcomes.



Health care workers are encouraged to support positive decision-making by clients and implement interventions that remove barriers to early initiation of ART.

### **3.3.1 Preparation of Adults, Adolescents and Children for ART**

#### **Baseline Assessment for ART**

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

- Retesting for HIV to verify HIV status
- Assessment of patient's readiness for initiation of ART.
- Development of patient-centered adherence strategy

It is noteworthy that the first few months of therapy are important especially as certain occurrences during the period can influence the outcome of treatment. Adverse drug reactions, immune reconstitution inflammatory syndrome (IRIS) and opportunistic infections following commencement of treatment may confuse health care workers and patients leading to poor adherence and treatment failure. Patients should be warned to expect these complications but reassured that they are usually transient and would abate in the course of treatment. The importance of adherence for positive treatment outcomes must be emphasized and health workers are encouraged to develop individualized treatment adherence plans for each patient. Patients should be advised that poor adherence to treatment at any time following initiation of ART is associated with treatment failure, rapid development of drug resistance, ill-health and possibly death.

HIV positive adolescents and adults who are not willing and ready to start ART should receive ongoing counselling and education to promote retention in care.

#### **Further Baseline Assessment**

*Note: This assessment should not delay the commencement of ART.*

Further baseline assessment includes:

- Complete history and physical examination: Anthropometric assessment (weight, height/length, OFC, chest & mid-upper arm circumference). History of renal cardiovascular disease, 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 determined especially for adolescents
- Baseline CD4+ cell count estimation
- Screening for TB and Hepatitis (B and C) should be done. GeneXpert MTB/Rif should be used for asymptomatic cases of TB
- Determination of nutritional, psychosocial, growth and immunization status of patient (including determination of BMI for adults)
- Rectal and vaginal examination (including Inspection with Acetic Acid- VIA or/and PAP smear where possible)
- Determination of WHO clinical stage of disease
- Pregnancy assessment, family planning and counselling services, where required.
- Conducting baseline laboratory assessments



### **3.3.2 Initiating ART In Adults**

ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4+ cell count.

As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with a CD4+ cell count of  $\leq 350$  cells/mm<sup>3</sup>.

Initiating ART early in PLHIV is associated with reduced mortality and ill health. Untreated HIV infection may be associated with development of serious co-morbidities such as cardiovascular, kidney and liver diseases, cancers and mental illness. Early initiation of ART serves the useful purpose of preventing the occurrence of these diseases. An additional advantage of early initiation of ART is that it substantially reduces the risk of sexual transmission to HIV-negative partners.

It should be noted that there is increased risk of adverse drug reaction when certain ARV drugs usually NNRTIs are initiated at high CD4+ cell counts. It is recommended that all patients with CD4+ cell counts above 500 cells/mm<sup>3</sup> starting Nevirapine containing regimens should be monitored closely in the first couple of months for early detection and management of adverse drug events.

### **3.3.3 Initiating ART in adolescents (10-19 years of age)**

ART should be initiated in all adolescents living with HIV, regardless of WHO clinical stage and at any CD4 + cell count.

As a priority, ART should be initiated in all adolescents with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and a CD4 + cell count of 350 cells/mm<sup>3</sup>.

In Nigeria, like in most other sub-Saharan African (SSA) countries, HIV/AIDS programming for adolescents have remained largely inadequate; resulting in poor uptake of services, high loss to follow-up rates and suboptimal adherence among this age group.

It is therefore recommended that implementation of early ART in adolescents should be prioritized to ensure that effective and age-appropriate counselling approaches are a prominent component of the ART package for this age group.

Health workers are advised to leverage on the control that parents and caregivers exercise on their wards to improve adherence to treatment in this age group. They should therefore ensure that parents and caregivers are involved in developing a treatment adherence plan for their wards.



### **3.3.4 Initiation of ART in infants and children younger than 10 years of age**

ART should be initiated in all children with HIV, regardless of WHO clinical stage, or at any CD4+ cell count.

As a priority, ART should be initiated in the following situations

- All children < 2 years of age
- All children younger than 5 years of age with WHO clinical stage 3 or 4 disease or CD4+ cell count  $\leq 750 \text{ cells/mm}^3$  or CD4+ percentage  $< 25\%$
- All children 5 years and older with WHO HIV clinical stage 3 or 4 disease or CD4+ cell count  $< 350 \text{ cells/mm}^3$

Infants and young children living with HIV are more likely to die within the first two years of life from the disease in the absence of any intervention. As they grow older the risk of disease progression and mortality, in the absence of treatment, falls to rates similar to those of young adults.

Aside from preventing illness and death in very young children, earlier initiation of ART can mitigate the negative effects of HIV infection on growth, pubertal and nervous system development.

### **3.3.5 Recommendations for use of ART in TB/HIV co-infection**

ART should be started in all TB patients (adults, adolescents and children) living with HIV, regardless of CD4+ cell count. TB treatment should be initiated first, followed by ART as soon as possible within the first 2 weeks of treatment.

There is strong evidence that initiation of ART within two weeks of TB treatment is associated with marked reduction in overall TB-related morbidity and mortality. Also, there is significant reduction in the occurrence of AIDS-related illnesses among persons who initiated ART early.

It should be noted that early initiation of ART in TB/HIV co-infection could be associated with a higher risk of IRIS. Therefore health workers should strive to recognize and manage it early.



**Table 3.1 When to initiate ART in adults and adolescents (including pregnant women) and children**

Target population	Recommendation
All HIV positive adult and adolescents (including pregnant women)	<p>Initiate ART in all regardless of WHO clinical stage and at any CD4+ cell count.</p> <p>As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with a CD4+ cell count of <math>\leq 350</math> cells/mm<math>^3</math></p>
All HIV positive Children	<p>Initiate ART in all children regardless of WHO clinical stage and at any CD4 cell count.</p> <p>As a priority, ART should be initiated in the following situations</p> <ul style="list-style-type: none"> <li>• All children <math>&lt; 2</math> years of age</li> <li>• All children younger than 5 years of age with WHO clinical stage 3 or 4 or CD4+ cell count <math>\leq 750</math> cells/mm<math>^3</math> or CD4+ percentage <math>&lt; 25\%</math></li> <li>• All children 5 years and older with WHO HIV clinical stage 3 or 4 disease or CD4+ cell count <math>&lt; 350</math> cells/mm<math>^3</math></li> </ul>

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 two weeks of initiating TB treatment). For most HIV/HCV co-infected people, including those with cirrhosis, the benefits of ART outweigh concerns regarding drug-induced liver injury.

### 3.4 Recommended ART Regimen for Adults, Adolescents and Children

The choice of regimens for ART should be informed by potency, safety, convenience of dosing and interactions with other medications. Fixed dose combinations (FDCs) and once daily regimens are generally preferred because of simplicity of administration, prescription practices and procurement. In addition FDCs promote adherence to ART and help reduce incidence of drug resistance.

ART regimens are generally classified as first, second and third line. The first line regimens are used in ARV naive patients while second and third line regimens are used in individuals who have failed first and second line regimens respectively.

Prior to commencing ART, patients should be informed that the first line ART regimens represent the best option of remaining virally suppressed. Patients should therefore be supported to adhere fully to treatment.



### **3.4.1 First-line ART regimens for adults**

TDF + 3TC + EFV or TDF + FTC + EFV as fixed dose combinations are the preferred first line regimen for initiating ART in treatment naive adults.

In the event that the preferred regimens above are contraindicated or not available, the following alternative options are recommended;

- TDF + 3TC (or FTC) + DTG
- AZT\* + 3TC + EFV
- TDF + 3TC (or FTC) + EFV<sub>400</sub>
- AZT\* + 3TC + NVP
- TDF + 3TC (or FTC) + NVP
- ABC + 3TC + EFV

### **3.4.2 First Line ART Regimen for Adolescents**

The recommended first line regimens for adolescents include the following;

TDF + 3TC + EFV or TDF + FTC + EFV presented as a once daily fixed dose combination is the preferred first initiation of ART. The alternative first line regimens for adolescents;

- TDF + 3TC (or FTC) + DTG
- TDF + 3TC (or FTC) + EFV<sub>400</sub>
- AZT + 3TC + NVP or EFV
- ABC + 3TC (or FTC) + DTG
- ABC + 3TC (or FTC) + EFV<sub>400</sub>
- TDF + 3TC (or FTC) + NVP
- ABC + 3TC (of FTC) + NVP

### **3.4.3 First line ART for children 3-10 years of age**

ABC + 3TC + EFV is the preferred first line regimen

The alternative options include the following

- ABC + 3TC + NVP
- AZT + 3TC + EFV
- AZT + 3TC + NVP
- TDF + 3TC (or FTC) + EFV
- TDF + 3TC (or FTC) + NVP

### **3.4.4 First line ART regimen for children less than 3 years of age**

ABC + 3TC + LPV/r or AZT + 3TC + LPV/r is recommended as first line regimen.

The alternative first line regimens for this age group

- ABC + 3TC + NVP
- AZT + 3TC + NVP



In special circumstances where preferred and alternative regimes are not available or suitable the following regimen can be used;

- ABC + 3TC + RAL\*
- AZT + 3TC + RAL\*

*\*RAL is approved for use in infants and children from the age of 4 weeks, but there is very limited evidence to inform the use of raltegravir (RAL) as a first-line drug in infants and young children. The use of this INSTI could be considered where available in instances of poor tolerability or administration challenges with LPV/r, particularly in settings where as a result of rapid expansion of maternal treatment, infants and children are at very high risk of carrying an NNRTI resistance virus.*

**Table 3.2 Recommended first line ART regimens for adults, adolescents, pregnant, breast feeding women and children**

First-line ART	Preferred first-line regimen	Alternative first-line regimens
<b>Adults</b>	TDF + 3TC (or FTC) + EFV	TDF + 3TC (or FTC) + *DTG AZT + 3TC + NVP (or EFV) TDF + 3TC (or FTC) + *EFV <sub>400</sub> ABC +3TC +EFV TDF + 3TC (or FTC) + NVP
<b>Pregnant/breastfeeding women</b>	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + NVP
<b>Adolescents (10-19 years)</b>	TDF + 3TC (or FTC) + EFV	TDF + 3TC (or FTC) + *DTG TDF + 3TC (or FTC) + *EFV <sub>400</sub> AZT + 3TC + NVP or EFV ABC + 3TC (or FTC) + *DTG ABC + 3TC + (or FTC) + *EFV <sub>400</sub> TDF + 3TC (or FTC) + NVP ABC + 3TC (or FTC) + NVP
<b>Children 3 years to less than 10 years</b>	ABC + 3TC + EFV	ABC + 3TC + NVP AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + EFV (or NVP)
<b>Children less than 3 years</b>	ABC + 3TC + LPV/r AZT+3TC+LPV/r	ABC + 3TC + NVP AZT + 3TC + NVP AZT+3TC+RAL***

See annexes 4, 5, 6 & 7 for dosing and formulations for ARVs

Where viral load monitoring is available, consideration can be given to substituting LPV/r with EFV at 3 years of age after viral suppression is sustained

\*Safety and efficacy data on DTG and EFV400 for pregnant and breastfeeding women and TB co-infection are yet to be verified

\*\*\*RAL is approved for use in infants and children from the age of 4 weeks, but there is very limited evidence to inform the use of raltegravir (RAL) as a first-line drug in infants and young children. The use of this INSTI could be considered where available in instances of poor tolerability or administration challenges with LPV/r, particularly in settings where as a result of rapid expansion of maternal treatment, infants and children are at very high risk of carrying an NNRTI resistance virus



**Table 3.3: Special Considerations**

Patient Category	Recommended Regimen
Patients with impaired renal function	*ABC + **3TC + EFV
Patients with osteoporosis (TDF induced or post- menopausal)	*ABC + **3TC + EFV

\*Indicated for patients with impaired kidney function (eGFR <60ml/min).

\*\*Dose adjusted 3TC.

See annex 8 for Dosing Of Antiretroviral Drugs for HIV-Infected Adults with Chronic Kidney Disease (CKD) or End-Stage Renal Disease (ESRD)

There is currently limited experience with use of EFV400mg and DTG in adolescents. While no age or weight restrictions apply to the use of EFV400mg/day which can be used starting from weight of 20kg, the use of DTG (50 mg) is approved only for adolescents who are older than 12 years and who weigh more than 40kg. In addition, safety and pharmacokinetic data on co-infection and pregnancy are still pending.

TDF based regimens should be used with caution in individuals with hypertension and diabetes; TDF is contraindicated in patients with evidence of chronic kidney disease. AZT should be avoided in individuals with severe anaemia (Hb <8g/dl). Where TDF and AZT are contraindicated as in chronic kidney disease, ABC can be used as a substitute. However provision should be made for dose adjustment of 3TC in cases of renal impairment.

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 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.

In suspected cases of renal impairment dosage modifications are recommended for many ARV drugs. The administration of ART in the presence of renal failure should be done in consultation with specialist.



**Table 3.4 Summary of Recommended ART Regimens for children and adolescents who need TB treatment**

<b>Recommended Regimens for Children and Adolescents initiating ART while on an anti TB treatment</b>				
Younger than 3years	*Triple NRTI (AZT+3TC+ABC)			
3years and older	Two NRTIs + EFV (AZT+3TC+EFV)			
For infants and children infected with HIV younger than 3 years, ABC + 3TC + AZT is recommended as an option for children who develop TB while on an ART regimen containing NVP or LPV/r. Once TB therapy has been completed, this regimen should be stopped and the initial regimen should be restarted.				
<b>Recommended Regimens for children and Adolescents initiating TB treatment while receiving ART</b>				
Child on Standard NNRTI-based Regimen Two NNRTI + EFV or NVP	Younger than 3years	Continue NVP, ensuring that the dose is 200mg/m <sup>2</sup> OR *Triple NRTI ( AZT+3TC+ABC)		
	3years and older	If the child is receiving EFV continue the same regimen. If the child is receiving NVP substitute with EFV		
<b>Recommended Regimens for children and Adolescents initiatingTB treatment while receiving ART</b>				
Child on Standard PI-based Regimen Two NRTIs+LPV/r	Younger than 3years	Triple NRTI (AZT+3TC+ABC) OR Continue LPV/r adding RTV to achieve full therapeutic dose. **		
	3years and older	If the child has no history of failure of an NNRTI-based Regimen: Substitute with EFV Or continue LPV/r until an LPV/r ratio of 1:1 is attained**  If the child has a history of failure of an NNRTI-based Regimen: Continue LPV/r adding RTV until an LPV/r ratio of 1:1 is attained **		

See annexes 5, 6 & 7 for paediatric ARV dosage and formulations

\*Triple NRTI is only recommended for the duration of TB treatment; an age appropriate PI or NNRTI based Regimen should be restarted when rifampicin based therapy ends.

\*\*Increase RTV until it reaches the same dose as LPV in mg in a ratio of 1:1

## 3.5 Monitoring Patients on ART

### 3.5.1 Monitoring and Follow-Up in Adults

Once ART is initiated, assessment should look out for:

- Any persisting or new signs/symptoms of HIV related conditions
- Potential drug toxicities.
- Optimal Adherence
- Response to therapy (Clinical, Immunological and Virologic).
- Weight changes, growth and development including height in children
- Abnormal Laboratory parameters



**Table 3.5: Recommended Schedule for Monitoring Adults on ART: Clinical Assessments**

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

Laboratory monitoring tests may differ according to the level of the health care facility and should be done according to the following schedule:

**Table 3.6: Recommended Schedule for Monitoring Adults on ART: 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 <sup>1</sup>	X			X	
WBC, Platelets	X	As clinically indicated					
ALT	X	As clinically indicated					
Creatinine (CalcCrCl)	X					X	
HbsAg and HCV	X						
Urinalysis	X		X <sup>3</sup>			X <sup>3</sup>	
Syphilis test	X						
VIA/Pap Smear	X	Annual thereafter					
AST, ALP, FBS, Amylase, Pregnancy test, Lipid profile, U/E, GeneXpert, Chest X-Ray		As clinically indicated					

<sup>1</sup> Essential

<sup>2</sup>

<sup>3</sup>

For patients on AZT; Patients on NVP; patients on TDF

‡ Desirable: Baseline viral load can be performed especially for those with prior exposure to ARVs but is not routinely recommended. 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.



### 3.5.2 Monitoring in Children on ART

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 3 months following initiation of ART or earlier if indicated

### 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 3.8; however, baseline laboratory tests should not delay ART initiation in children. 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)

### 3.5.3 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 of adverse drug events
- Review ARV dosages for changes in body weight.
- Provide adherence support and monitoring



**Table 3.7: Recommended Schedule for Monitoring Children on ART: Clinical Assessments**

	Pre-Treatment (Baseline)	Week 2	Week 4	Week 8	Week 12	Every 12 Weeks <sup>+</sup>
History and Physical Exam	X	X	X	X	X	X
Anthropometric Measurements (Wt, Ht, Length, OFC, MUAC <sup>*</sup> ; Chest circumference)	X	X	X	X	X	X
Nutrition (Feeding, diet)	X	X	X	X	X	X
Immunization status <sup>**</sup>	X					
Adherence monitoring	X	X	X	X	X	X
Psychosocial assessment <sup>***</sup>	X	X	X	X	X	X
Clinical Screening for TB and other OIs (assessment INH and CTX Prophylaxis)	X	X	X	X	X	X

\*Most appropriate for children aged 1 – 5 years

\*\*Ascertain completion of routine immunization, otherwise refer accordingly

\*\*\*Most appropriate for adolescents

+More frequent clinic visits and examination may be required for unstable patients

**Table 3.8: Recommended Schedule for Monitoring Children on ART: 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+ Cell count/CD4%*	X			X	X	X		
Hb/PCV	X	X <sup>1</sup>	X			X		
WBC + differentials, Platelets	X			As clinically indicated				
ALT	X			As clinically indicated				
Creatinine (Calc CrCl)	X					X		
HbsAg and HCV	X							
Urinalysis	X			X <sup>3</sup>			X <sup>3</sup>	
AST, ALP, FBS, Amylase, Pregnancy test <sup>1</sup> , Lipid profile, U/E, Mantoux, GeneXpert, Chest X-Ray				As clinically indicated				

X Essential

<sup>1</sup> For patients on AZT; <sup>2</sup> Patients on NVP; <sup>3</sup> patients on TDF

\*Most appropriate for adolescents especially where pregnancy is suspected

‡ Desirable: Baseline viral load can be performed especially for those with prior exposure to ARVs but is not routinely recommended

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.



## Monitoring Schedule for Children on ART

Clinical assessment and laboratory monitoring schedule for children on ART is as provided for in Tables 3.7 and 3.8. 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 months 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.

## 3.6 Management of HIV Treatment Failure

### 3.6.1 Definition of Treatment Failure

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

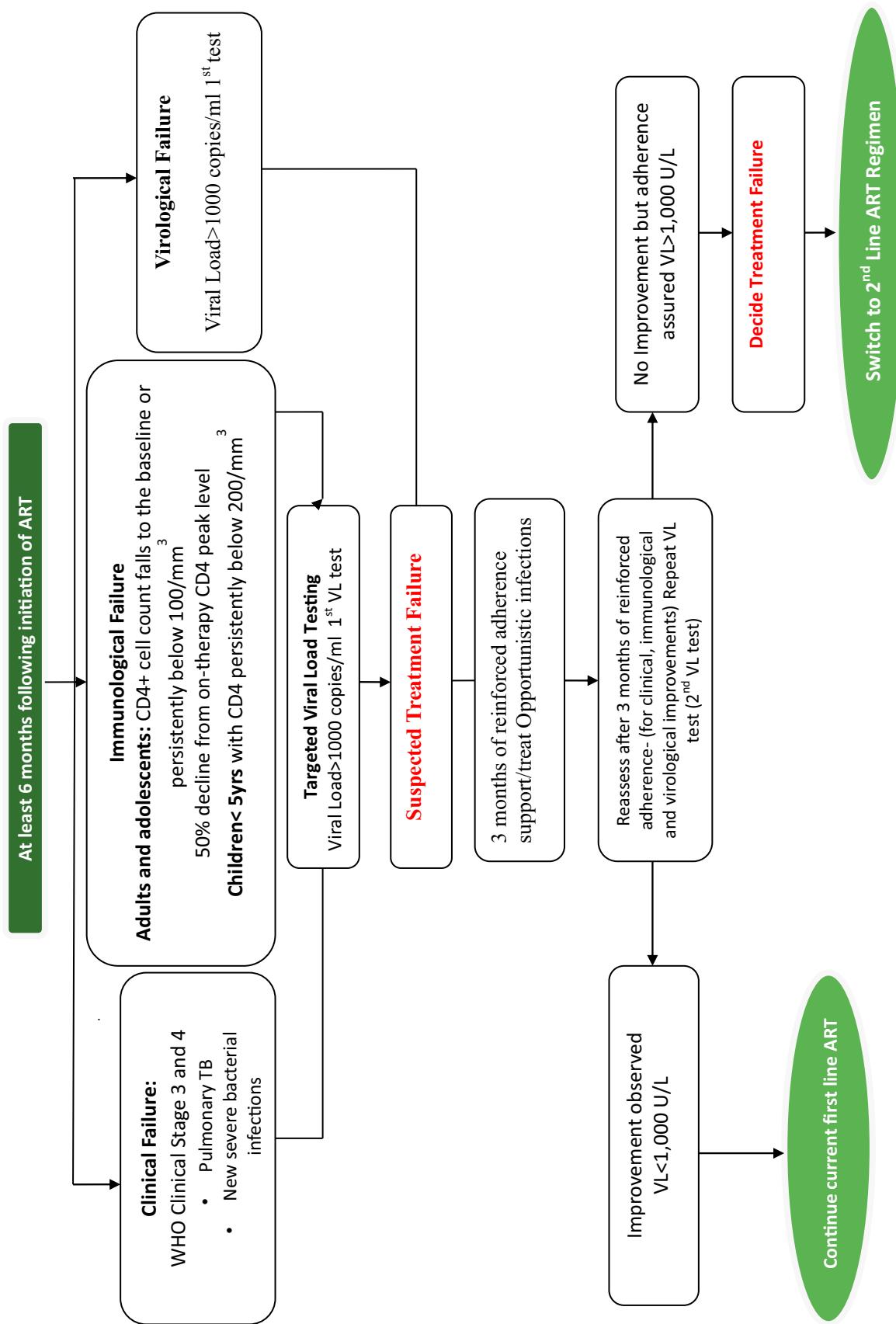
- Virologic failure
- Immunologic failure
- Clinical failure



**Table 3.9: Definition of Clinical Failure**

Failure	Definition	Comments
Clinical Failure	<p><b>Adults and adolescents</b> New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 condition) after 6 months of effective treatment.</p> <p><b>Children</b> 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</p>	The condition must be differentiated from IRIS 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	<p><b>Adults and adolescents</b> CD4+ cell count falls to the baseline (or below) Or Persistent CD4+ cell count below 100 cells/mm3 50% decline from on-therapy CD4+ cell count peak level</p> <p><b>Children</b> <b>Younger than 5 years</b> Persistent CD4+ cell count below 200 cells/mm3 or &lt;10% <b>Older than 5 years</b> Persistent CD4+ cell count below 100 cells/mm3</p>	Without concomitant or recent infection to cause a transient decline in the CD4+ cell counts.
Virological Failure	Plasma viral load above 1000 copies/ml based on two consecutive viral load measurements in 3 months, with adherence support following the first viral load test	An individual must be taking ART for at least 6 months before it can be determined that a regimen has failed Blips are a transient increase in viral load between 50 and 1,000 copies/ml and can occur during periods of inter-current infections.



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

## Causes of Treatment Failure

### 1. Viral factors

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

### 2. Non-viral Factors

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

This may be due to:

- Host factors: poor adherence to ART, malnutrition and malabsorption of drugs
- Choice of initial ART regimen, poor potency or improper dosing
- Drug-drug interactions

## 3.6.2 Substitution and switch of ARV drugs

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

1. Toxicity/adverse drug reactions
2. Co-morbidity
3. Pregnancy
4. 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.

## Drug toxicity / Adverse drug reactions

Toxicity refers to how poisonous or harmful a substance can be. In the context of pharmacology, drug toxicity occurs when a person has accumulated too much of a drug in their bloodstream, leading to adverse effects within the body. On the other hand an adverse drug reaction (ADR) is “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.”

In the event of drug toxicity and adverse drug reactions, the offending drug(s) must be discontinued and changed to other drugs from within first line ARV options. Second line drugs are preserved for treatment failures.



### 3.6.3 Second line ART regimen

**Table 3.10: Preferred Second line ART regimen for Adult and Adolescents including Pregnant women**

Target Population		Preferred Options
Adults and adolescents (including pregnant women)	If TDF used in first-line therapy	AZT + 3TC + LPV/r or AZT + 3TC + ATV/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 LPV/r

See annexes 4 & 7 for ARV formulations and dosage

\*When used with ATV/r or LPV/r, Rifabutin should be dosed at 150mg qod or 3x/week  
Choice of second line also depends on first line NRTI backbone (as in adults)

**Table 3:11 Second Line ART regimens for children**

Children	First-Line ART regimens	Second-line ART regimens
Children less than 3 years	ABC + 3TC +LPV/r	AZT or ABC +3TC +RAL <sup>a</sup>
	AZT + 3TC+ LPV/r	
Children 3 years and older	ABC + 3TC+ EFV	AZT+3TC+LPV/r
	AZT+3TC+ EFV	ABC or TDF <sup>b</sup> +3TC+LPV/r <sup>c</sup>

See annexes 5, 6 & 7 for ARV formulations and dosage for children

<sup>a</sup> If RAL is not available, no change is recommended unless in the case of advanced clinical disease progression or lack of adherence specifically due to poor palatability of LPV/r. In this case, switching to a second-line NVP-based regimen should be considered. Based on approval of the use of EFV in children less than 3 years, an EFV-based regimen could be considered as an alternative. However, more data are needed to inform how best to use EFV in this population.

<sup>b</sup> TDF may be given only to children older than 2 years.

<sup>c</sup> ATV/r can be used as an alternative to LPV/r in children older than 3 months. However, the limited availability of suitable formulations for children younger than 6 years, the lack of an FDC and the need for separate administration of the RTV booster should be considered when choosing this regimen.



### 3.6.4 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 drug sensitivity testing (genotype or phenotype resistance testing) is not readily available. In the event of treatment failure on 2<sup>nd</sup> 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 requisite experience and expertise in the management of advanced and complicated HIV disease

#### Consideration for third line

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:

**Table 3.12 Sequence of Switching ART from first Line to third Line regimens**

Population	First line regimen	Second line regimen	Third line regimen
Adults and Adolescents (>10years)	2 NRTIs + EFV	2 NRTI + ATV/r or LPV/r	DRV/r <sup>b</sup> + DTG <sup>c</sup> ± 1-2 NRTIs
	2 NRTIs + DTG	2NRTI + ATV/r or LPV/r	DRV/r + 2 NRTIs + NNRTI
Pregnant and Breastfeeding women	2NRTIs + EFV	2NRTIs + ATV/r or LPV/r	DRV/r + DTG ± 1-2 NRTIs
Children (0-10 years)	2NRTI + LPV/r	If less than 3 years 2NRTI + RAL <sup>d</sup>	RAL (or DTG) <sup>f</sup> + 2 NRTIs DRV/r <sup>g</sup> + 2NRTIs
		If older than 3 years 2 NRTI + EFV or RAL	
	2NRTI + EFV	2 NRTI + ATV/r or LPV/r	DRV/r + RAL(or DTG)±1-2NRTIs

<sup>b</sup> In PI-experienced patients, the recommended DRV/r dose should be 600 mg/100 mg twice daily.

<sup>c</sup> Safety and efficacy data on the use of DTG in adolescents younger than 12 years and pregnant women are not yet available.

<sup>d</sup> If RAL is not available, no change is recommended unless in the presence of advanced clinical disease progression or lack of adherence, specifically because of poor palatability of LPV/r. In this case, switching to a second-line NVP-based regimen should be considered. Based on approval of the use of EFV in children less than 3 years of age, an EFV-based regimen could be considered as an alternative. However, more data are needed to inform how best to use EFV in this population.

<sup>e</sup> ATV/r can be used as an alternative to LPV/r in children older than 3 months of age. However, the limited availability of suitable formulations for children younger than 6 years of age, the lack of an FDC and the need for separate administration of RTV booster should be considered when choosing this regimen.

<sup>f</sup> RAL can be used in children failing PI-based second-line treatment when DTG is not available and when RAL has not been used in a previous regimen. DTG is currently approved only for children 12 years and older; however, studies are ongoing to determine dosing in younger children, and approval for lower age groups is expected in the near future

<sup>g</sup> DRV/r should not be used in children younger than 3 years of age.



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## CHAPTER FOUR

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# PHARMACOVIGILANCE IN ANTIRETROVIRAL THERAPY

## 4.1 INTRODUCTION

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. Pharmacovigilance is an arm of patient care that aims at making the best use of medicines for the treatment or prevention of disease. Good pharmacovigilance will identify the risks and the risk factors in the shortest possible time so that harm can be avoided or minimized.

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 as the country commences ART for all HIV positive persons. All healthcare providers (doctors, pharmacists, nurses and counsellors etc.) at various service delivery points should therefore assess patients for adverse drug reactions at every encounter and report all suspected adverse events using the National Individual Case Safety Report Form.

There are two methods of pharmacovigilance namely: active and passive 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.

## 4.2 Adverse drug reactions (ADR)

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.”

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. ADRs that pose a serious threat to the health and well-being should be discontinued without delay and necessary consultations made regarding next line of actions.

### Classification of Adverse Drug Reactions

The World Health Organization classifies ADRs into four categories based on severity. 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 4.1: WHO Severity Grading of ADR**

SEVERITY GRADE	CHARACTERISTICS
<b>1 – Mild ADR</b>	Transient or mild discomfort (<48 hours) No limitation of activity No medical intervention or therapy required
<b>2 – Moderate ADR</b>	Mild to moderate limitation of activity Some assistance may be needed No or minimal medical intervention required
<b>3 – Severe ADR</b>	Marked limitation of activity Some assistance usually required Medical intervention or therapy required Hospitalization possible
<b>4 – Life Threatening ADR</b>	Extreme limitation of activity Significant assistance required Significant medical intervention or therapy required Hospitalization or hospice care probable.

### 4.3 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 (table 4.2).

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

#### Laboratory monitoring of toxicity:

Laboratory monitoring of patients receiving ARVs for either HIV treatment or prophylaxis is very important for early detection and prevention of some ADRs. Abnormal laboratory values may be early warning signals preceding the clinical manifestations of some ADRs in patients receiving antiretroviral drugs. Symptom related monitoring is useful (but not routinely required) for assessing safety and toxicity of ART, especially in high-risk clients.

The table below shows the ARV drug class, clinical abnormality and the laboratory test that could be used for its monitoring.



**Table 4.2 Common abnormalities associated with ARV drugs and necessary laboratory tests.**

<b>Drug class</b>	<b>Drug</b>	<b>Abnormality</b>	<b>Laboratory Tests</b>
NRTI	Zidovudine	Anaemia, leukopenia, neutropenia, Myopathy	Full blood count CPK
	Lamivudine	Few	Nil specific
	Abacavir	Hepatotoxicity Hypersensitivity	Liver enzymes CPK,
	Tenofovir	Renal Toxicity	Creatinine, Urinalysis
	Emtricitabine	Hepatotoxicity	Liver enzymes
NNRTI	Efavirenz	Hepatotoxicity Hypercholesterolemia	Liver enzymes Serum cholesterol
	Nevirapine	Hepatotoxicity	Liver enzymes
PI	Ritonavir	Hepatotoxicity Hyperglycaemia Hyperlipidaemia	Liver enzymes Urinalysis, BSL- blood sugar level Serum lipids CPK, Uric acid
	Atazanavir/ritonavir	Electrocardiographic abnormalities (PR and QRS interval prolongation)  Indirect hyperbilirubinaemia (clinical jaundice) Nephrolithiasis	ECG
	Lopinavir /ritonavir	Hepatotoxicity Pancreatitis Arrhythmias Dyslipidaemia Diarrhoea	Liver enzymes Serum amylase ECG Lipid profile
	Darunavir/ritonavir	Hepatotoxicity Severe skin and hypersensitivity reactions	Liver enzymes
Integrase inhibitors	Raltegravir	Rhabdomyolysis, myopathy, myalgia.  Hepatotoxicity Severe skin rash and hypersensitivity reaction	CPK  Liver enzymes
	Dolutegravir	Hepatotoxicity Hypersensitivity reactions	Liver enzymes



The severity grading of laboratory test abnormalities may guide prompt intervention and prevent the negative consequences of ADR. The guide (Annex 3) can be used to estimate the severity grade of laboratory adverse events

### **Steps to Recognize ADRs**

1. Take adequate history and do a thorough physical examination of the patient
2. Establish time relationships, between start of therapy to the time of onset of the suspected reaction.
3. Carry out appropriate laboratory investigations when indicated
4. Check the known pharmacology of the suspected drugs

### **What Should Be Reported About ADRs?**

1. All serious or unexpected (unusual) reactions that one suspects for established or well-known drugs
2. All suspected reactions, including minor ones for new drugs
3. If an increased frequency of a given reaction is observed
4. All suspected adverse reactions associated with drug-drug, drug-food or drug-food supplement interactions
5. Adverse drug reactions during pregnancy and lactation
6. ADRs occurring from overdose or medication error
7. Lack of efficacy of a medication, or when suspected pharmaceutical defects are observed
8. Reactions suspected of causing death, danger to life, admission to hospital, prolongation of hospitalization, or birth defects.
9. 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.

## **4.4 Principles of management of Adverse Drug Reactions**

### **1. Ensure routine screening of all patients receiving antiretroviral drugs for signs/symptoms indicating possible adverse reactions using ADR Screening Form**

- 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:
  - a) Determine the severity of the adverse event(s) using WHO Severity Grading of ADRs
  - b) 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.
  - c) 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)

### **2. Antiretroviral drugs (ARVs) regimen may be continued in cases of grade I or II adverse event**



**3. 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.

**4. 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).

**5. 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.

**6. 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

**7. 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.

**8. If there are no new ADR(s)**

- Continue case management of the patient



9. Ensure strict adherence to the above standard procedures for detecting, evaluating and reporting ADRs in ART/PMTCT Clinical Settings
10. Establish a functional hospital – based pharmacovigilance committee (with a term of reference) in all ART/PMTCT centres to coordinate ARV clinical pharmacovigilance. This committee is very vital to the success of pharmacovigilance and management of ADRs in a clinical setting.

## **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 Efavirenz is more likely to cause CNS 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. Manifestation of NRTI adverse drug reaction is dependent on the organ involved; there can be myopathy presenting with muscle weakness, bone marrow disorders causing depression of haemopoiesis and leading to anaemia, leucopenia 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+ cell count > 250cells/mm<sup>3</sup> and men with CD4+ cell count > 400cells/mm<sup>3</sup>. Other common reactions include skin rash, and CNS disorders.

### **Protease Inhibitors (PIs)**

Pis are potent CYP3A4 inhibitors 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 diarrhea, 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), gynecomastia in males, fat accumulation in the breast in females and fat accumulation in subcutaneous tissue (peripheral lipomatosis). Management of acute ADRs includes reassurance and symptomatic treatment as it clears within 4-6 weeks of therapy.



**Table 4.3 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 neutropenia; CD4+ cell count $\leq 200$ cells/mm <sup>3</sup> ]  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
Emitricitabine (FTC)	Similar to lamivudine	Occasional hyperpigmentation of skin (palms/ soles)	
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 ABC. If TDF is being used in second-line ART (after d4T + AZT use in first-line ART), substitute with ABC.  Use alternative drug for hepatitis B treatment.



Antiretroviral Drug	Primary toxicities	Minor toxicities	Monitoring/Management
Abacavir (ABC)	<p>Life-threatening hypersensitivity reaction may occur in 3-9% of patients [Risk factors - presence of HLA-B*5701 Gene]</p> <p>Lactic acidosis may also occur with/without hepatic steatosis</p>		<p>Discontinue therapy if hypersensitivity develops. Abacavir should never be used in that individual again.</p> <p>If ABC is being used in first-line ART, substitute with TDF or AZT. If ABC is being used in second-line ART, substitute with TDF</p>
Nevirapine (NVP)	<p>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</p> <p>DRESS syndrome (drug rash, eosinophilia and systemic symptoms) manifesting as fever, arthralgia, etc.</p> <p>Hepatotoxicity [Risk factors: Underlying hepatic disease; HBV and HCV co-infection; Concomitant use of hepatotoxic drugs; CD4 &gt;250 cells/mm<sup>3</sup> in women; CD4 &gt;400 cells/mm<sup>3</sup> for men; First month of therapy (if lead-in dose is not used)]</p>		<p>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.</p> <p>Change to EFV. If the person cannot tolerate either NNRTI, use boosted PIs</p>
Efavirenz (EFV)	<p>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]</p> <p>Hepatotoxicity [Risk factors: Underlying hepatic disease – HBV and HCV co-infection Concomitant use of hepatotoxic drug]</p> <p>Convulsions [Risk factor: History of seizure]</p> <p>Hypersensitivity reaction, Stevens-Johnson syndrome. Mobiliform rash may appear but usually not life-threatening</p> <p>Potential risk of neural tube birth defects (very low risk in humans)</p> <p>Male gynaecomastia.</p>	Dizziness	<p>Rash in 10% but rarely severe in &lt;1%; CNS symptoms often resolve 2-4 weeks.</p> <p>EFV is contraindicated in patients who already have psychiatric manifestations.</p> <p>Change to NVP. If the person cannot tolerate either NNRTI, use boosted PIs</p>



Antiretroviral Drug	Primary toxicities	Minor toxicities	Monitoring/Management
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	Clinical jaundice is cosmetic and not related to hepatitis or liver damage. Substitute only if adherence is compromised  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
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, diarrhoea and skin rash	Diarrhoea is 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
Dolutegravir (DTG)	Hepatotoxicity Severe allergic reactions (hypersensitivity)	Insomnia, headache	Monitor liver function and toxicity may worsen with existing hepatitis B or C



## 4.5 What patients need to be told about adverse drug effects

Health workers need to tell patient:

- That drugs have side effects but the benefits of taking the drugs are by far greater than the problems caused by not taking them
- That most side effects are mild and will be over within a month
- About common adverse effects of the drugs they are taking. In trying to do this, they should not frighten them.
- Specific things to do to prevent some side effects e.g. avoid taking EFV with a fatty or very oily meal; Take EFV at bedtime to avoid or reduce dizziness, abnormal dreams, inability to concentrate
- What they should do if they encounter any adverse effects e.g. if they experience mild rash, they can try to keep their skin dry, avoid walking long distances under the sun which can induce sweating, use calamine lotion
- Encourage patients to always tell you about any adverse effects they experience while taking their drugs. This is especially important because some may already be planning to stop taking their drugs

## 4.6 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, preventive measures, where applicable and what to do when it occurs or is suspected. The healthcare provider should be very knowledgeable on this
- Be vigilant and look out for these adverse effects when initiating therapy and during follow-up.

## 4.7 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. See Annex 1 and 2 for examples of non-ARV vs ARV drug interactions.

**Table 4.4 Important ARV vs. ARV drug interactions**

Drug	Interaction	Action
<b>EFV; NVP</b>	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.
<b>TDF</b>	Concomitant 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.

Additional resources for other possible drug interactions can be found in the following sites.



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## CHAPTER FIVE

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# ADHERENCE TO ANTIRETROVIRAL THERAPY

## 5.1 INTRODUCTION

Adherence is the patients' behavior of taking drugs correctly based on mutual agreement between the patient and health care provider. It is the act of taking the right drugs, at the right dose, at the right frequency and at the right time.

Adherence to antiretroviral therapy is absolutely necessary for achieving sustained suppression, delaying onset of drug resistance, enhancing immune recovery, and improving the overall health and quality of life of the individual. Poor or non-adherence to ART results in suboptimal viral suppression. Viral replication in the presence of sub-optimal doses of ART may lead to emergence of drug resistance and loss of future treatment options.

## 5 .2 Adherence Preparation for ART

It is strongly recommended that patients should undergo thorough adherence preparation before they commence ART. It is also recommended that adherence preparation should be implemented as ongoing multidisciplinary task that involves as many relevant health workers as possible that are involved in the care of the patient including the doctor, pharmacists, laboratory scientist, nurses and the officer officially designated as adherence counsellor.

Health workers should note that the success of any adherence strategy adopted depends on the:

- Information and education provided to clients before the initiation of ART.
- Assessment of their understanding of information provided
- Willingness and readiness for the client to commence treatment.
- Assessment and addressing barriers to initiating ART

Adherence counselling is central to any adherence strategy and should;

- Provide of basic information on HIV and its manifestations.
- Provide information on ARV medication which should include dosing, frequency, duration and side effects of ARV medications including how the medications should be taken and what to do in case of missed doses.
- Provide information on ART and benefits of early initiation.
- Highlight the importance of 100% adherence, which implies not missing any dose. Emphasize non-adherence is the single most important factor that can lead to development of drug resistance.

All persons on ART should receive adherence support. Such support may come from family, friends, treatment partners, and support groups. Adherence supporting IEC materials in the form of posters and patient information leaflets is also essential.



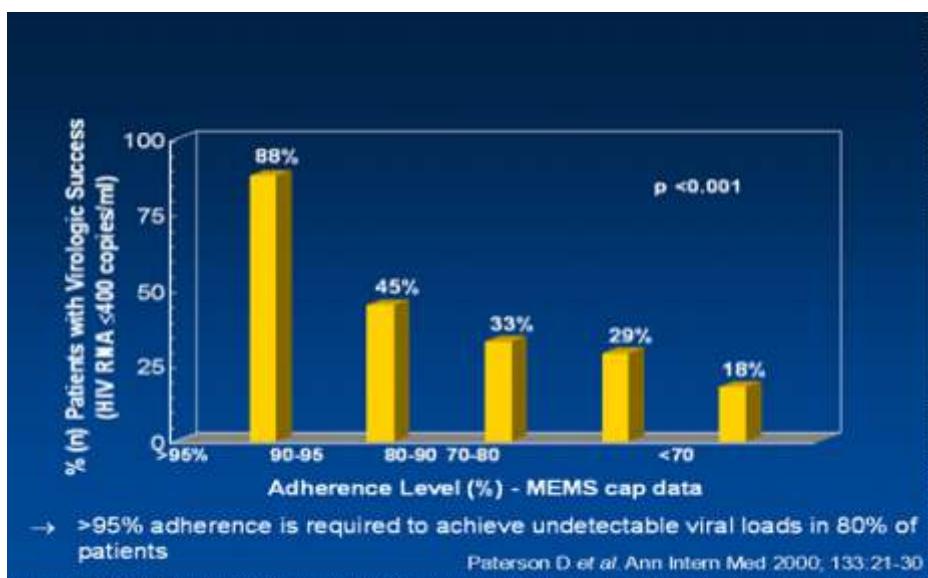
## 5.3 On-going adherence for clients on ART

Continuous adherence counselling is essential in ART and should be accessible to every patient on ART. This should include adherence assessments and documentation at every clinic visit, emphasis on importance of continued adherence and involvement of support systems (relatives, friends, peers and/or community support personnel). Barriers to adherence should also be assessed and addressed.

## 5.4 Monitoring of Adherence

Sustained viral suppression is dependent on adherence to ARVs (Figure 5.1). Adherence monitoring provides an opportunity to reinforce the positive behavior of the adherent patient and to flag patients that require support to improve adherence. 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.

**Figure 5.1 Correlations between Adherence and Virologic Success**



Effective monitoring of adherence involves a combination of approaches based on resource capacity (human/ financial), acceptability by client and providers and comprehension of local context. These include:

- Viral load monitoring: This is considered the gold standard for monitoring adherence and treatment success. Where the viral load is not effectively suppressed ( $> 1000$  copies/ml) an adherence intervention should precede a repeat viral load test. Viral load monitoring has a high likelihood to motivate adherence.
- Pharmacy refill records: These records document the dates a client collected their ARVs. Irregular collection may indicate adherence challenges. As with other adherence assessment methods, pharmacy refill records may over-estimate adherence, as collecting



- ARVs does not guarantee that they are being taken or taken correctly. This is however an acceptable proxy.
- c) Self-reporting: This is a quick and inexpensive approach to adherence monitoring. It is easily carried out in clinical settings and frequently used in routine care; however, it is subject to recall bias.
  - d) Pill counts: This involves a physical count of the remaining pills at each pharmacy refill visit. It is used to compare the actual to the expected consumption of ARVs for a given period. The effectiveness of pill counting is limited by the fact that some clients may discard tablets not taken prior to their routine clinic visit leading to over-estimated adherence. Additionally, the time required by health providers to conduct pill counts may not be available, especially in resource-limited settings.

Other approaches may include electronic methods e.g. Medication Event Monitoring System (MEMSCap). This involves the use of an electronic device that monitors the dates and time the pill bottle is opened. The bottle opening represents the medicine intake.

#### **5.4.1 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-centered care when more than one family member is infected with HIV
- Continuous and effective adherence counselling, which includes knowledge and understanding of HIV infection, course of treatment, and expected adverse reactions and what to do if in the event of an adverse reaction occurring.
- Drug regimen simplicity e.g. Fixed Drug Combination (low pill burden)
- The use of drugs with less adverse effect.

#### **5.4.2 Factors associated with poor adherence**

##### **Patient factors**

- Self-efficacy (belief in one's ability to succeed) regarding adherence.
- Substance abuse e.g. Active drug or alcohol use.
- Lack of social support.
- Incarceration.
- Pregnancy related conditions.
- Inability of patients to identify their medications.
- Lack of patient education.
- Forgetfulness
- Stressful life events
- Self-stigmatization
- Health status e.g. severe illness, dementia, mental health.



### Treatment Factors

- Drug toxicity
- High pill burden
- Long duration of treatment
- Complexity of the treatment
- Medication side effects.

### Patient-Provider Relationship

- Poor patient-caregiver relationship
- Lack of trust
- Poor conception of maintenance of client's confidentiality
- Lack of empathy/ warmth
- Poor communication skills
- Stigma and discrimination
- Lack of client's openness/ cooperation

### Clinical Environment

- Distance to facility
- Poor quality of adherence counselling
- Clinic staff attitude
- Cost of treatment
- Perceived benefits versus barriers e.g. discrimination and stigmatization
- Perceived lack of confidentiality
- Unpleasant past experiences
- Long waiting time

### 5.4.3 Recommendations for improving adherence

- Treatment education for patients and treatment partners
- Treatment-supporter involvement.
- Peer health education/peer counsellors
- Routine assessment and reinforcement of adherence during follow up
- Use Fixed Dose Combination (FDC) and drugs with lower dosing frequency.
- Reminders and patient engagement tools (e.g. a cell phone, SMS text messages, alarm clock, calendars etc.)
- Convenient monthly ARV packs
- Follow up visits before ARV supplies are exhausted
- Positive feedback on health improvements
- Nutritional assessment, care and support
- Prevent and/or adequately manage ADR.
- Address life-style factors e.g. alcohol abuse
- Adapting therapy to the client's lifestyle
- Minimizing out-of-pocket payments at the point of care as much as possible.
- Encourage participation in support groups
- Improved social support
- Directly Observed Therapy –where possible
- Cognitive behavioral therapy and behavioral skill training



#### 5.4.4 Recommendations on clinic visits and medication refill (Pick-up)

It is important to strike a balance between the need for patients to present to doctors for proper ongoing clinical assessment and the burden of too frequent patient visits on the patient, the health worker and the health system. The following are therefore recommended for stable patients on ART

- a) 3 monthly clinic visits.
- b) 3 monthly medication pick-up.

This duration of clinic and medication pick-up can be modified and individualized depending on prevailing circumstance.

Stable patients are defined as clients that are:

- On ART for at least one year
- Are virally suppressed (VL<1000 copies/ml)
- Are immunologically stable (CD >500 where viral load is not available)
- Are clinically stable with absence of opportunistic infections
- Are adherent to ART

#### 5.4.5 Adherence in Specific Populations

While stigma, discrimination and health facility challenges are cross cutting issues affecting adherence, some factors are peculiar to specific populations e.g.

##### Infants and young children

Committed and dedicated caregivers are critical for treatment adherence in children. Identification of responsible caregivers and a family centered approach would improve adherence. The following poses challenges to adherence in children

- Poor taste and large volume of liquid formulations
- Large pill size, pill burden and difficulty in swallowing pills.
- Changing dosage requirement in relation to weight gain
- Inadequate nutrition

##### Adolescents

Adherence is especially challenging for adolescents for many reasons including;

- Psychosocial factors such as peer pressure
- Lack of adolescent friendly health services including skilled health workforce.
- Transition from paediatric to adolescent care
- Lack of adolescent tailored treatment literacy and adherence training tools
- Disclosure issues especially to parents and peers



**Pregnant and postpartum women:**

Peculiar adherence challenges exist during pregnancy and adherence usually worsens postpartum. Adherence challenges may include;

- Nausea and vomiting
- Depression
- Non-disclosure to partner
- Inadequate awareness and knowledge of HIV and PMTCT
- Stigma and discrimination
- Poor health provider capacity and attitude
- Domestic violence

**People with substance use and mental health conditions**

- Use of alcohol and substances abuse can lead to forgetfulness and diversion of monetary resources
- Poor comprehension of treatment plans
- Drug interaction and ADRs

**Key populations (which includes FSW, MSM, IDU, LGBT)**

- Stigma and discrimination
- Poor access to health services
- Absence of health care which targets their specific needs

Health workers are required to take note of the adherence challenges peculiar to each of the groups and design for each patient an individualized adherence plan that adjusts for their lifestyle, work and social environment.



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## CHAPTER SIX

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# PREVENTION OF MOTHER TO CHILD TRANSMISSION OF HIV INFECTION

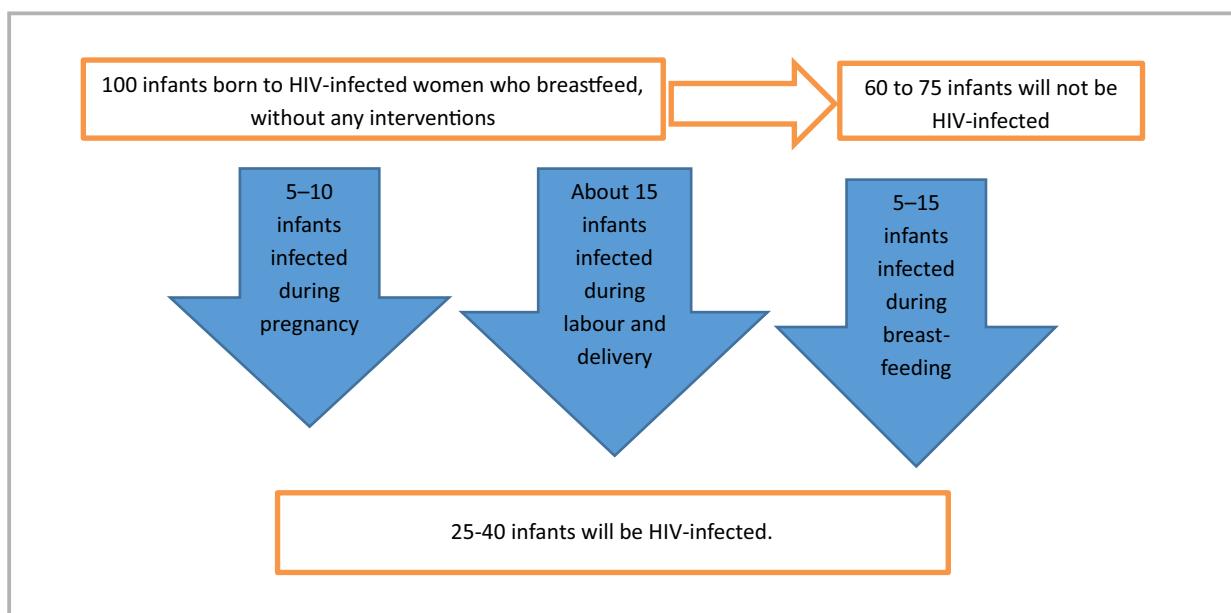
## 6.1 INTRODUCTION

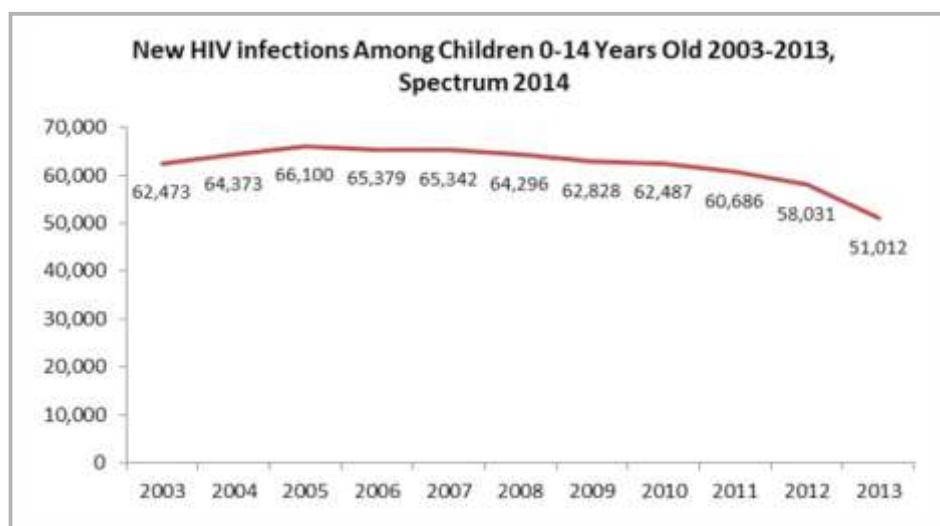
A HIV positive pregnant woman can transmit HIV to her newborn child during pregnancy, labour, delivery, and breastfeeding. In order to prevent this WHO introduced a set of interrelated interventions designed to block transmission of HIV from a HIV infected mother to her child during the period of pregnancy and breastfeeding. These interventions are offered together as a single package of care known as Prevention of Mother to Child Transmission of HIV (PMTCT).

In the absence of PMTCT, the risk of mother to child transmission of HIV is 25-40% and as such it is recommended that all pregnant women should be actively screened for HIV and commenced on ART immediately if they are positive.

Nigeria has the second largest global burden of HIV/AIDS with an estimated 380,000 children living with HIV by the end of 2014 making the country home to over 30% of the global burden of HIV infected children. The high burden of mother-to-child transmission of HIV in Nigeria is due to high rates of heterosexual transmission, high prevalence of HIV in women of reproductive age, high total fertility rate, low PMTCT coverage and prolonged breastfeeding culture.

**Figure 6.1: Rate of Mother to Child Transmission Of HIV**



**Figure 6.2: 10-year trend of new HIV infections among children in Nigeria (Spectrum estimation)**

## Factors associated with increased risk of PMTCT

There are many factors that are associated with increased risk of PMTCT and they operate at different stages of the period of transmission risk; during pregnancy, labour and delivery and breastfeeding. Factors that increase risk during pregnancy include high maternal viral load (the result of new infection or advanced disease), infection of the placenta, maternal malnutrition and antepartum haemorrhage. In addition to high maternal viral load, early rupture of membrane >4 hours before labour, chorioamnionitis, prolonged labour, invasive delivery procedures including use of forceps and episiotomy are factors that increase transmission risk during labour and delivery. Others include preterm birth, first infant in multiple birth and pre-term birth. Risk factors during breastfeeding include but are not limited to high maternal viral load (new infection or advanced disease), extended duration of breastfeeding, early mixed feeding, breast abscesses, nipple fissure, mastitis, poor maternal nutritional status and oral disease in the infant

### Benefits of PMTCT to the mother include:

- Identification of HIV positive mothers for targeted interventions to reduce risk of transmission of infection to their infants and to access treatment, care and support services
- Promotion of positive behaviour change and reduction in risk of HIV transmission
- Increase use of dual protection methods of family planning and STI prevention
- Promotion of optimal infant feeding practices and support
- Promotion of access to early preventive and medical care

### Benefits of PMTCT to the Infant include:

- Prevention of HIV transmission to infants
- Promotion of early diagnosis and intervention for the HIV exposed infants
- Improvement of child health and survival.

### Benefits of PMTCT to the Family include:

- Promotion of communication between couples and testing of both partners
- Reduction in the risk of sexual transmission to zero-discordant partners
- Provision of opportunity for testing other family members



- Contribution to reduction of stigma and discrimination
- Provision of infant feeding support.

**Benefits of PMTCT to the community include:**

- Promotion of the understanding of the HIV and AIDS epidemic among those living with HIV and AIDS within the community thereby strengthening community support structures
- Promotion of uptake of risk reduction practices
- Promotion of acceptance and uptake of HIV testing services
- Contribution to reduction of stigma and discrimination
- Provision of infant feeding support.

**Benefits of PMTCT to the health system include:**

- Provision of opportunity to strengthen the health system.

## 6.2 Pre-ART Care for HIV-positive pregnant women

### 6.2.1 Initial examination of HIV pregnant women

All HIV- positive pregnant women should have full physical examination. In addition to routine antenatal services, special focus should be placed on HIV related illnesses including symptoms and signs of opportunistic infections (OIs) especially tuberculosis. Special attention should also 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, and others
- Other sexually transmitted infections
- Weight gain or loss

### 6.2.2 Laboratory Investigations

HIV positive pregnant women should be tested for syphilis (VDRL) and have haemoglobin or haematocrit estimation and urinalysis done. The following investigations are valuable (See table 6.1):

- Hepatitis B and C screening
- Full blood count (FBC)
- Blood film for malaria parasites
- Tests for sexually transmitted infections e.g. gonorrhoea and chlamydia
- Liver function test
- Renal function test
- Lipid profile



- CD4+ cell counts
- Viral load

**Table 6.1: 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 chapter 3				
LFT	As clinically indicated				
E/U/Cr	As recommended by chapter 3				
Lipid Profile	As clinically indicated				

\*\*\*newly diagnosed HIV positive women enrolled into care, should have at least one viral load test at gestational age of 32 to 36 weeks

### 6.3 Use of Antiretroviral Therapy for PMTCT

Pregnancy is an absolute indication for ART. ART should be initiated in all HIV pregnant and breastfeeding women regardless of WHO clinical stage and at any CD4+ cell count and continued for life. This is also regardless of gestational age.

ART should be initiated urgently in all pregnant and breastfeeding women, even if they are identified late in pregnancy or postpartum, because the most effective way to prevent mother-to-child HIV transmission is to reduce maternal viral load.

#### Recommended first line regimen for pregnant and breastfeeding women.

The preferred first line ART regimen for HIV positive pregnant or breastfeeding women is a combination of TDF+ 3TC +EFV. The alternative first line ART regimens include AZT + 3TC + EFV, AZT + 3TC + NVP, and TDF + 3TC + NVP. Table 6.2 below shows preferred first line and alternative first line regimens for Pregnant and breastfeeding women.

**Table 6.2 Recommended first-line ART regimen in pregnant and breastfeeding women**

First-line ART	Preferred first line regimens	Alternative first-line regimens
Pregnant or breastfeeding women	TDF + 3TC + EFV TDF + FTC + EFV	AZT + 3TC + EFV AZT + 3TC + NVP TDF + 3TC + NVP TDF + FTC + NVP

See Annexes 4 and 7 for ARV dosage and formulations



### **ARV prophylaxis for the HIV exposed infant**

All HIV exposed infants should receive ARV prophylaxis. Infants born to mothers with HIV who are at high risk of acquiring HIV should receive dual prophylaxis with AZT (twice daily) and NVP (once daily) for the first 6 weeks of life, whether they are breastfed or formula fed.

It is recommended that infants delivered to HIV positive mothers who are stable on ART should receive Nevirapine prophylaxis. Nevirapine prophylaxis is administered daily. These infants irrespective of the type of feeding should receive daily NVP from within 72 hours of birth to 6 weeks of age.

If infants are receiving replacement feeding, they should be given 4 to 6 weeks of infant prophylaxis with daily NVP (or twice-daily AZT). (When NVP is not available and AZT has to be used, HB should be monitored closely for early detection of anaemia.)

- For babies with weight <2,500g, give NVP 10mg or 1ml once daily
- For babies with weight ≥2,500g, give NVP 15mg or 1.5ml once daily.

**Table 6.3 NVP Dosing for Infant HIV Prophylaxis**

Infant Age	Daily Dosing
Birth to 6 weeks:	
Birth weight <2,500 grammes	10 mg (1 ml) once daily
Birth weight ≥2,500 grammes	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.

### **Special situations for extended ARV prophylaxis for HIV exposed Infants at High Risk of MTCT**

Breastfed infants who are at high risk of acquiring HIV should continue infant prophylaxis for an additional 6 weeks (total of 12 weeks of infant prophylaxis) using AZT (twice daily) and NVP (once daily). High-risk infants are defined as those:

- Born to women with established HIV infection who have received less than four weeks of ART at the time of delivery  
OR
- Born to women with established HIV infection with viral load >1000 copies/mL in the four weeks before delivery, if viral load measurement available;  
OR
- Born to women with incident HIV infection during pregnancy or breastfeeding;  
OR
- Identified for the first time during the postpartum period, with or without a negative HIV test prenatally.



**Table 6.4 ARV prophylaxis for high risk Infants**

Infant Age	Nevirapine daily dosing	Zidovudine daily dosing
<b>Birth to 6 weeks (dual prophylaxis):</b> Birth weight <2,500grms Birth weight >2,500 grms	10mg (1ml) once daily 15mg (1.5ml) once daily	10mg (1ml) twice daily 15mg (1.5ml) twice daily
<b>6 weeks to 12 weeks</b>	20mg (2ml) once daily	20 mg (2ml) twice daily

*Note: Infants whose mothers received NVP-containing regimen should be managed with twice daily Zidovudine rather than NVP.*

#### Cotrimoxazole Prophylaxis for HIV exposed infants

Cotrimoxazole prophylaxis is recommended for HIV-exposed infants from 6 weeks of age and should be continued until HIV infection has been excluded by an age-appropriate HIV test 12 weeks after complete cessation of breastfeeding.

The recommended doses are shown in table 6.5 below:

**Table 6.5 Dosing for Cotrimoxazole Prophylaxis in HIV-Exposed Infants and HIV-Infected Children**

SN	Infant Age / Weight	Dosage
1	For infants below 6 months or < 5 kg	120mg daily
2	For children 6 months –5 years or 5 -15 kg	240 mg daily

## 6.4 Comprehensive Care of the HIV Positive Pregnant Woman

### 6.4.1 Comprehensive approach to prevention of MTCT

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

- 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

#### A. Primary prevention of HIV infection in women of reproductive age and their partners include the following:

**Use of the “ABC” approach** to enhance safer and responsible sexual behaviour and practices. This includes

- A = Abstinence - refraining from having sexual intercourse
- B = Be faithful - being faithful to one faithful partner
- C = Condom use - using condoms correctly and consistently.



**· #Safe and responsible sexual practices include:**

- Delaying the onset of sexual activity until marriage
- 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 to HIV testing services (HTS). Making HIV testing services widely available especially to women attending antenatal clinic ensures that they know their HIV status. All HIV pregnant women should be linked to PMTCT services on site or by referral.

**· 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 also serves as motivation to adopt safer sex , family planning practices, and encourages partner testing.

## B. Prevention of unintended pregnancies among HIV positive women

Preventing unintended pregnancy among women living with HIV improves the lives of these women and their children and is essential for eliminating mother-to-child transmission of HIV. Nigeria has a high unmet need for family planning. Unintended pregnancy rate among women living with HIV reaches an estimated 51-90% in some settings, accounting for 27% of maternal death, which can be prevented by meeting the unmet need for family planning.

It is the responsibility of health services 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 as this is their sexual and reproductive rights. This implies;

- Providing good quality, user-friendly, and easily accessible family planning services to HIV positive women that can prevent unwanted pregnancy.
- Providing and promoting consistent 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.
- Integrating dual protection messages into family planning counselling services
- Offering contraception including emergency contraception to all HIV positive mothers in the immediate postpartum period to prevent unintended pregnancy. Lactational amenorrhoea does not guarantee adequate contraception even in women who exclusively breastfeed. Refer to medical eligibility criteria for contraceptive use in HIV positive women

## C. Prevention of HIV transmission from infected mothers to their infants. These include;

- HIV testing services
- HIV and Infant feeding counselling
- Modification of obstetric practices
- Administration of ART to all HIV positive pregnant women irrespective of their WHO clinical stage and CD4+ cell count



- Administration of single or dual ARV prophylaxis to all infants delivered to HIV positive women.

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

### Package of services for mothers

- ART for all HIV positive women
- 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 using DBS for DNA PCR at 6 to 8 weeks of age and 12 weeks after breastfeeding has ended. HIV antibody test can be used for HIV screening for children older than 9 months where virologic test is not available. HIV antibody test is the recommended diagnostic testing 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 all HIV infected children (see Chapter 3)
- Symptom management and palliative care if needed

### 6.4.2 Antenatal Care for HIV positive pregnant 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 pregnant 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.

*Note*

- 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

#### **6.4.3 Management of HIV positive women in labour, delivery and within 72 hours of delivery**

The management of Labour should follow usual obstetric guidelines. Analgesia should be given in labour if required and epidural analgesia is not contraindicated (*See Table 6.6 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 HIV-positive women who are concerned about their condition and risks of HIV transmission to their children. HIV positive pregnant women should not be stigmatized nor discriminated against by medical staff including 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 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.

##### ***Induction of Labour***

As prolonged rupture of membranes is associated with increased risk of MTCT, careful assessment of the desirability of Caesarean 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 ART should be allowed to deliver vaginally where there is no obstetric contraindication. Vaginal delivery remains the primary delivery mode of choice.



### **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. However, adolescent pregnant women should be monitored closely and special care taken to confirm that their pelvis is sufficiently developed and that they will not require instrumental 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. 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. 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 a longer course of antibiotics is recommended.

#### **6.4.4 Specific Modification of Obstetric Care for HIV Positive Women**

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



## 6.5 Care and Support of the HIV-Exposed Infant

### 6.5.1 Immediate and on-going care of the new-born of HIV positive women

The immediate care of the HIV exposed new-born follows standard practice regardless of the mothers' HIV status. At delivery all newborns should:

- Have their mouths and nostrils wiped with gauze after delivery of the head.
- Be handled with latex gloves until maternal blood and secretions are washed off.
- Have the cord clamped immediately after baby is delivered and avoid milking the cord.
- Have the cord cut under cover of a lightly wrapped gauze swab to avoid blood spurting.
- Be kept warm.
- Be suctioned if indicated using a mechanical/electrical suction unit at a pressure below 100mmhg or bulb suction. Mouth operated suction is contraindicated.
- Be cleaned with warm chlorhexidine solution or wiped dry with a towel or surgical cloth to remove maternal body fluids.
- Place the baby on the mother's chest for skin to skin contact soon after delivery.
- In this position the baby will latch on to one of the mother's breast to initiate feeding unless the mother opted for alternative feeding method. Have vitamin k administered, ensuring injection safety.

**Table 6.6: Procedure for safe delivery Interventions for Safe Vaginal Delivery**

Interventions during labour/delivery	Care of the baby at delivery
<ul style="list-style-type: none"> <li>• Perform vaginal cleansing with warm (0.25%) chlorhexidine solution to prevent genital infections</li> <li>• Avoid the following: <ul style="list-style-type: none"> <li>- Frequent vaginal examinations</li> <li>- Episiotomies (unless absolutely necessary)</li> <li>- Instrumental delivery (unless when necessary)</li> </ul> </li> <li>• Avoid milking the cord before clamping.</li> <li>• Clamp cord immediately after baby is delivered and cut, under cover of wrapped gauze swab to avoid blood spurting.</li> </ul>	<ul style="list-style-type: none"> <li>• Wipe baby's mouth and nostrils with gauze at delivery of the head.</li> <li>• Handle all babies with gloves regardless of mother's HIV status until blood and secretions are washed off</li> <li>• Keep all babies warm soon after delivery</li> <li>• 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</li> <li>• Place the baby on the mother's body for skin-to-skin contact soon after delivery.</li> </ul>

### 6.5.2 Infant feeding in the context of HIV

Appropriate infant feeding is critical to child survival because the natural food for infants is breast milk. In the context of maternal HIV infection, infant feeding can become complex. HIV infection may be transmitted through breast milk from mother to child and this risk approach 5-15% in the absence of any intervention. Breast milk substitute has the benefit of zero HIV transmission but carries with it the risk of increased morbidity and mortality from malnutrition, diarrhoea and pneumonia.



- It is recommended that mothers of HIV exposed infants breastfeed their babies exclusively for the first six (6) months of life.
- Complementary feeds should be introduced at 6 months in addition to breast milk
- Breastfeeding complemented by household foods should be continued till 12 months, after which child should be weaned off breast milk.

Mothers who breastfeed should be aware that:

- From 5-15% of infants breastfed by HIV-infected mothers may acquire HIV infection through breastfeeding without intervention;
- ARV provided during labour and to the mother/infant pair throughout the period of breastfeeding provides protection for the infant from MTCT of HIV.
- The risk of transmitting HIV to her infant during breastfeeding is higher in certain conditions such as:
  - When the woman is more ill (by clinical or laboratory measures)
  - When she has mastitis, a breast abscess, or other similar conditions
  - When the child has ulcers in the mouth
  - When breastfeeding is prolonged

## Exclusive breastfeeding

### Benefits

- Breast milk is easily digestible and gives infants all the nutrients and water they need. They do not need any other liquid or food for the first 6 months.
- Breast milk is always available and does not need any special preparation.
- Breast milk protects infants and children from diseases, particularly diarrhoea and pneumonia.
- Breastfeeding provides the close contact that deepens the emotional relationship or bond between mother and child.
- Breastfeeding reduces mother's risk of some cancers and helps space her pregnancies.
- Breastfeeding prevents the infants from acquiring allergic diseases e.g. asthma.
- Breastfeeding reduces the risk of infants acquiring lymphomas.

### Challenges

Risk of MTCT exists.

- The risk of transmitting HIV through breastfeeding is increased if the mother has a breast infection (e.g., mastitis) or cracked and bleeding nipples and breast abscess.
- Working mothers may need to find a strategy to continue to breastfeed exclusively when there is no crèche at their work places.

Breastfeeding may not be feasible when HIV – infected mothers become too ill with AIDS or AIDS related illnesses. If for any reason an HIV positive mother cannot breastfeed an alternative feeding method is indicated e.g. breast milk substitute. Breast milk substitute means feeding infants who are receiving no breast milk with commercial infant formula that provides most of the nutrients infants need until the age at which they can be fully fed on family foods. Unlike breastfeeding, it does not provide protection against infections. During the first 6 months of life, Breast milk substitute should be with a suitable commercial infant formula. After 6 months the suitable commercial formula should be complemented with other foods.



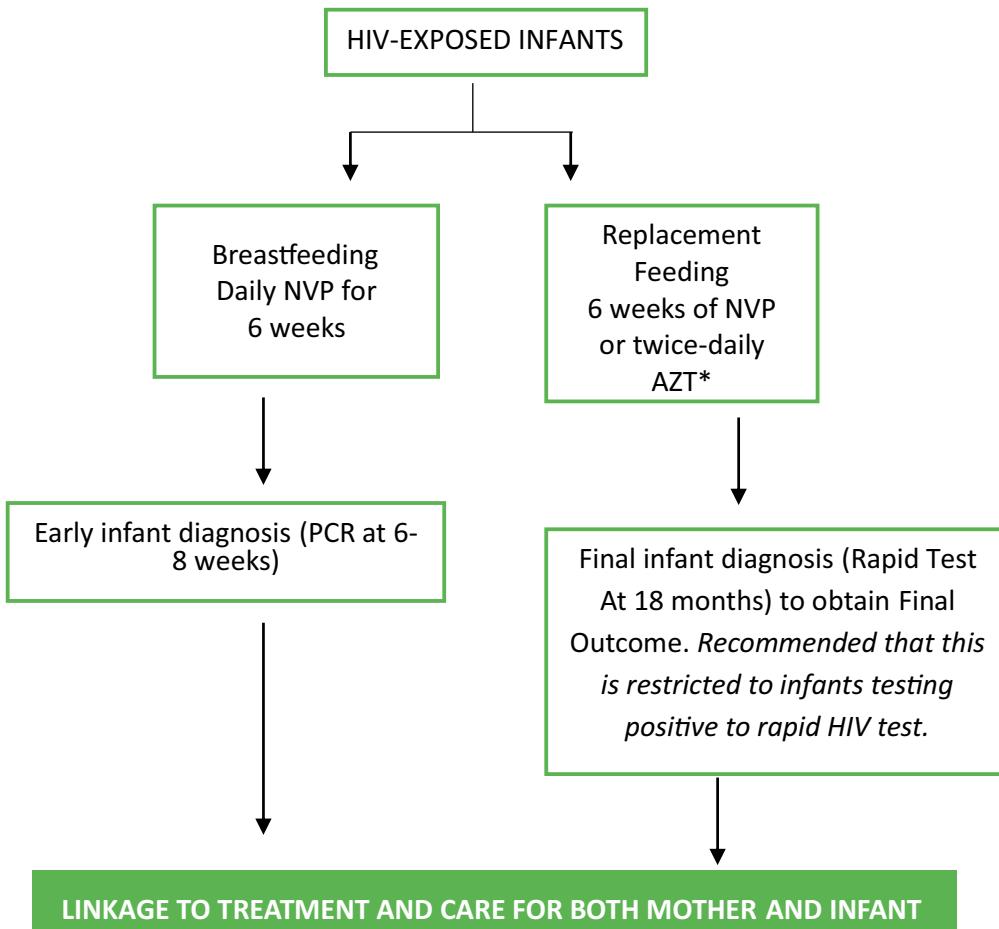
## Disadvantages of breast milk substitute

- Commercial formula does not contain antibodies, which protect infants from infection. An infant who is fed on commercial formula exclusively is more prone to common infection. In resource constraint settings, evidence has shown that babies fed on this have higher morbidity and mortality from diarrhoea, pneumonia and malnutrition
- Supply of formula may not be regular
- Commercial formula is expensive.
- Families need soap for cleaning cups and utensils used in preparing the formula.
- Safe preparation of commercial formula requires clean water and fuel.
- Formula should be made fresh for each feed, according to manufacturer's directions, and preparation is both day and night.
- In some settings, family neighbours, or friends may question a mother who does not breastfeed about her HIV status.
- Breast milk substitute offers the mother no protection from pregnancy.

### 6.5.3 Early Infant Diagnosis (EID)

All HIV-exposed infants should have initial DNA PCR testing at 6 weeks of age (or earliest opportunity thereafter) and 12 weeks after complete cessation of breastfeeding.

**Figure 6.3. Flowchart for early infant diagnosis for HIV-exposed infants**



## 6.5.4 Immunizations for HIV Exposed Children

All HIV exposed children should be immunized as early in life as possible to protect them against vaccine-preventable diseases. They should be assessed to ensure they are fully immunised for age according to the national immunisation schedule (NPI).

Children who have, or are suspected to have HIV infection but are not yet symptomatic should be given all appropriate vaccines, including Bacillus Calmette Guerin (BCG), oral polio vaccine (OPV), and measles and yellow fever vaccines.

Children with advanced and symptomatic HIV infection (CD4 < 200 or < 14%, or Stage 3 or 4 disease), should not be given live vaccines (BCG, varicella-zoster, OPV, measles and yellow fever vaccine). Oral polio vaccine may cause disease in HIV infected children. Symptomatic HIV infected children should therefore be given the inactivated polio vaccine (intramuscular).

Pneumococcal conjugate vaccine (PCV) and the pentavalent vaccine, which contains H. influenzae antigens have recently been added to the NPI schedule and is recommended for asymptomatic HIV exposed babies.

**Table 6.7 National Routine Immunization Schedule**

Vaccine	#Doses	Age	Minimum Interval bw doses	Route	Dose	Site
<b>BCG</b>	1	At birth or as soon as possible after birth	-	Intradermal	0.05ml	Upper L arm
<b>OPV</b>	4	Birth, 6, 10&14wks	4 weeks	Oral	2 drops	Mouth
<b>Pentavalent</b>	3	6,10,&14 wks	4 weeks	IM	0.5ml	Outer thigh
<b>PCV</b>	3	6,10,&14 wks	4 weeks	IM	0.5ml	Outer thigh
<b>IPV</b>	1	14 weeks	-	IM	0.5ml	Outer thigh
<b>Measles</b>	1	9 months	-	SC		Upper L arm
<b>Yellow Fever</b>	1	9 months	-	SC	0.5ml	Upper R arm
<b>Vit. A</b>	2	9 months and 15months	6months	Oral	100000 IU 150000 IU	Mouth

OPV0 and Hep B0 must be given at birth or within two weeks of delivery. Human Papilloma Virus (HPV) vaccine to be given in females age 9-26 is not recommended during pregnancy. Certain live vaccine preparations; anthrax, smallpox are not recommended for HIV positive adults.



## 6.6 Linkage of PMTCT with comprehensive HIV Treatment, Care and Support Services for Mothers and Infants

The follow-up treatment, care, and support for HIV-positive mothers after delivery and the care of their children is important as part of continuum of care package.

PMTCT services can be offered in the following level of health care delivery:

- Health facilities offering PMTCT with no capacity for comprehensive HIV care (PHCs).
- Health facility with capacity for comprehensive HIV care (Secondary/Tertiary health facilities).

Mother/infant pairs from health facilities with no capacity for comprehensive HIV care should be linked with comprehensive health services that provide HIV/AIDS treatment, care and support. This is because it is important that treatment and care extend beyond prevention of MTCT for women, infants, and family members at risk for or infected with HIV.

### **Benefits of establishing linkages with comprehensive healthcare services**

- It creates synergy and helps ensure that the HIV-positive mother and her infant access the range of promotive, preventive, and curative services that meet their diverse health needs and help them to remain in optimal health.
- It increases the range of resources available to the HIV-positive mother, promotes acceptance of PMTCT interventions at the community level and helps reduce stigma and discrimination.
- It ensures uninterrupted HIV treatment, care and support services for the mothers and HIV-positive infants.

Mother/infant pairs who are receiving care and treatment in lower levels health facilities should be able to access secondary and tertiary level facilities for more advanced services, as the situation requires. In addition, mothers, after completion of PMTCT interventions and the final outcomes have been determined for the babies (and HIV-infected babies), should be linked to health facilities providing comprehensive HIV services.

*For details on Linkages, Networks and Referral Services in HIV care, see Chapter 9*



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# CHAPTER SEVEN

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# PREVENTIVE MANAGEMENT IN HIV/AIDS

## 7.1 INTRODUCTION

Preventive management of HIV/AIDS, is a broad term for different interventions that protect individuals from contracting / transmitting HIV infection. It is also includes interventions that protects the HIV positive individual from common opportunistic infections including tuberculosis. It is recommended that all persons who come in contact with health services be allowed access to any combination of HIV prevention interventions most suitable to their needs. The necessity for simultaneous employment of different approaches and intervention types for prevention of HIV infection has led to the concept of combination prevention.

### 7.1.2 Combination prevention

The UNAIDS defines Combination prevention as a rights-based, evidence-informed, and community-owned programme that uses a mix of biomedical, behavioural, and structural interventions, prioritised to meet the current HIV prevention needs of particular individuals and communities, so as to have the greatest sustained impact on reducing new infections.

**Behavioral interventions** include a range of behavior change communication activities designed to promote HIV risk-reducing and protective behaviors. These activities span, and often combine, mass media, community mobilization, advocacy and interpersonal communication (IPC) such as one-to-one or one-to-group educational activities. Social media and mobile technology are important tools that should be integrated in HIV prevention programmes and can be particularly critical in informing about and providing prevention services to key populations.

**Biomedical interventions** include several medical interventions that can prevent HIV infection, decrease infectiousness, and/or reduce the risk of infection. These interventions that directly influence the biological systems through which the virus infects a new host, such as blocking infection (e.g., male and female condoms), decreasing infectiousness (e.g., ART as prevention), or reducing acquisition/infection risk (e.g., voluntary medical male circumcision). These interventions include; proper use of male and female condoms, HIV testing services, voluntary medical male circumcision (VMMC), prevention of mother-to-child transmission, STI diagnosis and treatment, antiretroviral therapy (ART) for pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP), microbicides, and vaccines.

**Structural interventions** are strategies recommended for change in social, legal, political and economic factors that increase vulnerability to HIV. These intervention address stigma and discrimination, key populations, gender based violence and inequality. They are also designed to support income-generating activities, promote the integration referral, adherence and retention in health services.



Effective implementation of combination prevention in the country will require political commitment and leadership, programme coordination and management, partnerships and collaboration, adequate human resource capacities, advocacy, community and social mobilization, functional commodity supply management systems, M&E and research.

## 7.2 Pre Exposure Prophylaxis

Pre exposure Prophylaxis (PrEP) is the pre-emptive use of antiretroviral (ARV) drugs to reduce the probability of HIV negative individuals acquiring HIV infection especially persons who engage in high-risk activity. A systematic review and meta-analysis of PrEP trials using TDF containing antiretroviral drug combination demonstrated that PrEP is effective in reducing the risk of acquiring HIV infection. The level of protection did not differ by age, sex, regimen (TDF or FTC + TDF) and mode of acquiring HIV (Rectal, penile or vaginal exposure). The level of protection was strongly correlated with PrEP drug adherence.

### Guidance for offer of PrEP

It is recommended that pre-exposure prophylaxis (PrEP) should be offered as an additional prevention choice for HIV negative persons who are exposed to prolonged and substantial risk of acquiring HIV infection as a part of a combination of other available HIV prevention methods. PrEP should not be offered in an ad-hoc manner neither should it be prescribed haphazardly as prevention for every isolated individual act of risky sexual behaviour. It should be administered as a long-term therapy for persons who engage in sustained long term high risk life style.

It is recommended that PrEP should be offered only to the category of individuals listed below;

1. Serodiscordant couples
2. Commercial sex workers
3. Injecting drug users
4. Individuals who engage in anal sex on a prolonged and regular basis

In initiating PrEP, health workers should ensure the following;

- Confirm HIV negative status before commencement of PrEP. PrEP should only be offered to HIV negative individuals
- Persons eligible for PrEP should be screened for Hepatitis B. People with detectable HBsAg and alanine transaminase (ALT) elevated more than twice the upper limit of normal or clinical signs of cirrhosis could benefit from long-term therapy for HBV.
- Conduct baseline serum creatinine and urinalysis before starting PrEP and repeat three monthly for the first twelve months, then annually thereafter. To be eligible for PrEP an individual must have normal renal functions.
- Persons eligible for PrEP should be offered comprehensive HIV counseling, with emphasis on adherence and actions to take in the event of occurrence of adverse reactions.
- Patient is offered and encouraged to continue to implement all of the other risk reduction interventions such as safer sex practices, VMMC etc.
- Prior to initiating PrEP all potential beneficiaries are informed and advised that PrEP does not guarantee absolute protection from HIV and that persons on PrEP can still acquire HIV. Beneficiaries should also be informed that full protection from PrEP starts after 7 doses.



- PrEP should be discontinued if the person taking PrEP is no longer considered as belonging to the most at risk population (MARPS)

## **Administration and Monitoring of PrEP**

When used daily and consistently, PrEP can reduce the risk of HIV among high-risk individuals by as much as 90%. PrEP can be even more effective if it is combined with other HIV prevention methods like condom use, drug abuse treatment, and treatment for people living with HIV to reduce the chance of passing the virus to others. Health workers initiating PrEP should;

- Prescribe safe and effective drugs
- Provide adequate information about the drugs and regimen to improve safer use
- Provide adequate and ongoing adherence preparation and reinforcement
- Provide access to risk-reduction support services to help reduce exposure to infection
- Regular monitoring of patients to detect HIV infection, drug toxicities and levels of risk behavior to inform management choices

## **Approved Drugs for PrEP**

Preferred daily oral dose regimen for PrEP is the combination of TDF + FTC

The alternate regimen for PrEP is a daily dose of TDF.

These drugs are to be taken indefinitely until the individual no longer qualifies as high risk for HIV. On no condition should any other antiretroviral regimen be used for PrEP other than the ones already stated.

## **Clinical Monitoring of PrEP**

Patients on PrEP should be monitored closely. It is recommended that once on PrEP patients should return for follow-up every 3 months, however, at the beginning clients may benefit from more frequent visits starting one month after initiation, to assess and confirm HIV-negative test status, assess for early side effects, discuss any difficulties with medication adherence, and attend to patients concerns.

All patients on PrEP should be monitored at certain intervals for specific purposes

### **Every 3months:**

- Repeat HIV testing and assess for signs or symptoms of acute infection to rule out and document that patients are still HIV negative
- Repeat pregnancy testing for women who may become pregnant
- Provide a prescription or refill authorization of daily TDF/FTC for no more than 90 days (until the next HIV test)
- Assess side effects, adherence, and HIV acquisition risk behaviors
- Provide support for medication adherence and risk-reduction behaviors
- Respond to new questions and provide any new information about PrEP use

### **Every 6 months**

- Monitor eCrCl
  - If other threats to renal safety are present (e.g., hypertension, diabetes), renal function may require more frequent monitoring or may need to include additional tests (e.g., urinalysis for proteinuria)
  - A rise in serum creatinine is not a reason to withhold treatment if eCrCl remains  $\geq 60$  ml/min.



- If eCrCl is declining steadily (but still  $\geq 60$  ml/min), consultation with a nephrologist or other evaluation of possible threats to renal health may be indicated.
- Conduct STI testing recommended for sexually active adolescents and adults (i.e., syphilis, gonorrhea, chlamydia)

#### **Every 12 months**

Evaluate need to continue PrEP as a component of combination prevention for the individual

#### **When to discontinue PrEP**

It is not advisable to discontinue PrEP while an individual is still exposed to influences with a high risk of HIV infection. However there are situations when individuals can or should discontinue PrEP:

- Personal patient choice often against advice
- Individual no longer at high risk of acquiring HIV infection
- Moderate to severe and intolerable adverse drug reactions
- Consistent poor adherence despite adequate counseling
- Patient become HIV positive in the course of receiving PrEP

Documentation for persons on PrEP should be as rigorous as for persons who are on ART. Upon discontinuation of PrEP, the following information should be documented; HIV status at time of discontinuation and reasons for discontinuation.

For persons wishing to resume PrEP following discontinuation the same pre-initiation evaluation should be conducted afresh.

### **7.3 Post-Exposure Prophylaxis**

Post Exposure Prophylaxis (PEP) is the short-term use of ARV drugs to prevent HIV infection in persons accidentally exposed to a 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 inoculum of virus and thereby prevent establishment of chronic HIV infection.

It is recommended that post exposure prophylaxis for HIV infection should be offered and initiated as early as possible in all individuals with an exposure that has the potential for HIV transmission, preferably within 72 hours.



### 7.3.1 Post Exposure Prophylaxis for Occupational HIV exposure

There is evidence that, in the occupational setting, HIV transmission is significantly associated with 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 (breast milk, genital secretion, cerebrospinal, amniotic, peritoneal, synovial, pericardial and plural fluids)

#### **Steps to take 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% glutarylaldehyde.
- 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 post exposure 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 Post Exposure Prophylaxis**

Evaluating exposed person's eligibility for HIV post exposure 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 <1000 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

### Recommendations for PEP

- Immediately after exposure to HIV, all exposed individuals should take 3drug ARV combination for PEP.
- 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.
- Enhanced adherence counseling and support should be provided for PEP users
- If the preferred regimen is not available, it is better to administer an alternative regimen than to wait.

### Recommended 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 counseling 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 counseling, 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.

### Recommended Drug Combinations for PEP

It is recommended that three-drug ARV regimen should be used for post-exposure prophylaxis.

TDF + 3TC (or FTC) is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis for adults and adolescents. EFV is recommended as the preferred third drug for HIV post-exposure prophylaxis for adults and adolescents. However, where available, LPV/r, RAL or DRV/r can be considered as alternative options.

In children  $\leq$ 10 years AZT + 3TC is recommended as the preferred backbone regimen for HIV post exposure prophylaxis. Alternative backbone regimen for this age category will include ABC + 3TC or TDF + 3TC (or FTC). EFV is recommended as the preferred third drug for HIV post-exposure prophylaxis for children younger than 10. An age-appropriate alternative regimen can be identified among LPV/r, ATV/r, RAL or DRV.



**Table 7.1 Recommended Drug Combinations for PEP in Adults & Adolescents**

<b>Recommended 3-Drug ARV Combinations</b>
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.
<i>Where Efavirenz is contraindicated, either of the 2drug combinations may be combined with ATV/r or LPV/r</i>

- NVP should not be used in children above the age of 2 years.
- A 28-day prescription of antiretroviral drugs should be provided for HIV post-exposure prophylaxis following initial risk assessment.
- Enhanced adherence counseling is suggested for individuals initiating HIV post-exposure prophylaxis.

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 7.2: Recommended Schedules of Investigations Following HIV Exposure**

<b>Period</b>	<b>Recommended Investigations</b>
Baseline	HIV, HBV and HCV 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

### 7.3.2 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 should be discussed with the patient:**

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

**Recommendations**

- A three-drug ARV regimen should be used for post sexual exposure PEP (see table 7.1).
- As with all cases of sexual assault, it is important to arrange for continuous counseling and support for the victim.
- Emergency contraception should also be considered.

**Clinical considerations**

- As with PrEP, there is concern about the potential risk of hepatic flares among people with chronic HBV once TDF-, 3TC- or FTC-based PEP is stopped. Assessment of HBV infection status should not be a precondition for offering TDF-, 3TC- or FTC-based PEP, but people with established chronic HBV infection should be monitored for hepatic flare after PEP discontinuation. Among people with unknown HBV status and where HBV testing is readily available, people started on TDF-, 3TC- or FTC-based PEP should be tested for HBV to detect active HBV infection and the need for ongoing HBV therapy after discontinuing PEP.
- NVP should not be used for PEP in adults, adolescents and older children because of the risk of life-threatening serious adverse events associated with HIV-negative adults using this drug.
- EFV is widely available as a third agent, as this drug is used as part of the preferred first-line ART regimen. EFV is well tolerated for treatment but has limited acceptability for use as PEP, as there are concerns about giving a drug associated with early neuropsychiatric adverse events to HIV-negative people who may have anxiety related to HIV exposure.
- NVP has been widely used to prevent the transmission of HIV from mothers to HIV uninfected infants and should be used for preterm babies or infants younger than two weeks of age where LPV/r oral liquid cannot be used. However, because the NVP toxicity profile beyond infancy remains unclear, its use should be avoided in children older than 2 years of age.



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## CHAPTER EIGHT

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# MANAGEMENT OF COMMON HIV CO-INFECTIONS AND CO-MORBIDITIES

## 8.1 INTRODUCTION

Persons living with HIV (PLHIV) are more prone to develop infections than persons not infected with the virus largely because of the immune system damage associated with HIV infection. Most of the infections that occur in PLHIVs are called opportunistic infections because they depend on compromised immune system. The appearance of opportunistic infections in HIV infected persons is directly related to the extent of immune deficiency that is the degree of depletion of CD4+cells. The lower the CD4+cell count, the higher the likelihood of the appearance of opportunistic infections. Most opportunistic infections in PLHIVs begin to appear at CD4+cell counts of <350cells/mm<sup>3</sup> and many of the opportunistic infections (OIs) 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. When opportunistic infections occur in PLHIVs they should be treated immediately since they can cause considerable damage to the immune system and lead to rapid increase in viral replication and disease progression and death.

GeneXpert MTB/RIF has enhanced the diagnosis of TB in HIV positive patients and its widespread use in the country should improve health outcomes for HIV/TB co-infected patients.

Chronic non-communicable diseases (NCDs), including cardiovascular disease (CVD), hypertension, diabetes, chronic obstructive pulmonary disease (COPD), kidney disease and mental health illnesses present important considerations in adults and adolescents living with HIV and requires early assessment and management. Pre-disposing factors such as lack of physical activities, smoking, and unhealthy dietary habits should be addressed.

Early initiation of ART, appropriate treatment of identified opportunistic infection and comorbidities, lead to reversal of immune system damage with reconstitution and prevention of AIDS related death.

## 8.2 Preventing Opportunistic Infections

The relationship between HIV and OIs is bi-directional; HIV depresses the immunity of an individual thereby increasing predisposition to opportunistic infections while OIs and other similar infections may lead to acceleration of HIV disease progression.

It is therefore important that health workers have a good understanding of the role of chemotherapy in the prevention and treatment of opportunistic infections, because while



chemoprophylaxis directly prevent pathogen-specific morbidity and mortality, they also contribute to reduced rate of progression of HIV disease.

For instance, there is irrefutable evidence that chemoprophylaxis with trimethoprim-sulfamethoxazole (cotrimoxazole) can both decrease OI-related morbidity and improve survival. The reduced progression of HIV infection would reduce the risk of subsequent OIs. There are currently two main strategies for preventing opportunistic infections; cotrimoxazole preventive treatment (CPT), which provides protection to a wide range of bacterial infections and Isoniazid Preventive Treatment (IPT), which is useful for treating latent tuberculosis.

### **8.2.1 Co-trimoxazole Preventive Therapy**

#### **Background and Rationale**

Cotrimoxazole preventive therapy (CPT) is a fixed-dose combination of two antimicrobial agents (sulfamethoxazole and trimethoprim) used for the prevention of some AIDS-associated opportunistic diseases (*Pneumocystis jirovecii* pneumonia [PCP] and toxoplasmosis) and the reduction of HIV-associated mortality in people with low CD4+ cell counts. CPT is also used to treat a variety of bacterial, fungal and protozoan infections.

CPT is a feasible, well-tolerated and inexpensive intervention to reduce HIV-related morbidity and mortality in people living with HIV. Co-trimoxazole is an off-patent drug and is widely available in Nigeria.

#### **Recommendations for offer of Co-trimoxazole**

##### **Co-trimoxazole prophylaxis for adults**

Co-trimoxazole (CTX) prophylaxis is recommended for adults (including pregnant women) with severe or advanced HIV clinical disease (WHO stage 3 or 4) and/or with a CD4+ cell count  $\leq 500$  cells/mm<sup>3</sup>.

- Due to high prevalence of malaria and severe bacterial infections in Nigeria, co-trimoxazole prophylaxis should be initiated regardless of CD4+ cell count or WHO stage. Priority should be given to adults (including pregnant women) with severe or advanced HIV clinical disease (WHO stage 3 or 4) and/or with a CD4+ cell count  $< 500$  cells/mm<sup>3</sup>
- Routine cotrimoxazole prophylaxis should be given to all HIV-infected patients with active TB disease regardless of CD4+ cell count.
- Co-trimoxazole prophylaxis may be discontinued in adults (including pregnant women) with HIV who are clinically stable on ART, with evidence of immune recovery and viral suppression.
- Due to high prevalence of malaria and severe bacterial infection in Nigeria, co-trimoxazole prophylaxis should be continued regardless of CD4+ cell count or WHO clinical stage.

##### **Co-trimoxazole prophylaxis for HIV-infected infants, children and adolescents**

- Co-trimoxazole prophylaxis is recommended for infants, children and adolescents with HIV, irrespective of clinical and immune conditions. Priority should be given to all children younger than 5 years old regardless of CD4+ cell count or clinical stage, and children with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and/or those with a CD4+ cell count  $\leq 500$  cells/mm<sup>3</sup>



Due to high prevalence of malaria and severe bacterial infections in Nigeria, cotrimoxazole prophylaxis should be continued until adulthood, irrespective of whether ART is provided.

- Cotrimoxazole prophylaxis is recommended for HIV-exposed infants 6 weeks of age and should be continued until HIV infection has been excluded by an age-appropriate HIV test to establish final diagnosis after complete cessation of breastfeeding.

Cotrimoxazole prophylaxis is recommended in all persons with active TB regardless of CD4+ cell count and continued until criteria for discontinuation in adults and children is met.

In HIV positive individuals who have adverse drug reactions to cotrimoxazole, options for prophylaxis of PCP include dapsone, dapsone plus pyrimethamine plus leucovorin and atovaquone. For those who will be started on dapsone, do a G6PD deficiency test. Dapsone should be avoided in individuals with G6PD deficiency.

### **Starting Patients of CPT**

Before commencing a client on CPT the health worker should undertake the following actions;

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

In addition the patient should be counselled for;

- Drug adherence and given detailed information of the likely side effects of co-trimoxazole and action to take in the event of the occurrence of any. Common side effects associated with CPT include: skin eruptions, which may be severe (Stevens Johnson syndrome) nephritis, hepatitis, anaemia and other signs of bone-marrow suppression, and hyperkalaemia.

### **Dosing of CPT**

Dose of co-trimoxazole (CPT) in the Adult:

Co-trimoxazole 960 mg daily (two single strength or one double strength tablet) daily

For infants below 6 months or < 5 kg (co-trimoxazole 120 mg daily)

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

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

For anyone over 14 years or >30 kg (co-trimoxazole 960 mg)

### **8.2.2 Isoniazid Preventive Treatment of TB (IPT)**

Isoniazid Preventive Therapy (IPT) is the use of isoniazid to prevent the development of active TB disease in HIV positive individuals. TB is a disease that is driven by HIV and so is very frequently associated with HIV. Not only is TB closely associated with HIV, TB is a significant cause of illness and death among PLHIVs.



IPT is effective in preventing the development of active TB in HIV positive individuals. It is however not a treatment for active TB and it is therefore necessary to exclude active TB before commencing a patient on IPT.

The adult dose of Isoniazid 300 mg given daily prevents the progression of latent TB infection to active clinical disease. The combined use of IPT and ART has also been shown to have both TB prevention and mortality benefits, including in people with higher CD4+ cell counts. TST should not be a requirement for initiating IPT for people with HIV. For a patient to benefit from IPT, he/she must;

1. Be HIV positive.
2. Not have active TB.
3. Be counselled and motivated to adhere to treatment.

## **Recommendations for offer of Isoniazid Preventive Treatment of TB**

### **Recommendations for adults and adolescents:**

- Adults and adolescents living with HIV should be screened with a clinical algorithm; those who do not report any one of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered IPT.
- Adults and adolescents living with HIV who are unlikely to have active TB or in whom active TB has been safely ruled out should receive at least six (6) months of IPT as part of a comprehensive package of HIV care. IPT should be given to such individuals regardless of the degree of immunosuppression, and also to those on ART, those who have previously been treated for TB and pregnant women.

### **Recommendations for children:**

- Children living with HIV who do not have poor weight gain, fever or current cough are unlikely to have active TB. Children living with HIV who have poor weight gain, fever or current cough or contact history with a TB case may have TB and should be evaluated for TB and other conditions. If the evaluation shows no TB, they should be offered IPT regardless of their age.
- Children living with HIV who are  $\geq 12$  months of age and who are unlikely to have active TB on symptom-based screening and have no contact with a TB case should receive six months of IPT (10 mg/kg/day) but not more than 300 mg/day as part of a comprehensive package of HIV prevention and care.
- In children living with HIV who are  $< 12$  months of age, only those who have contact with a TB case and who are evaluated for TB (using standard lab investigations) should receive six (6) months of IPT if the evaluation shows no TB disease.
- All children living with HIV, after successful completion of treatment for TB, should receive IPT for an additional six months.

### **Commencing Isoniazid Preventive Treatment,**

It is recommended that health workers should undertake the following actions first;

1. Verify/Confirm HIV Status.

2. Counsel clients on TB/HIV interactions.



3. Exclude active TB by asking the client about:

- a) Cough, weight loss, fever and night sweats.
- b) Check for lymph node enlargement.
- c) For patients who answer no to (a) and (b) above, assess for contraindications to IPT, counsel on adherence, and commence IPT.
- d) For those with symptoms/signs in (a) and (b) above:
  - Do sputum examination (Where available, the new molecular test for TB (GeneXpert 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.

4. Counsel patient/caregiver on:

- Importance of Treatment adherence
- Side effects of INH: peripheral neuropathy, jaundice, rash and what is expected in such circumstance
- 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).

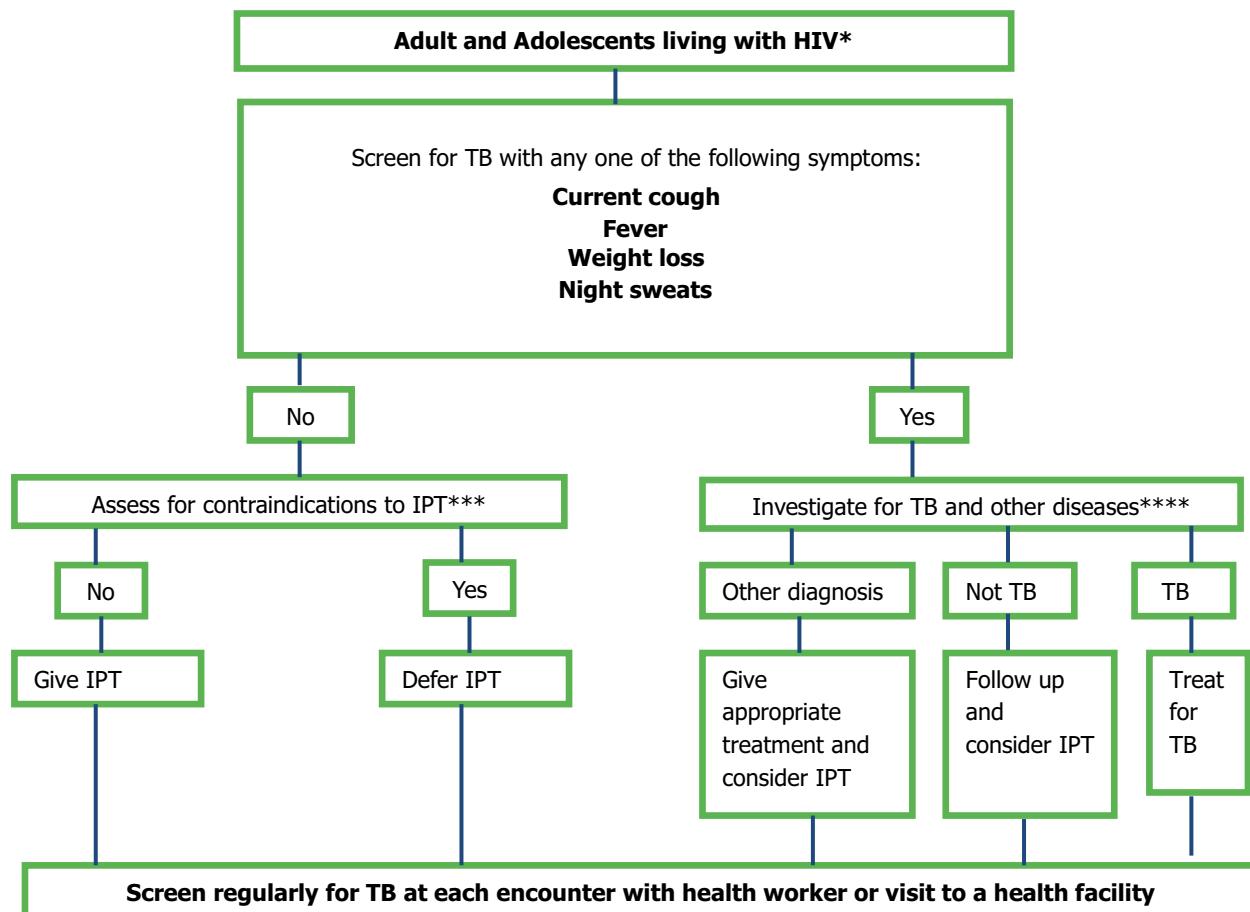
5. During the monthly visit, health worker is to monitor the patients for:

- 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 a Medical Doctor for assessment.

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.

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



**Figure 8.1 Algorithm for TB screening among adults and adolescents living with HIV****Foot note for the algorithm**

\* All PLHIV are eligible for ART irrespective of CD4+ cell count. Infection control measures should be prioritized to reduce M. tuberculosis transmission in all settings that provide care.

\*\* All that are PLHIV with presumptive TB should be sent for GeneXpert MTB/RIF test.

\*\*\* Contraindications include: active hepatitis (acute or chronic), regular and heavy alcohol consumption, and symptoms of peripheral neuropathy. Past history of TB and current pregnancy should not be contraindications for starting IPT.

\*\*\*\* Investigations for TB must be done in accordance with the National TBL & BU management and control guidelines.



**Table 8.1: Common HIV related Opportunistic Infections: Clinical Features, Treatment, and Prophylaxis**

Infection/ Conditions	Causative organisms	Symptoms and signs	Diagnosis	Treatment and Prophylaxis	Comments
Tuberculosis	M. Tuberculosis	Depends on the organ(s) affected- Pulmonary TB(PTB) or Extrapulmonary TB(EPTB). Any current cough fever weight loss night sweats In children additional feature include failure to gain weight	The primary diagnostic tool should be GeneXpert MTB/RIF (Sputum, gastric aspirate etc). Other investigations include Sputum AFB(where GeneXpert MTB/RIF is not available), CXR, FNAB Lateral Flow lipoarabinomannan (LF-LAM), Loop-mediated isothermal amplification(TB-LAMP)	Drug susceptible TB (DS-TB): 2 RHZ/E/4 RH-for new and previously treated adult PTB and EPTB cases. 2 RHZ + E /4 RH-for new and previously treated paediatric PTB and EPTB cases. 2 RHZ/E/10 RH -for adult meningitis and Osteo-articular TB 2RHZ + E /10 RH-for paediatric meningitis and osteo-articular TB	History of contact with an adult who has chronic cough should increase index of suspicion. LF-LAM-for patients with CD4 <100 where available. GeneXpert MTB/RIF for gastric aspirate, CSF,Lymph Node and other samples - where available. Refer to algorithms for TB screening and Management of PLHIV with presumptive TB below. Drug resistant TB (DR-TB): DR-TB are managed under a specialized care in health facility and community with 8Km-Z-Lfx-Pto/12 Z-Lfx-Cs-Pto Refer to National TB and BU management and control Guidelines for detail.



Infection/ Conditions	Causative organisms	Symptoms and signs	Diagnosis	Treatment and Prophylaxis	Comments
Cryptococcal meningitis	<i>Cryptococcus neoformans</i>	Headache, fever, delirium, neck pain, convulsion, photophobia	Clinical Lab: CSF Serology/ India Ink stain	Prophylaxis: Isoniazid Preventive Therapy(IPT) for prophylaxis (Adult – 300mg/day for 6 months; Pediatric – 10mg/kg/day for 6 months) (Refer chapter 7 for detail)	Serum or plasma CrAg screening in ART naïve adults followed by pre-emptive antifungal therapy to reduce the development of disease should be considered in patients with CD4+ cell count less than 100cells/mm <sup>3</sup> . OR Fluconazole high dose alone when amphotericin B is not available: For localized non-meningeal disease, or in patients with isolated serum CrAg positivity (where active cryptococcal meningitis has been excluded). Oral Fluconazole



800mg/d for 2 weeks, followed by 400mg dly for 8 weeks, followed by maintenance of 200mg dly for 1 year and till CD4+ cell count is >200 cells/ $\mu$ l or CD cell count percentage >25% in children.	initiation should be deferred until there is evidence of a sustained clinical response to antifungal therapy, and after 4 weeks of induction and consolidation treatment with amphotericin B-containing regimens combined with flucytosine or fluconazole, or after 4–6 weeks of treatment with a high-dose oral fluconazole induction and consolidation regimen. Refer to infectious disease specialist where necessary	The regimen should include TDF and 3TC, and where TDF is contraindicated, substitute for TDF and add Entecavir	HBsAg quantification if available Liver biopsy if necessary Baseline alpha-fetoprotein (AFP) if possible Refer for specialist care if complicated. Some may require Peg-Interferon treatment.	
Hepatitis B Virus	There may be no signs and symptoms except as in chronic liver disease.	Screen for HBsAg. If positive, screen for the following: HBsAg Anti HBsAg Anti HBCAg Anti HCV HBV-DNA LFT Abdominal ultrasound		(For additional information, please refer to national treatment guidelines on viral hepatitis)



Infection/ Conditions	Causative organisms	Symptoms and signs	Diagnosis	Treatment and Prophylaxis	Comments
Hepatitis C Virus		There may be no signs and symptoms except as in chronic liver disease.	Anti HCV LFT Abdominal ultrasound. HCV RNA (Refer if positive) FBC	Direct acting antiviral (DAA); Sofosbuvir/Daclatasvir, Sofosbuvir/Ledipasvir (FDC), Sofosbuvir + Ribavirin Peg Interferon + Sofosbuvir+Ribavirin  Baseline AFP if possible	Side effects of antifungal drugs: Mild - Nausea, vomiting, diarrhoea, abdominal pain Severe - Hepatotoxicity, agranulocytosis, seizures
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 400,000-600,000 units, 4 – 5 times/day, chew in mouth several minutes and then swallow OR Fluconazole 200 mg PO on Day 1, then 100 mg daily for 7-10 days	



Infection/ Conditions	Causative organisms	Symptoms and signs	Diagnosis	Treatment and Prophylaxis	Comments
B. Oesophagitis (oesophageal candidiasis)	Candida albicans	White patches, in mouth, retro-sternal pain on swallowing, food refusal, excessive salivation	Suspected presence of oropharyngeal thrush, odynophagia Oesophagoscopy	Paediatric: Nystatin 100,000-200,000 IU gargled or delivered to the cheeks in children 4-5 times/day for 14 days, OR Pastilles (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	With fluconazole, hepatotoxicity, nausea, vomiting abdominal pain, pancytopenia may occur Avoid use of ketoconazole with NVP Paediatric:
				Adult: 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	



Infection/ Conditions	Causative organisms	Symptoms and signs	Diagnosis	Treatment and Prophylaxis	Comments
Acute watery Diarrhoea	Viruses: Rotavirus Enteroviruses Other viruses	Bacteria: <i>Enterobacteriae</i> <i>E. Coli</i> <i>C. jejuni</i>	Frequent watery stools	Clinical Laboratory: Stool m/c/s Serology	Rehydrate (SS, ORS or Resomal as required) Zinc supplement 20mg daily for 10-14 days for paediatric patients
Dysentery	<i>E. histolytica</i> <i>G. Lamblia</i> <i>Isospora</i> <i>belli</i> <i>Cryptosporid</i> <i>ia</i> <i>Salmonella</i> <i>spp.</i> <i>Shigella</i>	<i>C. jejuni</i> <i>Cyclospora</i> <i>Microsporidia</i> <i>C. albicans</i> <i>M. avium</i> <i>complex</i> <i>S. Stercoralis</i> <i>Clostridium</i> <i>deficile</i>	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



Infection/ Conditions	Causative organisms	Symptoms and signs	Diagnosis	Treatment and Prophylaxis	Comments
Herpes zoster (Shingles)	<i>Varicella zoster virus</i>	Painful vesicular lesions in a dermatomal distribution, on face and trunk	Clinical	<p>Adult: Acyclovir: 800mg 5 times/day for 7 days + amitriptyline 25mg nocte</p> <p>OR</p> <p>10 mg/kg IV q8hr for 7 days Analgesics – NSAIDS, carbamazepine, amitriptyline Local application of calamine lotion; Topical application of Acyclovir cream For painful vesicular unilateral lesions on face or trunk. Add gentian violet topical application, tab pregabalin 75mg BD (adult) 7 to 10 days, Paediatrics: Tab Acyclovir 30mg/kg/day tds x 7 days</p>	<p>Refer intractable cases for specialist care.</p> <p>Refer cases of herpes zoster involving the eye and ear for specialist care.</p>



Infection/ Conditions	Causative organisms	Symptoms and signs	Diagnosis	Treatment and Prophylaxis	Comments
Herpes simplex Genitalis	Herpes simplex virus- (HSV)	Blisters or painful sores on or around the genitals, rectum ,	Clinical	Acyclovir Tab 400mg tds for 7 – 14 days OR 200mg 5 times daily for 7 -14 days	
Tinea corporis Tinea capitis	<i>Malassezia furfur</i> <i>Trichophyton rubrum</i>	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 b.d to skin for 3-5 weeks Oral therapy: itraconazole/ fluconazole	Extra caution for possible NVP interactions with ketoconazole (see section on drug interactions) Internationally ketoconazole relatively contraindicated since 2013 due to increased idiosyncratic reactions
Seborrhoeic dermatitis	Allergic reaction to yeast infection ( <i>Pityrosporum</i> )	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.



**Table 8.1.....cont...**

Infection/ Conditions	Causative Organisms	Symptoms and Signs	Diagnosis	Treatment	Comments
Pneumocystis pneumonia PCP	<i>Pneumocystis jirovecii</i> (formerly <i>carinii</i> )	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.	First choice: high-dose co-trimoxazole 100 mg/kg/day SMX and 20 mg/kg/day TMP in 2 – 4 divided doses, iv or orally for 21 days (use CTX 960mg, 2 tabs 3 times/day for 21 days)  OR Dapsone 2mg/kg o.d. max. 100mg/ day x 21 days with Trimethoprim 15mg/kg/day in 3 divided doses, OR Pentamidine 4mg/kg/o.d. I.V. 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 or Dapsone 100mg daily	Complications of drug treatment - Severe reactions: Stevens-Johnson syndrome Toxic epidermal necrolysis Anaemia, hepatitis, haemolysis in G6PD deficient patients
Stomatitis, Aphthous ulcers	<i>Herpes simplex virus 1 and 2</i>	Recurrent, painful, oral vesicular lesions, shallow ulcers Oesophagitis: odynophagia	Clinical; Laboratory: Tzank 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	<i>Herpes simplex virus 1 and 2</i>	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 8.1..... cont....**

Infection/ Conditions	Causative Organisms	Symptoms and Signs	Diagnosis	Treatment	Comments
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 <u>Laboratory:</u> 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 – Ophthalmological examination; same drug therapy as above.	
Measles	<i>Measles virus</i>	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	<i>Varicella virus</i>	Fever, centrifugal (starts from trunk to extremities) umbilicated rash in crops	Clinical	Supportive therapy Reduce fever with antipyretics Antibiotics for bacterial infections	
Anal/Genital warts	<i>Human papilloma virus</i>	<u>Anal/Genital:</u> Crops of papules or nodules with a rough surface <u>Verruca planar:</u> Widespread flat hypo/hyper-pigmented rash on face, trunk and limbs, not itchy, dry, often scaly	Clinical In addition, laboratory	Apply Salicylic acid preparation, or Liquid nitrogen, Cryotherapy or Electrocautery Add podophyllin and podophyllotoxin and imiquimod.	
Cutaneous warts ( <i>Verruca plana</i> )			Xpert HPV tests.		



**Table 8.1..... cont....**

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. Strongly consider cryptococcal skin infection if there are constitutional symptoms. Add Gentian Violet daily application until the lesions resolve.	Antibiotics for bacterial super-infection.
Toxoplasmosis	<i>Toxoplasma gondii</i>	Fever, reduced alertness, headache, focal neurological deficits, seizures, chorio-retinitis	Clinical: Response to empiric therapy. Serology: rising IgG titre CT scan	Non Pregnant Adult: TMP-SMX(5mg/kg TMP & 25mg/kg SMX) PO BID for 6 weeks OR 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  <b>Pregnant Adult:</b> Spiramycin 1 g orally every 8 hours If the amniotic fluid test result for <i>T gondii</i> 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	Complications of treatment - Nausea, vomiting, abdominal pain; Megaloblastic anaemia, pancytopaenia, rash, Stevens Johnson Syndrome, photosensitivity



		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  <b>Paediatrics:</b> 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	Viral pneumonia is self-limiting – requires only supportive care  <b>Bacterial:</b> Out-patient therapy with CTX or Amoxicillin or Amoxicillin/clavulanic acid. For in-patient therapy:  2 <sup>nd</sup> and 3 <sup>rd</sup> generation cephalosporin as 2nd line. (Azithromycin or clarithromycin). Respiratory quinolones (levofloxacin) in adults.
Pneumonia	Respiratory viruses Bacteria: <i>S. pneumoniae</i> <i>H. influenza</i> <i>S. aureus</i> <i>M. catarrhalis</i> <i>Kl. pneumonia</i> <i>P. aeruginosa</i>	Fever, chills, cough and pleuritic chest pain, difficulty/ fast breathing. Crepitations, bronchial breath sounds  Clinical Laboratory: blood culture. Chest x ray -sputum examination	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. Quinolones is a 2 <sup>nd</sup> line anti TB drug hence rule out TB before using quinolones(levofloxacin)



**Table 8.1.....cont....**

<b>Conditions/ Infections</b>	<b>Causative Organisms</b>	<b>Symptoms and Signs</b>	<b>Diagnosis</b>	<b>Treatment</b>	<b>Comments</b>
Acute Pharyngo– tonsillitis	Respiratory viruses Bacteria: <i>Strep. pneumoniae</i> <i>H. influenza</i> <i>Moxerella Catarhalis</i> <i>Klebs. pneumoniae</i>	Fever, cough, vomiting, refusal of feeds, drooling of saliva, inflamed tonsils/ pharynx.	Clinical Laboratory: Throat swab for m/c/s	Amoxicillin or Amoxicillin/clavulanic acid. 2nd generation cephalosporin 3rd and 4th generation cephalosporin, and respiratory quinolones (levofloxacin)	
Acute otitis media	Respiratory viruses Bacteria: <i>Strep. pneumoniae</i> <i>H. influenza</i> <i>Staph. Aureus</i> <i>Moraxella catarhalis</i> <i>Klebs. pneumoniae</i>	Fever, vomiting, cough, ear-tugging; Hyperaemic tympanic membrane, purulent ear discharge	Clinical Laboratory: Ear swab for m/c/s	Amoxicillin or Amoxicillin/ clavulanic acid 2nd generation cephalosporin 3rd and 4th generation cephalosporin, and respiratory quinolones (levofloxacin)	
Chronic suppurative otitis media	<i>S. pneumoniae</i> <i>H. influenza</i> <i>S. Aureus</i>	<i>M. Catarhalis</i> <i>Kl. pneumoniae</i> <i>P. aeruginosa</i>	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



*Table 8.1.....cont....*

Infections/ Conditions	Causative Organisms	Symptoms and Signs	Diagnosis	Treatment	Comments
Malaria	Mainly <i>P. falciparum</i>	Fever, chills and rigor, headache, nausea and vomiting	Clinical Laboratory: malaria parasite in blood film RDT.	Uncomplicated: Artemisinin-based Combination Therapy Complicated: Injectable Artesunate <i>Avoid ACT containing amodiaquine in patients taking zidovudine or EFV.</i> <i>Avoid ACT containing sulfadoxine-pyrimethamine combination if patient is on CPT.</i> <i>Avoid Intermittent Preventive Treatment(IPT) for malaria in pregnancy if the patient is on CPT.</i>	Refer to higher level facility if complicated There is increased risk of neutropenia with AZT and increased risk of hepatotoxicity with EFV.
Sepsis	<i>S. pneumoniae</i> <i>H. influenzae</i> <i>Salmonella</i> <i>N. meningitidis</i>	<i>Staph aureus</i> Gram negatives (e.g. <i>E. coli</i> ) Anaerobes	Fever Shock  Clinical assessment <u>Laboratory:</u> FBC Blood culture Urine culture <i>Organ-specific signs/focus of infection determines needed test(s).</i>	While awaiting m/c/s results, either:  Penicillin + Gentamycin  Amoxicillin/clavulanic acid + genticin  Metronidazole for anaerobes  <i>2<sup>nd</sup> or 3<sup>rd</sup> generation cephalosporin and amoxicillin-clavulanic acid with/out other antibiotics depending on the focus of infection.</i>	Refer to tertiary facility if necessary If in shock, provide supportive therapy



**Table 8.1.....cont....**

Infections/ Conditions	Causative Organisms	Symptoms and Signs	Diagnosis	Treatment	Comments
Impetigo	<i>Streptococcus spp,</i> <i>Staph. Aureus</i>	Skin pustules crusts Fever rarely	Clinical	Clean sore with antiseptics Drain pus if fluctuant Ampicillin/cloxacillin Cefuroxime, cefixime, amoxicillin-clavulanic acid and flucloxacillin. Topical agents such as Mupirocin or Retapamulin.	Refer to tertiary facility if necessary
Acute bacterial Meningitis	<i>S. pneumoniae</i> <i>H. influenzae</i> <i>Salmonella</i> <i>N. meningitidis</i> <i>Staph aureus</i>	Fever, headache, vomiting, irritability, altered sensorium, convulsions Nuchal rigidity, bulging fontanelle(in children)	Clinical assessment Laboratory: FBC Blood culture CSF analysis	Penicillin & Chloramphenicol or 3rd generation cephalosporin + Gentamycin Supportive treatment	Treat super-imposed bacterial infection with oral antibiotics Treat all household members even if asymptomatic Ivermectin is not recommended for children below 15kg and pregnant or lactating women
Scabies	<i>Sarcoptes scabiei</i>	Intense itchy lesions most prominent in inter-digital web, spaces of the fingers, wrist, buttocks and axillary area; Papular rashes or generalised (Norwegian) Presentation could be more generalized in the context of HIV/AIDS	Clinical, Laboratory: Microscopy on KOH prep. of skin scrapings	25% 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. If poor response to topical treatment then oral ivermectin tablet 200mcg/kg stat, repeat after 7–14 days +/- 25% benzyl benzoate or Crotamiton . Wash and sun-dry/iron clothings, beddings and fomites.	



**Table 8.1.....cont....**

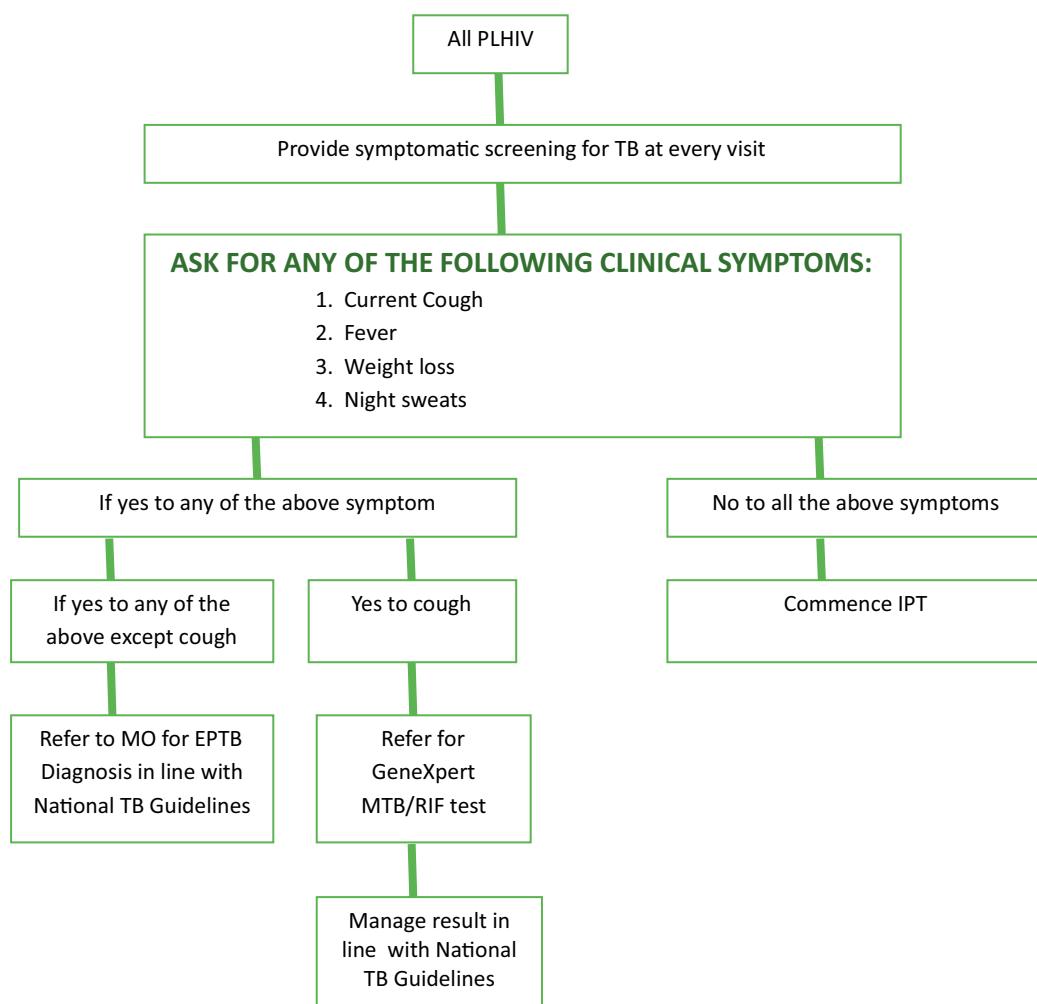
Infections/ Conditions	Causative Organisms	Symptoms and Signs	Diagnosis	Treatment	Comments
Mycobacterium Avium Complex	<i>M. Avium spp.</i>	Disseminated form – recurrent fever, chronic diarrhoea, lymphadenopathy, weight loss/failure to thrive, abdominal pain, Respiratory symptoms may occur	Clinical Laboratory: 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.	Nausea and vomiting  Optic neuritis may occur with ethambutol
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 Diagnosis of exclusion. Chest X Ray: reticulo- nodular infiltrates, bilateral hilar/mediastinal lymphadenopathy;	Steroids (prednisolone 2mg/kg/day x 6 weeks, taper off) Oxygen Bronchodilators (salbutamol) Chest physiotherapy Referral to specialist (paediatric pulmonologist)

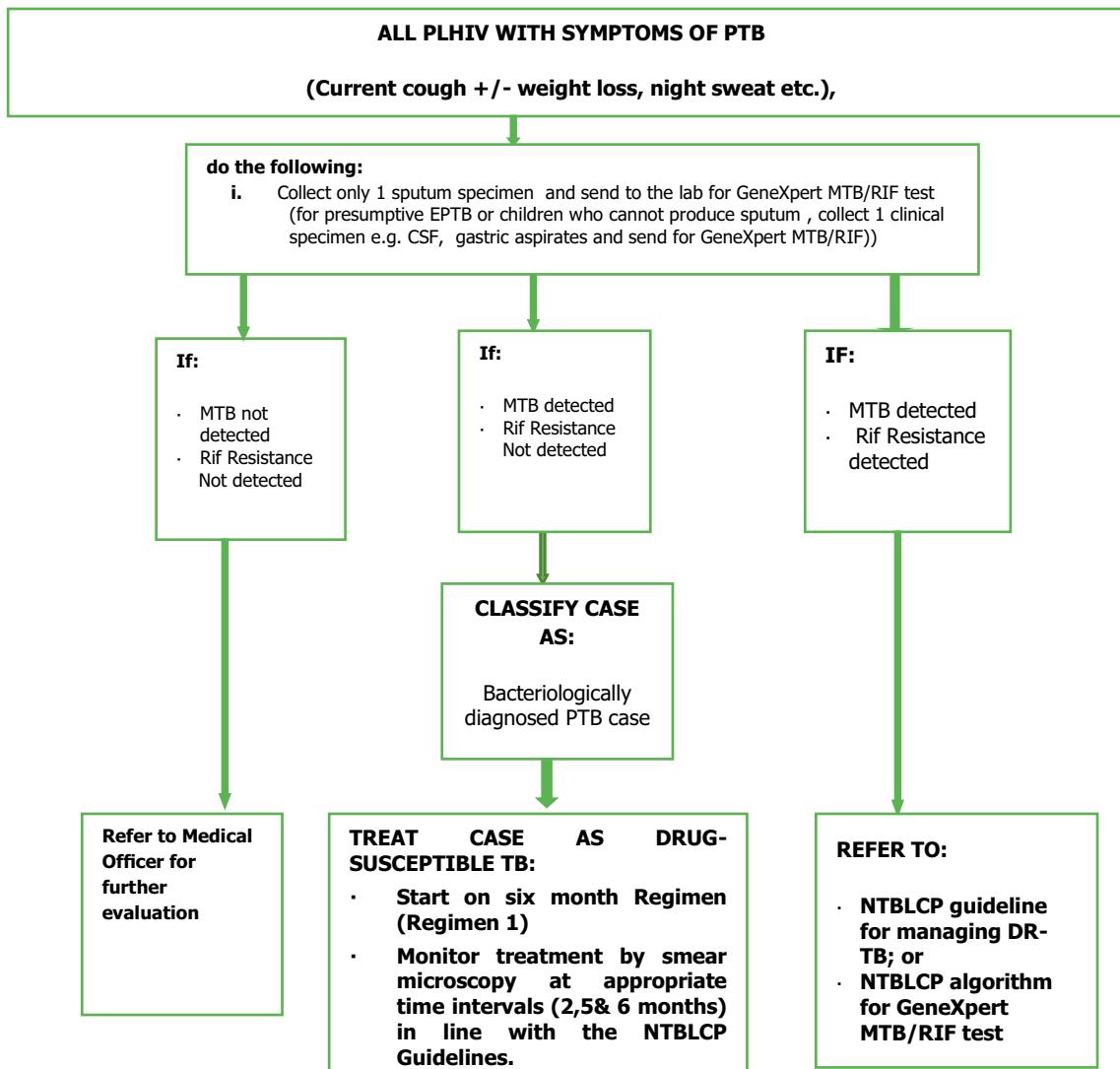


**Table 8.2 Common HIV Related Co-Morbidities**

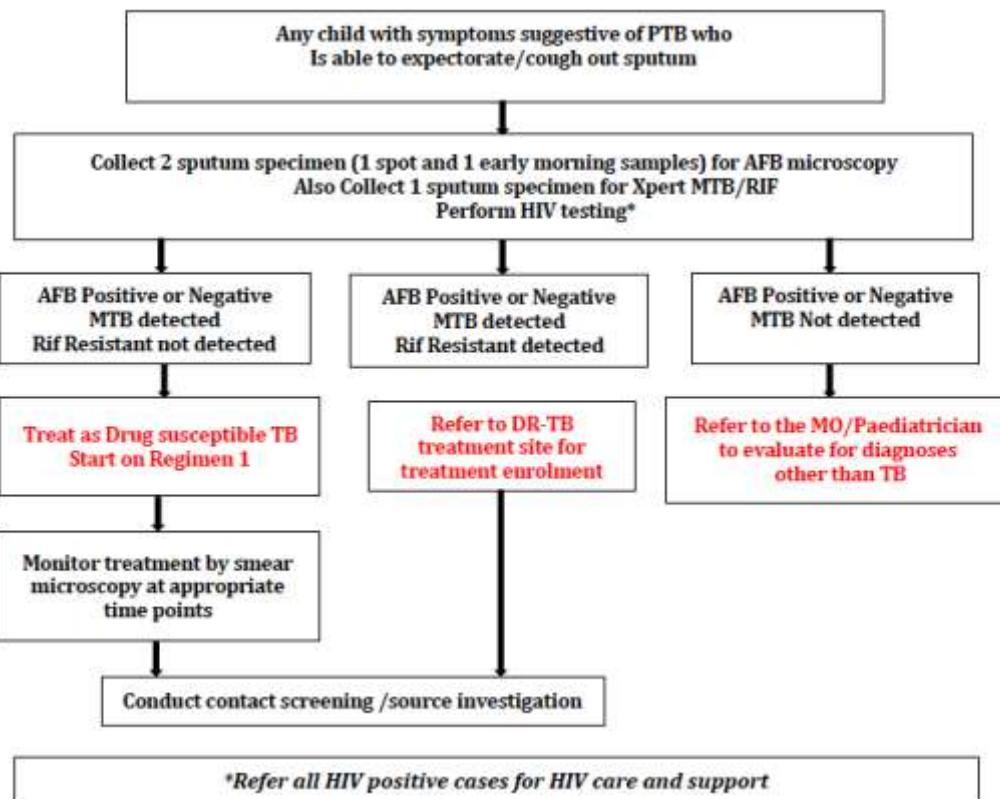
Comorbidities	Example	Comment
Cardiovascular	Hypertension Heart failure Cardiomyopathy Arrhythmias Arteriosclerosis/Ischaemic heart diseases/Cerebrovascular diseases	Asses all PLHIV for risk of CVD and implement risk reduction strategies. Treat uncomplicated hypertension and heart failure refer others for specialist care
Mental health illness	Depression	All PLHIV should be assessed and managed for depression directly or by referral for specialist care.
Others	Type 2 diabetes, Asthma Chronic obstructive pulmonary disease(COPD)  Breast and Cervical cancers  Kaposi Sarcoma Lymphoma	Clients should be assessed and managed for these diseases including referral for specialist care where necessary. All women with HIV should be screened for cervical cancer regardless of age. Clients should be assessed and managed for these diseases including referral for specialist care where necessary.

**Figure 8.1: Algorithm for TB screening among adult living with HIV/AIDS**

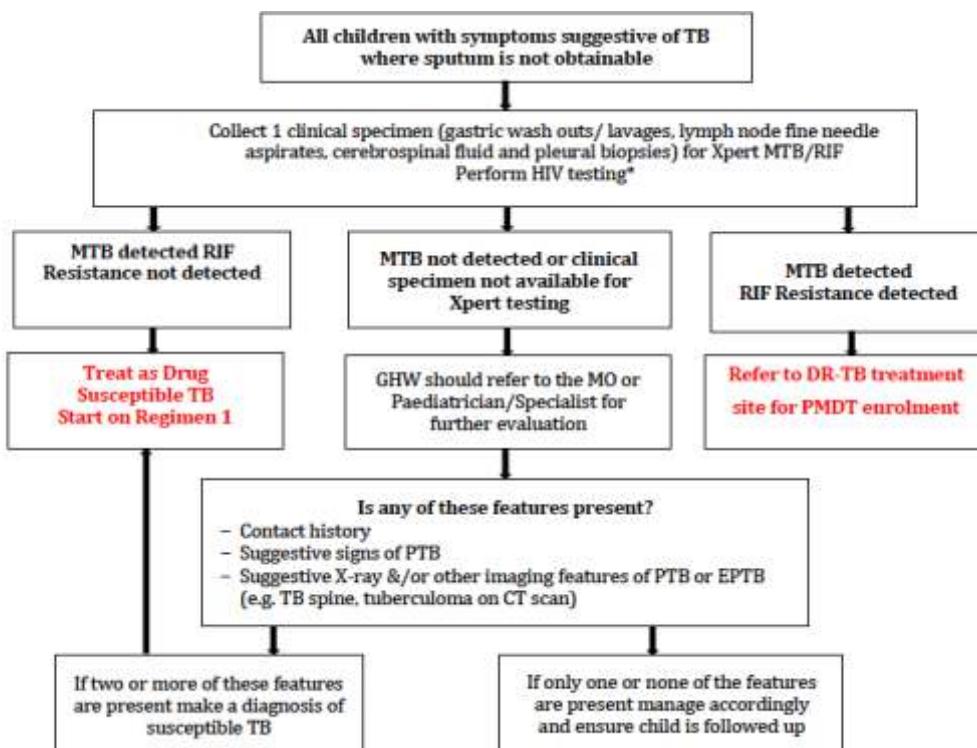


**Fig. 8.2: Diagnostic algorithm for management of PLHIV with Presumptive PTB**

**Figure 8.3 Algorithm for diagnosis of PTB in children in whose sputum is available.**



**Fig 8.4 Algorithm for diagnosis of PTB in children in whose sputum is not available**



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## CHAPTER NINE

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# SERVICE DELIVERY

## 9.1 INTRODUCTION

According to WHO, less than 30% of people diagnosed with HIV in low and middle income countries navigate the full continuum of care. Globally, less than 50% of adults are retained in care four years after initiation of antiretroviral therapy (ART) and even in developed countries, the achievement of global targets is limited by the complex challenges associated with large scale public health interventions. In fact only 27% of all persons on ART in the USA are virally suppressed.

In Nigeria there are considerable obstacles to treatment access that also compromise the quality of services, these obstacles include; inadequate human resource for health, over centralization of service with congestion of large urban clinics. With nearly 1 million patients on treatment, it is necessary to adopt service delivery models that improve access, enhance adherence, maximize resources, improve retention and strengthen systems.

Decentralization, task shifting to nurse-led teams and community delivery and more efficient procurement and supply management are innovations to ART service delivery that will support massive scale up of services required to achieve the UNAIDS 90-90-90 targets by 2020.

## 9.2 Differentiated care

Differentiated care is the delivery of a minimum package of HIV/AIDS treatment care and support services according to the diversity of the care needs of people living with HIV. Broadly, there are four categories of people living with HIV/AIDS with specific service needs:

1. Newly diagnosed patients who are generally well at presentation, in WHO stage 1 and 2 with probably high CD4+ cell counts. Preparation for ART requires readiness and willingness to initiate treatment. Adherence and retention in care are essential in committing to lifelong ART.
2. For another category, patients who present with advanced disease, the priority is to prevent death and reduce illness. This category of patient requires accelerated clinical response with initiation of ART, treatment of opportunistic infection and other care and support services. Late presentation may be traceable to individual, health facilities and other related factors.
3. A third category includes patients who have been unstable on ART. They will require close monitoring for identification and treatment of opportunistic infection, viral load and adherence monitoring.



4. A fourth category are stable patients who require less clinic visits. Stable patients are those who have received ART for at least one year and have no adverse drug reactions that requires regular monitoring, no current illnesses or pregnancy, are not currently breastfeeding and have good understanding of lifelong adherence and evidence of treatment success (two consecutive viral load measurements below 1000 copies/mm(see table 9.1 below).

The package of care for stable individuals can include the following:

- Stable patient should visit for clinical consultation every 3 months;
- Clients should pick up medication every 3 months;
- Continue 6-monthly CD4+ cell count monitoring until viral load testing becomes widely and sustainably available

While less frequent clinic visits are recommended for stable individuals, rapidly growing children (0–5 years old) and adolescents will need to be monitored more frequently for treatment dosing/weight changes and adherence support.

**Table 9.1: Differentiated approaches to HIV care**

People living with HIV	Care package elements
Newly diagnosed presenting well	<ul style="list-style-type: none"> <li>• Initiation of ART</li> <li>• Adherence and retention support</li> <li>• TB screening and IPT</li> </ul>
Newly diagnosed presenting with advanced disease (CD4+ cell count below 200 cells/mm or WHO diseases stages 3 and 4)	<ul style="list-style-type: none"> <li>• Initiation of ART</li> <li>• Clinical package to reduce mortality and morbidity</li> <li>• Opportunistic infection screening and management.</li> <li>• TB screening diagnosis and treatment</li> <li>• Cotrimoxazole and Isoniazid prophylaxis</li> </ul>
Unstable individuals	<ul style="list-style-type: none"> <li>• Adherence and retention support</li> <li>• viral load testing</li> <li>• switch to second or third-line ART if indicated, monitoring for HIV drug resistance (HIV-DR)</li> <li>• Opportunistic infection screening and management. TB screening diagnosis and treatment., Cotrimoxazole and Isoniazid prophylaxis</li> </ul>
Stable individuals	<ul style="list-style-type: none"> <li>• Reduced frequency of clinic visits and community ART delivery models</li> </ul>



### 9.3 Decentralization

Decentralization involves the devolution of part responsibility for the offer of HIV treatment and care from the tertiary and secondary level ART centers to the primary level health facilities. Under this arrangement, PHCs can now offer additional ART services such as initiation of ART and routine ARV refills. Implementation of decentralized ART service involved shifting of specific HIV management tasks from physicians to non-physician providers, from nurses to CHEWs and subsequently to trained peer educators, patients and community-based caregivers. Task shifting and sharing have rapidly increased the number of sites providing ART services and scaled up PMTCT service provision in Nigeria. ART provision at the PHC reduces the distance that patients have to travel by ensuring that services are brought closer to patients' homes. In addition, decentralizing HIV treatment and care also strengthens community involvement by linking community based interventions with health facilities including PHCs and community pharmacy outlets thereby optimizing access to services, care-seeking behavior and retention in care.

HIV treatment and care services providers should implement recommendations of the National Guidelines for the decentralization of ART services.

**Table 9.2 Minimum Package of Care by Health Facility**

Primary level	Secondary level	Tertiary level
<ul style="list-style-type: none"> <li>• HCT</li> <li>• Initiation of ART including PMTCT</li> <li>• Routine ARV-re-fill</li> <li>• Adherence counseling</li> <li>• ARV Prophylaxis for HEI</li> <li>• Basic laboratory investigations</li> <li>• Prevention and treatment of OIs</li> <li>• Prevention and treatment of malaria</li> <li>• DOTS</li> <li>• Adherence counseling</li> <li>• Psycho-social counseling</li> <li>• Home-based care services</li> <li>• Nutritional support</li> <li>• Palliative care</li> <li>• M &amp; E</li> <li>• Growth monitoring</li> <li>• Linkage to secondary level facility</li> </ul>	<ul style="list-style-type: none"> <li>• HCT</li> <li>• Initiation of ART including PMTCT</li> <li>• Routine ARV-re-fill</li> <li>• Adherene counseling</li> <li>• ARV Prophylaxis for HEI</li> <li>• Basic laboratory investigations</li> <li>• Hepatitis screening</li> <li>• CD4+ count estimation</li> <li>• X-ray,</li> <li>• ART</li> <li>• Prevention and treatment of OIs including TB</li> <li>• Prevention and treatment of malaria</li> <li>• Nutritional management</li> <li>• Adherence counseling</li> <li>• M &amp; E</li> <li>• Linkage to tertiary level facility</li> </ul>	<ul style="list-style-type: none"> <li>• HCT</li> <li>• Initiation of ART including PMTCT</li> <li>• Routine ARV-re-fill</li> <li>• Adherence counseling</li> <li>• ARV Prophylaxis for HEI</li> <li>• Basic and advanced laboratory investigations</li> <li>• Hepatitis screening</li> <li>• CD 4+ count estimation</li> <li>• X-ray</li> <li>• LFT</li> <li>• ART</li> <li>• Prevention and treatment of OIs including TB</li> <li>• Prevention and treatment of malaria</li> <li>• Nutritional management</li> <li>• Adherence counseling</li> <li>• M &amp; E</li> <li>• Viral load</li> </ul>

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



## 9.4 Task shifting and Task sharing

As the country scales up HIV prevention, treatment, care and supports services, health workforce shortage becomes a major challenge. Task shifting and task sharing involve the redistribution of tasks within health workforce teams. Task shifting and task sharing will address the high patient-to-doctor ratio, reduce the high default rates among patients already on ART and improve patient satisfaction. Task shifting and sharing have rapidly increased the number of sites providing ART services and scaled up PMTCT in Nigeria. In the context of HIV, task shifting and sharing allow specialized health workers more time to focus on advanced clinical conditions while non-physician providers attend to more stable patients.

The national policy on task shifting recommends that registered nurses can;

- Perform routine screening tests including HIV testing services
- Assess client's readiness to commence ART
- Initiate first line ART for clients without complications
- Issue prescription for ARV regimen based on the national guideline on the pharmacy order form (POF) and refer to pharmacy.
- Maintain (refill) ART in HIV positive clients without complications
- Substitution of ARV regimen according to national guidelines
- Screen and treat opportunistic infections following national algorithms
- Refer cases beyond their competence and all PLHIV with complications to the appropriate levels of care
- Health workers should refer to the policy on task shifting for details of recommendation for other health cadres

## 9.5 Retention in care, treatment and support

Patient retention refers to the proportion of people who continue ART among those who ever started. It is the number of patients on ART and alive either in the same facility or documented transferred out to another facility offering ART services. Retention in care is critical to the overall success and impact of HIV programme. While ART can dramatically improve outcomes for people living with HIV, retention in care and on treatment and excellent adherence to ART is required for optimal clinical outcomes in patients with HIV infection.

Retention in care and on treatment allows provision of medications for opportunistic infections, prompt initiation of ART, evaluation for medication toxicities and identification of treatment failure. Finally, retention in care provides opportunities for linkage to community support structures. Factors that contribute to loss from care and treatment include the following:

- Long distance to clinic
- Inadequate/lack of funds for transportation to clinic
- Forgetting clinic appointments
- Ill health
- Peer pressure especially in adolescence
- Substance abuse and mental health problems



- Stigma, discrimination and lack of disclosure
- Inadequate information and knowledge of the need for life long ART treatment
- Inconvenient clinic hours, especially for patients with busy schedules
- Family responsibilities and/or the need to care for others sick family members.
- Incarceration
- Long waiting time during clinic appointments

A combination of interventions is required to address individual, institutional and community level related factors responsible for poor retention in care and treatment. This is particularly important among specific population groups for example pregnant and breastfeeding women, infants and children, adolescents and men.

The following interventions at the community level may improve retention in HIV care;

- Treatment literacy- providing basic HIV education and teaching patients the skills that will help them be successful in care.
- Patient advocates
- Treatment and peer support groups

## **9.6 Linkages for HIV testing, networks and referral Services**

Early linkage to treatment and care after HIV diagnosis prevents HIV transmission, disease progression and improved health outcomes for PLHIV. Several factors may prevent early linkage to treatment and care including stigma, discrimination, concerns with disclosure and lack of understanding of the diagnosis of HIV. Health facility related factors include; long waiting times, long clinic appointments, clinic personnel attitude etc.

Structural barriers preventing linkage to treatment include distance to clinic, transportation cost amongst others

Linking HIV testing to treatment and care can be improved through the following:

- Integration of HIV services with other relevant services in all health facilities especially TB, STI and MCH.
- Decentralization of ART provision to lower level cadre health facilities.
- Deployment of mobile health technologies such as mobile phones, text messaging particularly for adolescents and young adults.
- Promoting partner testing and notification.
- Community interventions such as: comprehensive HIV testing services, initiation, distribution, and dispensing of ART.
- Family support and family centered case finding/index case finding
- Support groups for parents of HIV+ children and adolescents

Referral is the process whereby the treatment, care and support needs of the clients are assessed and prioritized, and they receive assistance in accessing such services. Referral should also include proactive actions necessary to facilitate initial contact with treatment, care and support service providers. Referral can also be understood at three levels of interfaces between clients

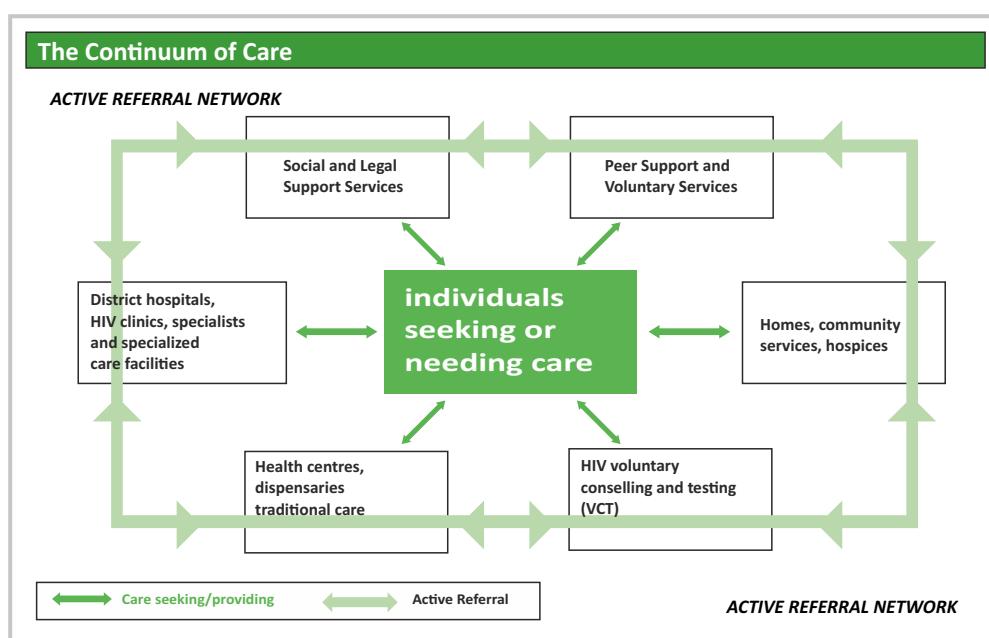


and the health care system: the community, the client/provider and the institution.

Patients who are receiving care and treatment in primary health centers 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 able to access non-medical care and support services that exist outside the facilities such as legal aid, income generating activities etc.

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 linkage and referral systems between health facility and existing community based support for PLHIV.

**Figure 9.1: The Continuum of HIV Care**



## Reasons for referral

### Clinical services

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

### Reproductive health services

Adolescents, men, pregnant women 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 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, alcohol and other substances of abuse should receive or be referred to substance or alcohol abuse prevention and treatment services. Innovative interventions such as opioid substitution and needle exchange should be considered as prevention interventions during program implementation.



### 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

### Legal support services

Clients who test positive may require legal support services for counseling on how to prevent or deal with discrimination in employment, gender-based and domestic violence, housing and public accommodation.

### Social support services

HIV positive clients should be referred to the appropriate institutions for social support including linkage to income generating activities, nutritional, housing, transportation, childcare and psychosocial support. Additional services may include peer support and voluntary services.

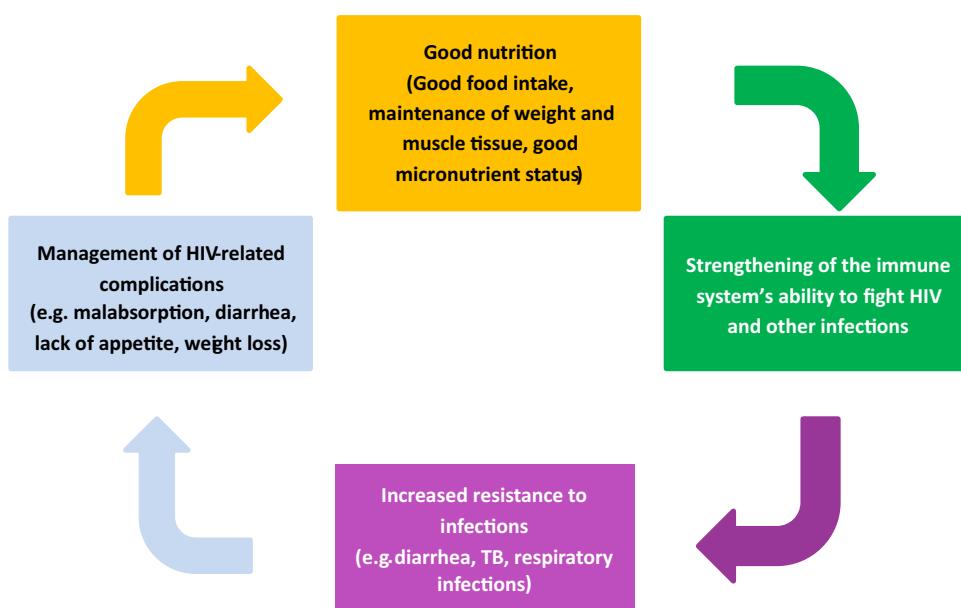
### Positive Health Dignity and Prevention (PHDP)

This provides prevention counseling, 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 re-infection and/or transmitting HIV infection. PHDP activities include short term and ongoing behavioural counseling 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.

## 9.7 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 counseling as soon as the diagnosis of HIV is made and at subsequent contact with care providers.

**Figure 9.2: Relationship between nutrition and HIV/AIDS**



Successfully treating a child requires a commitment and involvement of a responsible caregiver. Parents and other family members of children living with HIV may themselves be infected with HIV and sub-optimal HIV care and treatment for family members could result in sub-optimal care for the child. Other challenges include lack of nutritional support, limited choice of pediatric formulations, poor palatability of liquid formulations, high pill or liquid volume burden, large pill size, frequent dosing requirements and difficult in swallowing tablets. The nutritional needs of infants, young children, adolescents and adults alike must be adequately addressed during initial evaluation and this should be balanced with the need for their medication. All PLHIV should benefit from nutritional assessment, counseling and support (NACS).

The following are some nutritional guides 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
- Fats and oils in meals provide energy
- Use salt sparingly
- Drink lots of water
- Do not drink alcohol and avoid cigarette smoking
- Food, drinking water and beverages should be hygienically prepared
- Strategies for improving and monitoring nutritional status
- Weight monitoring
- Nutrition education and counseling
- Prompt treatment of OIs that interfere with nutrition (mouth disorders, diarrhoea etc)
- Nutritional Support (macro- and micronutrients)
- Economic empowerment
- Regular exercise and physical activity

## Outcomes of nutritional assessment

### Categories of anthropometric assessment

- Undernourished/underweight
- Normal
- Overweight

**Table 9.3 Outcomes of anthropometric assessment**

Assessment outcome					
BMI	<18.5 (Underweight)	18.5-24.9 (Normal)	25-29.9 (Overweight)	>30 (Obese)	>40 (Morbidly obese)
MUAC (under 5)	<11.5cm (Underweight)	11.5-12cm (Normal)	>13cm (Overweight)		
MUAC (pregnant women)	<23cm (Underweight)				



#### **Indications for therapeutic nutritional support**

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

### **9.8 Standard Precautions**

Infection prevention and control measures aim to ensure the protection of those who might be vulnerable to acquiring an infection both in the general community and while receiving care due to health problems in a range of settings. All health facilities in the private and public sector should adopt a policy for the prevention of accidental occupational exposure to blood, body fluid and airborne pathogens.

Minimum standards of precautions that must be observed by health workers include:

- Routine hand washing with soap and water before and after contact with any patient
- Use of barrier precautions including Personal Protective Equipment (PPE).
- Safe handling and disposal of sharp instruments and equipment, including needles and syringes
- Access to vaccination for health care workers against vaccine-preventable diseases eg hepatitis B and TB
- Access to Post-Exposure Prophylaxis for health care workers
- Access to screening for HIV, TB, hepatitis B and other infections for health care workers
- Provision of a safe working environment. This includes having policies and procedures in place to ensure safety and health of employees within the workplace.

Health facilities owe their employees the responsibility of developing and disseminating policy on universal safety precautions, infection prevention and control and workplace safety.

### **9.9 Client and family-centered care (CFCC)**

The family centered approach to care is an approach to the planning, delivery and evaluation of health care that is grounded in mutually beneficial partnerships among health care providers, patients and families. The core concepts involve:

- Dignity and respect
- Information sharing
- Participation and
- Collaboration

The CFCC addresses the individual needs of the patients in the context of the needs and circumstances of the family. The health care worker should:

- Listen to and honor patients' and family perspectives and choices
- Communicate and share complete and unbiased information with patients and families in a way that are affirming and useful
- Ensure and encourage participation of the patients and families in decision-making about their own health
- Collaborate with the patient, their families and the community in the development of policies and programs that affect their health



The CFCC approach is encouraged in all settings but especially with provision of adolescents and youth friendly services and MNCH services,

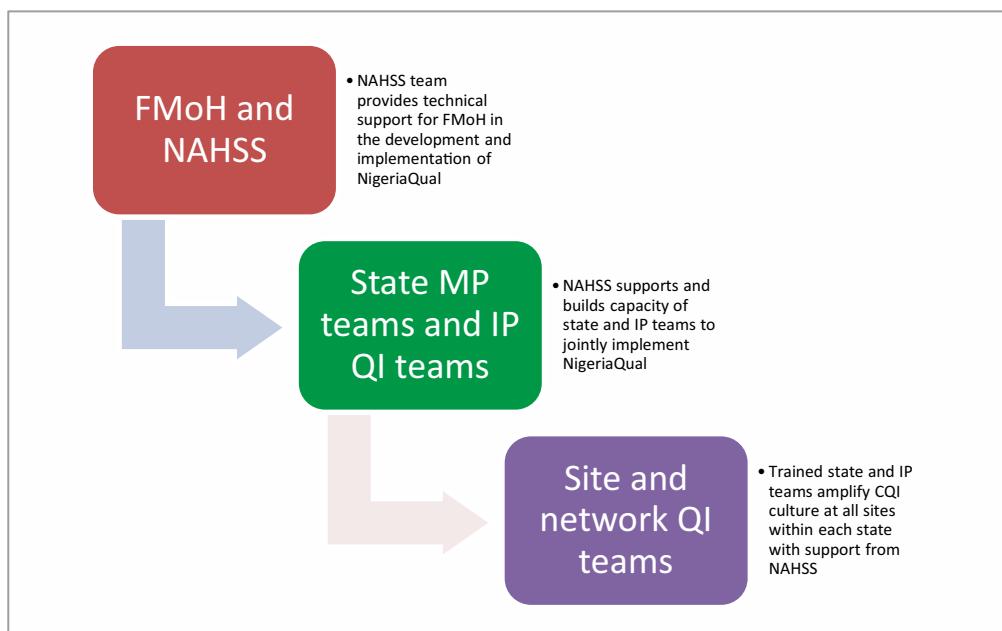
## 9.10 Improving quality of health care services

This section focuses on key principles, approaches and interventions highlighting quality assurance and quality improvement practices based on implementation and program experience. Quality of care emphasizes that services should be effective in achieving desired health outcomes and that health care practices should be people-centered and safe. Continuous quality improvement should be integrated into routine service delivery. The framework in use in Nigeria for quality improvement programs is the NigeriaQual.

NigeriaQual builds upon the HealthQual framework and has the following components:

- Performance measurement
  - Indicator development, data collection, analysis and reporting
- Quality improvement
  - Problem identification, prioritization, implementation of tests of change
  - Plan, Do, Study, Act (PDSA) cycle guides sustainable ongoing change
- Quality management structure
  - Quality improvement teams at sites
  - Multi-disciplinary management teams at facility, local government, state and federal government levels

**Figure 9.3: NigeriaQual implementation structure**



Within the context of HIV care service delivery in Nigeria, people-centered care includes:

- Building healthcare provider skills for effective service delivery and communication with people
- Providing information and supporting people to make informed decisions about their health, their engagement with health care and management of their disease
- Offering a patient appointment system and acceptable frequency of clinic visits. There should be a systems in place to track patients who default on their appointments
- Avoiding long waiting times during clinical consultation, medication pickups and laboratory services. Health facilities are encouraged to implement strategies that decongest ART clinics, pharmacies and other service delivery points.
- Integrating service delivery when people require multiple services eg TB and HIV treatment, family centered care etc.
- Providing comprehensive, integrated services as appropriate and relevant

## **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 quality HIV prevention, treatment and care. At all levels of service provision (whether health facility or community-based), there should be adequate human resource to cater for the needs of PLHIV. Evidence-based interventions should be implemented to boost human resource for HIV/AIDS services.

### **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 providers should be conducted using nationally approved training curriculum and manuals
- Training curricula should be adolescent and youth friendly and should ensure that health workers are able to provide age and context appropriate services to adolescents

### **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 deployment policies that enhance retention of personnel in HIV service

## **9.11 Procurement and Supply Management Systems/Logistics Management Information system**

Existing procurement and supply management systems need to be adapted to cope with the demands of the Test and Treat strategy to ensure that HIV commodities including ARVs are



continuously available in sufficient quantities at all times when they are needed. These commodities must be quality assured. Safe and rational use of these medicines must be ensured to optimize patient outcomes and resource utilization. Adequate systems including financing should be in place to ensure the following:

- Product selection in line with the essential medicines list and global best practices
- Efficient quantification to determine HIV/AIDS commodity needs
- Adequate supply planning for procurements to ensure commodity security reducing stock outs and expiries
- Pharma-grade warehousing at the central level and good storage practices at the facility level
- Cost-effective and efficient last mile distribution leveraging private sector efficiencies
- Coordinated Logistics Management Information Systems (LMIS) with data repositories at the national FMOH and state Logistics Management Coordination Units (LMCU) collecting and aggregating periodic facility level data to inform re-supply and supply chain decisions
- Pharmacovigilance data should also be collected at facility level, submitted to LMCUs for onward transmission to the state NAFDAC in a timely manner
- LMCUs are responsible for ensuring that adequate LMIS tools are made available and accessible to facilities
- Regular stock status monitoring and reporting should be undertaken at facility level and tracked by LMCUs for decision-making
- Regular PSM TWGs meetings at state and national level for effective and efficient coordination and management of the PSM system
- Monitoring and Supportive Supervisory Visits (MSVs) for continuous quality improvement of PSM systems
- Adherence to the provisions of the national HIV/AIDS LMIS Standard Operating Procedures manual

## **9.12 Laboratory and Diagnostics Services**

### **General principles**

- To ensure that diagnostic services are accurate and reliable, relevant QA systems need to be developed and strengthened
- Ensure the use of only high-quality diagnostics and equipment
- Support the expansion of diagnostic services to include testing at the point of care.
- Training and certifying health-care workers who perform testing
- Ensure high-quality diagnostics and plans for implementing these, including QA
- Ensuring appropriate deployment of diagnostic technologies to increase their efficient and optimal use
- Expanding current laboratory networks to support and monitor the decentralization and integration of testing services and to provide access to testing when diagnostic services are unavailable at service delivery sites
- Allocating appropriate resources to ensure the availability of testing services, including human and financial resources; and
- Guidance on operations and service delivery



### **Increased access to HIV viral load testing for all people on ART for monitoring purposes**

- Strengthen laboratory referral systems and procedures for collecting and processing specimens to increase access to viral load testing
- Provide for and strengthen a dedicated, efficient, safe and cost-effective specimen referral system
- Provide reliable specimen transport with adequate conditions for whole blood, plasma and dried blood spot specimens as well as for rapidly and dependably reporting test results back to the referring site with linkage to care. Rapid reporting of results is essential for timely care
- Viral load testing should be used to monitor treatment response and diagnose treatment failure. In addition to plasma, the use of dried blood spot samples for viral load testing should be implemented as a priority intervention for expanding access to VL testing
- There should be ongoing strengthening of existing laboratory services and phased expansion of monitoring services in peripheral facilities
- Strengthen and leverage on existing EID networks
- Ensure that laboratories have adequate infrastructure, technical expertise and QA and QI programmes
- Ensure an increased access of peripheral facilities in remote locations to viral load testing

### **Planning for appropriate use of CD4+ cell count testing as access to viral load testing increases**

As countries move to eliminate CD4+ cell count-dependent treatment initiation thresholds and viral load monitoring replaces monitoring with CD4+ cell count, it is anticipated that the demand for CD4+ cell count testing will decrease. As this transition takes place, programme, laboratory and PSM staff should take into account the following programmatic considerations;

- As demand decreases, reductions in CD4+ cell count testing capacity can be staged through several strategies based on site-level demand, age of the instrument and failure rates
- Although sample referral networks for CD4+ cell count and viral load testing may overlap, the sample types require different transport capabilities. Programmes need to ensure adequate network capability for sample referral for viral load testing prior to scaling down CD4+ cell count testing
- Programme planning should include a realistic transition of financial support from CD4count testing to viral load monitoring. Cost savings may not be evident immediately, as the cost per test for CD4+ cell count testing will increase as volumes decrease
- Quantification and forecasting (active supply planning) will be essential to account for commodity shifts. This is particularly important in the early phases of the transition when historical data will not reflect current commodity needs. Supply chain needs, including cold-chain transport and storage, must also be considered during the transition.

### **Ensuring appropriate deployment of diagnostic technologies**

- Ensure there are no frequent stock-outs of reagents by planning for efficient procurement of essential equipment and laboratory commodities



- Maintenance should be embedded in the contractual agreement with the manufacturers supplying diagnostics

Prior strategic planning is essential to ensure that appropriate space and trained laboratory staff are ready when the procured equipment is delivered for use in the country.



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## CHAPTER TEN

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# MONITORING AND EVALUATION

## 10.1 INTRODUCTION

The Monitoring and Evaluation of the HIV programme enables the country to measure the level of effectiveness of interventions and linkages between services. This will enable the country track progress toward achieving its programme goals and set targets. It also provides information that can be used to provide a basis for informed decision making on the programme and allocation of resources. New strategies in the management of HIV call for a shift in the M&E system in order to adequately measure and assess the impact of the interventions.

Monitoring and evaluation for the HIV programme will be in line with the National Strategic plan; therefore some details below may vary as the National M&E strategy is updated. In addition, routine monitoring should be complemented by periodic systematic evaluations and programme reviews to assess the performance and effects of HIV programmes. Sometimes there may be need to triangulate routine programmatic and survey data in order to ascertain accuracy of HIV data.

## 10.2 Selection of indicators

In 2015, the country adapted national global indicators for M&E reporting of the HIV programme. The national indicators adopted relate to the following:

1. HIV testing services;
2. Treatment and care for pregnant and breastfeeding women (prevention of mother-to-child transmission [PMTCT])
3. Paediatric, adolescent and adult HIV treatment and care;
4. TB/HIV coinfection;
5. Other comorbidities and coinfections;
6. post-exposure and pre-exposure prophylaxis (PrEP);
7. Services for key populations;
8. linkage, enrolment and retention in care;
9. toxicity monitoring;
10. HIV-DR
11. viral suppression; and
12. impact evaluation (mortality, prevalence and incidence)

Refer to the National HIV M&E indicator reference sheets for a list of the adapted 50 indicators.

## 10.3 Data Management

HIV data management is a process that includes the collection, collation, analysis, dissemination and use of HIV data for planning and implementing HIV services. Data are disaggregated by age, sex, location (LGA, state and national), breast feeding, and pregnancy status to improve decision making.



### 10.3.1 Data Collection

Patients' information is collected using 2 types of tools;

1. Patient Management and Monitoring (PMM) tools
2. Programme Monitoring and Evaluation (PME) tools.

PMM tools provide information on individual patients and help in improving diagnosis and management of HIV patients. This information is monitored over time and enables clinicians to assess patient's response to treatment.

PME tools provide information on the services provided to HIV positive patients. This system provides data that can be used to routinely monitor and evaluate the effectiveness, efficiency and acceptability of HIV service provision at all levels of healthcare. Efforts should be made by all HCWs at service delivery points to ensure proper documentation of all HIV services provided. Facility M&E staff are responsible for the collection of M&E data from all service delivery points for monthly reporting.

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

#### Data Collection Tools

The following are current tools used for M&E in the national HIV programme:

**Table 10.1 Tools used for M&E in the national HIV programme**

HTS	PMTCT	ART
<b>PMM</b>  Client Intake form Request & Result form Client Referral form  <b>PME</b>  HTS Register Daily HIV & Syphilis Test Worksheet Referral Register HTS Monthly Summary form	<b>PME</b>  PMTCT Monthly Summary form General ANC Register  <b>PMTCT</b> PMTCT HTS Register PMTCT ART Cohort Register Child Follow Register Partner Register PMTCT Delivery Register	<b>PMM</b>  Care card Adult Initial Clinical Evaluation form Paediatric Initial Clinical Evaluation form Lab Order & Results form Pharmacy Order form HIV Care & Treatment transfer form Client Tracking & Termination form  <b>PME</b>  Care card Enrolment Register ART Register ART monthly summary form Pharmacy Daily Worksheet HIV Care & Treatment Client Tracking Register Post Exposure Prophylaxis Register Cohort analysis report



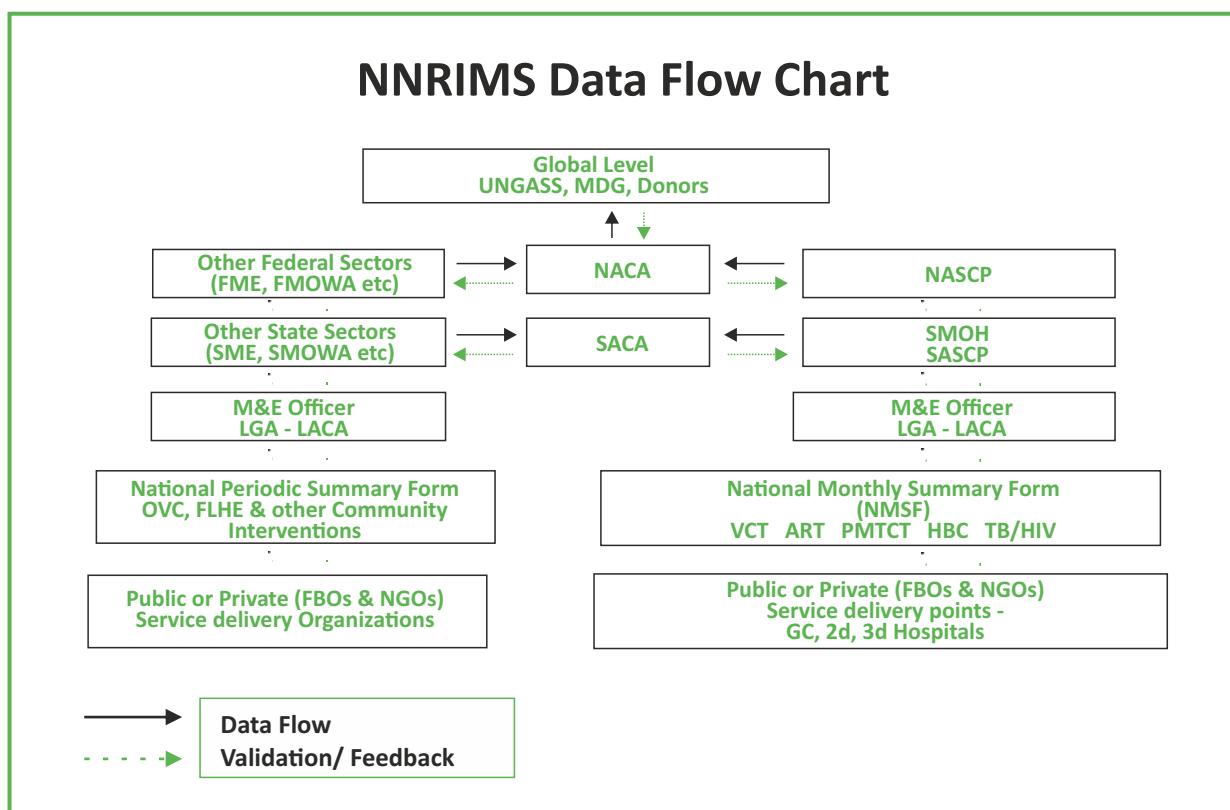
### 10.3.2 Data Security, Collation & Reporting Flow

Handling of PMM/PME tools requires confidentiality and efficiency in order to give the clients a sense of security. A filing system for HIV programme records should be developed and followed within each facility. All records must be kept confidential and stored in a secure room with lockable cabinets. Backup records should be secured from damage or loss.

At the end of each month, routine HIV programme data should be validated for completeness and quality, and collated into monthly summary forms. Completed monthly summary forms should be forwarded to the Local Government Area (LGA), where data from all the HIV sites in the LGA are collated and transmitted to the State Ministry of Health. At State M&E review meetings HIV data should be validated, collated and analysed by all relevant HIV programme stakeholders. States should in turn forward to the National HIV/AIDS Division of the FMOH.

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

**Figure 10.1 – Data Flow Chart for HIV reporting**



### **10.3.3 HIV Data Dissemination and Use**

The significance of data cannot be fully realized until it is disseminated to all relevant stakeholders for effective planning and decision making. This ultimately leads to an improved HIV programme. Data use should be encouraged at all levels especially at the health facilities where these data are generated to improve patient management and monitoring.

## **10.4 HIV M&E Logistics**

Harmonized M&E tools should be made available to all sites delivering HIV services. These tools facilitate the reporting of routine data which help track progress and identify challenges in implementation at the facilities and nationally. Indicator Reference Sheets and User Guides should be made available to end-users to aid understanding of programme indicators and also help in the completion of M&E tools. The FMOH in collaboration with relevant stakeholders should ensure training and retraining of healthcare workers on data management and use.



# ANNEXES

**Annex 1:**  
**Non-ARV vs. ARV Drug Interactions**

Drug	Interaction	Action
Rifampicin	<p>Decreases plasma level of all PIs by at least 75% (except ritonavir, which it decreases by 35%).</p> <p>Rifampicin also decreases plasma levels of EFV (25%), and NVP (20%–58%) and DLV (96%).</p> <p>Plasma concentration of DTG is known to be significantly reduced by rifampicin</p>	<p>Contraindicated with all PIs in general.</p> <p>Rifampicin can be used with EFV. Maintain EFV dose at 600 mg once daily and monitor for virologic response.</p> <p>It is not recommended that Rifampicin be used with NVP.</p> <p>Increasing the dose of DTG to twice daily schedule may be necessary</p>
Rifabutin	<p>It reduces levels of all PIs and NNRTIs by 15 to 35%, except DLV that is reduced by 80%</p> <p>LPV/r increases Rifabutin level by 300%; ATV increases Rifabutin level by 250%</p> <p>EFV reduces Rifabutin level by 38%.</p>	<p>Rifabutin should not be used with DLV</p> <p>Rifabutin dosage should be reduced to 150 mg OD or 3x/week when used with LPV/r, ATV or ATV/r</p> <p>Rifabutin dose should be increased to 450–600 mg once daily or 600 mg three times a week when EFV is used.</p>
Clarithromycin	<p>ATV/r: increase Clarithromycin AUC by 94%; Cmax: increased by 50%; Cmin: decreased by 62%. ATV increases clarithromycin effect through the inhibition of CYP450 3A4.</p> <p>DRV/r: increase clarithromycin AUC by 57%;</p> <p>LPV/r: increase clarithromycin level expected;</p> <p>EFV and NVP decrease clarithromycin levels by 39% and 31% respectively</p>	<p>Monitor for clarithromycin-related toxicities or consider alternative macrolide (e.g., azithromycin).</p> <p>Reduce clarithromycin dose by 50% with CrCl 30-60 mL/min. Reduce clarithromycin dose by 75% in patients with CrCl &lt;30 mL/min.</p> <p>Monitor for effectiveness or use alternative agent, such as azithromycin, for MAC prophylaxis and treatment with EFV, NVP.</p>
Simvastatin, Lovastatin	<p>Boosted PI (ATV/r, LPV/r): Significant increase in levels of statins</p> <p>EFV decrease level of simvastatin by 68%; NVP, ETR decrease levels of simvastatin and lovastatin possible</p>	<p>Contraindicated. Do not co-administer. Use pravastatin or low dose atorvastatin during concurrent PI therapy</p> <p>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.</p>



**Annex 1:*****Non-ARV vs. ARV Drug Interactions .....CONTINUED***

Drug	Interaction	Action
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 OD 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 to avoid its adverse effects or avoid if patient can tolerate the decision
Antacids	ATV, ATV/r, DTG, RAL: when given simultaneously, Antacids decrease 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



**Annex 1:*****Non-ARV vs. ARV Drug Interactions .....CONTINUED***

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.
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.
Oestrogen-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: DTG 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 co - administer; may consider Lopinavir/ritonavir capsules
Multivitamins	DTG and RAL; when given simultaneously with multivitamins, cations in multivitamins decrease the level of the drugs in plasma	Give DTG or RAL at least 2 hours before or 6 hours after ingestion of multivitamins



**Annex 2.**  
**ARV drug-food interaction**

Drug	Interaction	Action
Tenofovir (TDF)	High fat meal increase AUC ( <i>total drug exposure over time</i> ) 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 DTG St John's wort decreases levels of NNRTI (NVP, Efv, ETR)	Avoid concurrent use during PI therapy Do not co-administer.



**Annex 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
<b>HAEMATOLOGY</b>					
Haemoglobin	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 $\times 10^9$ /L	1 - 1.5 $\times 10^9$ /L	0.75 – 0.99 $\times 10^9$ /L	0.5 - 0.749 $\times 10^9$ /L	<0.5 $\times 10^9$ /L
Platelet count	100–450 $\times 10^9$ /L	70–99 $\times 10^9$ /L	50 – 69 $\times 10^9$ /L	30 – 49 $\times 10^9$ /L	< 29 $\times 10^9$ /L
Total WBC	4.0 – 11.0 $\times 10^9$ /L	2.0- 3.9 $\times 10^9$ /l	1.0 – 1.9 $\times 10^9$ /L	< 1.0 $\times 10^9$ /L	-
<b>CHEMISTRY</b>					
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 (hyperglycaemia)	4 – 6 mmol/l	6-8.9 mmol/l	8.91-13.88mmol/l	13.89-27.76mmol/l	> 27.76mmol/l
Glucose (hypoglycaemia)	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	.....	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 62-133 $\mu$ mol/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 Hypernatremia	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



**Annex 4****Dosages of ARVs for Adults and Adolescents**

Generic name	Dose
<b>Nucleoside reverse-transcriptase inhibitors (NRTIs)</b>	
Abacavir (ABC)	300 mg twice daily or 600 mg once daily
Emtricitabine (FTC)	200 mg once daily
Lamivudine (3TC)	150 mg twice daily or 300 mg once daily
Zidovudine (AZT)	250–300 mg twice daily
<b>Nucleotide reverse-transcriptase inhibitors (NtRTIs)</b>	
Tenofovir (TDF)	300 mg once daily
<b>Non-nucleoside reverse-transcriptase inhibitors (NNRTIs)</b>	
Efavirenz (EFV)	400 or 600 mg once daily
Nevirapine (NVP)	200 mg once daily for 14 days, followed by 200 mg twice daily
<b>Proteases inhibitors (PIs)</b>	
Atazanavir/ritonavir (ATV/r)	300 mg/100 mg once daily
Darunavir + ritonavir (DRV/r)	800 mg + 100 mg once daily <sup>a</sup> or 600 mg + 100 mg twice daily <sup>b</sup>
Lopinavir/ritonavir (LPV/r)	400 mg/100 mg twice daily
	<b>Considerations for individuals receiving TB therapy</b> - In the presence of rifabutin, no dose adjustment required.  - In the presence of rifampicin, adjusted dose of LPV/r: (LPV 800 mg + RTV 200 mg twice daily or LPV 400 mg + RTV 400 mg twice daily) with close monitoring.
<b>Integrase strand transfer inhibitors (INSTIs)</b>	
Dolutegravir (DTG)	50 mg once daily

*a For individuals with no previous use of protease inhibitors.*

*b For individuals with previous use of protease inhibitors.*



**Annex 5*****Simplified dosing of child-friendly ARV formulations for twice daily dosing in 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
		3.0–5.9 kg		6.0–9.9 kg		10.0–13.9 kg		14.0–19.9 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
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
ABC/3TC	Tablet (dispersible) 60 mg/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3
ABC/3TC	Tablet (dispersible) 120/60 mg	0.5	0.5	1	1	1	1	1.5	1.5	1.5	1.5
AZT	Tablet (dispersible) 60 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3
ABC	Tablet (dispersible) 60 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3
NVP <sup>b</sup>	Tablet (dispersible) 50 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3
LPV/r <sup>c</sup>	Tablet <sup>d</sup> 100 mg/25 mg Pellets <sup>e</sup> 40 mg/10 mg	–	–	–	–	2	1	2	2	2	2
	Pellets <sup>e</sup> 2	2	3	3	4	4	5	5	6	6	6
	Pellets <sup>e</sup> 3	3	3	3	4	4	5	5	6	6	6
	Pellets <sup>e</sup> 3	3	3	3	4	4	5	5	6	6	6

<sup>b</sup> 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 2015). More definitive evidence is expected from an ongoing trial.

<sup>c</sup> The LPV/r heat-stable tablet formulation must be swallowed whole and should not be split, chewed, dissolved or crushed.

<sup>d</sup> The adult 200/50 mg tablet could be used for children 14.0–24.9 kg (1 tablet in the morning and 1 tablet in the evening) and for children 25.0–34.9 kg (2 tablets in the morning and 1 tablet in the evening)

<sup>e</sup> The LPV/r pellets formulation should not be used for infants younger than 3 months. More details on the administration of LPV/r pellets is available at <http://www.emtct-iat.org/wp-content/uploads/2015/09/IATT-LPVr-Factsheet-Final-30-September-2015.pdf>.



**Annex 6*****Simplified dosing of child-friendly solid formulations for once daily dosing in children***

Drug	Strength of tablets (mg)	Number of tablets by weight band once daily					Strength of adult tablet (mg)	Number of tablets or capsules by weight band once daily
		3.0–5.9 kg	6.0–9.9 kg	10.0–13.9 kg	14.0–19.9 kg	20.0–24.9 kg		
EFV <sup>b</sup>	Tablet (scored) 200 mg	–	–	1	1.5	1.5	200 mg	2
ABC/3TC	Tablet (dispersible) 60 mg/30 mg	2	3	4	5	6	600 mg/300 mg	1
ABC/3TC	Tablet (dispersible) 120/60 mg	1	1.5	2	2.5	3	600 mg/300 mg	1

<sup>b</sup> EFV is not recommended for children younger than 3 years and weighing less than 10 kg. The United States Food and Drug Administration approved EFV for use for children younger than 3 years weighing more than 3.5 kg during the finalization of these guidelines (3.5–5.0 kg: two 50-mg capsules; 5.0–7.5 kg: three 50-mg capsules; 7.5–15.0 kg: one 200-mg capsule), but more data are urgently needed to inform recommendations for using EFV in this age group.



**Annex 7****Commonly used Adult and Pediatric ARV Formulations and Dosage**

	3-5.9kg	6-9.9kg	10-13.9kg	14-19.9kg	20-24.9kg	25-34.9kg	Adult ( $\geq 35\text{kg}$ )
<b>Fixed-dose Combinations</b>							
ABC/3TC	60/30mg	1 BD or 2 OD	1.5 BD or 3 OD	2 DB or 4 OD	2.5 BD or 5 OD	3 BD or 6 OD	5 BD
ABC/3TC	600/300mg						1 OD
AZT/3TC/NVP	60/30/50mg	1 BD	1.5 BD	2 BD	2.5 BD	3 BD	1 BD
AZT/3TC/NVP	300/150/200mg						1 OD
AZT/3TC	60/30mg	1 BD	1.5 BD	2 BD	2.5 BD	3 BD	1 BD
AZT/3TC	300/150mg						1 OD
TDF/3TC/EFV	300/300/600mg						1 OD
TDF/3TC/EFV	300/300/400mg						1 OD
TDF/3TC	300/300mg						1 OD
<b>Singles</b>							
ATV/r	300/100mg						1 OD
ABC	60mg	1 BD or 2 OD	1.5 BD or 3 OD	2 DB or 4 OD	2.5 BD or 5 OD	3 BD or 6 OD	5 BD
ABC	300mg			1 OD		1 BD or 2 OD	1 BD or 2 OD
DRV	600mg						1 BD
DRV/r	400/50mg						2OD
DTG	50mg						1 OD
EFV	200mg						1 OD
EFV	600mg						1 OD
NVP	50mg	1 BD	1.5 BD	2 BD	2.5 BD	3 BD	1 BD
NVP	200mg						1 BD
LPV/r	40/10mg	2BD*	3 BD	4 BD	5 BD	6 BD	
LPV/r	100/25mg			2AM/1PM	2 BD	3 BD	N/A
LPV/r	200/50mg				1 BD	2AM/1PM	2 BD
LPV/r	80/20 mg/ml		3-3.9kg: 1ml BD 4-5.9kg: 1.5ml BD				
RTV	100mg						1 OD
3TC	150mg					1 BD or 2 OD	1 BD or 2 OD

\* LPV/r pellets should not be used for infants younger than 3 months Infants receiving pellets should be developmentally able to swallow



**Annex 8****Dosing Of Antiretroviral Drugs for HIV-Infected Adults with Chronic Kidney Disease (CKD) or End-Stage Renal Disease (ESRD)**

Antiretroviral drug, dosing category	Dosage
<b>Zidovudine</b>	
<b>Usual dosage</b>	300 mg po b.d.
<b>Dosage for patients with CKD or ESRD</b>	
Creatinine clearance 15 mL/min	No adjustment
Creatinine clearance <15 mL/min	100 mg po q6 - 8h
Receiving hemodialysis	100 mg po q6 - 8h
Receiving peritoneal dialysis	100 mg po q6 - 8h
<b>Lamivudine</b>	
<b>Usual dosage</b>	150 mg po b.i.d./300 mg po q.d.
<b>Dosage for patients with CKD or ESRD</b>	
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.
<b>Tenofovir</b>	
<b>Usual dosage</b>	300 mg po q.d.
<b>Dosage for patients with CKD or ESRD</b>	
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 days
Receiving peritoneal dialysis	Unknown, use with caution



## **Annex 9**

## ***Adverse Drug Reactions Screening Form***



**ADVERSE DRUG REACTIONS SCREENING FORM**

**State:** \_\_\_\_\_ **L.G.A.:** \_\_\_\_\_ **Facility Name:** \_\_\_\_\_

**Patient ID:** \_\_\_\_\_ **Patient Name:** \_\_\_\_\_ **Age:** \_\_\_\_\_ **Sex:** \_\_\_\_\_

Insert Visit Date →		1-1	1-2	1-3	1-4	1-5	1-6	1-7	1-8	1-9	1-10	1-11	1-12	1-13	1-14
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):														
<b>Skin and Appendages</b>															
Pruritus															
Skin rash															
Steven-Johnson Syndrome															
<b>Musculoskeletal System</b>															
Athralgia															
Myalgia															
Myopathy															
<b>Cardiovascular System / Respiratory System</b>															
Chest pain / Chest discomfort															
Cough															
Dyspnoea / Shortness of breath															
Palpitation															
Tachycardia															
Tachypnea															
Wheezing															
<b>Central and Peripheral Nervous</b>															
Anorexia															
Anxiety															
Blurred vision															
Depression															
Dizziness															
Headache															
Insomnia															
Nightmares															
Pain / Tingling / Numbness															
<b>Gastrointestinal / Hepato-biliary / Renal System</b>															
Abdominal pain															
Constipation															
Diarrhea															
Dyspepsia															
Hepatomegaly															
Jaundice															
Nausea / Vomiting															
<b>Metabolic / Endocrine System</b>															
Lipodystrophy															
Polydipsia (excessive thirst)															
Polyuria (Increased micturition)															
<b>Systemic Signs /symptoms – General</b>															
Anemia															
Fatigue / Weakness															
Fever															
Malaise															
Rigors / Chills															
Sweating / Diaphoresis															
Others															
<b>Intervention</b>															
Hospitalization															
Referral to other facility															
Drugs initiated															
Others:															
<b>Signature of Healthcare Professional</b>															

#### KEY TO GRADING OF ADVERSE DRUG REACTIONS

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 required



**Annex 10**  
**Form for Reporting Adverse Drug Reactions**

**NATIONAL PHARMACOVIGILANCE CENTRE (NPC) NIGERIA**

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



**FORM FOR REPORTING OF  
 SUSPECTED ADVERSE DRUG  
 REACTIONS**

**IN STRICT CONFIDENCE**

Tel: 08036889171 or Fax: 09-5241188

1. ★ PATIENT'S DETAILS					
Full Name or Initials:		Patient Record No:			
AGE/DATE OF BIRTH:		SEX: M <input type="checkbox"/> F <input type="checkbox"/> WEIGHT (kg):			
HOSPITAL/Treatment Centre:					
2. ★ ADVERSE DRUG REACTION (ADR)					
A. DESCRIPTION		C. OUTCOME OF REACTION TICK AS APPROPRIATE			
		<input type="checkbox"/> Recovered fully <input type="checkbox"/> Recovered with disability (Specify) <input type="checkbox"/> Congenital Abnormality <input type="checkbox"/> Life Threatening (Specify) <input type="checkbox"/> Death <input type="checkbox"/> Others (Specify)			
DATE Reaction Started	DATE Reaction Stopped				
B. Was Patient Admitted Due to ADR		Yes <input type="checkbox"/> No <input type="checkbox"/>			
If Already Hospitalized, Was it Prolonged Due to ADR		Yes <input type="checkbox"/> No <input type="checkbox"/>			
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:			
<b>★: MANDATORY FIELDS</b>					





**NATIONAL AIDS AND STIs CONTROL PROGRAMME  
FEDERAL MINISTRY OF HEALTH  
NIGERIA**

**2016**