Integrated Guidelines for Prevention, Testing, Care and Treatment of HIV/AIDS in Liberia

2nd Edition

National AIDS and STI Control Program

Ministry of Health and Social Welfare
Republic of Liberia
December 2007

For questions or expert advice related to the Integrated Guidelines or the National prevention, care and treatment program, please contact the National AIDS and STI Control Program:

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Foreword

Worldwide, the HIV/AIDS epidemic is now a global crisis affecting all countries and to a greater or lesser degree. It constitutes one of the most formidable challenges to development and social progress in this century. In the most affected countries, the epidemic is eroding decades of development gains, undermining economies, threatening security and destabilizing families, communities and societies.

In some counties in Sub Saharan Africa, the epidemic has created a state of emergency. It strikes hardest at vulnerable groups, including women and children, thereby increasing pre-existing gender inequalities and exacerbating the problem of child labor.

In response to the AIDS epidemic, the Government of Liberia created the National HIV/AIDS/STI Control Program (NACP) in 1987 and the National AIDS Commission (NAC). The latter was re-constituted in June 2007 under the leadership of President Ellen Johnson-Sirleaf and Dr. Walter Gwenigale, the Minister of Health and co-chair of the NAC.

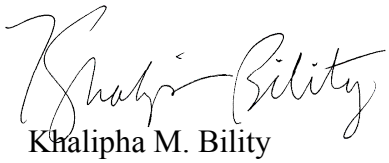
This document emanates from the collective commitment of many individuals and organizations to mount a nationally integrated response to the need for prevention, treatment, care and support to mitigate the impact of HIV/AIDS in Liberia. The first edition of these guidelines, produced in 2005, was a milestone for the national response in Liberia. After broad consultation, however, it became clear that changes in the treatment guidelines were crucial as part of the long-term effort to improve the quality of HIV/AIDS care and treatment services. Major changes from the first edition include:

- Updated HIV/AIDS treatment recommendations, which now correspond with the WHO 2006 recommendations and lessons learned from local experiences
- Encouragement of routine provided-initiated testing, and the promotion of testing as an integrated part of prudent public health practices
- Reconsideration of the first- and second-line antiretroviral therapy regimens: the NACP based these recommendations on the criteria of 1) doing no harm, 2) lowest pill burden, 3) least toxicity, 4) highest efficacy, and 5) the ability to still expand access to these medicines throughout the population
- Clear listing of contact information at the NACP, including a phone number and email address, through which questions and feedback may be received and properly addressed

The creation of an integrated guideline that discusses prevention, testing, care and treatment for all eligible patients – men, women, pregnant women, and children – reflects the eagerness of NACP to learn from other countries and chart for the future. The guidelines now include recommendations on major topics such as standard precautions, infant testing, follow-up scheduling for patients who are not yet eligible for antiretroviral treatment, specific treatment for HIV-1, HIV-2 and HIV-1/HIV-2 co-infection, adherence, co-management of patients with tuberculosis, treatment failure, and post-exposure prophylaxis.

These new guidelines will be used as the foundation for training health care providers throughout Liberia, and for the development of targeted interventions. The NACP looks forward to working with all health care providers involved in HIV counseling, testing, and treatment.

The treatment of HIV is a rapidly evolving field and the Technical Working Group used the most up to date information available when making its recommendations. Revisions will be made as new scientific evidence is gathered.



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Acknowledgements

In early 2007, a Technical Working Group was appointed to revise the national guidelines on care and treatment of HIV/AIDS in Liberia. The result of that effort is this document, the *Integrated Guidelines for Prevention, Testing, Care and Treatment of HIV/AIDS in Liberia*. This document is a product of not only the efforts of the members of the Technical Working Group, but also reflects the contributions of many other individuals, groups, and institutions. We can not possibly begin to express our gratitude to the dozens of individuals and organizations whose work – past and current – has contributed to the production of these Guidelines. The Ministry of Health and Social Welfare is particularly grateful for the support and guidance of the following institutions:

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UNDP
UNICEF
University of Massachusetts
University of Pennsylvania Department of Infectious Diseases
WHO

The *Integrated Guidelines* also draw upon the knowledge accumulated within the following documents, guidelines, and publications:

Addis Ababa City Administration Health Bureau (2006) *Standard Operating Procedures for Decentralizing ART Initiation and Follow Up Care to Public Health Centers and Private Facilities*. Addis Ababa, Ethiopia.

Bartlett JG and Gallant JE (2007) *Medical Management of HIV Infection*. Baltimore, MD: Johns Hopkins Medicine Health Publishing Business Group.

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We are deeply grateful for the generosity of the above institutions, organizations, individuals and authors.

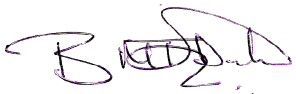

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Table of Contents

List of Tables

List of figures

Acronyms and Abbreviations

/r	Ritonavir	HIV	Human Immunodeficiency Virus
3TC	Lamivudine	HIV-1	Human Immunodeficiency Virus Type 1
ABC	Abacavir	HIV-2	Human Immunodeficiency Virus Type 2
ADC	AIDS-related Dementia Complex	HMIS	Health Management Information Systems
AFASS	Acceptable, Feasible, Affordable, Sustainable, and Safe	HSV	Herpes Simplex Virus
AFB	Acid-Fast Bacilli	IEC	Information, Education and Communication
AIDS	Acquired Immunodeficiency Syndrome	INH	Isoniazid
ANC	Antenatal Clinic	IPD	Inpatient Department
ART	Antiretroviral Therapy	IRIS	Immune Reconstitution Inflammatory Syndrome
ARV	Antiretroviral	KS	Kaposi's Sarcoma
AZT	Zidovudine	LFT	Liver Function Test
BID	Twice daily	LIP	Lymphocytic Interstitial Pneumonitis
BMI	Body Mass Index	LPV/r	Lopinavir/ritonavir, Kaletra
CBO	Community Based Organization	M&E	Monitoring and Evaluation
CDC	Center for Disease Control	MCH	Maternal and Child Health
CHO	County Health Officer	MOHSW	Ministry of Health and Social Welfare
CHT	County Health Team	MTCT	Mother to Child Transmission (of HIV)
CNS	Central Nervous System	NACP	National AIDS and STI Control Program
CPT	Cotrimoxazole Preventative Therapy	NFV	Nelfinavir
CTX	Cotrimoxazole	NGO	Non-Governmental Organization
CXR	Chest X-Ray	NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
d4T	Stavudine	NRTI	Nucleoside Reverse Transcriptase Inhibitor
DBS	Dried Blood Spot	NtRTI	Nucleotide Reverse Transcriptase Inhibitor
ddI	Didanosine	NVP	Nevirapine
DOTS	Directly Observed Therapy, Short-course	OCV	Oral Contraceptive Pill
EFV	Efavirenz	OHL	Oral Hairy Leukoplakia
ELISA	Enzyme-Linked Immunosorbent Assay	OI	Opportunistic Infection
EPI	Expanded Program on Immunization	OPD	Outpatient Department
FBC	Full Blood Count	ORS	Oral Rehydration Therapy
FBO	Faith-Based Organization	PA	Physician Assistant
FDC	Fixed Drug Combination	PCP	Pneumoscystis Jiroveci Pneumonia
FI	Fusion Inhibitor	PCR	Polymerase Chain Reaction
FTC	Emtricitabine	PEP	Post-Exposure Prophylaxis
GFATM	Global Fund to fight AIDS, Tuberculosis, and Malaria	PGL	Persistent Generalized Lymphadenopathy
GFR	Glomerular Filtration Rate	PI	Protease Inhibitor
HAART	Highly-Active Antiretroviral Therapy	PICT	Provider-Initiated Counseling and Testing
Hb	Hemoglobin	PLHA	People Living with HIV/AIDS
HBC	Home-Based Care	PMTCT	Prevention of Mother to Child Transmission (of HIV)
HBV	Hepatitis B Virus	PPE	Pruritic Papular Eruption
HCT	HIV Counseling and Testing	QD	Once Daily
HCV	Hepatitis C Virus	RPR	Syphilis test

sd-NVP	Single Dose Nevirapine	TMP-SMX	Trimethoprim – Sulfamethoxazole (Cotrimoxazole)
SJS	Stevens-Johnson Syndrome	ULN	Upper Limit of Normal
SOP	Standard Operating Procedure	VCT	Voluntary Counseling and Testing
SQV	Saquinavir	VZV	Varicella Zoster Virus
STI	Sexually Transmitted Infection	WBC	White Blood Count
TB	Tuberculosis	WHO	World Health Organization
TDF	Tenofovir Disoproxil Fumarate	ZDV	Zidovudine, AZT
TLC	Total Lymphocyte Count	ZN(stain)	Ziehl-Neilsen Stain

SECTION 1: Introduction

1. Introduction

The First Edition "National Protocol for HIV/AIDS ARV Care in Liberia" for the safe and effective use of ARV drugs was issued in 2005. It has played an important role in setting a national standard and guiding HIV care services, and serving as a tool for training, quantifying and forecasting ARV drugs procurement needs and costs.

The decision to update the National Protocol was made by the Ministry of Health, National AIDS and STI Control Program, and Liberian care providers after the WHO 2006 updates of:

- *Antiretroviral Therapy for HIV Infection in Adults and Adolescents in Resource Limited Settings*;
- *Antiretroviral Therapy for HIV Infection in Infants and Children in Resource-Limited Settings;*
- *Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants in Resource-Limited Settings*
- *Guidelines on Cotrimoxazole Prophylaxis for HIV-Related Infections Among Children, Adolescents and Adults in Resource-Limited Settings*

The desire to update the ART guidelines stems from local experiences and needs, together with the current level of knowledge and experience in using ARV drugs in resource-limited settings.

The Second Edition aims to integrate the national protocols for adults, adolescents, children, infants, and pregnant women into one comprehensive document. In addition, the 2nd edition focuses on providing HIV care and treatment services in a family centered approach to care. The most relevant issues for making ART widely available in Liberia, such as expansion of services to rural areas and expansion of the roles of nurses and physician assistants in ART initiation and management, have been considered in preparing the 2nd edition.

Finally, in the 2nd edition the first and second line drug regimens have been updated taking into account current level of scientific knowledge, best practices, and local experiences. Selected sections of the 2nd edition will also be available in different formats, such as condensed pocket-size manuals, posters and flow charts.

1.1 Objectives of the Integrated Guidelines

- To provide a standardized approach to the use of antiretroviral drugs in the comprehensive HIV/AIDS service delivery setting;
- To promote evidence-based, safe and rational use of antiretroviral drugs;
- To serve as a training tool and a reference material for health service providers, program managers, and people living with HIV/AIDS (PLHA);
- To guide the procurement of drugs and medical supplies in an efficacious, cost effective, and sustainable manner.

1.2 Target audience of the Integrated Guidelines

- Health care workers (physicians, physician assistants, nurses, midwives, pharmacy personnel, counselors, laboratory technicians and case managers) providing care to people infected with and affected by HIV;
- HIV/AIDS program managers, health planners, and researchers;
- Organizations involved in antiretroviral drug (ARV) procurement and supply management, and antiretroviral therapy (ART) service delivery;
- Local and international agencies involved in HIV/AIDS prevention, treatment, care and support.

1.3 About HIV/AIDS

1.3.1. The virus

AIDS (Acquired Immune Deficiency Syndrome) is caused by a virus, HIV (Human Immunodeficiency Virus) which was first isolated in 1983. It has been identified in over 200 countries and territories worldwide and is spreading rapidly in many affected populations, particularly in developing countries. The first case of HIV was identified in Liberia in 1986.

HIV belongs to an unusual group of viruses called retroviruses. There are two main strains of HIV. HIV-1 has caused the majority of infections and AIDS cases, however HIV-2 is concentrated in select countries. Of the other known related viruses, a type of retrovirus found in many other primates (simian immunodeficiency virus, SIV) may be the most likely contender for the origin of HIV. HIV has numerous varieties and has been shown to mutate, or change, within an individual during the progression of infection.

Both HIV-1 and HIV-2 have the same modes of transmission, are associated with similar opportunistic infections, and both lead to AIDS. However, HIV-2 is transmitted less easily, and the period between initial infection and illness is longer.

1.3.2. HIV-1

The HIV virus multiplies by replicating in the body at a rate of approximately 10^9 times per day, but frequently fails to produce identical copies of itself. These non-identical copies are referred to as mutations and may persist in the infected individual as 'subtypes,' which are genetically slightly different from the original (parent) virus. At least 10 genetically distinct subtypes of HIV-1 within the major group (group M) are known and designated A to K. In addition, group O (Outliers) contains a distinct group of very heterogeneous viruses and a new group of viruses labeled "N" for "New" was reported in 1998. These subtypes are unevenly distributed throughout the world. For instance:

- Subtype B: is found mostly in the Americas, Japan, Australia, Caribbean, Europe;
- Subtypes A and D: predominate in sub-Saharan Africa;
- Subtype C: predominates in South Africa and India and currently accounts for more than half of all new HIV infections worldwide;
- Subtype E: predominates in Central African Republic, Thailand, and other countries in Southeast Asia;
- Subtypes F (Brazil and Romania), G, and H (Russia and Central Africa), I (Cyprus), and O (Cameroon) are of very low prevalence.

Certain subtypes may be associated predominantly with specific modes of transmission. For example, subtype B may be associated with homosexual contact and intravenous drug use (via blood) while subtypes E and C are more with heterosexual transmission (via mucosal route). In Africa, one finds most subtypes, though subtype B is less prevalent.

1.3.3. HIV-2

HIV-2 is another human retrovirus that causes human immune deficiency due to depletion of CD4 cells. It is found primarily in West Africa. Compared with HIV-1, HIV-2 is less transmissible, is associated with a lower viral load and a slower rate of both CD4 cell decline and clinical progression.

1.3.4. HIV transmission

Among adults, HIV is spread most commonly during unprotected sexual intercourse with an infected partner. During intercourse, the virus can enter the body through the mucosal linings of the vagina, vulva, penis, rectum, or, rarely, via the mouth and possibly the upper gastrointestinal tract after oral sex. The likelihood of transmission is increased by factors that may damage these linings, especially other sexually transmitted diseases that cause ulcers and inflammation. Research suggests that immune cells, which live in the mucosal surfaces such as macrophages and dendritic cells, may begin the infection process after sexual exposure by binding to and carrying the virus from the site of infection to the lymph nodes where other immune system cells become infected.

HIV can also be transmitted by contact with infected blood, by the sharing of contaminated needles or syringes among IV drug users, after occupational exposure among health workers and by contaminated blood transfusions.

HIV positive women can transmit HIV to their babies during pregnancy, at birth, and through breastfeeding. Up to 40 % of untreated pregnant women infected with HIV will transmit the infection to their babies. Approximately 50% of these children will die before the age of two if they do not receive antiretroviral treatment.

1.3.5. Life cycle of HIV infection

HIV begins its infection of a susceptible host by binding to the CD4 receptor on the host cell. CD4 is present on the surface of many lymphocytes, which are a critical part of the body's immune system. Recent evidence indicates that a co-receptor is needed for HIV to enter the cell.

Following fusion of the virus with the host cell, HIV enters the cell. The genetic material of the virus, which is RNA, is released and undergoes reverse transcription into DNA. An enzyme in HIV called reverse transcriptase is necessary to catalyze this conversion of viral RNA into DNA.

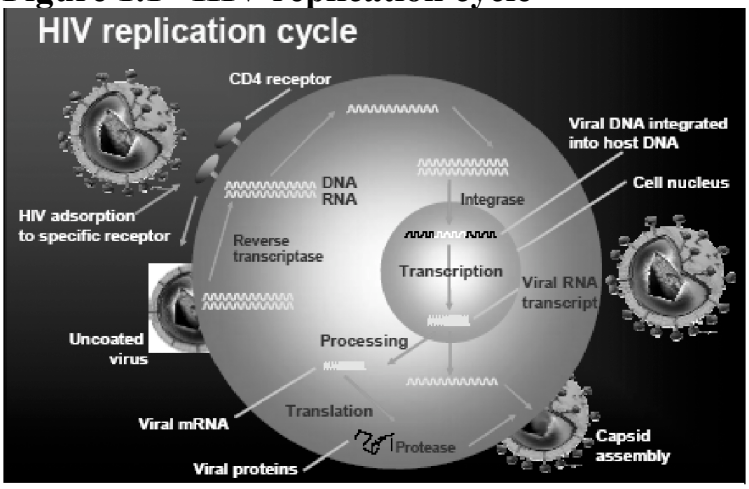
Once the genetic material of HIV has been changed into DNA, this viral DNA enters the host nucleus where it can be integrated into the genetic material of the cell. Once this happens, the cell can either become activated or can remain inactive. Activation of the host cells results in the transcription of viral DNA into messenger RNA, which

is translated into viral proteins. The new viral RNA forms the genetic material of the next generation of viruses. The viral RNA and viral proteins assemble at the cell membrane into a new virus. Amongst the viral proteins is HIV protease, which is required to process other HIV proteins into their functional forms. Protease inhibitors, one of the most potent types of ARV medications, act by blocking this critical maturation step. Following assembly at the cell surface, the virus then buds forth from the cell and is released to infect another cell.

Those CD4 cells that remain inactive act as a reservoir for HIV. The virus can persist within the cell for many years in a latent state. Because latent virus is not actively replicating, it cannot be targeted by antiretroviral drugs. Persistence of virus in latently infected cells is the major barrier to eradication or cure of HIV. For this reason, based on our current knowledge, patients must remain on anti-retroviral therapy (ART) for life.

Unless the HIV cycle is interrupted by treatment, the viral infection spreads throughout the body and results in the destruction of the body's immune system.

Figure 1.1 HIV replication cycle



1.3.6. Natural progression of HIV/AIDS disease

The natural history of untreated HIV infection is divided into the following stages:

- Viral transmission
- Acute retroviral syndrome
- Recovery and Seroconversion
- Asymptomatic chronic HIV infection
- Symptomatic HIV infection/AIDS
- Death

Once HIV enters the body, it infects a large number of CD4 cells and replicates rapidly. During this acute or primary phase of infection, the blood contains many viral particles that spread throughout the body, seeding various organs, particularly the lymphoid ones. This rapid initial viral replication causes an equally rapid destruction of CD4 cells, leading to a high concentration of virus in plasma and a low CD4 count. Two to six weeks after exposure to the virus, 50 to 80% of newly HIV positive people suffer a flu-like syndrome related to this infection (acute retroviral syndrome). Symptoms include: fever, headache, myalgias (muscle aches), skin rash, pharyngitis (sore throat), and diarrhea. Other symptoms, such as paralysis, meningitis

(infection of the lining around the brain) and opportunistic infections as a consequence of severe immune suppression are much less common. As antibodies are produced and become detectable in the patient's blood (from around 6 weeks onwards), the level of virus falls, the CD4 count begins to increase and the clinical symptoms and signs resolve. This period is known as seroconversion.

This response by the immune system is mainly the result of killer T lymphocytes (CD8 cells) and antibodies produced by B lymphocytes. However, the immune response to the HIV virus is not complete and effective because the high rate of mutations that occur during replication of HIV allows many viral particles to escape the immune system defenses. Finally the virus may remain latent within the chromosomes of infected cells as explained above, where it is hidden from the immune system. A person may then remain free of HIV-related symptoms for many months or years even though HIV continues to replicate within the lymphoid tissue.

After seroconversion, a period of asymptomatic chronic infection follows. During this time the virus continues to replicate and infect the CD4 cells as above. With time, the immune system becomes unable to produce new CD4 cells at the same rate at which they are being destroyed, so the number of CD4 cells begins to decline and the rate of viral replication increases until the immune system is damaged to the point where HIV related disease and eventually AIDS develops.

Almost all (if not all) HIV-positive people will ultimately develop HIV-related disease and AIDS. The rate of this progression depends on the type and strain of the virus and certain host characteristics. Factors that may cause faster progression include age less than 5 years or over 40 years, nutritional status, other infections, and possibly genetic factors. As HIV infection progresses and immunity declines, people become more susceptible to opportunistic infections.

The median interval from HIV-infection to the development of severe immune deficiency is estimated to be about 7 to 8 years. The survival time after onset of severe AIDS-characteristic illnesses is also variable but, prior to the development of effective antiretroviral therapy, average survival time was about 2-4 years in most developed countries and about 6 months or less in developing countries.

1.3.7. Opportunistic infections

Most illness in HIV infection is caused by opportunistic infections occurring when the body's defenses are low, and not by the HIV virus itself. Therefore, opportunistic infections should be aggressively treated before even considering ARV treatment. The WHO staging system for HIV infection recognizes HIV disease progression and may be used to assess newly diagnosed HIV clients and their eligibility for preventive and ARV therapies. Knowledge and extensive use of the WHO staging system is the basis of clinical care for HIV. In addition, regular measurement of body weight and laboratory measurement of immunological and virological status where possible are critical to HIV clinical care.

SECTION 2: The approach to HIV prevention

2. The approach to HIV prevention

2.1 Standard precautions to prevent nosocomial transmission of HIV

Standard precautions are a simple set of effective practice guidelines (creating a physical, mechanical and chemical barrier) to protect health care workers and patients from infection by a range of pathogens including blood borne pathogens. Standard precautions are used when caring for all patients regardless of diagnosis.

Consider every person (patient or staff) potentially infectious and susceptible to infection.

2.1.1. Components of standard precautions

1. Hand hygiene including hand washing, hand antisepsis, antiseptic hand scrub and surgical hand scrub
2. Personal protective equipment including gloves, gowns, aprons, goggles and masks
3. Careful handling and disposal of sharp instruments
4. Safe disposal of infectious waste contaminated with body fluids
5. Proper handling of soiled linen
6. Sterilization and disinfection

2.1.2. Implementation of standard precautions

In practice, implementation of standard precautions includes the following interventions:

2.1.2.1. Hand washing

Hands should be washed with soap and clean water:

- Before and after contact with each patient
- Before and after each procedure
- Before wearing and after removal of gloves
- When hands are visibly soiled
- Before preparing, handling, serving or eating food and before feeding a patient
- Before leaving the area of work
- Adequate supply of disposable tissues is encouraged in order to avoid reusable towels

2.1.2.2. Use of protective barriers such as gloves, gowns, aprons, goggles and masks

Gloves should be worn during all procedures involving contact with blood or other potentially infected body fluids. Gloves must be discarded after each patient, or decontaminated, washed and properly sterilized. Gloves are not required for routine care activities in which contact is limited to a patient's intact skin. Clean, non-sterile gloves will be worn:

- For examination and non surgical procedures
- Contact with blood, body fluids, secretions, excretions, mucous membranes, draining wounds, or non-intact skin

- For handling items visibly soiled with blood, body fluids, secretions or when the health worker has skin lesions on the hand

Protective clothing such as waterproof gowns, aprons, boots, goggles and/or masks should be worn only where there is likelihood of exposure to large amounts of blood or body fluids such as in operating room, labor room or laboratory.

2.1.2.3. Careful handling and disposal of sharp instruments

- All sharps should be handled extremely carefully to avoid prick injuries.
- Needles should not be bent, broken or removed from syringes. If they must be removed from syringes, then use forceps.
- Holders must be used for all blades.
- All needles and other sharp instruments should be deposited in puncture resistant sharps containers to be placed near the working place. The containers should be clearly labeled, easily accessible and incinerated when three quarters full.

2.1.2.4. Safe disposal of waste contaminated with body fluids

Soiled waste that is contaminated with blood, body fluids, laboratory specimen or other tissues, should be placed in leak proof containers with special labels and incinerated, or buried in a pit covered with soil that is 8 feet deep and at least 30 feet away from any water source. Liquid waste such as blood or body fluids should be poured down a drain connected to an adequately treated sewer or pit latrine.

2.1.2.5. Proper handling of soiled linen

Soiled linen should be touched as little as possible. It should be collected in bags and not rinsed or sorted out at the patient care area. If possible, linen with large amounts of blood should be transported in leak proof containers, and if not available they should be folded with the soiled parts inside, and handled carefully with gloves. Soiled linen should be soaked in hot water with sodium hypochlorite solution (e.g. bleach) for not less than thirty minutes, then washed separately in hot water and then air-dried.

2.1.2.6. Sterilization and disinfection

The human immunodeficiency virus does not survive well outside the human body. Nevertheless, it is mandatory that health care workers and family members caring for HIV positive persons take precautions in order to prevent accidental spread of the virus. All material used repeatedly must be properly disinfected and/or sterilized. Thorough cleaning with soap and hot water removes a high proportion of microorganisms. All equipment should be dismantled before cleaning. Sterilization will destroy HIV. Recommended methods of sterilization include steam under pressure, e.g. autoclave or pressure cooker, or dry heat such as oven.

Recommended disinfectants are Bleach 10% (corresponds to a 0.5% sodium hypochlorite solution) and 1% Lysol. Commonly used methods are boiling and chemical disinfection with hypochlorite solution. If there is a need for boiling equipment, then they must be cleaned and then boiled for at least 20 minutes.

Detergents and hot water are adequate for routine cleaning of floors, beds and toilets. In case of spillage of blood or body fluids, the area should be cleaned with chlorine-

based disinfectant and followed by thorough cleaning with soap and hot water. Pour hypochlorite 1:10 on the site, clean with paper towels. Then pour hypochlorite solution again and clean. CIDEX can also be used.

Gloves must be worn during cleaning of equipment and if splashing with body fluids is likely, additional protective clothing such as waterproof aprons, gowns, boots, protective eyeglasses and/or masks should be worn. Method of decontamination can be decided based on the following criteria:

Table 2.1 Criteria for selecting decontamination method

Level of risk	Items	Decontamination method
High	Instruments which penetrate the skin/body	Sterilization and single use of disposables
Moderate	Instruments which come in contact with non-intact skin or mucous membrane	Sterilization, boiling or chemical disinfections
Low	Equipment which comes in contact with intact skin	Thorough washing with soap and water

2.2 Laboratory safety procedures

Safety precautions are essential and should be followed at all steps starting from specimen collection to storage, transporting and disposal of biohazard wastes so as to minimize occupational risks. The risk of transmission of HIV, hepatitis B virus (HBV) and other transfusion transmissible infections can be minimized if laboratory workers use the above safety precautions/procedures at all times. Also:

- All laboratories handling infectious materials should always have a biohazard spill kit containing paper towels, gloves, tweezers, disinfectant and heavy-duty biohazard disposal bags.

Supervisors should report any HIV exposure events to the medical director. Supervisors should ensure that Post-Exposure Prophylaxis (PEP) logbooks are maintained. See **Section 22**: Post-exposure prophylaxis.

2.2.1. Phlebotomy safety procedures

Gloves should always be worn during phlebotomy to reduce the incidence of blood contamination of hands. However, gloves cannot prevent penetrating injuries caused by needles or other sharp instruments. A fresh pair of gloves should be used for each patient. Gloves are particularly important in the following situations:

- For performing phlebotomy when the worker has cuts, scratches or other breaks in the skin (after covering the cuts with bandages)
- Where the worker judges that hand contamination with blood may occur e.g. on an uncooperative patient
- When performing finger or heel prick on infants and children

Use disposable, single-use blood collection safety sets (safety needles, vacuum tubes and holders) wherever possible. Where syringes and needles have to be used, always use a one-handed method to re-cap the needle after collection. Remove the needle from the syringe before dispensing blood into tubes.

2.2.2. Sample storage procedures

- Always store samples in tightly closed and labeled tubes kept upright in racks.
- Always keep a record of stored samples.
- Always dispose of used or old specimens in a timely fashion by autoclaving and/or incineration.
- Storage should be at the appropriate temperature.

2.2.3. Sample transportation procedure

If blood is to be transported from the clinic to laboratory or from one laboratory to another, it is recommended that:

- Specimens should be stored appropriately and according to up-to-date Standard Operating Procedures (SOPs) before shipping.
- Dispatch and receipt records should be maintained.
- Specimens should be shipped in safe containers as per sample transport guidelines.

SECTION 3: The approach to HIV care

3. The approach to HIV care

3.1 Scope of care and treatment

People suffering from HIV related illnesses can access care at different levels of the health care system in Liberia. These include: public or private hospitals and health centers (OPD or inpatient units), clinics, home based care programs, antenatal clinics, VCT sites, TB and STI clinics. In order to provide effective and quality HIV and AIDS Care and Treatment, services need to be organized in such a manner as to ensure regular and standardized treatment, follow-up, and referral of patients.

The creation of a system of referral and care that is integrated within and strengthens the existing Liberian health care network will ensure that people living with HIV can be treated throughout the course of their illness. Close collaboration needs to be ensured for essential services such as DOTS for TB, reproductive health and family planning and home care services.

3.2 Care and Treatment Programs

The following Core elements of care and treatment will be established at Care and Treatment Programs in Liberian facilities:

- Basic education regarding the mechanism of HIV infection and disease progression and how to live positively with the disease
- Education about behavior change to reduce transmission of HIV
- Orientation to the care and treatment program
- Education and counseling on life-long disease management
- Education and counseling about interventions that may delay the progression of disease and reduce comorbidities such as proper nutrition, food safety, clean water and malaria prevention
- Routine clinical care and nutritional assistance for malnourished patients
- Prophylaxis for OIs as indicated by these guidelines
- Management of disease symptoms and opportunistic infections
- Assessing eligibility for ART (in terms of clinical, immunological, virological and psychosocial factors)
- Recording and reporting to MOH according to the established system, and proper monitoring and evaluation.
- Continued counseling and support (the psychosocial aspects of care)

3.3 Clinical categories of patients

Each of the patients that are seen for care will fall into one of three clinical categories with specific clinical goals of treatment as outlined below. Patients in any of the three categories are strongly advised to come to the treatment clinic whenever their clinical situation deteriorates.

3.3.1. Clinically asymptomatic HIV (mildly immunosuppressed)

HIV positive individuals who are asymptomatic and/or have high CD4 cell counts will come to the clinic for periodic monitoring. The goals of care for these patients are to delay progression by treating and/or preventing opportunistic infections,

prevent onward transmission of HIV, provide advice on healthy life styles and to enhance the likelihood of success of future treatment by improving adherence to prophylactic medications and visits.

3.3.2. Symptomatic HIV (moderately immunosuppressed)

HIV positive individuals who have significantly compromised immune systems but may not be eligible for ART will come to clinic for closer monitoring. The goals of care are to delay progression by preventing and treating opportunistic infections and to enhance the likelihood of success of future treatment by improving adherence to medications and visits.

3.3.3. Advanced or severe HIV (treatment-ready patients)

HIV positive individuals who are eligible for ART as detailed in the criteria in later chapters will be started on treatment and monitored at a treatment facility. The goals of treatment and care are to reduce morbidity and mortality by aggressively suppressing viral load, and prevent and treat opportunistic infections in order to maximize the benefits of treatment by encouraging consistent adherence to ART.

3.4 Accreditation of healthcare facilities as care and treatment sites

In order to reach the HIV positive patients who are expected to require ART, it will be necessary to have many healthcare facilities, public and private, of various sizes and capabilities with care and treatment programs spread equitably throughout the country. These facilities will each have to meet a minimum set of criteria in order to provide quality care and treatment services for PLHA. Thus, many health facilities will need to be strengthened before they can start and/or expand ART-services. In order to have as many health facilities as possible qualify for the provision of ART to HIV/AIDS patients, the National AIDS and STI Control Program (NACP) will use a strengthening and accreditation procedure. The objectives of this procedure are to:

- Determine the availability and quality of the essential elements to start and/or expand ART;
- Identify areas for strengthening and improvement to upgrade health facilities to be able to provide comprehensive care to PLHA; and
- Issue accreditation to health facilities to enable them to start/expand ART, once they have met a minimum set of criteria.

The need for the minimum standards requirement is not to limit the number of institutions that can deliver care and treatment. Rather, it has the dual role of: 1) assuring that care and treatment services are delivered with an appropriate quality and standard, and 2) allowing identification of needs/gaps at each institution in order to facilitate channelling of resources to meet these needs.

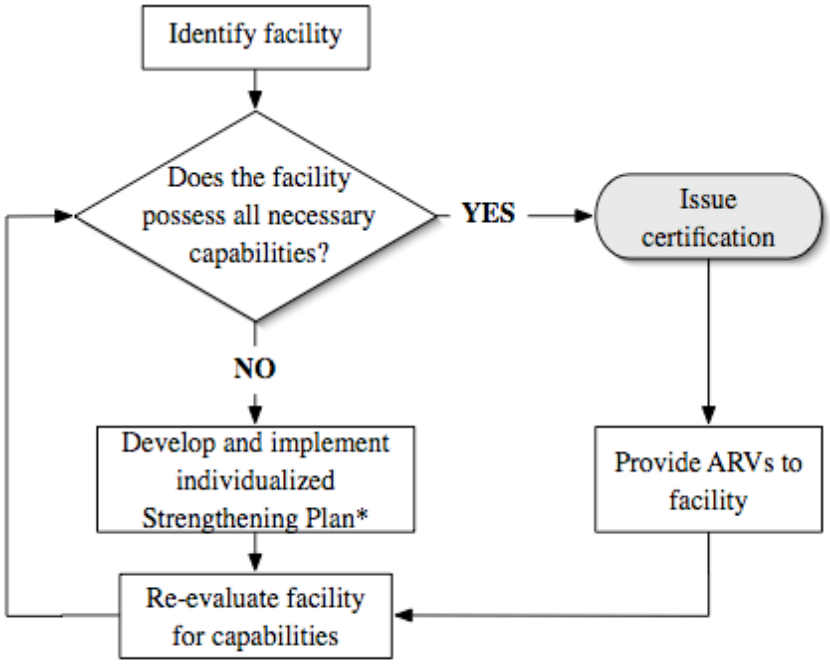
Compliance with the minimum standard is a prerequisite for initiating ART. The minimum standard is defined in terms of the following capacities:

- Human resources
- Infrastructure, medical equipment and supplies
- Clinical, Laboratory, Pharmacy, and HIV services
- Patient records, reporting, and monitoring and evaluation (M&E) systems
- Referral systems

3.4.1. Selection and strengthening process

NACP has developed a system to identify, strengthen, and accredit facilities to introduce Care and Treatment Programs and provide ARVs. The objective is to establish clinics to prescribe ARVs, monitor patient condition, and provide other care and treatment for HIV positive patients (see **Figure 3.1** Preparing facilities for certification).

Figure 3.1 Preparing facilities for certification



*Includes recruiting and training health care workers, obtaining equipment and improving overall facilities.

In conjunction with other divisions of the MOHSW, the NACP will target the public facilities where ARV therapy will be administered. This targeting will be undertaken in full consultation with authorities at the national and county level.

The targeted health facilities will be assessed by a multidisciplinary assessment team, in which representatives of the MOHSW and County Health Teams will participate. During the assessment visit a comprehensive assessment tool will be completed as well as a checklist with minimum criteria for starting ART. These forms will contain the basic information for the preparation of a Strengthening Plan.

The Strengthening Plan will be the key tool in preparing facilities for participation in the ART program. It will be jointly prepared and agreed upon by representatives of the NACP, the County Health Team and managers of the target facility to ensure the needs and remedies for each facility are correctly identified and prescribed. Over time as the program expands, it is planned that County Health Officers, working as extensions of NACP, will take a major role in the targeting of facilities as well as in the preparation of Strengthening Plans.

Each Strengthening Plan will develop detailed strategies for addressing issues such as:

Human Resources:

- Designation of a facility leader to take responsibility for preparation of the strengthening plan and supervision of the facility's participation in the HIV/AIDS Care and Treatment Program.
- The recruitment of personnel for the Care and Treatment Team and other supporting units of the facility.
- Training of Care and Treatment Team members.
- Orientation and training of other healthcare workers at the facility and in nearby facilities to support the Care and Treatment Program.

Infrastructure and Equipment:

- Identifying or establishing appropriate clinic space.
- Development of a laboratory plan and sample transportation schedule, if needed.
- Building a secure pharmacy.
- Inventory of existing equipment, ordering of new equipment.
- Maintenance plan for equipment.

Services:

- Participation in PMTCT program.
- Preparation for linking with TB, antenatal, and STI clinics.
- Linkages with other facility operations (wards, other clinics, support units etc).
- Linkages with community resources (HCT, social support, etc.).
- Participation in locally based continuous care and IEC activities.

Program Operations:

- Preparation of a facility-specific implementation plan for HIV/AIDS care and treatment.
- Use of national and facility based monitoring and evaluation tools.

Planning for strengthening should not be limited only to looking at the facility itself. For example, an analysis of the availability of HCT services in the area must be undertaken and preparations made for increasing the number (or effectiveness) of sites if necessary. These activities will require coordination with other sections of the MOHSW, community leaders and resources, NGOs and other HCT service providers.

Other important activities outside the facility might include:

- Enlisting resources to help educate families and communities about the basics of HIV/AIDS medicine, particularly the role treatment can play and the difficulties inherent in lifelong treatment for affected individuals and their families.
- Coordinating HIV activities with other MOHSW strengthening activities including implementation of the Basic Package of Health Services

The Strengthening Plan will spell out in detail the implementation steps that are necessary to bring the facility to the point where it can be certified as ready to receive, prescribe and distribute ARVs. The plan will also assign responsibility for each implementation step and develop a time line that will show when the process will be completed. The NACP, working closely with the CHTs, will be responsible for monitoring progress in implementing the Strengthening Plan and ensuring adherence to the approved timeline.

3.4.2. The accreditation process

The key values the NACP will look for in considering an application will include:

- Quality – Does the facility have a treatment system in place that will ensure quality health care for HIV/AIDS patients?
- Quantity – Is the facility prepared to treat a significant number of HIV+ individuals upon accreditation, and to increase the patient load as the staff gains experience?
- Accessibility – Will essential treatment be made available on an equitable basis to all Liberians regardless of ability to pay?
- Accountability – Are procedures and safeguards in place to ensure that funds, equipment, supplies, and medicines are properly used and accounted for?

With these values in mind, the strengthening plan should help prepare a facility to meet the minimum criteria outlined below. The NACP will encourage flexibility and maximum integration with existing healthcare resources in the plan for meeting the minimum criteria. Target facilities should tailor their solutions to reflect the facility's individual needs and characteristics. In this way, best practices can be developed to aid in the scaling up efforts.

For the first year, the target facilities will be Regional and County Hospitals, therefore the checklist with minimum criteria highlights what each facility should have in place as a minimum at the County Hospital level.

3.4.3. Minimum criteria to start/expand ART at hospitals

3.4.3.1. Organization of HIV/AIDS care services within facility

1. Space for registration of HIV/AIDS patients
2. Clearly described patient flow plan (including referral within the facility)
3. Project manager to coordinate the HIV/AIDS care and treatment services at the facility (this can be a member of the C&T team and does not need to be a doctor)

3.4.3.2. Human resource capacity, training and continuous education

1. Motivated Care and Treatment team consisting of at least: - 2 clinicians capable of initiating ART, evaluation of patients, and prescription refill (MD, PA, or RN) - 2 counselors (HCT and adherence counseling) - 2 laboratory technologists/technicians - 2 pharmacists/pharmaceutical technicians/dispenser - 2 data-clerks* **Note:** The Care and Treatment team must support the work of the ART clinic but need not work there exclusively. It is important that more than one person is trained to carry out all of the above roles to ensure continuity of quality services in the event of staff turnover or temporary absence.
2. Above team has been trained according to approved national curricula
3. Guidelines to be made available: National HIV/AIDS care and treatment guidelines, PMTCT guidelines, Blood Safety Guidelines, HCT guidelines

*Recommended but not required

3.4.3.3. Clinical HIV/AIDS care and treatment services

1. Consultation services
2. TB-diagnosis and treatment services
3. STI-diagnosis and treatment services
4. PMTCT Services*
5. Palliative care services*

* Recommended but not required

3.4.3.4. Physical Infrastructure and Equipment (need not be exclusive to Care and Treatment Program)

1. Confidential examination room (1 room/ART provider) including desk, chairs and exam couch
2. Confidential ART counseling room including desk, chairs, shelf, and lockable filing cabinet

• Exam tools:
  • BP cuff
  • otoscope
  • stethoscope
  • thermometer
  • adult weigh scale and height measurement
  • pediatric weigh scale and height measurement if providing pediatric ART
  • speculum

• Supplies: gloves; condoms*

* Recommended but not required

3.4.3.5. Patient records and reporting systems

1. An established and working medical record system
2. Locked area with limited access for medical records
3. M&E and HMIS Formats (as developed and implemented by NACP) • Pre-ART and ART registration logbook • Pre-ART and ART Intake Form • Follow Up Card • Unique ART card • Communications Flowchart and Contact Information • Monthly Reporting Forms • Laboratory Test Request Form • Radiology Test Request Form • ART Prescription Forms • PEP logbook

3.4.3.6. Continuum of care: organization of HIV/AIDS care services

1. Clear referral system for inter-institution, intra-institution, specialized referral facilities, and community referrals (linkage with HBC, NGO's, CBO's, FBO's and other community-based organizations), including referral slips, feedback forms, receiving and disposition slips
2. System for patient tracking in place
3. System for receiving and filing results from on-site or referral lab

3.4.3.7. Laboratory services

1. Adequate space
2. Types of Tests: • CD4* and CD4%* • Liver enzymes • Full Blood Count • Hemoglobin • AFB Smear • Malaria Smear • Pregnancy Test • Screening for Blood Safety • Serology for HIV (at least three different rapid tests) • HIV DNA PCR (DBS)* • RPR (syphilis test) • Stool, Urine, CSF • X-ray*

3. Equipment: • Generator • Reliable petrol supply • Sterilizing Equipment/Autoclave* • Microscope • Centrifuge* • Hematology analyzer* (semi-automated or automated) • Chemistry analyzer* (semi-automated or automated) • Refrigerator including freezer compartment • Air conditioner • Lockable room or cabinet for record storage
4. M&E/HMIS/Formats (as developed by NACP, will be required): • Laboratory Registration Book • Laboratory Testing Logbooks • Monthly Reporting Forms • Laboratory Request Forms • Unique ART card • Communications Flowchart and Contact Information
5. Systems: • Use of Standard Operating Procedures (SOPs) • Internal and external quality systems

*Recommended but not required

Regional Hospital level (criteria listed above, plus below criteria)
1. Emergency water reserve
2. Electricity supply back up (generator, solar)
3. Automated hematology (low volume)
4. Automated biochemistry (low volume)
5. CD4 testing (low volume)
6. Refrigerator including freezer compartment for samples
7. Refrigerator including freezer compartment for reagents
8. Freezer, -20^{o}C

3.4.3.8. Pharmacy services

1. Storage space for 1.5 month supply of ARVs
2. Drug Formulary: • First line ARV drugs • Post-exposure prophylaxis • Cotrimoxazole • Fluconazole* • Acyclovir* • Amoxicillin* • Prednisolone* • Pyridoxine* • Amitriptyline* • TB drugs* • Malaria drugs*
3. Functional ARV-tracking system
4. Use of Procurement and Supply Management SOP (national ARV-pharmacy instructions for GFATM commodities)

5. M&E/HMIS/Formats (as developed by NACP, will be required) • Bin card • Stock card • Receiving form • Registration forms • Monthly reporting formats • Unique ART card • Communications flowchart and contact information • ART prescription forms • PEP logbook
6. Refrigerator
7. Air Conditioner

* Recommended but not required

3.4.3.9. Finances

1. Internal quality control arrangement in place
2. External quality control arrangement in place
3. Budget earmarked for strengthening clinical HIV/AIDS services

3.5 Organization of Care and Treatment Programs

3.5.1. Patient visit plan

Once a patient is identified, he or she will be referred to the Care and Treatment Program which, in all but the largest care settings, should be within the OPD, (see **Section 5:** Patient enrollment in Care and Treatment Program, and **Appendix 4**). At the initial visit a triage nurse will assess patients needs, register basic information, issue relevant forms, weigh and direct patient for baseline investigations and clinical consultation (see **Section 7:** Patient assessment for treatment). All patients will be started on appropriate medications to prevent OIs. (See **Section 9:** Prophylaxis against HIV-associated infections with cotrimoxazole preventive therapy.)

Patients who are eligible for and agree to initiate therapy will meet with a counselor to discuss adherence, medication dosing and adverse event management (see **Section 6**: Counseling: adherence and disclosure). Patients initiated on ART will be scheduled for follow-up after two weeks, then frequently within the first six months for clinical care and monitoring of response to therapy (see **Section 15**: Monitoring of patients on ART). During these visits, they will see a nurse, an evaluating clinician as required, pick up their medication, and meet with a counselor (see **Section 6**: Counseling: adherence and disclosure). If the patient's condition has stabilized, after six months he or she will be requested to visit the clinic at less frequent intervals for medication and counseling and as needed for clinical care. Every six months, CD4+ counts and basic blood tests will be performed and patients will see a clinician for follow-up and evaluation of response to therapy.

For HIV positive people who do not immediately qualify for treatment, regular monitoring of their status will be required every 3 months as detailed in **Section 8**: Monitoring of adults and children not yet eligible for ART.

All patients are to be advised to come to the clinic immediately should their condition deteriorate prior to their next scheduled visit.

3.5.2. Adherence management and lifestyle counseling

Patients on ARV treatment will be strongly encouraged to identify an adherence assistant or "treatment buddy." The adherence assistant is any person identified by the patient to help him/her with ARV medications, e.g. a family member, friend, colleague, or community member. When necessary, patients with special needs can be assisted by counselors, social workers or community health workers. (See **Section 6**: Counseling: adherence and disclosure, for further details.)

3.5.3. Medical records system

A Patient Identification Card, Patient Record Form, Patient Register (for pre-ART and patients on ART) and an ART Reporting Form, have been designed for the purpose of patient identification, patient monitoring and program monitoring respectively.

3.5.4. Patient identification card

This card has a pre-printed unique patient identification number. The Card is issued at the first visit, at the registration section of the facility. The Card is for patients on ARV treatment and HIV positive persons who are not yet on treatment but are being monitored by the program. The Card will be kept by the patient and used for identification purposes at every visit. It is important that the patient carries relevant treatment information with him/her whenever he sees a new clinician, e.g. when he or she transfers to another facility. The same initial identification number will be retained to avoid loss of follow up and double recording of the patient.

3.5.5. Patient record forms (intake and follow up)

These forms will be completed at the first visit (Intake Form) and at all follow up visits (Follow Up Form) for any HIV positive person attending the treatment clinic. Each form has a unique ID number, copied from the Identification Card. The Form is kept in a file and retained in the facility registry or dedicated HIV/AIDS cabinet and is to be retrieved at each visit using patients' unique ID number. Key information on patient management is filled in by the attending clinician.

3.5.6. Patient register books (pre-ART and ART)

These books aggregate the key information from the patient record. Information is written daily into the register after each visit. The summary format enables information to be easily collected for monthly reporting. Information for patients not yet eligible for treatment will be recorded in the pre-ART register. Information for patients on ART will be recorded in the ART register. Similar register books will be designed for PMTCT and HIV Testing and Counseling services.

3.5.7. Monthly services update forms (Care and Treatment, PMTCT, HIV testing and counseling)

These forms capture information for program monitoring. The Forms are currently printed in pads containing carbon triplicate sets. The designated person will copy all

required information from the Patient Registers to the Reporting Forms. First and second copies of filled forms are removed and sent to the CHO for approval and then to NACP at the end of every month, while third copies remain at the facility. Each facility participating in the Care and Treatment Program should identify a person to be responsible for reporting and handling of the Forms.

3.5.8. Linkages across a continuum of care

Successful linkages with a variety of partnering programs and care sites are encouraged at all levels. Partnerships between clinicians, HCT facilities, the treatment facilities and support programs in the community need to be established in order to ensure a continuum of care through functional referral mechanisms.

Care providers must be sensitive to the fact that PLHAs are often understandably reluctant to be transferred between providers and programs early in the process of counseling. Healthcare providers who diagnose HIV and counselors who work with PLHAs must be prepared to invest in trusting relationships and to proceed with referrals only when clients are ready.

PMTCT Programs/Antenatal Clinics

The MOHSW plans to establish Prevention of Mother to Child Transmission (PMTCT) programs in all hospitals in Liberia whereby antenatal clinics will also serve as counseling and testing sites. Strong referral systems must be put in place to ensure that any HIV positive individuals seen at the antenatal clinic are appropriately enrolled by the Care and Treatment Program.

ART availability will allow for expansion of the PMTCT program, with counseling aimed at enrolling the entire family in continuing care and treatment, most closely associated with the antenatal clinic. Availability of DNA polymerase chain reaction (PCR) testing will facilitate early diagnosis of HIV infection among children born to HIV positive mothers. In the absence of PCR testing, WHO Clinical Staging will be used in initiating ARV treatment. Close referrals and coordination between the PMTCT and the Care and Treatment services will make each program more effective and efficient.

HIV Counseling and Testing (HCT) Programs

HCT programs, including Voluntary Counseling and Testing (VCT) and Provider Initiated Counseling and Testing (PICT) play a crucial role in identifying people living with HIV and directing them to care and treatment. Strong referral processes will need to be established between all HCT programs and the appropriate treatment sites to ensure that HIV positive individuals are either enrolled for treatment, or have their condition monitored as appropriate.

STI Services

All patients diagnosed with STIs should undergo HIV counseling and testing. Facilities engaged in ART should ensure that close referral linkages are developed with STI treatment services. Because STIs increase the risk of transmitting HIV, **all patients in HIV care should also be screened and treated for STIs.**

Tuberculosis Clinics

Tuberculosis clinics will serve as an important channel for identifying HIV positive individuals. **All patients diagnosed with TB should undergo HIV counseling and testing.** HIV positive individuals should be referred to a care and treatment clinic for further management.

Community Based Programs and Home-Based Care

PLHA and their affected families and households have a variety of needs beyond the provision of clinical care. Such needs include psychological, spiritual, nutritional, educational, economic and legal care and support. Thus, a continuum of care for people living with HIV is an essential element of any care and treatment program.

A comprehensive and holistic program of care for PLHAs in Liberia will only be possible when the MOHSW, private and faith-based health institutions, and community groups are fully engaged. The intention is to decentralize care as much as possible with more sophisticated levels of care available by referral. The aim is for patients to have access to care at whatever level is appropriate to their needs.

Community based care programs and faith based groups can provide very helpful comprehensive care and support within the community and household level, including:

- Basic support, such as food, hygiene and shelter
- Clinical support such as preventive therapy and simple medications
- Adherence and psychosocial support
- Referral to access HCT, Family Planning, and Clinical facilities
- Community education in care and ART fundamentals
- Prevention activities
- Promotion of PLHA support groups
- Palliative care and support to PLHA and their caregivers

Each facility delivering HIV care and treatment services should be encouraged to develop a plan to link with and support organizations dealing with community based care. An inventory or directory of service providing organizations in the local community needs to be established to facilitate networking and referrals and a copy should be held at the Care and Treatment Program. Health care workers should aim to conduct supervisory visits to community and home care providers as part of their role and responsibility to ensure the continuum of care.

SECTION 4: Identification of HIV positive individuals

4. Identification of HIV positive individuals

4.1 Strategies for identifying HIV positive Liberians

For Liberians to benefit from ART, early diagnosis and treatment of all HIV positive individuals is essential. Early knowledge of HIV infection can result in tremendous public health benefits through decreasing risk behaviors that could transmit HIV to those people who remain uninfected. Uninfected persons may also benefit from HIV testing, because knowledge of their status may encourage them to modify or reduce risk behaviors. Expanding opportunities for widespread testing, coupled with access to free treatment – and the knowledge that it exists – will help to identify HIV positive individuals in the population.

4.2 Approaches to HIV counseling and testing (HCT)

Liberia has adopted a national testing strategy employing two key approaches:

1. **Voluntary counseling and testing (VCT)** is a system by which an individual can find out his/her HIV status and receive pre- and post-test counseling. Informed consent (written or oral) for testing is required in this setting.
2. **Health care provider-initiated counseling and testing (PICT)** is based on a health care provider's recommendation to a patient.
    - Routine provider-initiated counseling and testing is encouraged in all health care settings.
    - Health care providers should offer an HIV test to **every patient** who requests health care, but especially patients in:
        - Inpatient wards
        - TB clinics
        - STI clinics
        - Antenatal care clinics
        - Therapeutic feeding centers
        - Maternal and under five child health clinics (special attention should be paid to recognizing the manifestations of HIV in children)
    - All patients have the option to decline testing.
    - Pre-test counseling can be provided in a group format (e.g. a health talk) but post-test counseling should be performed in private settings.
    - Pregnant women who test HIV negative during the first trimester should be retested in the third trimester to rule out the possibility of a false negative diagnosis (testing negative during the window period) or a new infection.

4.3 Consent and counseling

- All patients undergoing HIV testing must give their consent (oral or written) before a test is performed on their specimens.
- Doctors, nurses, midwives and PAs should be trained to offer pre-test and post-test counseling. Ideally this should be included in pre-service training.

4.3.1. Pre-test counseling

Counseling before testing should be provided to individuals who are considering being tested for HIV. The counseling should provide information on basic technical aspects of screening and the possible personal, medical, social, psychological, and legal implications of being diagnosed either positive or negative.

- In healthcare settings (hospitals and clinics): health care providers should provide appropriate counseling so patients understand they will undergo a test for HIV.

- In VCT centers: counselors should perform more extensive pretest counseling, which includes explaining how the diagnosis is made, risk factors for HIV, the course of the disease, available treatments, and the need for life-long therapy.

The counselor should:
- Determine the individual's background information on HIV and AIDS.
- Provide information on HIV and AIDS in a manner easy to understand by using simple, common and accepted language.
- Take appropriate history to assess the likelihood that the individual has been exposed to HIV, such as risky sexual relations, injecting drug abuser, having received blood transfusion, or having been exposed to non-sterile invasive procedures.
- Inquire about a person who would be able to provide emotional and social support for the individual.

4.3.2. Post-test counseling

Post-test counseling must be provided:
- In **all** circumstances irrespective of the test result
- In a **private** manner acceptable to the patient
- To the care giver, in the case of a patient who is a minor (see below for more details about minors undergoing testing)

The type of counseling will depend on the outcome of the test:

If the results are negative, the following issues must be covered:

1. *"Window period"*: Following a possible exposure to HIV, there is a period of up to 3 months during which the negative test result based on antibody testing cannot be relied upon as the immune system may not yet have formed HIV specific antibodies. The client could be infected with HIV, but still test antibody negative. The client should be strongly advised to repeat the test three months later to confirm the results, but ensure safer sexual practices during that period.

2. Further exposure to HIV infection can be prevented only by avoiding high-risk behavior. Issues on safer sex practices and healthy lifestyles must be covered.

If the results are positive:

1. It should be acknowledged that receiving positive results is emotionally devastating and requires intense support. Positive results may be associated with fear, sense of loss, grief, guilt, depression, denial, anxiety, anger, suicidal thinking and loss of self-esteem, etc. After hearing his or her positive diagnosis, the patient may have difficulty focusing on anything else, and may not be able to absorb other information. Post-test counseling messages (see below) should be reiterated at subsequent visits.

2. The focus of post-test counseling should be three fold:
   - Helping the person to live positively with HIV.
   - Assisting him/her in accessing available HIV and AIDS care and support services, including treatment.
   - Reducing/mitigating behaviors that put others at risk e.g., unprotected sex, continued breastfeeding, mixed feeding of infants.

It is essential that confidentiality be maintained during and after testing. Careful record keeping is essential to ensure confidentiality.

4.4 Identifying children who may be HIV positive

It is important to identify children that are HIV positive at an early stage to ensure that they and their families obtain optimal care. As the disease progresses more rapidly in children than in adults, they might be the first to be identified as HIV positive in the family.

Providers should be pro-active in efforts to detect children with HIV:

- All HIV exposed children should be identified by PMTCT records and be registered in the Care and Treatment Program. HIV exposed children should be reviewed regularly to detect any change in clinical condition and ensure ongoing cotrimoxazole preventive therapy.
- Children with severe pneumonia, severe malnutrition, chronic/persistent diarrhea and TB must be tested for HIV infection
- Children less than 14 years born to parents diagnosed with HIV infection should be tested
- Orphans and vulnerable children are at special risk of HIV infection
- All adults living with HIV should be counseled to bring <u>all</u> children for testing. Likewise, parents and siblings of children diagnosed as HIV positive should be tested

Early identification makes it possible to:

- Develop an action plan for regular follow-up and ART if required.
- Commence interventions to prevent common childhood infections.
- Approach the family to establish whether others are HIV positive and offer clinical and social support.

Providers should ask, look and feel for features of symptomatic HIV infection in all children. The following questions should be asked at every pediatric visit.

- Pneumonia now?
- Ear discharge ever?
- Low weight for age?
- Losing weight, or unsatisfactory weight gain?
- Floppy, weak or tired?
- Unable to sit up by 6 months?
- Unable to stand up by 12 months?
- Unable to say one word by 15 months?
- Ribs showing?
- Fast breathing?
- Persistent diarrhea now or in the past 3 months?
- Enlarged lymph glands in 2 or more sites?
- Oral thrush (white sores in mouth)?
- Parotid enlargement?

If 2 or more features are present, child should be referred for HIV testing.

4.5 Special circumstances regarding HIV testing

4.5.1. Minors

Rights regarding providing consent for testing

- If a child is 14 years old or older, they may give their own consent for HIV testing.
    - Any child who is married, pregnant, works as a commercial sex worker, is a street teenager, family head or with a history of sexual intercourse is regarded as a "mature (or emancipated) minor" and can consent for HIV testing.
- HIV testing for children below 14 years of age who are not included in the "mature minor" category can only be performed with the knowledge and consent of their parents or guardians.
- Exceptions:
    - If children below 14 years of age present with convincing signs or symptoms of HIV infection but the parents or guardians refuse to consent to the test, the Department of Social Welfare should be contacted to facilitate testing. Every effort should be made to explain to the parents or guardians the necessity and benefit of knowing the child's HIV status.
    - Children who have been sexually abused and put at risk of HIV infection shall receive adequate counseling, be encouraged to test for HIV infection, and assisted in accessing appropriate care and treatment services. At the discretion of the health care provider, parents or guardians should be asked for their consent prior to testing.

Right to defer request for testing of a minor

The counselor or health care provider has the right to refuse a request for testing if he/she believes that the result is not being obtained with the best interest of the child in mind. Examples may include test requests linked to child adoption or testing of orphans in residential institutions.

Disclosure

Minors should be encouraged to disclose the result of HIV testing to their parents or guardians. However, the test result shall not be disclosed to third parties, unless the counselor or health care provider determines this to be to the benefit of the child. See **Section 6:** Counseling: adherence and disclosure for further details.

Increasing opportunities for VCT

Youth friendly VCT services shall be made widely available to adolescents and young adults.

4.5.2. Medical emergencies

In the event that a patient is unable to give his/her consent (e.g., unconscious or acute confusional state):

- Non-consensual HIV testing of patients who are too unwell should be undertaken only in a situation where there is doubt about the diagnosis or if there is evidence of chronic dementia or where results of a HIV test will change the management of the patient.
- Treatment should be initiated for any suspected OI where there is evidence of immunosuppression and a diagnosis of HIV is strongly suspected. When the patient is sufficiently recovered to give consent, counseling and testing should be performed as per usual.

In the event of an occupational exposure of a health care worker, if the source patient cannot give his/her consent to testing, an HIV test can be performed. (Refer to **Section 22**: Post-Exposure Prophylaxis for more information).

In both of these situations, the clinician must be the only person to decide whether an HIV test will be performed on the patient and results must not be disclosed to relatives. Consent should not be sought from relatives with the exception of a situation when a minor's health is at risk. **All patients must receive post-test counseling** at the first appropriate opportunity.

4.6 Importance of differentiating HIV-1 vs HIV-2

The majority of HIV infections in Liberia are likely due to HIV-1; however, HIV-2 is endemic in many West African countries. Testing algorithms have been developed to differentiate HIV-1 vs. HIV-2 infection and treatment recommendations are provided for both HIV-1 and HIV-2.

It is essential to determine the type of HIV infection (HIV-1, HIV-2, or HIV-1/HIV-2 coinfection) for each patient. This information should be recorded clearly in the patient record. Different medicines are needed to treat different types of HIV.

4.7 Testing algorithm for HIV in adults and children over 18 months

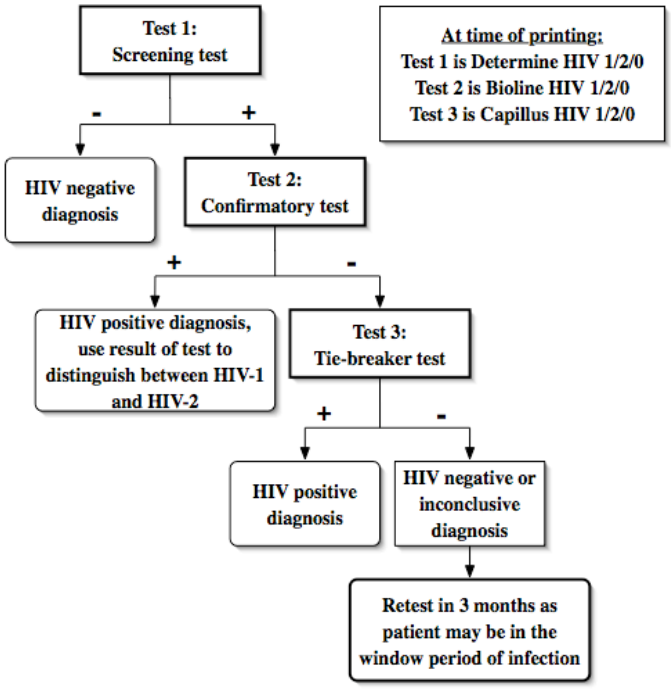
The detection of antibodies to HIV is the method of choice for diagnosis of HIV infection in adults and children over 18 months of age. **An individual over 18 months of age may be diagnosed as HIV positive if HIV antibodies are detected by one rapid test followed by a second confirmatory test**. Testing should proceed as outlined in Figure 4.1.

The first test is used to detect antibodies to both HIV-1 and HIV-2. If it is positive, a second test should be done to confirm seropositivity and to distinguish HIV-1 infection from HIV-2 infection. If Test 1 and Test 2 give different results, a third test should be performed.

Special notes on testing:

- Patients with negative or inconclusive test results should be encouraged to return and be re-tested 3 months later. They might be in the "window period" of early infection. Antibodies cannot be detected during this time.
- Ongoing inconclusive tests (1 positive, 2 negative) are likely biologically false positives and do not need to be treated for HIV.
- Where the health care provider cannot conclusively determine the serostatus of a patient, a reference assay such as an ELISA test or PCR should be conducted, if available. Arrangements should be made through the NACP.

Figure 4.1 Algorithm for diagnosis of HIV-1 and HIV-2 infections in: 1) adults, 2) children >18 months of age (or three months after completed breastfeeding), or 3) children <18 months of age if PCR not available



Note: Bioline test should be read at 10 minutes. If read more than 15 minutes after blood sample was deposited on the test, frequent errors may occur, such as the false positive diagnosis of HIV negative individuals.

4.8 Testing algorithm for HIV in infants and children less than 18 months (or who completed breastfeeding less than 3 months previously)

All infants who were born to HIV positive mothers (regardless of PMTCT regimen) need special attention during the first two years of life. Once they are approximately 6 weeks old, providers should consider testing them for HIV infection. At that time, all HIV exposed infants should be prescribed cotrimoxazole.

Testing HIV-exposed infants is complicated because maternal HIV antibody is transferred passively to the infant during pregnancy and breastfeeding—its presence does not mean that the infant is necessarily infected with the virus. The maternal antibody can remain in the infant's blood for as long as 18 months. Until then, the uninfected infant may falsely test positive on an antibody test. Infants and children remain at risk of acquiring HIV infection throughout the breastfeeding period. Thus, while a negative HIV test in the infant of a HIV positive mother at 18 months is usually confirmation that the infant is NOT infected, this is not the case if the infant is breastfeeding at the time of the test, or if breastfeeding was stopped less than 3 months before the time of testing.

4.8.1. Virological testing (PCR) available

Definitive diagnosis of HIV infection in children less than 18 months requires use of virological assays that detect the virus or its components. Liberia will be introducing dried blood spot testing (DBS) to facilitate use of a virological testing method called polymerase chain reaction (PCR) (see Testing Algorithm in **Figure 4.2**).

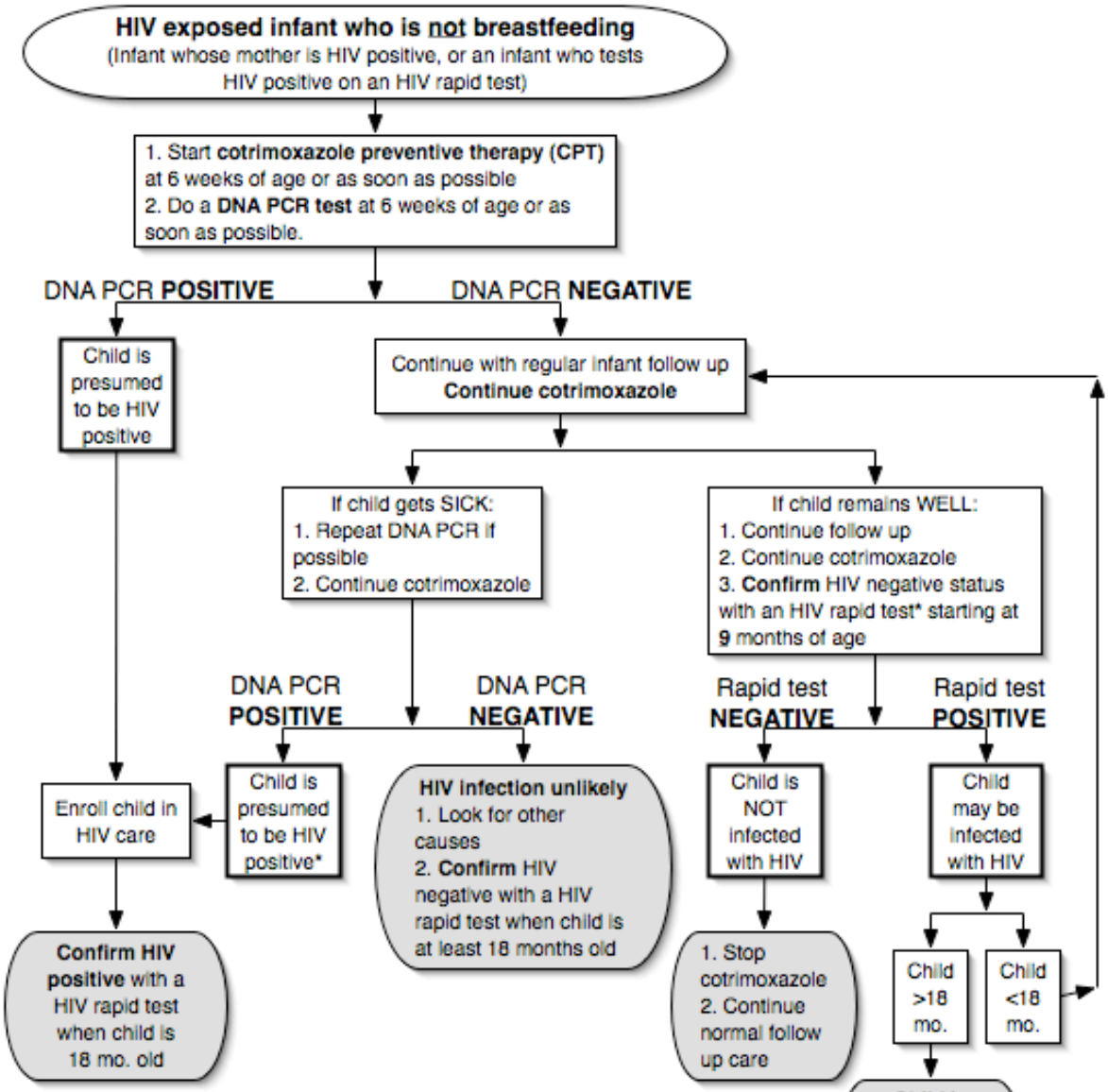
The first virological test should be conducted at approximately 6 weeks after birth. If a child is breastfeeding a negative virological test does *not* rule out HIV infection. Infants who are HIV negative on an initial PCR test should undergo repeat virological testing:

1. If they ever present with signs of HIV
2. At least 6 weeks after the complete cessation of breastfeeding

Note that if the infant is more than 9 months old and has not breastfed for at least 3 months, antibody testing can be performed. This situation is discussed in the following section.

If virological testing is not available and the provider is concerned about HIV infection in the infant, the child should be referred for further assessment.
(See Section 7.4)

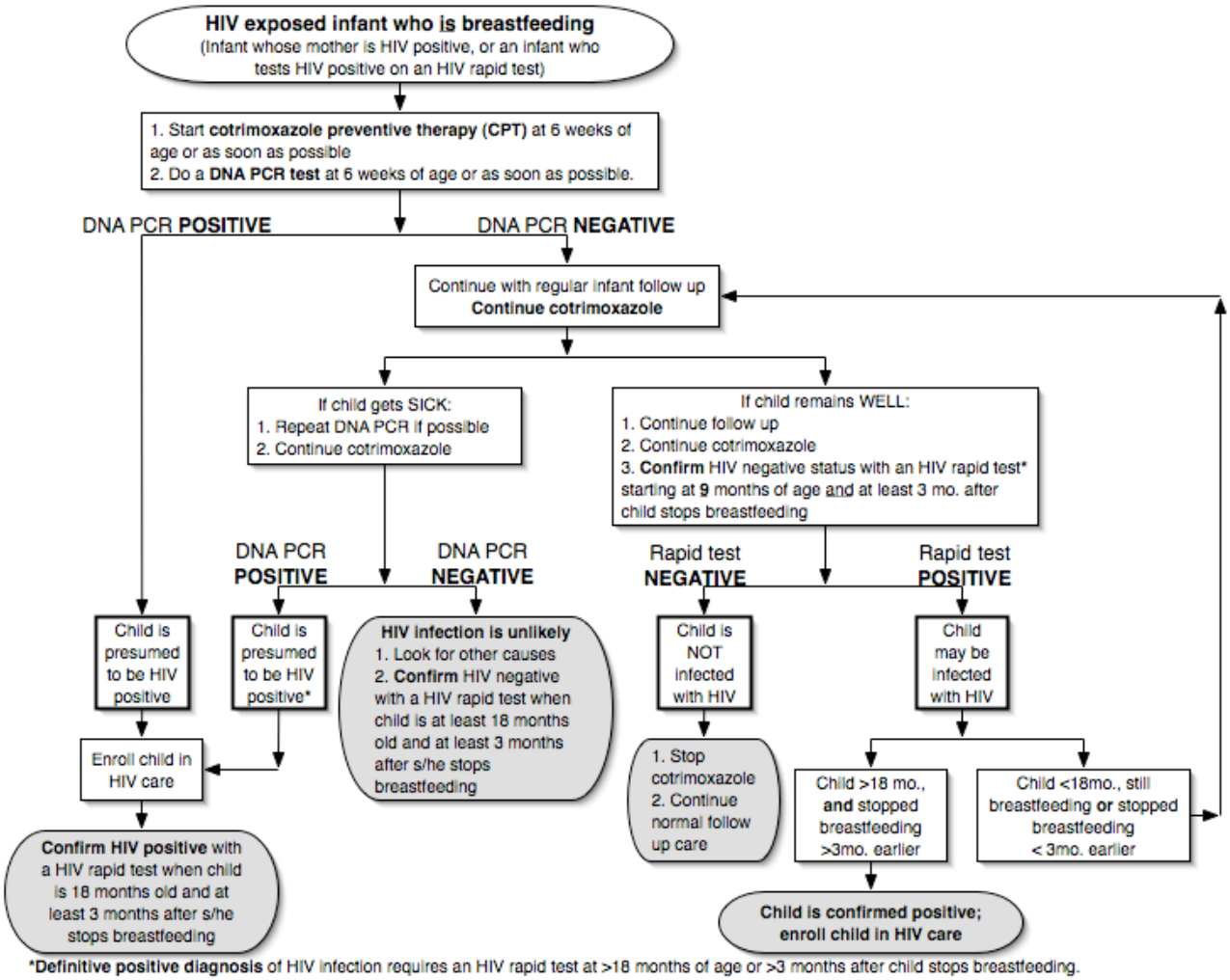
Figure 4.2 Testing algorithm where PCR testing available for HIV exposed infants and children less than 18 months who are <u>not</u> breastfeeding or who <u>stopped</u> breastfeeding >3 months previously



Note:
Definitive positive diagnosis of HIV infection requires an HIV rapid test at >18 months of age or >3 months after child stops breastfeeding.

Definitive negative diagnosis requires either:
1. a series of 2 negative DNA PCR tests, at least 6 weeks apart (with the 1st one 6 weeks after child stops breastfeeding) **or**
2. a negative antibody test after 9 months of age **and** at least 3 months after child stops breastfeeding

Figure 4.3 Testing algorithm where PCR testing available for HIV exposed infants and children less than 18 months who are breastfeeding or who stopped breastfeeding < 3 months previously



*Definitive positive diagnosis of HIV infection requires an HIV rapid test at >18 months of age or >3 months after child stops breastfeeding.

Definitive negative diagnosis requires either:
1. a series of 2 negative DNA PCR tests, at least 6 weeks apart (with the 1st one 6 weeks after child stops breastfeeding) **or**
2. a negative antibody test after 9 months of age **and** at least 3 months after child stops breastfeeding

4.8.2. Testing when virological (PCR) testing unavailable

Antibody testing cannot be used to make a *definitive* diagnosis of HIV in children less than 18 months of age. However, since the value of the test depends on how quickly maternal antibody levels decline in infants, it *may* be useful to use the antibody tests in infants as young as 9 months of age. Most uninfected infants will have lost maternal antibodies by this age, and a negative result can *exclude HIV infection* provided the infant ceased breastfeeding at least three months earlier.

Where virological testing is unavailable, presumptive severe HIV diagnosis may be made in an HIV antibody-positive child < 18 months who is symptomatic with 2 or more of the following:

- Oral candidiasis (thrush)
- Severe pneumonia requiring oxygen
- Severe wasting/malnutrition
- Severe sepsis requiring injectable antibiotics

4.8.3. Confirmatory testing for infants

<u>Confirmation of diagnosis is NOT required prior to starting ART in symptomatic children less than 18 months.</u> See Section 7.4.

If a child is diagnosed with HIV infection on the basis of one virological or antibody test—a confirmatory HIV antibody test should be performed when the child is at least 18 months of age and has discontinued breastfeeding for 3 months (see testing algorithm in **Figure 4.1**). If a child is confirmed to be HIV negative, the cotrimoxazole started at the age of 6 weeks can be stopped.

Table 4.1 Summary of laboratory diagnosis of HIV infection for all patients

Age	Definitive HIV diagnosis **positive** as follows:	Definitive HIV diagnosis **negative** as follows:
Adults and children > 18 months (and at least 3 months after cessation of breastfeeding) – See **Fig. 4.1**	Positive HIV antibody tests as per Testing Algorithm	Negative HIV antibody tests as per Testing Algorithm (although to be sure, testing should be repeated in 3 months)
Children < 18 months where virological testing is available – See **Fig. 4.2** or **4.3**, depending on whether child is breastfeeding	1) Positive HIV **virological** (PCR) test after the age of 6 weeks 2) Confirmatory positive **antibody** test after the child is >18 months	1) Negative HIV **virological** (PCR) test after the age of 6 weeks 2) Negative HIV **antibody** test after the child is >9 months and at least 3 months after cessation of breastfeeding
Children < 18 months where virological testing is not available	Cannot have definitive positive test until child is > 18 months. Follow antibody testing algorithm per adult guidelines when child is >18 mo.	Negative **antibody** test after the child is > 9 months and at least 3 months after cessation of breastfeeding

SECTION 5: Patient enrollment into the Care and Treatment Program

5. Patient enrollment into the Care and Treatment Program

All patients who test HIV positive should be **immediately** referred to an evaluating clinician associated with the Care and Treatment Program. All patients who enter the Care and Treatment Program should receive a unique ID number at their first visit and should be recorded in the pre-ART register. (If previously on ART and transferred from another facility, they should be given a chart with their old unique ID and recorded in the ART register).

The initial visit should focus on determining the patient's eligibility for ART and Cotrimoxazole Preventive Therapy (CPT).

5.1 First visit

All patients should be seen by 1) a counselor and 2) a clinician. A HIV Patient Care and Treatment Record should be filled out at the first visit, and updated at each subsequent follow-up visit.

The counselor will discuss:

- Registration and issuance of individualized patient identification number
- Basics of HIV and ART
- Positive living (see **Section 10)**
- Importance of adherence to clinic visits, medication, and positive living (see **Section 6** for further details)
- See **Appendix 4** for further detail

The clinician will perform:

- Complete physical and WHO clinical staging (see **Section 7**), including all questions in the Symptom Checklist (see **Table 5.1** below)
- Baseline laboratory tests (including CD4 and TLC if available, see **Table 8.1**)
- Cotrimoxazole prophylaxis, if necessary (see **Section 9**)
- Assessment and treatment of OIs, including TB (see **Section 19**, and **Appendices 13** and **14**)
- See **Appendix 4** for further detail

Ongoing counseling and patient preparation for life-long therapy **should be reinforced at every opportunity** by all members of the Care and Treatment Program. Adherence counseling is essential even if a patient is not yet eligible for ART.

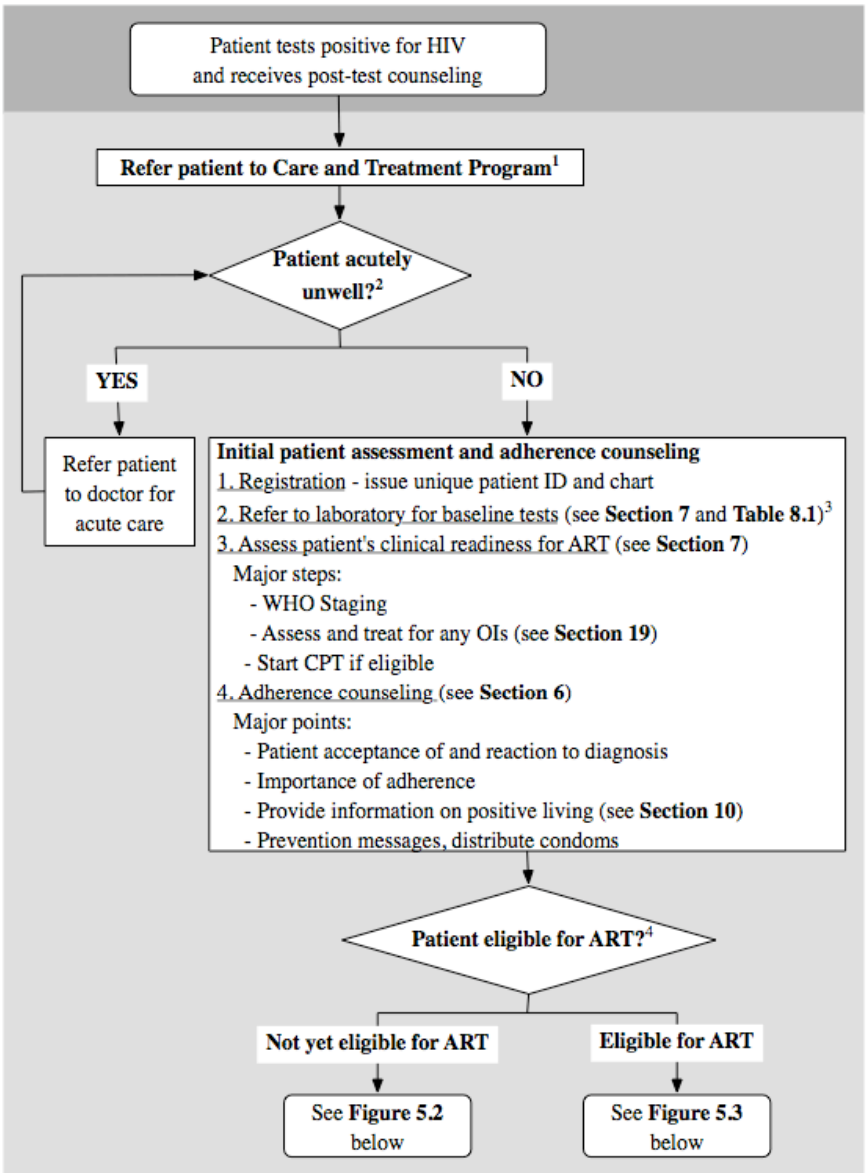
5.2 Patient follow up visits

The appropriate follow up plan should be designed based on patient's eligibility for ART (see **Figures 5.1, 5.2** and **5.3** below, **Appendix 4**, Schedule of actions for patient visits and **Section 7**, Patient assessment for treatment, for further details).

- If patient is not yet eligible for ART:
    - Schedule follow up at 2 weeks and then 4 weeks after initial visit if beginning cotrimoxazole preventive therapy (CPT). See **Figure 5.2**

below. More thorough follow up should be done every 3 months as described in **Section 8**. Also see **Section 9** for more details.
    - Schedule follow up visit for 3 months if patient is not eligible for either ART or CPT (or sooner as necessary, see **Section 8** for more details.)
- If patient is eligible for ART, proceed with Pre-ART visit 2 and ART visits as described in **Figure 5.3** below and **Appendix 4**.
- **Note:** patients not yet eligible for ART may come to the Care and Treatment Program with acute medical conditions. They should **always** be evaluated and staged to determine eligibility for CPT and ART.

Figure 5.1 Initial patient visit schedule



[1]Patients referred from other facilities should provide proof of positive HIV test, or a confirmatory test should be performed.

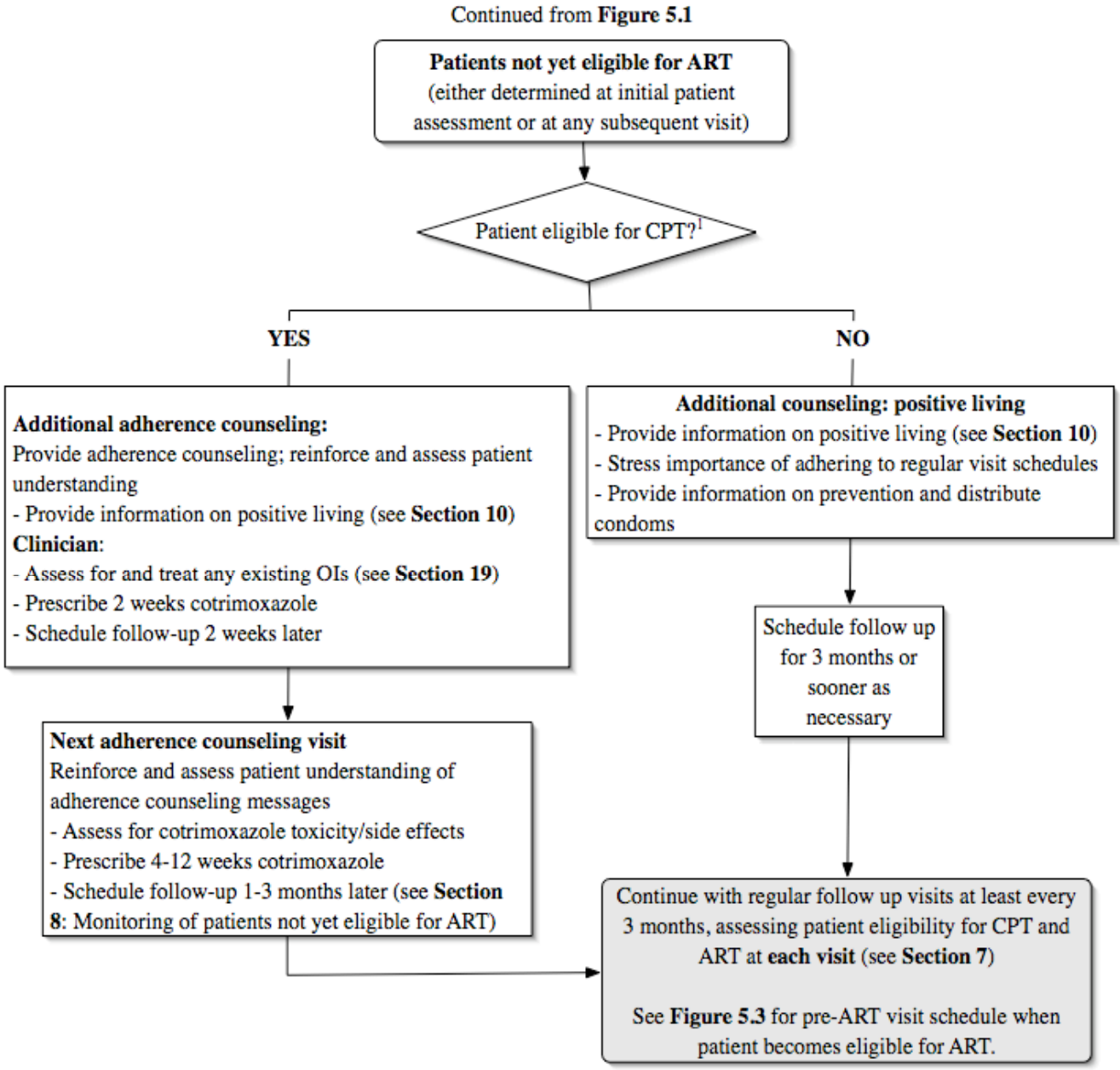
[2]In this case, patient will be registered and undergo laboratory testing and assessment as needed for his/her condition

[3]When lab tests are available on the same day, results can be used to assess patient eligibility for ART. If not possible, lab tests should be reviewed at the nxt visit.

[4]If patient is WHO stage 3 or 4 they are eligible for ART regardless of CD4 count. If patient is WHO stage 2, review lab tests before determining patient's eligibility for ART.

Also refer to **Appendix 4**: Schedule of actions for patient visits, for further details of each adherence counseling and pre-ART visit.

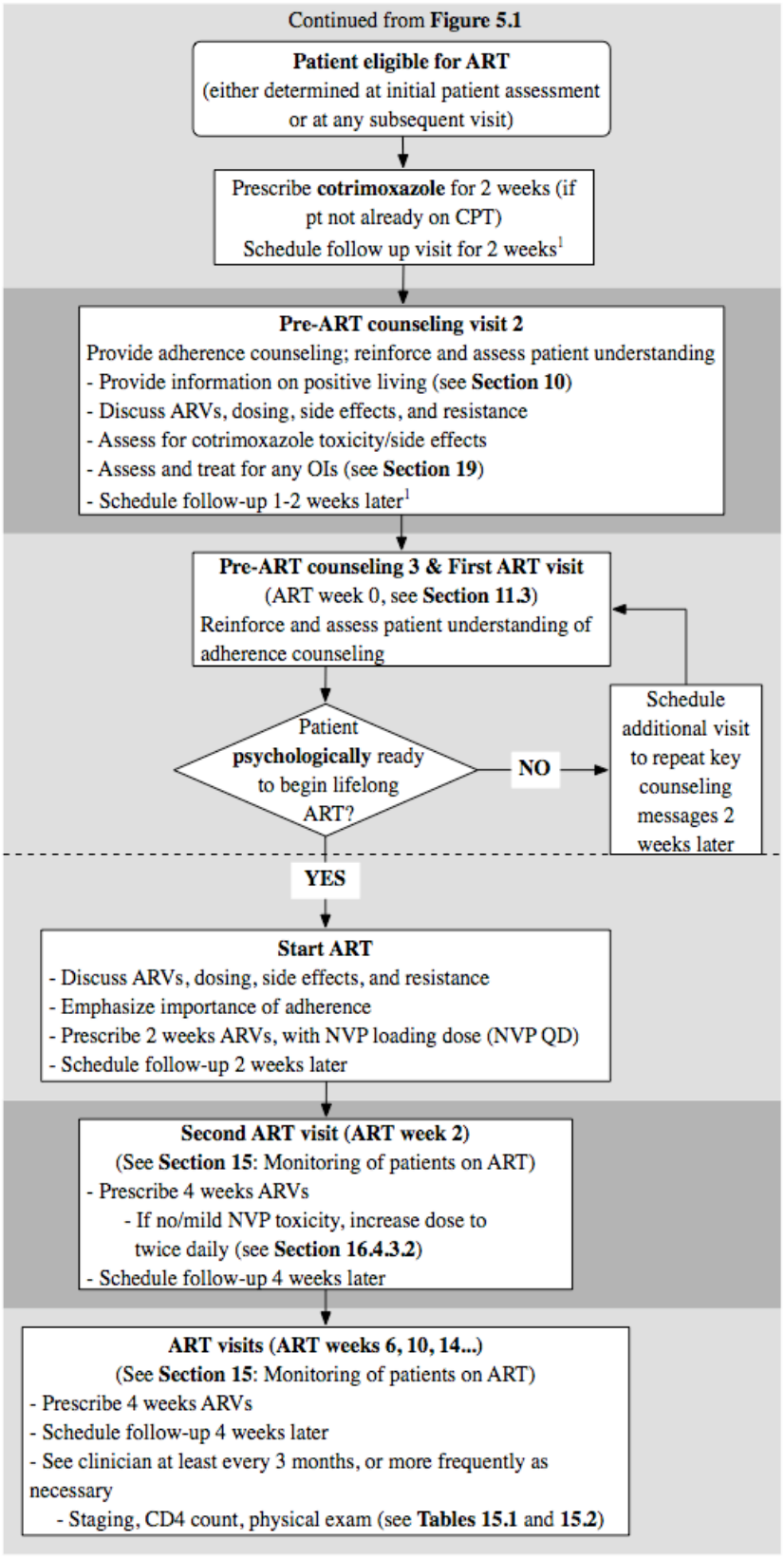
Figure 5.2 Visit schedule for HIV positive patients not yet eligible for ART



[1]All patients who are WHO stage 2, 3, or 4 are eligible for CPT. When in doubt, start patients on CPT.

Also refer to **Appendix 4**: Schedule of actions for patient visits, for further details on each adherence counseling and pre-ART visit.

Figure 5.3 Visit schedule for HIV positive patients eligible for ART



[1]If patient has been enrolled in Care and Treatment Program for an extended period of time before s/he becomes eligible for ART, the number and timing of pre-ART adherence counseling visits may be adjusted at the clinician and counselor's discretion.
Also refer to **Appendix 4**: Schedule of actions for patient visits, for further details of each adherence counseling and pre-ART visit.

SECTION 6: HIV Counseling: adherence and disclosure

6. HIV Counseling: adherence and disclosure

The main objectives of counseling in the context of HIV are:

- To assist the client to cope with their HIV status at the time of testing;
- To promote adherence once the patient is considered eligible to commence therapy;
- To educate the patient in preventing transmission of HIV to others;
- To minimize the risk of additional exposure to or reinfection by HIV.

The essential features of counseling include creating the environment for acceptance by the client, providing time to absorb news about the diagnosis of HIV, and allowing the client to react and express concerns. For additional summary information on pre- and post-test counseling and VCT and PICT, see **Section 4.2**. The information included in these guidelines is intended to be only an overview; for more detailed information on HIV Counseling and Testing, please refer to national Counseling and Testing guidelines.

6.1 Adherence

The importance of strict adherence to clinician appointments and to treatment with ARV drugs is essential. Near perfect pill taking is required to achieve maximal viral suppression – anything less than this leads rapidly to the development of viral resistance and hence, to much earlier treatment failure.

Adherence is a complex health behavior that is influenced by the regimen prescribed, patient factors, and characteristics of healthcare providers. Adherence support should begin before therapy is initiated and must be incorporated into every clinic visit.

6.1.1. Adherence counseling

Educating patients effectively and assessing their understanding can be very time consuming and labor intensive, but it is never time wasted. Counseling on HIV and the importance of adherence to care and treatment should begin on the first patient visit and should be reinforced during all visits by all members of the HIV focal team. It should be stressed that adherence is essential to not only ART but to clinic appointments, non-ART medications such as CPT, and healthy living.

Patients must be aware that ARV treatment is a life-long commitment. A person who takes ARV drugs erratically will not only receive minimal benefit, but also will still suffer the side effects and potentially limit his future treatment options. It is important that all patients demonstrate an understanding of these concepts before starting treatment. A patient who stops taking ARV drugs will rapidly lose any benefit he may have received. His increased immunity will disappear as the virus flourishes and CD4 cells are destroyed.

ARV providers that do not seriously address the complex issue of adherence <u>will fail</u> in their objective of helping their patients, and on a public health level they will cause the development of multi-drug resistant strains of HIV within the population they serve.

Adherence counseling is <u>not</u> only for patients who are eligible for ART. Every HIV positive patient should receive extensive adherence counseling (see **Figure 5.1**, Patient visit schedules and **Appendix 4**, Schedule of actions for patient visits, for details).

6.1.2. General measures to increase patients' readiness and adherence

- Don't rush into starting ARV drugs. Wait until a patient has shown that they are able to keep a number of appointments at the clinic, including adherence counseling sessions.
- All patients should have at least 2-3 adherence counseling sessions prior to starting ART. Each of these sessions should be at least one week apart (see **Figure 5.1** and **Appendix 4**). Issues to be discussed are outlined below. It may be practical for centers to develop their own tool (questionnaire) to be used to document patients' level of comprehension at each of these sessions. ART should not be started without documentation of readiness by the adherence counselor. (See **Appendix 4:** Schedule of actions during patient visits, which includes key messages for each counseling session.)
- Ensure the same adherence messages are given by all health workers. Even brief reinforcement of these messages at every clinic visit is recommended.
- Keep an organized appointments record. Without this the providers will be unaware of patients missing appointments, and hence not picking up drugs. See **Section 5**, Patient enrollment in Care and Treatment Programs, for details. If a patient defaults from a clinic visit, every effort should be made to contact them.

6.1.3. Key counseling messages

- ARVs are not a cure. HIV may be suppressed but is not eradicated from the body.
- The use of ARVs is associated with improved quality of life and long survival.
- ARVs should **not** be discontinued when the patient's clinical condition improves.
- ARVs should be taken daily **for life** to prevent development of resistance and treatment failure. The relationship between adherence and resistance should be well understood by the patient.
- Regular attendance at the clinic and adherence of at least 95% to all drugs in treatment regimen is essential to achieve good results.
- Disclosure to a trusted friend or relative improves adherence. Ideally a household member should accompany the patient to clinic appointments and help to support adherence to treatment on a daily basis. However, lack of disclosure should **not** be used to delay ART initiation.
- ARVs, like any other medication, are associated with side effects. Not all patients will experience them. If the side effects occur, it does not always mean that the medicines need to be changed. Patients/treatment supporters should be made aware of which side effects require immediate medical attention. For example, the knowledge that headaches and nausea are common, and that they will improve with time, can help patients to continue taking their ARVs.
- Symptoms of IRIS or drug toxicities should be discussed. The counsellor should be informed of the proposed regimen by the clinician prior to commencing adherence counselling so as to correctly inform the patient of likely side effects.

- ARVs interact with other medications. The patient should discuss non-prescribed drug intake (including traditional medicines) with the physician before taking them.
- Strategies to aid adherence (see below, "Patient-initiated adherence tools,") should be discussed with the patient and a concrete plan should be formed which is tailored to the individual's lifestyle.
- Patients should be shown samples of the drugs which they will be taking and asked to demonstrate which pills to take and when.
- HIV is a family disease. Patients should be encouraged to bring their partners and children in for testing.
- Practicing safer sex is important to prevent the reinfection of the patient and the new transmission of HIV to others. Condoms should be provided to all patients who may participate in sexual activity.

These issues should be thoroughly discussed by the counselor and any health worker who is directly involved with the patient. They should also be repeated during follow-up visits and whenever an opportunity arises. (See **Appendix 4** for details.)

At every visit, the provider should ensure that the patient has access to:

- Simple written information: Give written information to all patients who can read, or who have a friend/relative supporting them who is literate.
- Group sessions: Patients can be educated and counseled together, both before starting ARV drugs and as part of ongoing adherence support—this can be a very time efficient strategy.
- Patient support groups: Advise patient on community support groups and facilitate contact with them.
- Patient initiated adherence tools:
  - "Adherence calendars": Calendar sheets may be useful for patients as they can check each day when they have effectively taken their pills. This sheet is also a good indicator of patients' understanding on how to take the pills and if they have missed any. For illiterate patients, special signs and colors should be used to identify the drugs.
  - Other adherence strategies: Examples include pill cues (e.g. put tablets next to toothbrush if you brush your teeth twice a day) or an alarm clock, watch or phone.

Other important issues to discuss with patients that will help them develop a practical approach to treatment:

- Travel arrangements to and from the clinic: Determine how much the patient will pay for transportation and if it is sustainable. Consider the option of a facility nearer to the patient's home if it offers ART.
- Direct and indirect costs: Consider costs of treatment such as laboratory investigations, travel, time away from work. Help the patient be realistic about their ability to afford treatment so that they can plan appropriately.
- Review home, work or school situation: Ensure that these situations permit adherence. Address any barriers to adherence, including pill storage and safety from violence.

6.1.4. Methods of assessing adherence

Adherence assessment should be combined with adherence counseling at each visit. The idea is to identify those patients who are having the most difficulty with adhering to treatment so that they can be offered extra assistance.

- Self-Report: This is the simplest method, and most widely used. Patients are asked to report their own adherence—however, if used incorrectly it can be very inaccurate and will usually result in an overestimation of the level of adherence. For example, a patient who is asked: "***Do you forget to take your tablets?***" will likely answer "***No***". Questions need to be asked in a non-judgmental way in order to increase the accuracy of this method. For example: "***Many people find it hard to remember to take every single dose—when was the last time you missed a dose?***" You can also ask: "***What things can make it hard for you to remember your tablets?***" A trusting and supportive patient-provider relationship is vital to enable the assessment of adherence.
- Pill Counts: This method requires the health worker to count the number of pills remaining in the bottle or box. He or she then compares it to the number of pills that should be left if the patient took every dose since the last visit. Counting the pills is quick and easy, but is useless unless the health worker also calculates the "correct" number (the number of pills that should be left). This can be facilitated if the patient receives a defined and constant number of drugs each month.

  If done well, pill counting can help to reassure the provider that adherence is good, or identify those patients that need extra support. However, if it is approached insensitively, it can promote a relationship of distrust between the patient and provider. Be careful not to encourage situations in which patients may be tempted to "dump" missed pills prior to the visit.
- Clinical and biological markers: The development of new OI after a period of good immunity or a declining CD4 count (if the test is available) should alert the clinician to the possibility of poor adherence. Changing to a second line regimen will achieve nothing if the underlying cause of treatment failure is not addressed.

6.1.5. Preparation and practice to assist children and families

- Assess family's readiness for therapy
- Discuss medications
  - Who will administer the medications?
  - What medications will be given, what do they taste like?
  - When and how frequently will the medication be taken?
  - How will the medication schedule fit into school routine and caregiver's work schedule?
  - How will the medication be given?
  - How will the medications be stored?
- Practice taking medications
  - Taste testing
  - Observation of dosing, particularly for liquids
  - Training for pill swallowing
  - Behavioral reward system
  - Role play

6.1.6. Improving poor adherence

If adherence is found to be poor, every effort **must** be made to improve it.

- Re-educate patient and caregiver about importance of adherence and explain what happens if the patient does not take his/her ARVs more than 95% of the time (the medicines won't work for you as long, and the next regimen has many more pills and side effects).
- Clinicians should ask patients what further support the clinic could provide. Every effort should be made to meet patient needs.
- Evaluate appropriateness of support structures.
- Address medication-related issues.
- Use adherence support tools (above).
- Check family situation with social worker.
- Arrange home visits by a counselor and/or a social worker.
- Check for competing religious and cultural practices.
- Consider DOT. Identify and trace defaulters (use clinic appointment books, CHWs and lay counselors to help track and phone calls/ home visits).

6.2 Disclosure

All patients should be counseled and strongly encouraged to disclose their HIV status to a friend or relative prior to initiating ART. Disclosure will facilitate ongoing emotional support and good adherence for the patient, which can be essential to ensure good outcomes. Disclosure is a sensitive issue and will require special counseling that addresses the following issues:

- Disclosure to a friend or family member (a "treatment buddy") who can assist the patient in caring for him or herself may be crucial in ensuring adherence and in providing emotional support.
- Discuss the importance of disclosure to partners who may be at risk of continued exposure to HIV.
- Alert the patient to the existence of Partner Counseling and Testing services.
- Disclosure to third parties (e.g. employers or school staff) can help support good adherence to care and treatment. However, these situations should be approached very carefully by the patient/caregiver because it is essential to ensure confidentiality and non-discrimination.
- Identify an HIV positive peer that the patient could speak with and get advice.

6.2.1. The special situation of adolescents

Adolescents who are sexually active may acquire HIV infection and present for testing and care. The provider will often face a dilemma about when and how the parents or guardians should be informed. The problem is worse when the child does not want to disclose to parents/guardians but would like to benefit from ART. In view of the complicated nature of ART and the need for family support to maintain good adherence, it is recommended that:

- Every effort should be made by the counselor to discuss with the adolescent the need to involve the parents/guardians.
- Additional counseling time should be given to the adolescent to allow for deep understanding of the implications of ART.

Identification of a friend or relative as a treatment buddy should be strongly recommended prior to initiation of ART.

6.2.2. Special considerations for disclosure to children

Disclosing information to children improves management outcome. However, it is a sensitive issue which must consider both the needs, feelings, beliefs of the child and those of the parent(s)/guardians.

Disclosure of the child's HIV status is difficult for parents due to:

- Fear of impact of disclosure on child's psychological status and emotional health
- Fear of inadvertent disclosure to others by child
- Attempt to protect child from social rejection and stigma
- Guilt about the mode of transmission
- Difficulty coping with their own illness and those of their loved ones
- Established coping strategies within families (i.e. traditional silence around illness and disease, limited communication within families and denial as coping strategy)
- Belief that the child will not understand

Reasons to encourage disclosure:

- Opportunity to explain the facts about their illness and to dispel children's misconceptions about HIV
- Improvement of access to care and support services
- Enhancement of adherence to treatment and coping strategies
- Reduction of the negative psychosocial impacts of the disease

When and how to disclose to a child

Disclosure is more than revealing HIV status. It also involves an ongoing discussion of health and health-related issues. Ideally, status should be disclosed by the parents/guardians. They should begin the process as early as possible and continue discussion with the child about the condition and related issues. Simple explanation of the nature of HIV for younger children and disclosure about nature and consequences for older children is recommended. When to use the words "HIV" and "AIDS" will vary according to the needs of the child and family.

The child could be allowed to guide the discussion at the time of disclosure. The discussion should be tailored according to child's age, cognitive development, level of maturity, coping skills and the child's health status (a terminally ill child may benefit from discussion about death rather than specific diagnosis). Tools and language used may vary for different developmental capacities e.g., drawing, storytelling, play, and/or drama. Health care providers should provide the necessary support, including materials for the disclosure process.

Assisting families with disclosure

In preparing to disclose HIV status to a child, it is important for parents/caregivers to be able to explain HIV infection and handle the related questions and responses. Parents/caregivers must choose who needs to be there, what will be said, an appropriate place and time of disclosure and the plans after disclosure. Issues of disclosure to peers and others must also be addressed. A role for support groups and further on-going counseling should be outlined.

Table 6.1 Assessing readiness for disclosure to a child

Assessing readiness
The child • Is the child symptomatic? Taking medications? • How old is the child? • Is the child living with a sick parent or family member? • Is the child asking questions about HIV? • Does the child appear distressed, anxious or worried? • Is the child sexually active and at risk of contracting or spreading HIV?
The parent or caregiver • Has the parent or caregiver been tested for HIV? • Is the parent or caregiver HIV positive? Symptomatic/Taking medication? • Is the adult ill, is s/he in need of help from children in the household? • Is the HIV positive adult an important attachment figure for the child?
The family or household • Are there any adults in the household with HIV infection? Who is aware? • Are other children in the household HIV positive? Who is aware? • How many family members are taking HIV-related medications? • Is the family unit cohesive, or characterized by separations and/or conflicts?
The community • Are testing and treatment generally available in the community? • Are there people in the community who are open about their own HIV status? Does the child know anyone in the community who is open about his/her HIV status? • How strong is the stigma surrounding HIV in the community? • Are there risks to the family (isolation, discrimination) if inadvertent disclosure occurs? • Are there resources within the community for children – a youth group and or trusted adults they can talk to?

6.2.3. Planning for disclosure to a child

Disclosure is not an event or a one-time conversation. It is a process that takes time and constant communication in an age appropriate manner. Once the decision has been made to disclose to the child, it is important to understand that the topic will have to be visited repeatedly. It is important to give a clear message, listen actively, take cues from the child and avoid lecturing. The emphasis should be on asking and listening. The following examples can serve as a guide.

Preschooler (4-6 years old):
Younger children who are symptomatic often want to know what will happen to them. They do not necessarily need to be informed of their diagnosis, but the illness must be discussed with them. They may feel responsible for the parent's illness or just pretend nothing happened. It is important to give reassurance and take cues from younger children.

School aged children (7-13 years old):
Some may have difficulty coping with disclosure information, which can lead to changes in behavior (acting out in school, anger, crying fits, and/or no expression of emotion). Others may have concerns that other children in the school or community

will make fun of them. Encourage them to ask questions; do not be disappointed if they do not react in the manner you expect.

Adolescents (14 years and older):
Adolescents should know of their HIV status. They should be fully informed of the consequences of their status in order to appreciate its impact on many aspects of their health, including sexual behavior and treatment decisions. Be supportive and non judgmental.

Table 6.2 Preparing parent or guardian for disclosure

Preparation • Why disclose now? • What do you want to communicate to your child? • What will be the most difficult questions for you to answer when your child knows his/her HIV status? • How will this information affect the relationship between us? Acknowledge the difficulty of disclosure and affirm motivation to begin process.
Education • How to explain HIV transmission to a child • Anticipate questions and responses from child • Post disclosure expectations
Planning • When and where? • Who will be there? • What will you say? • Plans after disclosure
Follow-up • School and family functioning • Monitor medical treatment adherence • Disclosure to peers and others • Support groups/Counselling • Continue to reinforce the positives

SECTION 7: Patient assessment for treatment

7. Patient assessment for treatment

The process of initiating ART involves assessing patient readiness to commence therapy and an understanding of its implications (lifelong therapy, adherence, toxicities). Access to nutritional and psychosocial support and to family/peer support groups is important when decisions are being made about the initiation of ART. If health care providers are ever in doubt about a patient's readiness to start ART, treatment initiation should be deferred and more counseling should be provided.

For patients who are psychologically ready to start treatment:

- The best time to start ART is before patients become unwell or present with their first opportunistic infection.
- Laboratory parameters (CD4 counts) are the most useful marker of determining when to start ART. Clinical signs of severe HIV disease, however, are in themselves indications to start ART **even when laboratory criteria are not met.**
- Situations in which CD4 testing is and is not available are discussed below.

7.1 Initial clinical assessment of HIV positive adults, adolescents and infants: WHO clinical staging

Providers should conduct a thorough history and physical examination to exclude opportunistic conditions and to allow correct determination of WHO clinical staging. This should include the following:

- Assessment of symptoms and signs of OIs, TB and STIs
- Illnesses, especially those requiring hospitalization
- Other conditions: especially histories of Hepatitis B, injection drug use, alcohol abuse or psychiatric illness
- Medication history: previous use of ARV drugs (including ARV drugs for PEP or PMTCT interventions in women or children), as well as any other traditional or western medication
- In women, pregnancy status and the risk of pregnancy and reproductive plans
- For children, use growth chart to assess growth, development & immunization status; determine breastfeeding status
- Full physical examination: including height, weight, examination of skin and documentation of any pre-existing peripheral neuropathy

7.2 The importance of clinical staging

Clinical staging is intended for use where HIV infection has been confirmed by HIV antibody testing and it should be included in the baseline assessment (first visit) on entry into a care and treatment program for all adults and children. Clinical staging is used to guide decisions on:

- When to start co-trimoxazole prophylaxis
- When to start ART
- When to switch ART in situations where CD4 testing is not available or results are delayed

Clinical staging should be assessed at each patient visit (see below for staging, and **Appendix 4**: Schedule of actions for patient visits, for visit schedule).

Although ART improves the patient's clinical status, clinical staging is less useful in monitoring the efficacy of ART, defining treatment failure and determining when to switch ART. CD4 count is a better indicator in these situations.

7.3 Recommendations for initiating ART in adults and adolescents

7.3.1. Clinical staging

The WHO revised clinical staging for adults and adolescents provides details of the specific staging events and the criteria for recognizing them in adults and adolescents (see **Appendix 1**). Clinical staging should always be used in deciding whether to start ART.

Table 7.1 WHO clinical staging of HIV in adults and adolescents

CLINICAL STAGE 1 - ASYMPTOMATIC
Asymptomatic
Persistent generalized lymphadenopathy
CLINICAL STAGE 2 - MILD SYMPTOMS
Unexplained moderate weight loss (<10% of presumed or measured body weight)[a]
Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media and pharyngitis)
Herpes zoster
Angular cheilitis
Recurrent oral ulcerations
Papular pruritic eruptions
Seborrheic dermatitis
Fungal nail infections
CLINICAL STAGE 3 - ADVANCED SYMPTOMS
Unexplained severe weight loss (>10% of presumed or measured body weight)[a]
Unexplained chronic diarrhea for longer than one month[a]
Unexplained persistent fever (above 37.5°C intermittent or constant, for longer than one month)
Persistent oral candidiasis
Oral hairy leukoplakia
Pulmonary tuberculosis
Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis or bacteremia)
Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
Unexplained anemia (<8 g/dl), neutropenia (<0.5 x 10^9 per liter)[a]
and/or chronic thrombocytopenia (<50 x 10^9 per liter)
CLINICAL STAGE 4 - SEVERE SYMPTOMS
HIV wasting syndrome (BMI <18 kg/m^2, see **Appendix 2**)
Pneumocystis pneumonia
Recurrent severe bacterial pneumonia
Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site)
Esopheal candidiasis (or candidiasis of trachea, bronchi or lungs)
Extrapulmonary tuberculosis
Kaposi's sarcoma
Cytomegalovirus infection (retinitis or infection or other organs)
Central nervous system toxoplasmosis
HIV encephalopathy
Extrapulmonary cryptococcosis (including meningitis)
Disseminated non-tuberculosis mycobacterial infection
Progressive multifocal leukoencephalopathy

CLINICAL STAGE 4 - SEVERE SYMPTOMS (cont.)
Chronic cryptosporidiosis
Chronic isosporiasis
Disseminated mycosis (extrapulmonary histoplasmosis or coccidiomycosis)
Recurrent septicemia (including non-typhoidal *Salmonella*)
Lymphoma (cerebral or B-cell non-Hodgkin)
Invasive cervical carcinoma
Atypical disseminated leishmaniasis
Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy

[a]See **Appendix 2**: Assessing 10% weight loss and BMI for example calculations**.**

7.3.2. Immunological assessment

CD4 testing available:

CD4 testing is the ideal way to assess immunological status. A baseline CD4 cell count not only guides the decision on when to initiate ART but is also essential if CD4 counts are to be used to monitor ART. Patients whose CD4 cell counts are less than 350 cells/mm^3 are at increased risk of clinical disease progression. Although it is never too late to initiate ART, patients should preferably begin the therapy before the CD4 cell count drops to 200 cells/mm^3. In Liberia, patients with CD4 counts below 200 cells/mm^3 often present with severe symptoms. Thus, it is recommended that:

- All stage 3 or stage 4 patients with a CD4 count below 350cells/mm^3 start ART.
- Treatment can be considered in stage 2 patients with a CD4 count below 350 cells/mm^3 if the patient is symptomatic or if the CD4 count is falling rapidly.

If CD4 count NOT available:

In the absence of CD4 testing, **clinical staging** should be used to determine when to initiate in ART. In addition, a total lymphocyte count (TLC) below 1200 cells/mm^3 (1.2 x 10^9 cells/L) in patients with symptomatic HIV disease can be used as a guide to the **initiation** of ART. Specifically, the TLC is most useful in deciding when to initiate ART in symptomatic patients with WHO clinical stage 2 disease. <u>It is not useful and is not recommended for monitoring the response to ART or for deciding whether ART is failing.</u>

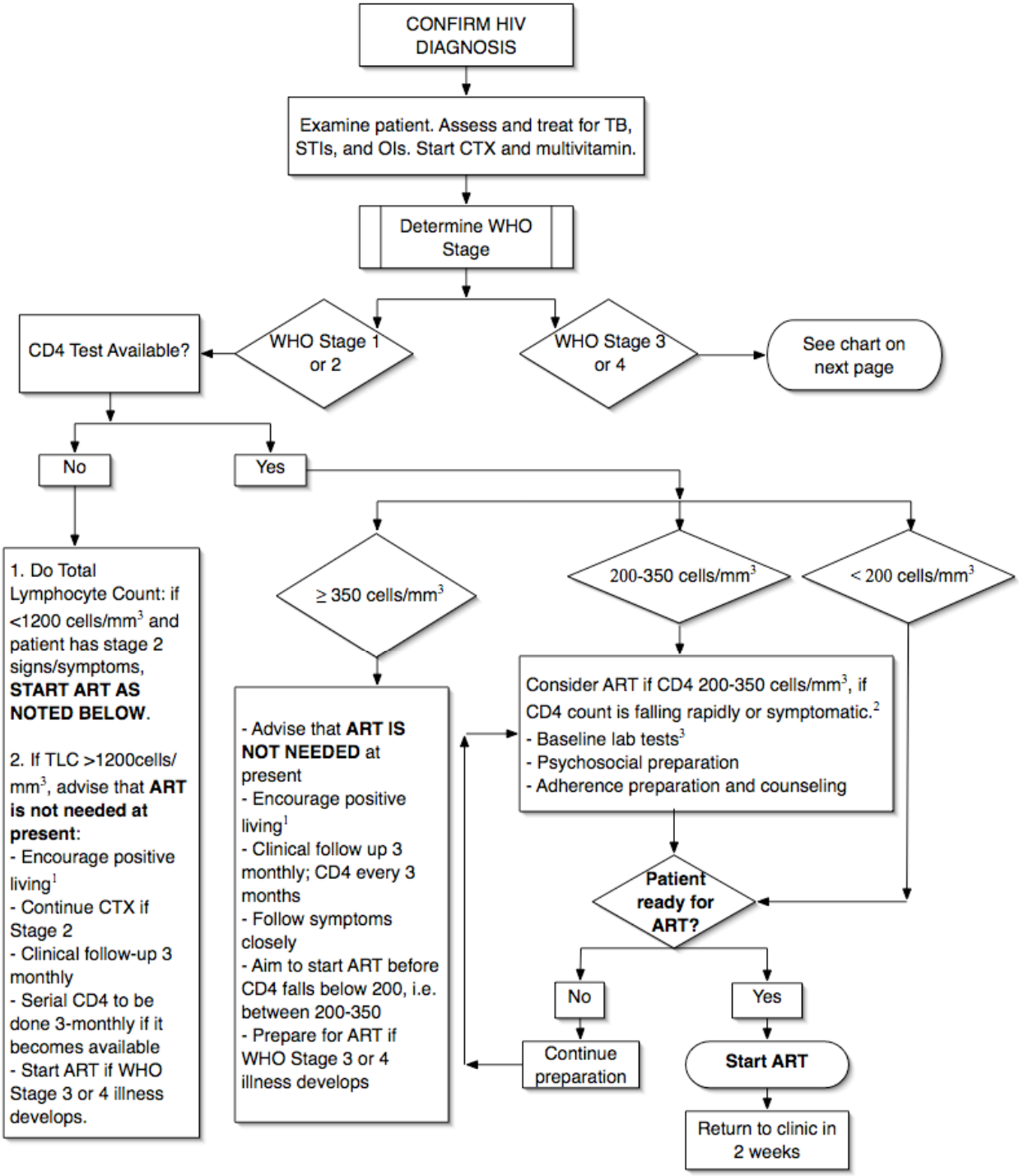
Table 7.2 Recommendations for the initiation of ART in adults and adolescents in accordance with clinical stages and the availability of immunological markers

WHO Clinical Staging	CD4 Testing Not Available	CD4 Testing Available
Stage 1: Asymptomatic	Do not treat regardless of TLC	Treat if CD4 count is <200 cells/mm^3
Stage 2: Mild Symptoms	Do not treat unless TLC <1200 cells/mm^3	Consider treatment if CD4 count[b] <350 cells/mm^3. Always initiate ART if CD4 <200/mm^3
Stage 3: Advanced Symptoms	Treat regardless of TLC	Initiate ART if CD4 <350/mm^3
Stage 4: Severe Symptoms	Treat regardless of TLC	Treat irrespective of CD4 cell count

a. A total lymphocyte count of 1200/mm^3 or less can be substituted for the CD4 count when the latter is unavailable and mild HIV disease exists. TLC is not useful in asymptomatic patients. In the absence of CD4 cell counts and TLC's, patients who are stage 2 should not be treated.

b. The initiation of ART is recommended for <u>all</u> HIV positive patients with CD4 counts < 350 cells/mm^3 and pulmonary TB (see **Section 18** for timing of ART and TB medication) or severe bacterial infection.

Figure 7.1 Summary – When to start ART for adults: WHO stages 1 and 2

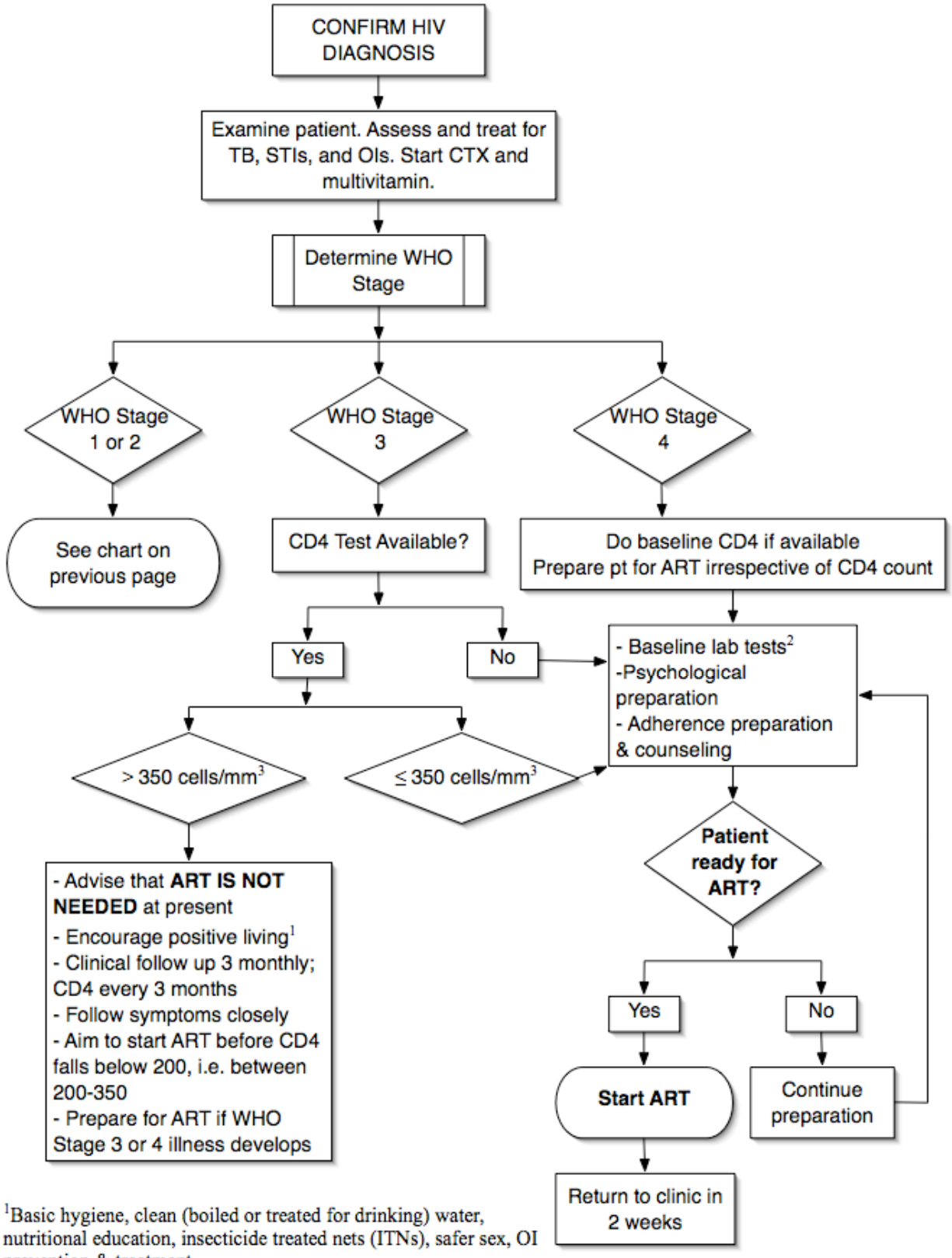


[1]Basic hygiene, clean (boiled or treated for drinking) water, nutritional education, insecticide treated nets(ITNs), safer sex, OI prevention & treatment

[2]If pulmonary TB or severe bacterial infection and CD4 <350cells/mm^3, start ART.

[3]Baseline lab tests: Hb (FBC), ALT (LFT), creatinine, and pregnancy test (if needed).

Figure 7.2 Summary – When to start ART for adults: WHO stages 3 and 4



[1]Basic hygiene, clean (boiled or treated for drinking) water, nutritional education, insecticide treated nets (ITNs), safer sex, OI prevention & treatment

[2]Baseline lab tests: Hb (FBC), ALT (LFT), creatinine, and pregnancy test (if needed).

7.4 Recommendations for initiating ART in children and infants

7.4.1. Clinical staging

Clinical staging provides details of the specific staging events and the criteria for recognizing them in children and infants. This staging is different from that of adults (see **Table 7.3**). Clinical staging should always be used in deciding when to initiate ART. Presumptive and definitive criteria for recognizing HIV-related clinical events in infants and children with established HIV infection are outlined in **Appendix 3**: Diagnostic criteria for the staging of HIV-related clinical events in children.

HIV-exposed children should be evaluated regularly. See **Section 14** for follow-up schedule for HIV-exposed infants. In the absence of DNA PCR testing, ART can be initiated based on a presumptive diagnosis of HIV disease (see **Table 7.4** below).

Table 7.3 WHO clinical staging of HIV in infants and children with established HIV infection

CLINICAL STAGE I - ASYMPTOMATIC
Asymptomatic
Persistent generalized lymphadenopathy
CLINICAL STAGE 2 - MILD SYMPTOMS
Unexplained[a] persistent hepatosplenomegaly
Papular pruritic eruptions
Extensive wart virus infection
Extensive molluscum contagiosum
Fungal nail infections
Recurrent oral ulcerations
Unexplained persistent parotid enlargement
Lineal gingival erythema
Herpes zoster
Recurrent or chronic upper respiratory tract infections
(otitis media, otorrhea, sinusitis or tonsillitis)
CLINICAL STAGE 3 - ADVANCED SYMPTOMS
Unexplained[a] moderate malnutrition not adequately responding to standard therapy
Unexplained persistent diarrhea (14 days or more)
Unexplained persistent fever (above 37.5°C intermittent or constant, for longer than one month)
Persistent oral candidiasis (after first 6-8 weeks of life)
Oral hairy leukoplakia
Acute necrotizing ulcerative gingivitis or periodontitis
Lymph node tuberculosis
Pulmonary tuberculosis
Severe recurrent bacterial pneumonia
Symptomatic lymphoid interstitial pneumonitis
Chronic HIV-associated lung disease including bronchiectasis
Unexplained anemia (<8 g/dl), neutropenia (<0.5 x 10^9 per liter)
and/or chronic thrombocytopenia (<50 x 10^9 per liter)
CLINICAL STAGE 4 - SEVERE SYMPTOMS
Unexplained[a] severe wasting, stunting or severe malnutrition not responding to standard therapy
Pneumocystis pneumonia
Recurrent severe bacterial infections (such as empyema, promyositis, bone or joint infection or meningitis but excluding pneumonia)
Chronic herpes simplex infection (orolabial or cutaneous of more than one month's duration or visceral at any site)

CLINICAL STAGE 4 - SEVERE SYMPTOMS (cont.)
Extrapulmonary tuberculosis
Kaposi sarcoma
Esopheal candidiasis (or candidiasis of trachea, bronchi or lungs)
Central nervous system toxoplasmosis (after one month of life)
HIV encephalopathy
Cytomegalovirus infection: retinitis or cytomegalovirus infection affecting another organ, with onset at age older than one month
Extrapulmonary cryptococcosis (including meningitis)
Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidiomycosis)
Chronic cryptosporidiosis
Chronic isosporiasis
Disseminated non-tuberculosis mycobacterial infection
Cerebral or B-cell non-Hodgkin lymphoma
Progressive multifocal leukoencephalopathy
Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy

a. Unexplained refers to where the condition is not explained by other causes.

Table 7.4 Clinical criteria for presumptive diagnosis of severe HIV disease in infants and children < 18 months of age

A presumptive diagnosis of severe HIV disease should be made if:

- The infant is confirmed HIV antibody positive; *and*
- Diagnosis of any AIDS-indicator condition(s) can be made; *or*
- **The infant is symptomatic with two or more of the following**:
    - Oral thrush[a];
    - Severe pneumonia[b];
    - Severe sepsis[c].

Other factors that support the diagnosis of severe HIV disease in an HIV seropositive infant include:

- Recent HIV-related maternal death; *or* advanced HIV disease in the mother;
- CD4 < 20% in infant.

In these cases, ART should be initiated

and confirmation of the diagnosis of HIV infection should be sought as soon as possible.

IMCI definition:

a. Oral thrush: Creamy white to yellow soft small plaques on red or normally colored mucosa which cannot easily be scraped off (pseudomembranous), or red patches on tongue, palate or lining of mouth, usually painful or tender.

b. Severe pneumonia: Cough or difficult breathing in a child with chest indrawing, stridor or any of the IMCI general danger signs; i.e., lethargic or unconscious, not able to drink or breastfeed, vomiting, and presence or history of convulsions during current illness; responding to antibiotics.

c. Severe sepsis: Fever or low body temperature in a young infant with any severe sign such as fast breathing, chest indrawing, bulging fontanelle, lethargy, reduced movement, not feeding or sucking breast milk, convulsions

7.4.2. Immunological assessment

When CD4 count is available:

Percentage CD4 (i.e. %CD4) values are more meaningful in children less than 5 years old than absolute CD4 count or total lymphocyte count, and should be used whenever possible. As normal values change with age, refer to the table below. CD4 % can be calculated manually in cases where the laboratory can perform absolute CD4 count and Total Lymphocyte Count:

$$\text{CD4\%} = \frac{\text{CD4 count}}{\text{Total Lymphocyte Count}} \quad \left(\text{same as}: \quad \text{TLC}\sqrt{\text{CD4 count}}\right)$$

In instances where CD4% are not available, absolute counts can be used (see **Table 7.5** below).

If CD4 count is not available:

In the absence of CD4 testing, clinical staging should be used to determine when to initiate ART.

Better data exist for the relationship of the TLC and HIV disease in children. TLC may be used as an indication of the need to initiate ART in infants or children up to 8 years old with WHO pediatric clinical stage 2 disease. ART should be initiated in all patients with stage 3 or 4 disease regardless of TLC, and in stage 2 disease where TLC indicates severe immunodeficiency as indicated in **Table 7.6** below.

Table 7.5 WHO immunological criteria of severe HIV immunodeficiency

Laboratory Measurement	Age Specific Recommendations to Start ART			
	<11 months	**12 – 35 months**	**36-59 months**	**≥ 5 years**
CD4 %[a,b]	<25%	<20%	<15%	<15%
CD4 count[a] (cells/mm^3)	<1500	<750	<350	<200
TLC[c] (cells/mm^3)	<4000	<3000	<2500	<2000

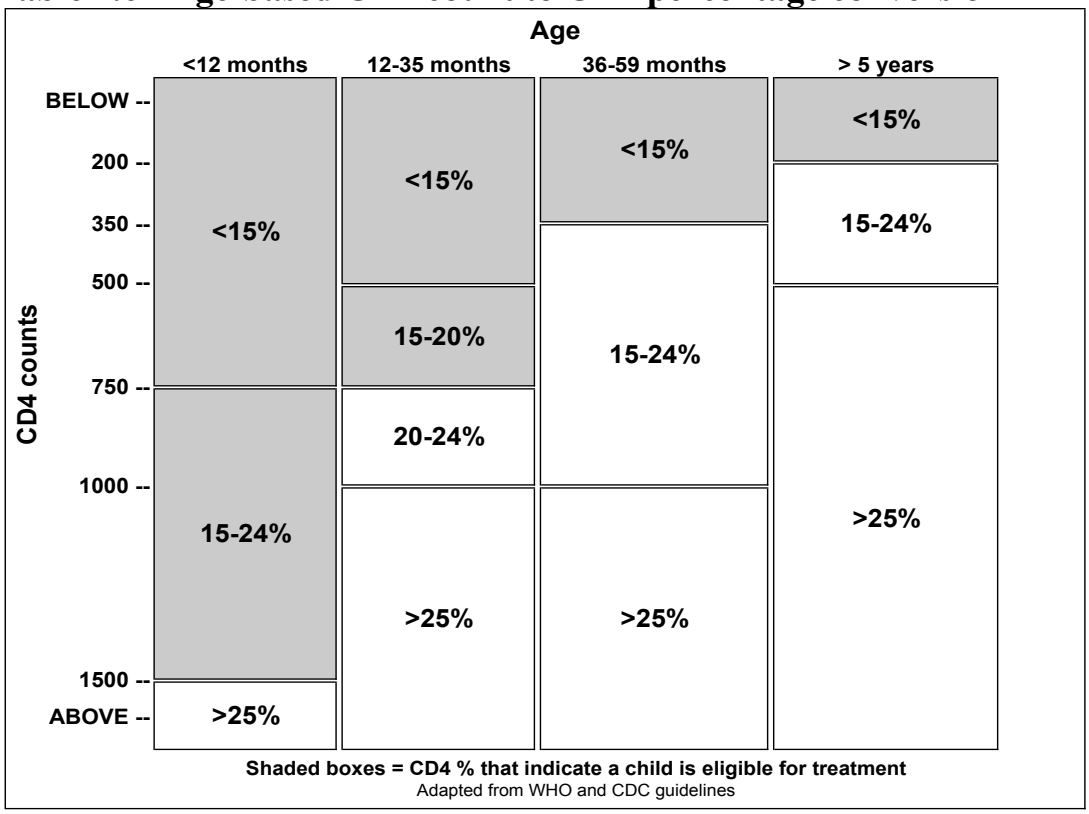
[a] ART should be started by these cut-off levels, no matter what clinical stage

[b] **CD4% is preferred for children < 5 years**

[c] There are less data available to make recommendations on the use of TLC for decision-making in children older than 8 years of age

Note: Initiation of ART based on the above TLC ranges is recommended only for WHO stage 2 infants and children, when CD4 measurement is not possible.

Table 7.6 Age-based CD4 count to CD4 percentage conversion



7.4.3. Summary - WHO recommendations for initiating ART in children

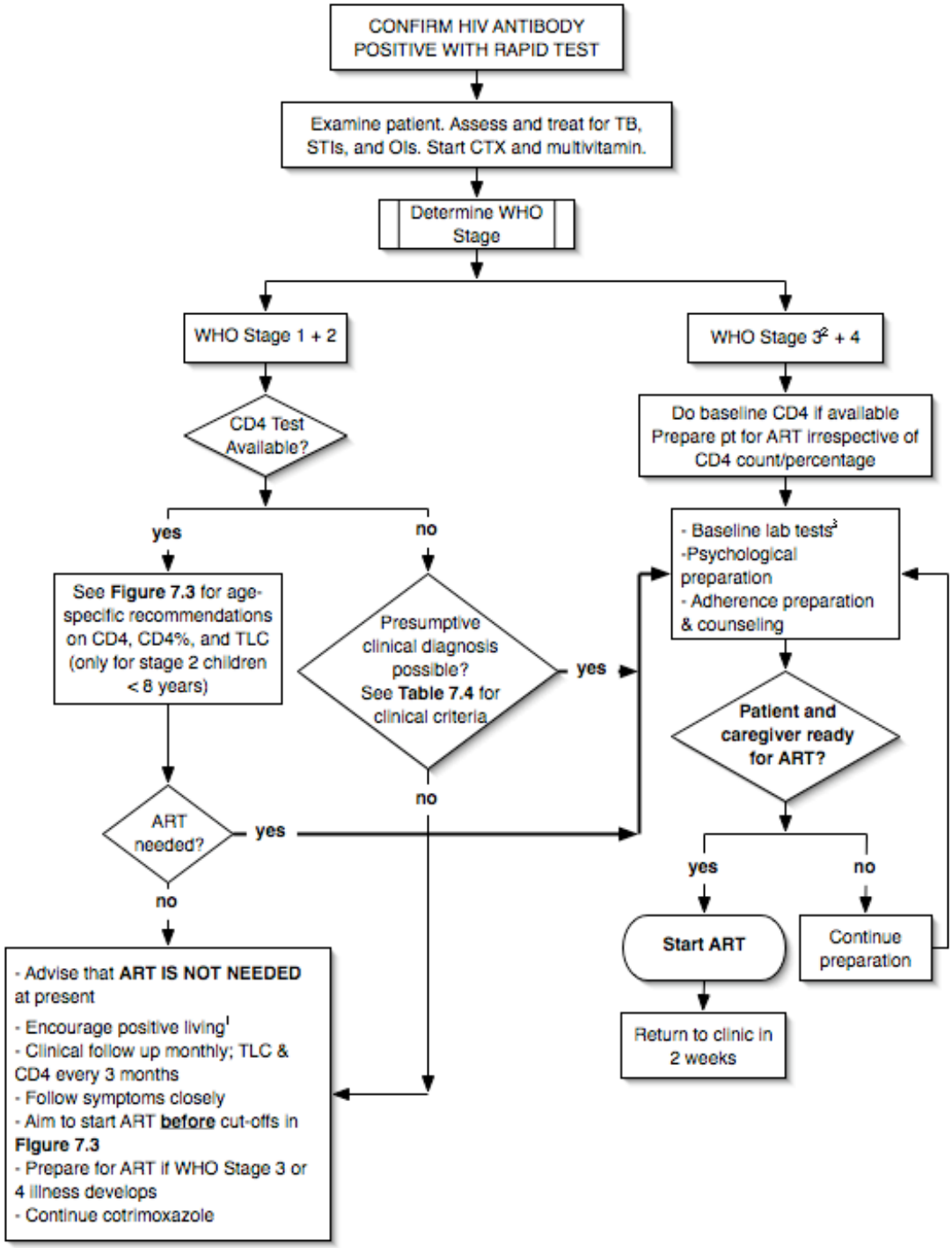
Given the rapid progression of HIV in children, when children are near the designated cutoffs, **initiate treatment**.

Table 7.7 Summary – Recommendations for initiating ART in presumed and confirmed HIV positive infants and children

WHO pediatric stage	Availability of CD4 cell measurements	Age-specific treatment recommendations	
		≤11 months	≥12 months
4[a]	CD4[b]	Treat all	
	No CD4		
3[a]		Treat all	Treat all, CD4-guided in those children with TB,[c] LIP, OHL, thrombocytopenia
	No CD4		Treat all[c]
2	CD4[b]	CD4-guided[d]	
	No CD4	TLC-guided[d]	
1	CD4[b]	CD4-guided[d]	
	No CD4[b]	Do not treat	

[a] Stabilize any opportunistic infection before initiation of ART.
[b] Baseline CD4 is useful for monitoring ART even if it is not required to initiate ART.
[c] In children with pulmonary or lymph node TB the CD4 level and clinical status should be used to determine the need for and timing of initiation of ART in relation to tuberculosis treatment (see **Section 18.1** Tuberculosis coinfection).
[d] Refer to **Table 7.6**, WHO CD4 criteria of severe HIV immunodeficiency, for CD4 and TLC values.

Figure 7.3 Summary – When to start ART in children, WHO stages 1, 2, 3 and 4



[1]Basic hygiene, clean (boiled or treated for drinking) water, nutritional education, insecticide treated nets (ITNs), safer sex, OI prevention & treatment

[2]For children older than 12 months with specific stage 3 conditions (TB, lymphocytic interstitial pneumonia, oral hairy leukoplakia or thrombocytopenia), ART initiation may be delayed if CD4 is above age-specific threshold value as indicated above in **Table 7.6**.

[3]Baseline lab tests: Hb (FBC), ALT (LFT), and creatinine.

SECTION 8: Monitoring of adults and children who are not yet eligible for ART

8. Monitoring of adults and children who are not yet eligible for ART

Patients who do not meet the clinical and laboratory criteria for initiation of ART should be reevaluated by an experienced health care worker with a clinical history and physical exam approximately every 3 months. Patients with acute illness should be assessed at any time as needed. If CD4 count testing is available, it should be performed every 3 months to follow the trend of the disease. If CD4 count is not available, clinical staging should be used at each visit to assess patient eligibility for ART. Patients should be monitored at each visit for the development of any stage 3 or 4 symptoms. See **Table 8.1** for a complete schedule of recommended counseling, clinical and laboratory monitoring activities for patients not yet eligible for ART. Patients who become eligible for ART (present with a stage 3 or 4 illness, or whose CD4 count falls below 350 cells/mm^3) should begin preparation for ART initiation (see **Section 11**: Antiretroviral therapy and recommended first line regimens for adults and children).

Table 8.1 Schedule of counseling, clinical, and laboratory monitoring activities for patients not yet eligible for ART

	Initial Visit	Follow Up
Counseling		
Positive Living and prevention of transmission	√	Every follow up visit
Contraceptive counseling	√	As needed
Clinical		
Complete physical exam	√	As needed
Focused physical exam	√	3 monthly (mouth, lymph nodes, skin, and conjunctiva at every visit)
Weight (kg)	√	Every follow up visit
Height (m)	√	Every follow up visit for children only
WHO clinical staging	√	Every follow up visit
Assess patient functional status (working, ambulatory, or bedridden)	√	Every follow up visit
Assess for OIs and STIs	√	Every follow up visit
Provide Medications		
Cotrimoxazole prophylaxis where indicated	√	1-3 months
Appropriate OI treatment	√	As needed
Laboratory testing		
Bioline testing (if needed)	√	Bioline testing should only be done if there is no record of type of HIV infection: HIV 1 or HIV 2.
CD4% + CD4 count (if available)	√	3 monthly
Full blood count	√	3 months, then every 6 months (for CTX toxicity)
TLC (if WHO stage 2)	√	-
Pregnancy test (if needed)	√	-
Chest x-ray (to rule out TB)	√	Repeat as needed
Malaria smear	√	Every visit where patient is febrile

Other Important Points

- If any client is not eligible for ARV drugs, they should be offered all other aspects of supportive treatment, including CPT if appropriate and early treatment of opportunistic infections. **Cotrimoxazole is given to all patients who are WHO stage 2, 3 and 4** (see **Section 9**: Prophylaxis Against HIV-associated infections with Cotrimoxazole Preventative Therapy).
- Some patients may be disappointed that they are not being started on therapy immediately. It should be explained that **starting ART is not an emergency** and that, in fact, starting a patient too soon can be harmful. ARVs always have a risk of drug toxicity. Also, the initial regimen will inevitably fail at some point. Starting ARV drugs before they are needed will decrease the patient's future therapy options.
- All patients, regardless of their eligibility for ARV drugs, should make use of available ongoing counseling services and support in all aspects of "positive living." Specifically, they should be helped to accept their HIV diagnosis, encouraged to change risky behaviors, and taught how to improve their hygiene and nutrition. (See **Section 10**: Positive living)
- Sexual partners and family members (**such as children of HIV positive parents**) should be encouraged to attend a clinic for VCT as well. Partner Counseling and Referral services should be utilized, when available.

SECTION 9: Prophylaxis against HIV-associated infections with cotrimoxazole preventive therapy (CPT)

9. Prophylaxis against HIV-associated infections with cotrimoxazole preventive therapy (CPT)

Cotrimoxazole (CTX or TMP-SMX) is an essential aspect of HIV care. Its use can improve survival independently of specific HIV treatment with ARVs. Specifically, the preventive activity of cotrimoxazole is effective against: bacterial pneumonia (streptococcus pneumonia), bacteremia (salmonella species), pneumocystis jiroveci pneumonia (PCP), diarrhea (salmonella, isospora belli), and toxoplasmosis. In children in particular, CPT also protects against malaria, otitis media, sinusitis, cellulitis, and septicemia.

9.1 Steps to initiating CPT

1. Identify potential recipients:
   - HIV+ adults, adolescents and children
   - HIV-exposed children from 6 weeks of age (see below: CPT in Children)
2. Take medical history
3. Conduct physical examination
4. Counsel on OIs in HIV infection
5. Treat pre-existing OIs (See **Section 19**)
6. Screen for contraindications to cotrimoxazole
   - Known allergy to sulfa-containing drugs (which include cotrimoxazole and sulfadoxine-pyrimethamine [Fansidar])
   - Kidney or liver disease
   - Seriously ill patients (Refer for specialized medical care)
7. Counsel patient on:
   - Drug adherence
   - Possible side effects of cotrimoxazole:
     - Skin eruptions, which may be severe (Stevens Johnson syndrome)
     - Nephritis (kidney disease)
     - Hepatitis (liver disease)
     - Anemia and other signs of bone-marrow suppression
     - Hyperkalemia

For most patients, the benefit of CPT should far outweigh the risk.

9.2 CPT in adults and adolescents

Indications for initiation:
- **All adults** with HIV stage 2, 3 and 4 disease regardless of CD4 count
- **All individuals** with HIV and a CD4 count <350 cells/mm^3
- **All pregnant women** with HIV unless CD4 is known to be >350cells/mm^3, regardless of the duration of the pregnancy

NOTE: a pregnant woman receiving cotrimoxazole, should not also receive S-P as malaria prophylaxis .

When in doubt, patients should be started on cotrimoxazole.

Cotrimoxazole Dosage:

1 double strength tablet (Trimethoprim (TMP) 160 mg + Sulfamethoxazole (SMX) 800 mg) QD **or** 2 single strength (TMP 80 mg + SMX 400 mg) tablets QD

Duration:

- CPT can be stopped if the patient has two CD4 counts above 350/mm^3 at least 3 months apart. If CD4 counts are not available or they never consistently rise above 350/mm^3, the CPT should be continued indefinitely.
- If the CD4 count falls below 350/mm^3 for two CD4 counts at least 3 months apart, the CPT should be restarted.

Criteria for Stopping:

- Severe cutaneous reactions
- Renal and/or hepatic failure
- Severe hematological toxicity (grade 4 toxicity)

Table 9.1 Management of cotrimoxazole-related rashes

Toxicity	Clinical Description	Recommendation
Grade 1	Erythema	Continue CPT with careful and repeated observation and follow-up. Provide symptomatic treatment, such as antihistamines, if available.
Grade 2	Diffuse maculopapular rash, dry desquamation	Continue CPT with careful and repeated observation and follow-up. Provide symptomatic treatment, such as antihistamines, if available.
Grade 3	Vesiculation, mucosal ulceration	Cotrimoxazole should be discontinued until the adverse effect has completely resolved (usually two weeks), and then desensitization can be considered (see below).
Grade 4	Exfoliative dermatitis, Stevens-Johnson syndrome or erythema multiform, moist desquamation	Cotrimoxazole should be **permanently** discontinued. Use alternative prophylaxis described below.

Table 9.2 Summary- when to start Cotrimoxazole Preventive Therapy according to clinical and immunological criteria

WHO clinical stage	No CD4 available	CD4 available
1	Clinician's discretion	Start* if <350 cells/mm^3
2	Start CPT	Start* if <350 cells/mm^3
3	Start CPT	Start* if <350 cells/mm^3
4	Start CPT	Start* if <350 cells/mm^3
Pregnant – any stage (see also **Section 12)**	Start CPT	Start CPT unless consistently >350 cells/mm^3

*CPT can be discontinued if patient has two CD4 counts >350 at least 3 months apart

9.3 Cotrimoxazole desensitization

Cotrimoxazole (CTX) provides patients many benefits. Every effort should be made to allow them to continue to use it safely if they suffer a reaction to it.

In case of non-life threatening reactions (grade 1, 2, or 3 toxicity) after initiation of CPT, treatment should be stopped for 2 weeks, then the patient may be rechallenged with CTX in a gradually increasing dose by using syrup formulation (see table below). A patient with toxicity grade 4 (life threatening events) should NOT be considered a candidate for CTX desensitization or re-trial of CPT. After desensitization, up to 70% of patients may again tolerate CTX.

Table 9.3 Plan for cotrimoxazole desensitization

Step	Dose
Day 1	80 mg sulfamethoxazole + 16 mg trimethoprim (2 ml of oral suspension)[a]
Day 2	160 mg sulfamethoxazole + 32 mg trimethoprim (4 ml of oral suspension)[a]
Day 3	240 mg sulfamethoxazole + 48 mg trimethoprim (6 ml of oral suspension)[a]
Day 4	320 mg sulfamethoxazole + 64 mg trimethoprim (8 ml of oral suspension)[a]
Day 5	One single-strength sulfamethoxazole-trimethoprim tablet (400 mg sulfamethoxazole + 80 mg trimethoprim)
Day 6 Onwards	Two single-strength sulfamethoxazole-trimethoprim tablets or one double-strength tablet (800 mg sulfamethoxazole + 160 mg trimethoprim)

[a]Cotrimoxazole oral suspension is 40 mg trimethoprim + 200 mg sulfamethoxazole per 5 ml.

9.4 Alternatives to CPT

In situations in which cotrimoxazole cannot be continued or should not be initiated, patients should be prescribed the following regimen, if available:

Pyrimethamine 50mg weekly and folinic acid 25mg weekly
(when CD4 ≤200 cells/mm^3)[1]

and

Dapsone 100mg QD (or 50mg BID) when CD4 <350 cells/mm^3

Pyrimethamine is effective as prophylaxis against toxoplasmosis, while dapsone will prevent PCP. Patients may be prescribed dapsone alone if pyrimethamine and folinic acid are not available, but clinicians should be aware that dapsone used alone is not as effective prophylaxis as cotrimoxazole. Therefore close attention should be paid to the possibility of OIs occurring in these patients. Pryimethamine/folinic acid prophylaxis can be discontinued once the patient's CD4 count is >200 cells/mm^3. Dapsone prophylaxis should be continued indefinitely or until patient has two CD4 counts >350 cells/mm^3 at least three months apart. When CD4 testing is not available, continue both pyrimethamine/folinic acid and dapsone indefinitely.

9.5 CPT in HIV exposed and HIV positive children

Indications:
- Any child identified as HIV positive
- All HIV-exposed children from 6 weeks of age (whether or not child was/is part of a PMTCT program)
  - Children born to HIV positive mothers, until 18 months of age when infection can be definitively excluded, or
  - HIV-exposed breastfed children at any age.

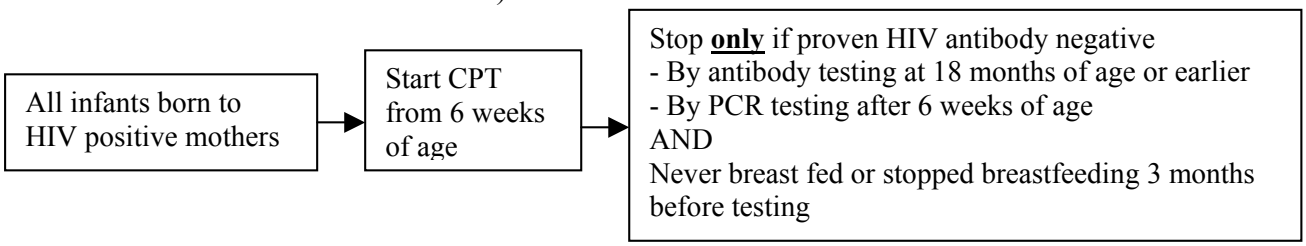
Dosage:
CTX syrup (SMX 200 mg, TMP 40 mg/5 ml) should be given once a day. The recommended dosage is 4 mg/kg of Trimethoprim once daily. If syrup is not available, crushed tablets may be used. Dosage is given by age in the following table.

[1] Hg should be taken prior to initiation, and again at 2, 4, 8, and 10 weeks (follow AZT algorithm in **Figure 16.1** for stopping pyrimethamine).

Table 9.4 Dose of cotrimoxazole for in infants and children

Age	Suspension Per 5ml (200/40mg)	Pediatric tablet (100/20mg)	Single Strength adult tablet (400/80mg)	Double Strength adult tablet (800/160mg)
< 6mo	2.5ml	1 tablet	¼ tablet	--
6 mo- 5yrs	5 ml	2 tablets	½ tablet	--
6-14 yrs	10 ml	4 tablets	1 tablet	½ tablet
>14 yrs	--	--	2 tablets	1 tablet

Duration of CPT in infants and children:
CPT may be discontinued in HIV exposed infants once HIV infection status has been definitively ruled out (by negative virologic testing after 6 weeks of life in a child who has never breastfed, or by negative rapid testing in a older infant who has not breast fed for at least 3 months).



Once an HIV positive child is initiated on CPT prophylaxis, this should not be discontinued until the age of 5. After the age of 5, follow adult recommendations (see **Section 9.2** above).

9.6 Alternatives to CPT in children

Toxicity criteria for stopping CPT in children are the same as for adults. In situations where CPT cannot be continued or used, children should be prescribed, if available:

- **Dapsone** (dosage in children: 2 mg/kg/day with a maximum of 100 mg/day) and
- **Pyrimethamine/folinic acid**; dosage in children[2]
  - Children older than 1 month:
    - Pyrimethamine 1mg/kg QD
    - Oral folinic acid 5mg ever 3 days.

9.7 Monitoring and follow-up for adults and children

- All patients should initially be seen in clinic monthly, and then every 3 months thereafter if the medications are tolerated (no skin rashes, nausea, or vomiting).
- Lab monitoring (haemoglobin and white blood cell count) should be repeated 3 months after initiation of CPT and thereafter every 6 months or when clinically indicated to assess for haematological toxicities.

[2] Hb should be taken prior to initiation, and again at 2, 4 and 8 weeks (follow AZT algorithm in **Figure 16.1** for stopping pyrimethamine).

SECTION 10: Positive living: nutrition, hygiene, risk reduction, malaria prophylaxis

10. Positive living: nutrition, hygiene, risk reduction, malaria prophylaxis

10.1 Nutrition

10.1.1. Adults

Since malnutrition can contribute to and result from progression of HIV disease, it is important to discuss eating habits with all patients. Providers should assess all patients' nutritional status and be familiar with food-related symptom management. They should create individualized nutrition care plans for each patient.

Background

- Chronic infection leads to increased nutritional requirements
- Micronutrient deficiency compromises host immunity
- Impaired nutrient absorption occurs during infection
- HIV positive individuals require 10-15% more calories/day
- HIV positive individuals with muscle wasting may require 50-100% more protein/day
- HIV and ART can both cause loss of appetite
- Some drugs have particular food restrictions

Economic realities

- HIV may affect ability to earn a living
- HIV may lead to loss of assets
- HIV may lead to disruption of social networks

Nutritional assessment

- Weigh patient at each visit
  - Record weight at each visit
  - Use growth curves to monitor infants and children
- Observe clinical condition
- Ask about food intake/hunger
- Ask about specific symptoms that may prevent food intake

Food-related symptom management

- Mouth pain: assess and treat for oral thrush
- Pain when swallowing: assess and treat for esophageal candidiasis
- Nausea, abdominal pain: assess and treat symptomatically
- Diarrhea: assess and treat symptomatically
- Anorexia: assess and treat symptomatically

Individualize the nutrition care plan

- Understand factors that may influence patients' ability to eat a sufficient diet.
- Know what foods your patient population consumes and how food is prepared.
- Know what foods are locally available, palatable, affordable and can be realistically incorporated into the diet.
- Promote fruit and vegetables as a source of vitamins and minerals.
- Promote safe drinking water.
- Promote avoidance of alcohol and illicit drugs.

Table 10.1 Recommended foods for maintaining good nutrition

Energy food	Body building food	Protective food
Cassava	Egg	Pawpaw
Plantain	Milk	Watermelon
Rice	Fish	Pineapple
Cereal	Meat	Okra
Eddoes	Bonnie	Oranges
Potato	Beans	Plums
Banana	Peanuts	Potato greens
	Bennie seed	Cassava leaves, etc.
		Eggplant

10.1.2. Infants and children

Nutrition is an important part of care for both HIV-exposed and HIV positive children. Growth problems in HIV positive children (growth failure and severe malnutrition not responsive to standard nutrition rehabilitation) may point to disease progression and the need for ART initiation or treatment failure in the child who is on ART. In HIV-exposed infants, growth failure may indicate development of HIV infection.

Effect of HIV on nutritional status

- HIV infection leads to malnutrition early in life.
- In HIV positive children experiencing weight loss, energy/caloric requirements are increased by 50 to 100 percent.
- HIV positive children are likely to have poor oral intake and malabsorption secondary to HIV infection and/or OIs.

Effect of nutritional status on HIV

- Decrease in CD4 cells, suppression of delayed hypersensitivity and abnormal B cell response, leading to reduced body defense and rapid disease progression.
- Wasting has been associated with reduced length of survival.
- Micronutrient deficiencies lead to increased oxidative stress, further damage to the immune system, increase in viral replication and decrease in CD4 count.

10.1.3. Nutritional assessment

10.1.3.1. Goals

- Decrease transmission of HIV via breastfeeding
- Decrease morbidity and mortality from diarrhea and other childhood illnesses, OIs, and HIV disease
- Ensure satisfactory growth and development

10.1.3.2. Assessment of growth and nutritional status

Nutritional status and growth, nutritional assessment and support should be an integral part of the care of HIV positive children. Growth monitoring at a minimum should involve measurement of weight, length/height and head circumference and

should be done at every visit. The pattern of growth plotted on a standard chart over a period of time is more useful than a single measurement.

- **Weight**- Weigh infant or child at every visit and plot on growth charts to see the pattern of growth. Use the Road to Health card growth charts for children.
- **Length/Height**- Measure recumbent length for infants until two years of age and standing height for children ≥ 2 years of age. Height should be measured monthly until six months of age then quarterly. Plot on growth chart.
- **Mid-Upper Arm Circumference** (MUAC) – This is another means of assessing nutritional status. WHO guidelines are pending.

10.1.3.3. Growth failure

Growth failure may be an indication of:

- HIV infection in an HIV-exposed infant (development of failure to thrive in a HIV-exposed infant after exclusion of other causes)
- Disease progression and need for ART in an HIV positive child (child who was clinical stage 2, develops stage 3 signs of severe malnutrition; low weight not explained by inadequate nutrition or other infections and not adequately responding to standard management)
- Treatment failure in a child on ART (lack of growth, or decline in growth rate in children who showed an initial response to treatment; moderate or severe unexplained malnutrition not responding to standard therapy; see **Section 17.2**)

Clinical indicators of growth failure

- Weight for age < 5% (on growth charts)
- Crossing two major percentile lines
- Weight for height < 5% (on growth charts)

If there is evidence of growth failure, evaluate the following:

- Nutrient intake
- Ongoing losses
- Failure to meet all developmental milestones (see **Appendix 12**: Developmental milestones and red flags)
- Physical exam looking for thrush, oral ulcers, skin changes, edema, GI bleeding and signs of a systemic infection

Children who have growth failure should receive intensive nutritional support.

10.2 Hygiene

Positive living entails accepting the realities of HIV infection and adjusting one's lifestyle to suit this reality. This includes adopting less risky lifestyle (behavioral change) as well as good personal and environmental hygiene, which are necessary to prevent opportunistic infections.

- Wash hands before eating
- Wash hands after using the latrine
- Use condoms for all sexual activities
- Bathe daily
- Use safe drinking water - for example: filter or boil water prior to drinking
- Use latrines to dispose of human waste

10.3 Reducing exposure to STI's and other strains of HIV

A key factor in maintaining the already weakened immune system during treatment of HIV infection is reducing exposure to new infectious agents and also eliminating exposure to novel strains of HIV (i.e., HIV-1 or -2, or drug resistant strains of HIV). This includes an ongoing commitment to:

- avoid sexual exposures, and
- use of condoms for all sexual activities, even with a stable partner

This becomes an especially important issue after beginning treatment with ART, when weight gain and restored health may reopen doors to new social and sexual relationships.

10.4 Malaria prevention

- Prescribe cotrimoxazole as appropriate (See **Section 9**).
- Encourage use of insecticide-treated bednets.
- Encourage patients to keep surroundings clean and free of standing water.

SECTION 11: Antiretroviral therapy (ART) and recommended first line regimens for adults and children

11. Antiretroviral therapy (ART) and recommended first line regimens for adults and children

11.1 Goals of therapy

- Primary goals of ART are to:
  - Reduce HIV-related morbidity and mortality
  - Improve quality of life
  - Restore and preserve immunologic function, and
  - Maximally suppress viral load.
- Secondary goals of ART are to decrease the incidence of HIV through:
  - The reduction of transmission in discordant couples, and
  - Reducing the risks of HIV transmission from mother to child.

The following strategies should be used to achieve these goals:

- Adequate counseling and creation of a supportive environment where patients can maximize adherence to antiretroviral regimens
- Rational sequencing of drugs for the preservation of future treatment options
- Monitoring of toxicities and adverse drug reactions
- Prescribers need to understand:
  - When to start antiretroviral drugs
  - Which drugs to use and in which order
  - How to manage common side effects of therapy
  - When to change therapy
  - Which drugs to use when changing therapy

11.2 Overview of the antiretroviral drugs (ARVs) and antiretroviral therapy (ART)

11.2.1. Difference between ARVs and ART

Antiretroviral drugs (ARVs) are used in several different ways. These medications can be used in prophylaxis (as in PMTCT, see **Section 13**, or PEP, see **Section 22**) or for treatment (as in ART, see below). When used for prophylaxis, ARVs are given for a *short period of time*, and a patient may be given only *one* or *two* drugs. Antiretroviral therapy (ART), in contrast, is continued for the patient's *whole life*, and follows a special protocol for providing *three* ARVs together to treat HIV directly. ART requires close monitoring of patients over a long period of time.

11.2.2. Antiretroviral drugs

Antiretroviral agents act by blocking the enzymes responsible for the replication and functioning of HIV. **Never use only one or two drugs** to treat chronic HIV infection; the only time less than 3 drugs is acceptable is in the setting of PMTCT and post-exposure prophylaxis.

Currently, available antiretroviral drugs belong to the following classes:

- Nucleoside Reverse Transcriptase Inhibitors (NRTIs) – These drugs block HIV reverse transcriptase and prevent the copying of the viral genetic code (RNA) into

the genetic code (DNA) of infected host cells by imitating the building blocks of the DNA chain. The resulting DNA is incomplete and cannot create new virus.

- Nucleotide Reverse Transcriptase Inhibitors (NtRTIs) - These drugs act at the same stage of the viral life cycle as the NRTIs. In clinical practice they are viewed as an expansion of the NRTI Class.
- Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIS) – These drugs block HIV reverse transcriptase and prevent the copying of the viral genetic code (RNA) into the genetic code (DNA) of infected host cells by binding to the enzyme and making the active site ineffective.
- Protease Inhibitors (PIs) – These drugs work at the last stage of the virus reproductive cycle. They block the enzyme protease and prevent the assembly and release of HIV particles from infected cells.
- Fusion Inhibitors: The newest class of drugs, these medications prevent the virus from entering the host cell. They are not yet available in Liberia.

Figure 11.1 Mechanism of action of ARVs

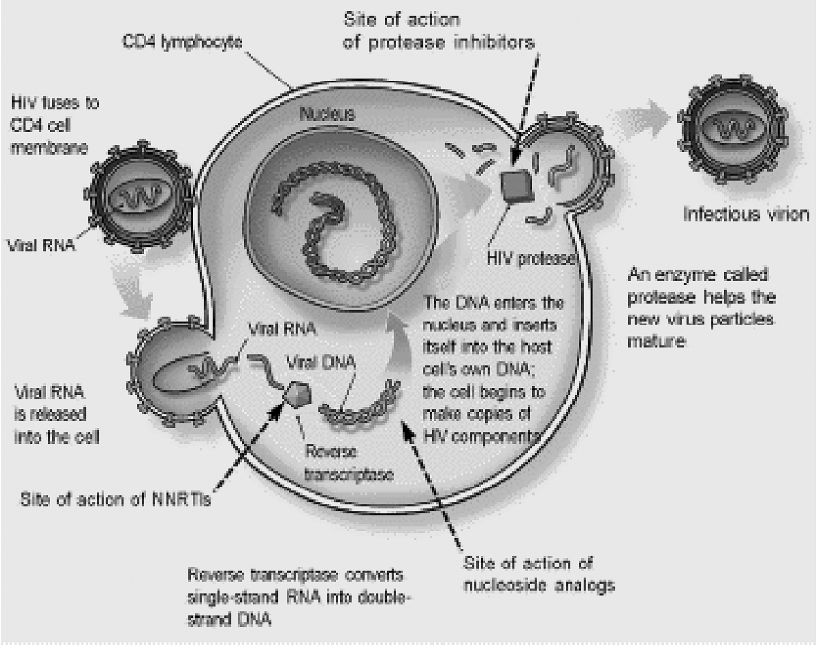


Table 11.1 Antiretroviral (ARV) drugs

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)*	Nucleotide Reverse Transcriptase Inhibitors (NtRTIs)*	Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	Protease Inhibitors (PIs)**	Entry Inhibitors
Zidovudine (AZT, ZDV)	Tenofovir (TDF)	Nevirapine (NVP)	Lopinavir/ritonavir (LPV/r)	Enfuvirtide
Didanosine (ddI)		Efavirenz (EFV)	Atazanavir/ritonavir (ATV/r)	
Emtricitabine (FTC)			Indinavir (IDV)	
Stavudine (d4T)			Nelfinavir (NFV)	
Lamivudine (3TC)			Amprenavir(APV)	
Abacavir (ABC)			Saquinavir (SQV)	

* NRTIs and NtRTIs are interchangeable, but are not interchangeable with NNRTIs.

** All protease inhibitors, with the exception of Nelfinavir, should be "boosted" with a low dose of ritonavir as this enhances their action. See **Table 16.6**: Characteristics of Available ARVs for more detailed information.

A number of these drugs are available as fixed dose combinations (FDCs). By prescribing drugs available in combination products, it is possible to reduce the number of pills a patient has to take each day and to improve adherence.

Table 11.2 Fixed dose combinations (FDCs) of ARVs for adults and children available in Liberia, 2008

Three-drug fixed-dose combinations	AZT (300mg) + 3TC (150 mg) + NVP (200 mg) BID d4T (30mg*) + 3TC (150 mg) + NVP (200 mg) BID d4T (6mg) + 3TC (30mg) + NVP (50mg) d4T (12mg) + 3TC (60mg) + NVP (100mg)
Two drug fixed-dose combination	AZT (300 mg) + 3TC (150 mg) given BID TDF (300mg) + 3TC (300 mg) given QD ⊗ d4T (30 mg*) + 3TC (150 mg) given BID d4T (6mg) + 3TC (30mg) d4T (12mg) + 3TC (60mg)
∗ FDCs are also available with d4T 40mg; however, this dose is no longer recommended. ⊗ TDF cannot be used in children or pregnant women due to its potential bone toxicity.	

NACP/NDS will make available updated lists of available drugs to Care and Treatment Program facilities on a quarterly basis.

11.2.3. Antiretroviral therapy (ART)

Antiretroviral therapy is prescribed as a combination of three drugs. Usually this will be in the form of either:

2 NRTI drugs plus 1 NNRTI drug
or
2 NRTI drugs plus 1 PI

All regimens prescribed in Liberia contain at least 2 NRTIs. It is not appropriate to use 2 NNRTI drugs together under any circumstance. There are occasional exceptional circumstances in which 3 NRTIs are used (discussed later in this chapter).

PIs should be preferentially reserved for use in second-line ART, after patients have failed first-line regimens of 2 NRTIs plus 1 NNRTI.

ARV combinations to be avoided or used with caution:

Significant drug interactions may occur when using some antiretrovirals in combination with each other or with other drugs.

- Certain combinations of NRTIs should not be used within three-drug therapy.
  - d4T + AZT (proven antagonism)
  - d4T + ddI (overlapping toxicities)
  - 3TC + FTC (interchangeable, but should not be used together) resistance to one means resistance to both
- The use of ddI should be reserved for second-line treatment.
- In second line regimens, it is possible to consider TDF + ddI with PIs, provided that caution and close clinical monitoring of toxicities are practiced. This combination can also result in suppression of CD4 production. When used together with TDF, all patients should receive ddI 250mg QD – the dose recommended for patients less then 60kg – in order to reduce potential toxicity.

11.3 Initiating ART

Before initiating therapy in any patient, the following should be done:

1. HIV diagnosis and HIV type confirmed (HIV-1 vs. HIV-2) and documented in the patient's chart
    - Note: symptomatic children <18 months suspected of HIV infection do not require a definitive HIV test prior to starting ART (see **Table 7.4**)
2. Patient confirmed eligible to start treatment (see **Section 7**)
3. Pre-ART counseling sessions completed; adherence emphasized and disclosure stressed. At least two adherence and counseling visits should be completed (at least 1 week apart, see **Section 5**, **Section 6** and **Appendix 4**) before ART is initiated on the third visit.
4. General orientation of the patient and family members, including:
    - Who and where to call for refills
    - Who and where to call for clinical problems
    - Who and where to call for social, spiritual and legal problems that might interfere with adherence to treatment.
5. Good history taken and physical exam performed; height and weight recorded
6. Laboratory tests (to establish baseline parameters for later monitoring):
    - Complete blood count
    - Chemistry profile with serum transaminases, glucose, creatinine and lipid profile (if available)
    - Pregnancy test in all women of childbearing age
    - CD4 and Total Lymphocyte Count (where available and applicable)
7. Screen for other infections
    - Chest x-ray to rule out tuberculosis (if available)
    - Blood smear to rule out malaria
8. Cotrimoxazole prophylaxis initiated
9. Multivitamins should be given (if available)
10. Treat any acute diseases (such as TB, PCP, candida, STIs, etc.) before commencing ARVs.

A second visit should be scheduled 2 weeks after the initiation of ART. It is important to recognize that ART should only be initiated if **all** clinical, immunological and adherence parameters are met.

Starting ART is not an emergency.

11.4 Reasons for temporary or permanent deferral of treatment

- Poor level of understanding/ poor adherence
- Current drug or alcohol abuse
- Untreated severe mental health illness
- Acute illness such as tuberculosis

11.5 Reasons for withholding treatment

- Terminal illness
- Patient refusal

11.6 Choosing an appropriate antiretroviral regimen

The choice of antiretroviral drugs/regimens is based on the following criteria:

- Therapeutic efficacy of each drug on HIV-1 and HIV-2
- Use in pregnant women, children, and TB coinfected patients
- Fixed dose combination (FDC) available
- Low pill burden
- Minimal and/or manageable side-effects
- Minimal storage constraints such as refrigeration
- Need to take medication with food

11.7 Preferred first line regimen for HIV-1 in adults and adolescents

Due to evidence that severe d4Ttoxicity is common and often irreversible, Liberia has revised its preferred first line regimens recommendations to **phase out the use of d4T.** Patients currently on ART and well tolerating of d4T can continue (though it is advised that the dose should be **immediately** decreased from 40mg to 30mg). d4T should be replaced with AZT or TDF if <u>any</u> symptoms of toxicity occur, (see **Section 16.4**: Description of specific drug toxicities and management).

For all treatment naïve patients, the preferred first line regimen choice is:

AZT + 3TC + NVP

(300mg BID + 150mg BID + 200mg BID*)

A caution on nevirapine:

***A 2-week initiating dose of NVP (200mg *<u>OD</u>*) must be used to reduce the risk of severe adverse reactions.**

- Nevirapine can, in some patients, cause severe adverse reactions such as Stevens-Johnson Syndrome or hepatitis. For this reason, **nevirapine is always prescribed using an *initiating* dose (half the usual dose) for the first 2 weeks of therapy.**
- If the patient tolerates the medication for the first 2 weeks, the triple combination regimen can be taken twice each day.
- If therapy is interrupted for any reason, the NVP initiating dose (200mg QD) must be repeated for two weeks; if well tolerated, the full dose (200mg BID) can be continued. (See **Figures 16.3** and **16.4**: Hepatotoxicity and skin toxicity associated with nevirapine management.)

<u>Interruption of ART should always be avoided</u>. (See **Section 20**: Interruption or discontinuation of ART.)

Dosing

Fixed dose combinations of the medications should be used whenever possible.

- **Phase one (2 weeks):**
  - AZT 300mg / 3TC 150mg / NVP 200mg QD (in morning) <u>and</u>
  - AZT 300mg / 3TC 150mg QD (at night)
- **Phase two:**
  - AZT 300mg / 3TC 150mg / NVP 200 mg BID if no or only mild nevirapine toxicity occurs (see **Section 16** and **Figures 16.3** and **16.4**)

- See **Figure 11.2** for more detailed description of how to choose the appropriate first line regimen for adults and adolescents with HIV-1.
- For more information on available ARVs and dosing, see **Appendices 7, 8,** and **9**.

11.8 Preferred first line regimen for HIV-1 in children and infants

Similar considerations were used for recommended first line regimens for children and infants, with three important notes:

- A d4T regimen is preferred because of its availability in fixed pediatric dose combinations for children who weigh over 3kgs.

d4T + 3TC + NVP

- Consult pediatric dosing chart for details of nevirapine initiating dose in children.

Children under 3kg should be given:

AZT + 3TC + NVP

(syrup form)

- TDF cannot be used in children because of potential bone toxicity.
- In cases of d4T toxicity, AZT should be used.
- EFV cannot be used in children less than 3 years old or smaller than 10 kg.
- Note: all dosages of pediatric medications must be calculated by weight (See **Section 14:** Care and treatment for HIV exposed and HIV positive children.) Fixed dose combinations may be dosed using a weight band dosing approach.
- See **Figure 11.3** for more detailed description of how to choose the appropriate first line regimen for children and infants with HIV-1.
- For more information on pediatric drug formulations and dosing, see **Appendix 7**: Summary of recommended first- and second-line ARV regimens for children, **Appendix 8**: Pediatric ARV drug formulations, side effects and special instructions for children, and **Appendix 9**: Pediatric dosing of ARV drugs.

11.9 Special considerations for first line HIV-1 treatments and suggested substitutions in case of toxcitiy

11.9.1. Patient with anemia (Hb less than 8 mg/dl)

Where baseline Hb is < 8 mg/dl:

- Where possible perform a full blood count including MCV to assess the nature of the anemia. Iron deficiency anemia is not a contraindication to AZT.
- Delay starting AZT and treat cause of anemia: parasites (hookworm or malaria), iron deficiency, folic acid deficiency. Check Hb again in 4wks. See **Figure 16.1** for details in initiating AZT and managing AZT toxicity.
- If cause unknown, give empirical therapy (mebendazole 100mg by mouth BID x 3 days) for presumed hookworm and treat with iron/folate for 1 month.
- If no improvement after one month, use:

TDF + 3TC + NVP

If capacity to investigate or treat anemia is limited, or in cases of severe HIV disease, patients should be started on a non-AZT regimen to avoid delays in treatment initiation.

Adult regimen options (in order of preference):

- TDF (300mg) / 3TC (300mg) QD plus NVP (200mg) BID
- d4T (30 mg)/3TC (150mg)/NVP (200mg) BID

Child regimen option:

- d4T/3TC/NVP BID (the whole fixed dose combination is weight-dosed)
- TDF cannot be used in children.

If anemia is treated and patient is started on **AZT**, obtain Hb at Day 0, weeks 2, 6, and 10 after initiation. If Hb drops <7g/dl after commencing AZT, **STOP** AZT, document toxicity, and replace with TDF or d4T. See **Figure 16.1**, Management of AZT toxicity, for more detail. If Hb is normal after 14 weeks, obtain Hb every 6 months.

11.9.2. First line drugs not available

It is anticipated that AZT and TDF will be widely available in Liberia by 2008. Until that time d4T 30mg can be substituted for either of them.
The regimen is:

- Adults: d4T (30mg)/3TC (150mg)/NVP (200mg) BID
  - 2 week initiating dose of NVP (200mg *QD*) must be given, if no/mild NVP toxicity dose should be increased to 200mg *BID*.
- Children: d4T/3TC/NVP, weight-based dosing

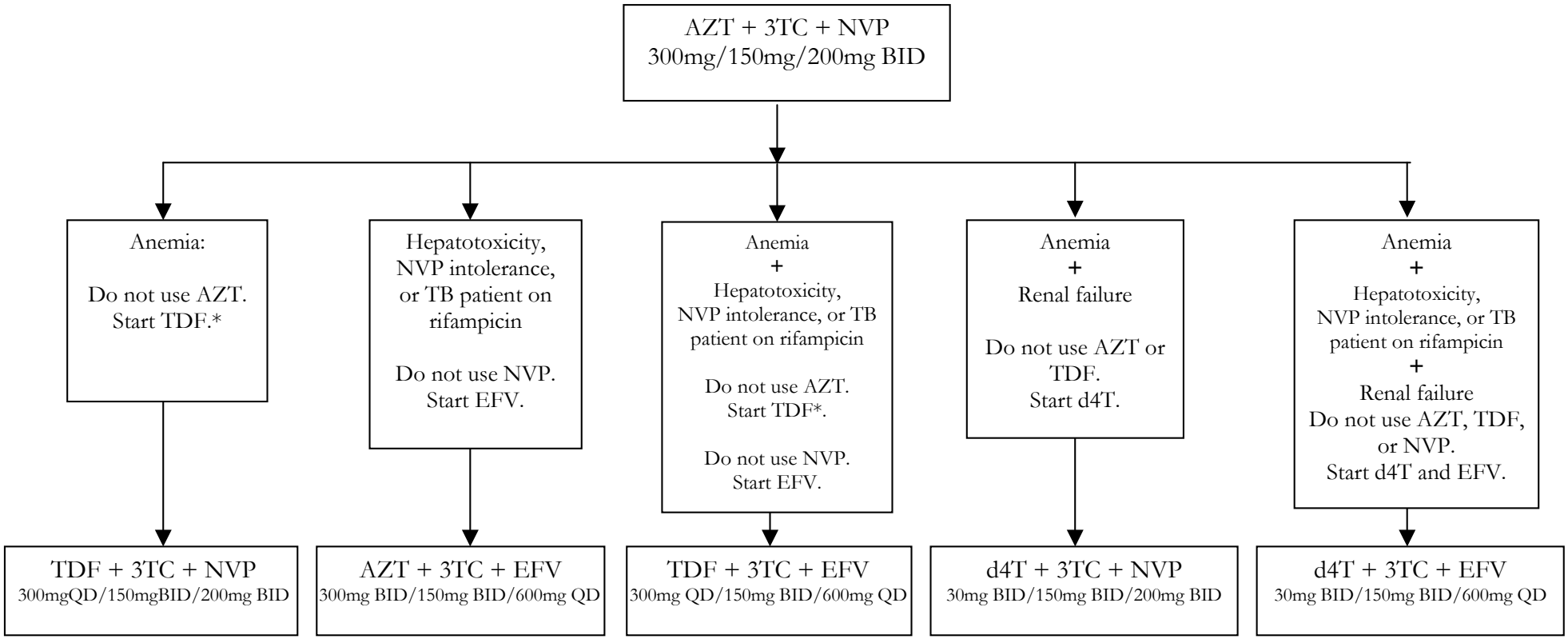
Note: Providers must be alert to complaints of peripheral neuropathy in patients taking d4T. If symptoms appear or symptoms are worsening, the d4T should be replaced. Bear in mind that peripheral neuropathy may be present prior to initiation of d4T. It can arise as a consequence of HIV infection itself, as well as diabetes, alcoholism, or nutritional deficiencies that can be exacerbated by taking isoniazid. This should NOT be considered as a contraindication to d4T but close observation is needed. (See **Section 16**: ARV treatment: toxicity and management.)

11.9.3. Other considerations and toxicities

Management of ART in women of childbearing age is addressed in **Section 12**, and the Management of ART in the presence of tuberculosis, hepatitis B, kidney disease, and liver failure is addressed in **Section 18**.

See **Figure 11.2** below for suggested substitutions within the first line regimen in case of toxicity.

Figure 11.2 Summary of preferred first line regimen options/substitutions for treatment of HIV-1 in adults and adolescents.



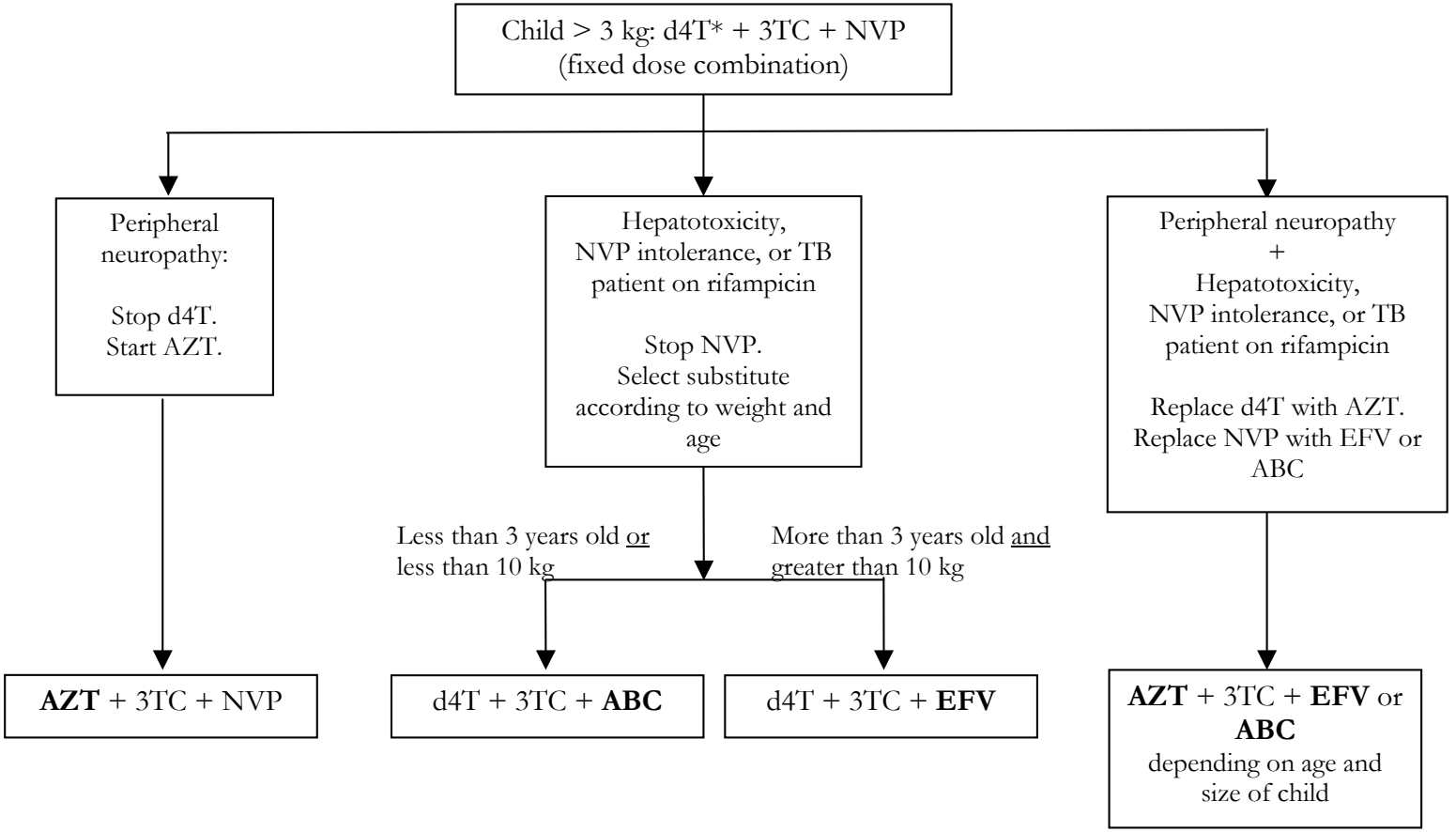
*TDF is expected to be available in Liberia in late 2007. Until that time, start d4T 30mg wherever TDF is mentioned.

•All adults should be given d4T 30mg BID, irrespective of weight.

•EFV should be avoided in women in the 1st trimester of pregnancy or who are of childbearing age and not using consistent contraception.

•Refer to **Section 16.4.3.2** for grading of NVP toxicity and hepatotoxicity. Refer to **Table 18.5** for grading of renal dysfunction.

Figure 11.3 Summary of preferred first line regimen options/substitutions for treatment of HIV-1 in children



*If child is less than 3kgs, AZT should be used (all drugs should be dosed in syrup form according to patient weight).

- All drugs should be dosed in Fixed Dose Combinations (as available) according to patient weight.
- EFV cannot be used in children who are either <10 kg or < 3years of age.

11.10 Preferred first line regimen for HIV-2 or HIV-1/HIV-2 coinfection

NNRTIs (Nevirapine and Efavirenz) are not effective against HIV-2. Treatment with triple NRTIs is not preferred for HIV-1 or HIV-2. Therefore, patients with HIV-2 alone or who are coinfected with HIV-1 and HIV-2 should be treated with 2 NRTIs and a PI:

The preferred first line regimen for HIV-2 *or* HIV-1 and HIV-2 coinfection:

Adults/Adolescents	AZT/3TC/LPV/r 300mg BID/150mg BID/200/50mg (heat stable)x2 pills BID
Infants and Children* > 3 yrs old	d4T/3TC/LVP/r
Infants and Children* < 3 yrs old	AZT/3TC/LVP/r

Note: ATV/r (300mg/100mg QD) can be substituted for LPV/r for adults. It is not currently licensed for use in children.
*See pediatric dosing guide, **Appendix 10**.

11.11 Special considerations for first line treatment of HIV-2 or coinfection of HIV-1/HIV-2

11.11.1. First line drugs not available

- When both LPV/r (Kaletra) and ATV/r are not available, NFV can be substituted temporarily until they are available again.
- The regimen is:
  - Adults and adolescents:
    - AZT (300mg BID)/3TC (150mg BID)/NFV (1250mg BID)
  - Children and infants:
    - Weight-based three times daily dosing for all children.

11.11.2. Patient with anemia (Hb < 8 mg/dl)

- Investigations and presumptive treatments should be carried out as discussed above under HIV-1.
- If no improvement after one month, substitute TDF (or d4T) for AZT.
- **Note:** If capacity to investigate anemia is limited, or in cases of severe HIV disease, patients should be started on a non-AZT regimen to avoid delays in treatment initiation
- Adult regimen options (in order of preference):
  TDF (300mg QD)/3TC (150mg BID)/LPV/r (400/100mg BID)
  d4T (30mg BID)/3TC (150mg BID)/LPV/r (400/100mg BID)
  - Child regimen option:
    d4T/3TC/NFV (weight-dosed)
    TDF cannot be used in children
- If anemia is treated and patient is started on **AZT**, obtain Hb at Day 0, week 2, 6, and 10 after initiation. If Hb drops <7g/dl after commencing AZT, **STOP** AZT, document toxicity, and replace with TDF or d4T. See **Figure 16.1**, Management of AZT toxicity, for more detail. If Hb normal after 14 weeks, obtain Hb every 6 months.

SECTION 12: Antiretroviral therapy in women of childbearing age and pregnant women

12. Antiretroviral therapy in women of childbearing age and pregnant women

The guiding principle for the treatment of women of childbearing potential or pregnant women is that therapeutic decisions should **always** be based on the woman's need and eligibility for ART.

The special circumstances of pregnancy or breast-feeding raise additional issues concerning toxicity to mothers and children, the choice of ARV drugs, and the prevention of HIV transmission from mothers to infants.

12.1 Special topics for counseling women of childbearing age

- Conception counseling
- Clinicians should always ask when the woman had her last menstrual period, and if not within past one month, a pregnancy test should be given
- Potential modes of transmission (focus on delivery and infant feeding)
- Provide information on the impact of HIV on the mother's and baby's health
- Encourage the woman to involve her partner or reliable close friend
- Explain how to access a support network and continued counseling as necessary
- Explain self-care initiative such as appropriate nutrition (see **Section 10**, Positive living)

12.2 Contraception for women of childbearing age receiving ART who do not want to become pregnant

- Effective and appropriate use of contraceptives is essential.
- ART may decrease the effectiveness of oral contraceptives.
- Condoms should be recommended to prevent HIV, but a second method of contraception (such as Depo-Provera or oral contraceptives) should be advised to prevent pregnancy.
- If Depo injections are used, adherence to the 3 monthly injections is critical, as ART can decrease the length of the injection's effectiveness.
- Abstinence is the best way to prevent pregnancy and the spread of HIV.

12.3 Antenatal care for women receiving ART who become pregnant

- HIV positive women should receive the same schedule of antenatal care as that given to HIV negative women.
- Additional care for OIs, toxicities or treatment failure may be necessary.
- Additional counseling time is required to discuss mother to child transmission.
- The integration of antenatal care, medical care for HIV-related conditions, social and psychological support is important.

12.4 General concepts for ART in pregnant women

Start cotrimoxazole prophylaxis (unless CD4 count known to be >350 cell/mm^3)
  - See **Section 9**.
  - Do not give S-P (Fansidar) if the woman is on cotrimoxazole.
- Always recommend, and, if possible, provide insecticide-treated nets.
- Screen and treat all pregnant women for STIs and TB.

12.5 When to start ART in pregnant women: clinical and immunological criteria

It is preferable to wait until after the 1st trimester to start ART. However, the decision to start ART should be based primarily on the woman's need and eligibility for antiretrovirals.

- Clinical criteria: stage 3 or 4 disease, or co-infection with TB
  Note: Weight loss, which may normally be a sign of severe disease, may appear less severe in pregnant women.
- Immunological criteria: CD4 count <350 cells/mm^3 or TLC <1200 cells/mm^3

Table 12.1 Initiating ART for pregnant women

WHO Clinical Stage	CD4 testing NOT Available	CD4 testing available
1	CPT*	TREAT if CD4 cell count <200 cells/mm^3
2	CPT*	TREAT if CD4 cell count <350 cells/mm^3
3	Three-Drug ART	TREAT if CD4 cell count <350 cells/mm^3
4	Three-Drug ART	TREAT irrespective of CD4 cell count

*See **Section 10:** Prophylaxis against HIV-associated infections with cotrimoxazole preventive therapy (CPT).

All pregnant women who are not yet eligible for ART should be provided with prophylactic ARVs for PMTCT starting at 28 weeks. See **Section 13**.

12.6 Starting ART in pregnancy

- In the first trimester, avoid EFV because of risk of congenital malformations
- EFV can be used safely in women
  - Using effective contraception (dual method should always be recommended)
  - In the 2nd and 3rd trimesters of pregnancy
- NVP carries an increased risk of causing liver toxicity in women with CD4 counts > 250 cells/mm^3:
  - Liver function tests should be checked closely when starting NVP and every 6 months after that. (See **Section 15**: Monitoring patients on ART, for laboratory monitoring schedule.)
- Do not use d4T and ddI in combination because of risk of lactic acidosis.
- Do not start a pregnant patient on TDF because of risk of decreasing bone density in the fetus (although if she is on it and tolerating it, the risk is not high enough to require a change).

12.6.1. Women who require initiation of ART during pregnancy

- Delay initiation of ART until 12 weeks (i.e. end of first trimester) unless the mother is severely immunosuppressed.
- For women who are severely immunosuppressed, the benefit of early therapy clearly outweighs any potential fetal risks. Thus, therapy may be initiated in the first trimester in these cases.
- ART is continued for life. After delivery the mother should be referred to the ART clinic for ongoing care.

12.6.2. Women who are not clinically eligible and require PMTCT only

HIV positive pregnant women who are not yet eligible for ART should receive ARV prophylaxis only for PMTCT purposes as per the protocol in **Section 13**.

12.7 Specific ART regimens for pregnant women

12.7.1. Pregnant women with HIV-1

First Line	AZT/3TC/NVP[1,2] 300mg BID/150mg BID/200mg BID
Second Line	ddI/ABC[3]/LVP/r 400mg QD[4]/300mg BID/ 400/100mg BID

[1]NVP should have a two-phase starting dosage (see **Section 11.7**)
[2]If CD4 count available and >250, replace NVP with EFV or LPV/r due to increased risk of liver toxicity.
[3]If ABC hypersensitivity is a concern, 3TC can be used in the 2nd line.
[4]ddI dosing is weight based. If patient is >60kg dose is 400mg QD, if <60kg give 250mg QD.

12.7.2. Pregnant women with HIV-1 who have anemia

- Diagnose cause of anemia
- Provide treatment for malaria and hookworm if needed
- Provide supplements of folate and iron if needed
- If Hb falling, substitute d4T 30mg for AZT. Recommended regimen:

d4T*/3TC/NVP** 30mg BID/150mg BID/200mg BID

*ABC (300mg BID) can be used in place of d4T
** NVP should have a two-phase starting dosage (see **Section 11.7**)

12.7.3. Pregnant women with HIV-1 who have active tuberculosis

- Start anti-TB treatment first.
- Start ART as soon as possible but not before TB therapy has been taken (and tolerated) for 2 weeks to avoid confusion about any drug toxicity that may occur and to decrease the risk of immune reconstitution inflammatory syndrome (IRIS).
- During labor, ART for PMTCT should be provided (see **Section 13**) **regardless of whether or not the woman has taken and tolerated 2 weeks of TB therapy**.
- See **Section 18** for more information on managing HIV and TB coinfection.

Recommended regimens for pregnant women **with TB** who require ART:

If in intensive phase of TB treatment: (**1st** trimester) AZT/3TC/**ABC** (**2nd** or **3rd** trimester) AZT/3TC/**EFV** If in continuation phase of TB treatment: AZT/3TC/**NVP**

It is essential that a provider refer to **Section 11**: Antiretroviral Therapy and recommended first line regimens in adults and children, before starting any of the regimens listed above. A schedule for baseline and follow-up laboratories can be found in **Section 15**: Monitoring patients on ART.

12.7.4. Pregnant women with HIV-2 or HIV-1/HIV-2 coinfection

NNRTIs are not effective and should not be used.

Recommended regimen:

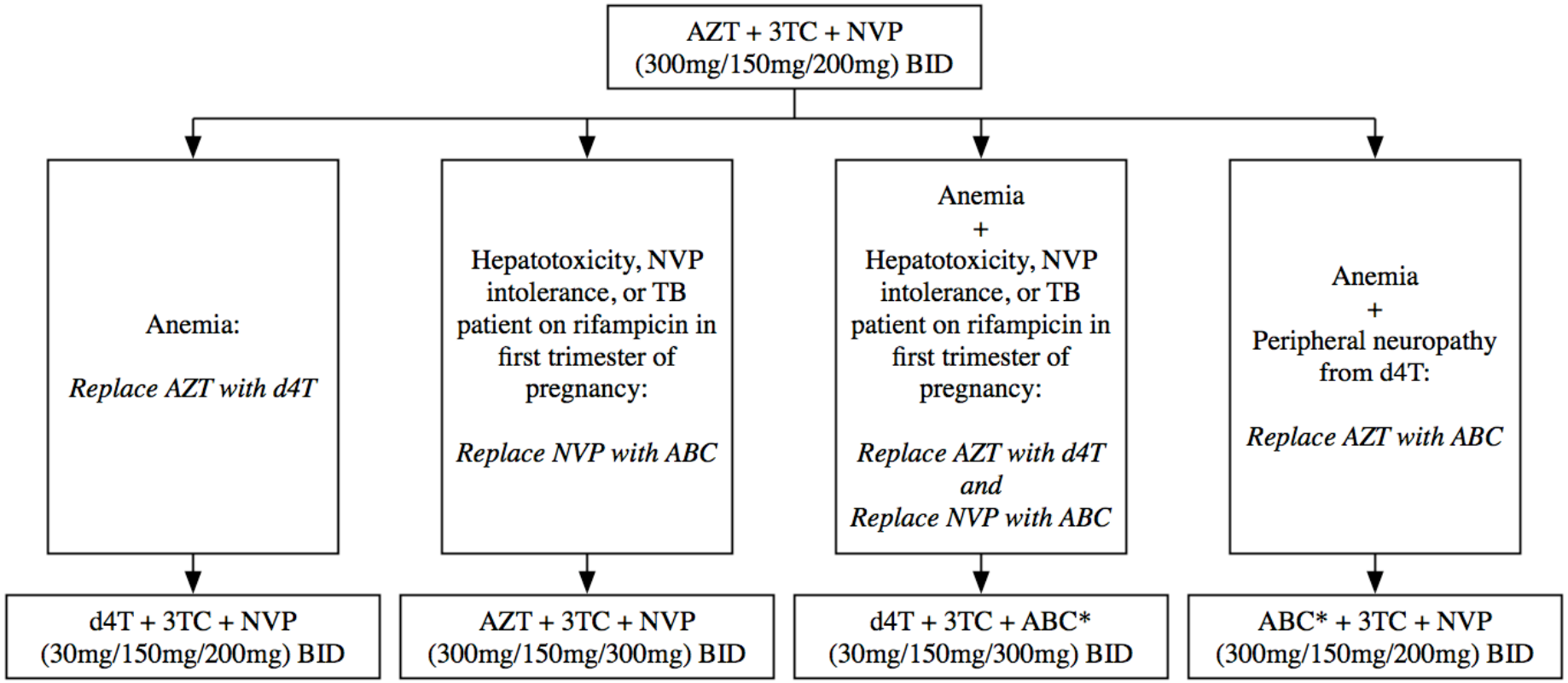
First Line[1]	AZT/3TC/LPV/r 300mg/150mg/400/100mg BID
Second Line	ddI/ABC[2]/LVP/r 400mg QD[3]/300mg BID/ 400/100mg BID

[1]ATV/r (300mg/100mg QD) can be used in place of LPV/r (Kaletra). When neither is available, NFV (1250mg BID) can be substituted. Triple NRTI can be used as a fourth option if PI regimen is not available. Triple NRTI regimen consists of AZT/3TC/ABC or d4T/3TC/ABC.

[2]If ABC hypersensitivity is a concern, 3TC can be used in the second line. However, patients failing a first-line therapy containing 3TC are more likely to have developed resistance to 3TC and FTC.

[3]ddI dosing is weight based. If patient is >60kg dose is 400mg QD, if <60kg dose is 250mg QD.

Figure 12.1 Summary of preferred first line regimen options/substitutions for treatment of HIV-1 in pregnant women requiring ART



*EFV may be used if in the 2nd or 3rd trimester of pregnancy.

12.8 Women who become pregnant while on ART

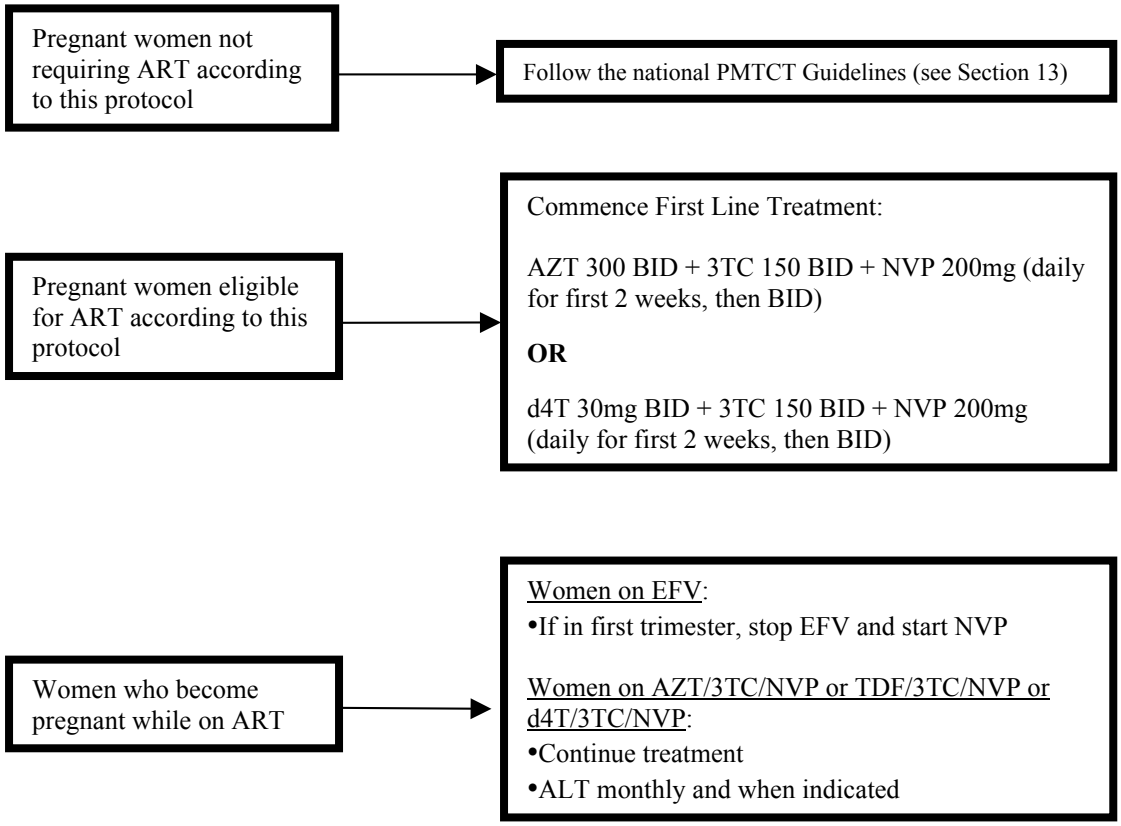
If women become pregnant on a regimen containing:

- **AZT** or **d4T:** The regimen should be continued throughout pregnancy.
- **NVP:** The ALT should be performed 3 monthly and as needed. NVP should be switched if ALT >5x ULN as per **Section 16.4.3.2**.
- **EFV:** as soon as pregnancy is suspected the EFV should be switched to NVP (though if pregnancy is only confirmed after first trimester, EFV can be continued).
- **TDF:** if tolerating it well, the regimen should be continued throughout pregnancy (the risk of decreasing bone density in fetus is not high enough to require a change).

Women who develop severe pregnancy-related nausea and vomiting (hyperemesis gravidarum) might require temporary discontinuation of treatment. When this occurs, all drugs should be stopped and restarted simultaneously. Treatment should be restarted after all symptoms of hyperemesis have subsided to ensure the drugs will be well tolerated.

All patients on ART should be assessed for treatment failure; where failure is confirmed, ART should be changed as early in pregnancy as feasible to allow time for maximal suppression of viral replication before delivery.

Figure 12.2 Summary: How to treat pregnant women with HIV-1



12.9 Returning to pre-pregnancy ARV regimens after delivery

Every change to a patient's regimen decreases the likelihood of adherence. Thus, returning patients to their pre-pregnancy regimens should occur only for the following reasons:

- The original substitution was made because of concern for pregnancy related toxicities, not because of treatment failure;
- The original regimen has fewer potential toxicities, is better tolerated, and is in consistent supply;
- The patient has good comprehension of the reasoning for the repeated changes to her regimen and a history of adherence to therapy.

12.10 Monitoring therapy during antenatal care and delivery

- ARVs can be provided in the antenatal clinic or through the general ART program. Patients should return 2 weeks after commencing therapy then monthly for ARV refill and standard ANC follow-up care. After 36 weeks gestation, visits should become weekly (according to patient's ability to schedule visits this frequently).
- At each follow-up visit, providers should assess:
    - Patient adherence to ART
    - Occurrence any adverse reactions to ARVs
- Routine lab testing should follow established ANC and ART monitoring guidelines (see **Section 15**, Monitoring patients on ART).
- Care should be taken to ensure ART is not interrupted when patient is admitted to the labor ward or after delivery.

12.11 Care and treatment for HIV exposed infants

All children born to HIV positive mothers, regardless of whether the mother is receiving ART or received ARV prophylaxis for PMTCT, are considered HIV exposed infants.

<u>All</u> HIV exposed infants born should receive appropriate ARV prophylaxis to prevent mother to child transmission and be followed regularly.

See the **next section** for PMTCT protocols (**Section 13**: ARV Prophylaxis to prevent transmission of HIV from mother to child, particularly **Figure 13.2**) and **Section 14**: Care and treatment of HIV exposed and HIV positive children, for information on appropriate follow up care for infants born to HIV positive mothers.

Starting at 6 weeks, HIV exposed infants should receive cotrimoxazole preventative therapy (CPT) (see **Section 9**: Prevention of opportunistic infections with cotrimoxazole preventive therapy, and **Section 14**: Care and treatment of HIV exposed and HIV positive infants and children).

SECTION 13: ARV prophylaxis to prevent transmission of HIV from mother to child (PMTCT)

13. ARV prophylaxis to prevent transmission of HIV from mother to child (PMTCT)

This section discusses how to prevent transmission of HIV from mother to child.

- In the absence of any intervention, the risk of an HIV positive woman transmitting the infection to her child is 15-30% in *non-breastfeeding* populations.
- Breastfeeding by an HIV positive mother increases the risk to a total of 20-45%.
- *The risk of MTCT can be reduced to under 2%* by interventions that include antiretroviral (ARV) prophylaxis given to women during pregnancy and labor and to the infant in the first weeks of life, and complete avoidance of breastfeeding.
- **ARV prophylaxis for PMTCT should be given to <u>all</u> children born to an HIV positive mother and to <u>all</u> pregnant HIV positive women not yet eligible for ART.**

Pregnant women who test HIV negative during the first trimester should be retested in the third trimester to rule out the possibility of a false negative diagnosis (testing negative during the window period).

All facilities should develop means of communicating the mother's HIV status between heath care workers as necessary, however, **<u>confidentiality must be maintained</u>**. Each pregnant woman should be counseled about the importance of PMTCT and encouraged to take responsibility to ensure that she and her baby receive the appropriate ARVs, particularly during and after delivery.

ARV prophylaxis and ART are **two different treatments**:

- ARV prophylaxis for PMTCT is a <u>short course</u> of ARVs given during pregnancy and shortly after delivery to prevent the transmission of HIV to the infant.
- ART is a <u>lifelong</u> ARV regimen given to improve the HIV positive patient's quality of life by restoring and preserving immunologic function. Management of women who are eligible for ART is discussed in the previous chapter.

Table 13.1 Factors that have an impact on mother to child transmission (MTCT)

Maternal Factors	Obstetrical Factors	Infant Factors	Infant Feeding Factors
High viral load Recent infection Advanced disease	Rupture of membranes >4 hours	Prematurity	Breast feeding
Poor nutrition	Episiotomy	First infant of multiple birth	Mixed feeding
Concurrent STI's	Invasive fetal monitoring	Immature GI tract	Maternal breast pathologies (mastitis)
Placental infection (esp malaria)	Intrapartum hemorrhage		Longer duration of breast feeding
	Instrument delivery		Maternal HIV infection during lactation
	Vaginal vs C-section		Mouth sores in infant

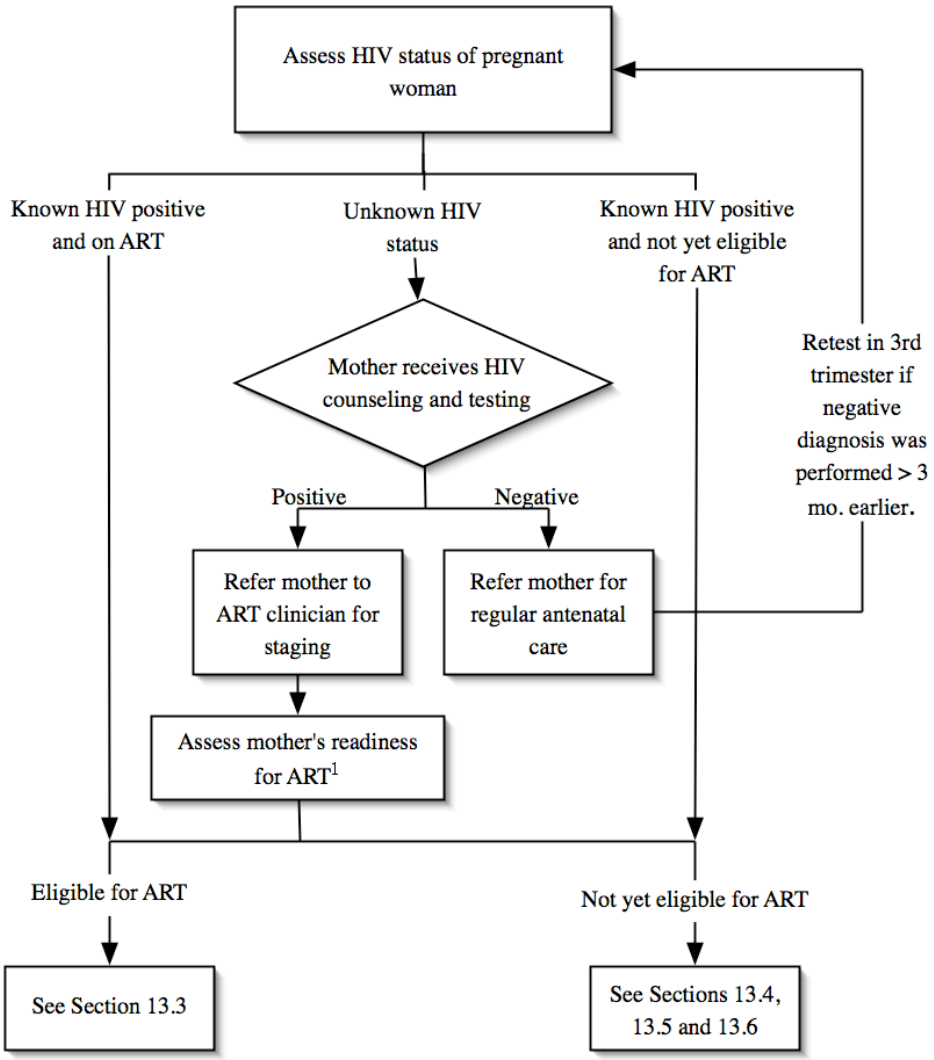
13.1 General rules concerning labor and delivery

- All women should be encouraged to deliver in hospital.
- Procedures likely to cause mixing of maternal and fetal blood should be avoided:
    - Do not perform elective episiotomies.
    - Do not routinely rupture membranes.
    - Avoid prolonged rupture of membranes. Caesarian section should be considered if necessary to avoid membranes being ruptured for 24 hours or more.
    - Do not milk placental blood toward the baby. The umbilical cord should be clamped immediately.

13.2 Overview of PMTCT

All pregnant women should be encouraged to test for HIV. Women who test positive should be immediately referred to the ART clinic and assessed for eligibility for ART. Women who are not yet eligible for ART should receive PMTCT. See **Figure 13.1**.

Figure 13.1 Overview of PMTCT for all pregnant women

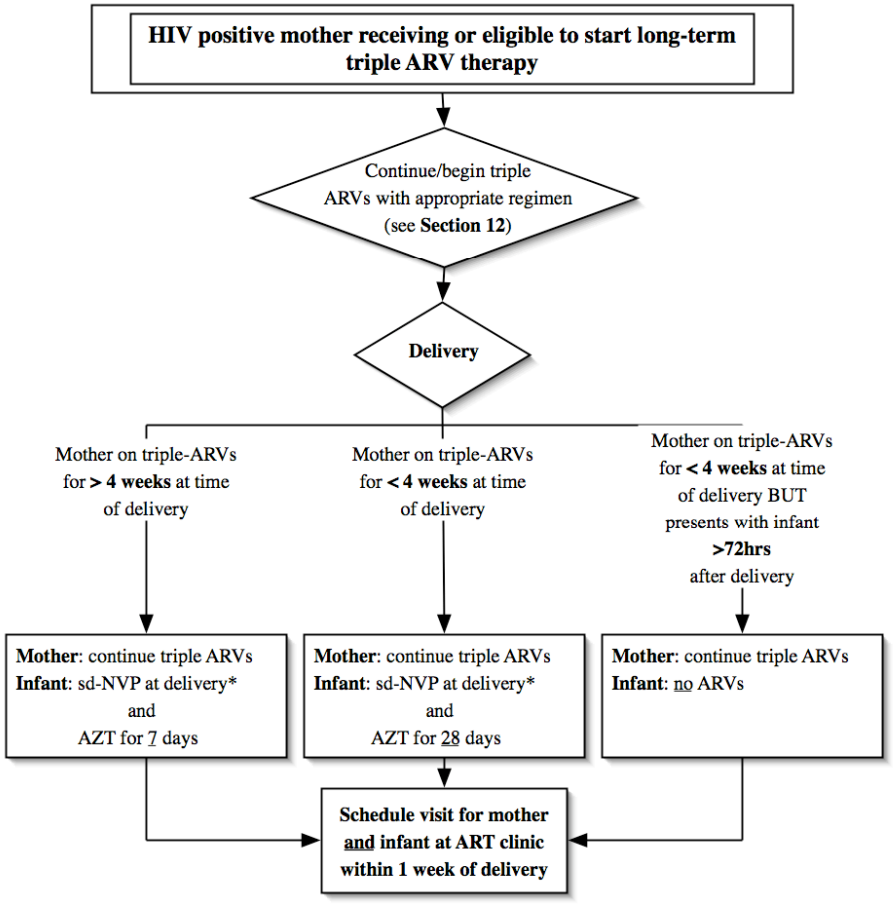


[1] See **Section 7**, Patient assessment for treatment and **Section 12**, ART in pregnant women.

13.3 PMTCT for HIV positive mothers who are receiving or eligible to start ART and their infants

- See **Section 12** for details on choosing ART regimens for pregnant women. The mother should continue this ART regimen throughout pregnancy and delivery.
- The infant should receive ARV prophylaxis as soon as possible after delivery:
    - Infants born to mothers who have received ART continuously for **more than** 4 weeks before delivery should receive sd-NVP 2mg/kg oral suspension **and** AZT 4 mg/kg BID for the first *7 days* after delivery.
    - Infants born to mothers who received ART for **less than** 4 weeks before delivery should receive sd-NVP 2mg/kg oral suspension **and** AZT 4 mg/kg twice daily for the first *28 days* after delivery.
- Infants of mothers infected with HIV-2 **only** should receive only AZT 4 mg/kg BID, and **not** the sd-NVP.
- If mother arrives at clinic more than 72 hours after delivery, do not provide medications to the infant; they will not be effective.

Figure 13.2 PMTCT for HIV positive mothers receiving or eligible for ART and their infants



Dosing for mother: same as regular triple ARV regimen (see **Section 12**)
Dosing for infant: AZT 4mg/kg twice daily, sd-NVP 2mg/kg oral suspension or 6mg.

*If mother is infected with HIV-2 only, the infant receives only AZT following delivery (no sd-NVP).
(If mother is infected with HIV-1 only, or if she is coinfected with HIV-1 and HIV-2, follow the flowchart above.)

13.4 PMTCT for mothers infected with HIV-1 who are not yet eligible for ART and their infants

Not all women who are HIV positive require ART. To eliminate HIV infection of infants and young children, HIV positive pregnant women who do not yet require lifelong antiretroviral therapy must be provided short-term antiretroviral medications to prevent transmission of HIV from mother to child (see **Section 12** for eligibility criteria).

It is very important for HIV positive mothers to register their infants at the ART clinic so that they may start cotrimoxazole preventive therapy from 6 weeks of age. The cotrimoxazole should be continued until HIV infection is confirmed negative.

13.4.1. Recommended regimens for mothers in consistent antenatal care

The recommended regimen described below begins at 28 weeks of pregnancy, which requires that women attend antenatal care services early in pregnancy. However, prophylaxis should be provided to all HIV positive women and their infants, whether women test positive before pregnancy, at some point during pregnancy, at the time of labor and delivery, or postpartum (see **Figure 13.4** below, for a summary of PMTCT for women not yet eligible for ART).

Antepartum – AZT 300 mg twice a day from 28 weeks of pregnancy (or as soon as possible thereafter. AZT twice daily can be started at any time up until labor.)

Intrapartum –

- AZT:
  - If delivery imminent (expected within 2-3 hours) give 600mg AZT once
  - If in early labor give 300mg AZT every 3 hours until delivery
- AND give 3TC 150 mg twice daily commencing at onset of labor
- AND give a single dose of nevirapine (sd-NVP) 200 mg at the onset of labor

Postpartum –

- Mothers: continue AZT 300 mg twice a day and 3TC 150 mg twice a day for seven days then stop both drugs. (Refer to **Section 13.7.3** for explanation)
- Infants: sd-NVP 2 mg/kg oral suspension immediately after birth and AZT 4 mg/kg twice a day for 7 days

See **Figure 13.4** below for summary of PMTCT for women not yet eligible for ART.

13.4.2. Recommended regimens for mothers who present late in pregnancy or shortly after delivery

Mothers who present in labor:

- AZT
  - If delivery imminent (expected within 2-3 hours) give 600mg AZT once
  - If in early labor give 300mg AZT every 3 hours until delivery
- AND give 3TC 150 mg twice daily commencing at onset of labor
- AND give a single dose of nevirapine (sd-NVP) 200 mg at the onset of labor

Postpartum –

- Mothers: continue AZT 300 mg twice a day and 3TC 150 mg twice a day for seven days then stop both drugs.
- Infants: sd-NVP 2 mg/kg oral suspension immediately after birth and AZT 4 mg/kg twice a day for 28 days

Mothers who arrive in care within 72 hours after delivery:

If the mother did not receive sd-NVP during labor, the mother can discontinue all ARVs and should be referred to the ART clinic. If an HIV positive mother did not receive any ARV prophylaxis for PMTCT but arrives in care within 72 of delivery, only the infant should receive ARVs. Give sd-NVP 2mg/kg as soon as possible and start AZT 4mg/kg BID for 28 days.

PMTCT should be the immediate priority for HIV positive pregnant women who present late in pregnancy or who arrive at the clinic soon after delivery. However, the mother's clinical or immunological eligibility for ART should be assessed as soon as possible after delivery. CD4 or TLC testing should be performed as soon as possible after delivery and if the mother is eligible for ART (see **Section 7**: Patient assessment for treatment), treatment should begin as with all other HIV positive patients. (See **Figure 13.4** below for summary of PMTCT for women not yet eligible for ART.)

13.5 Mothers coinfected with HIV-1/HIV-2 who are not eligible for ART

Follow guidelines for PMTCT for mothers infected with HIV-1 (see **Sections 13.3.1** and **13.3.2** above). The AZT and 3TC components of this regimen are critical, as the sd-NVP will have no effect on the HIV-2.

13.6 Mothers infected with HIV-2 who are not eligible for ART

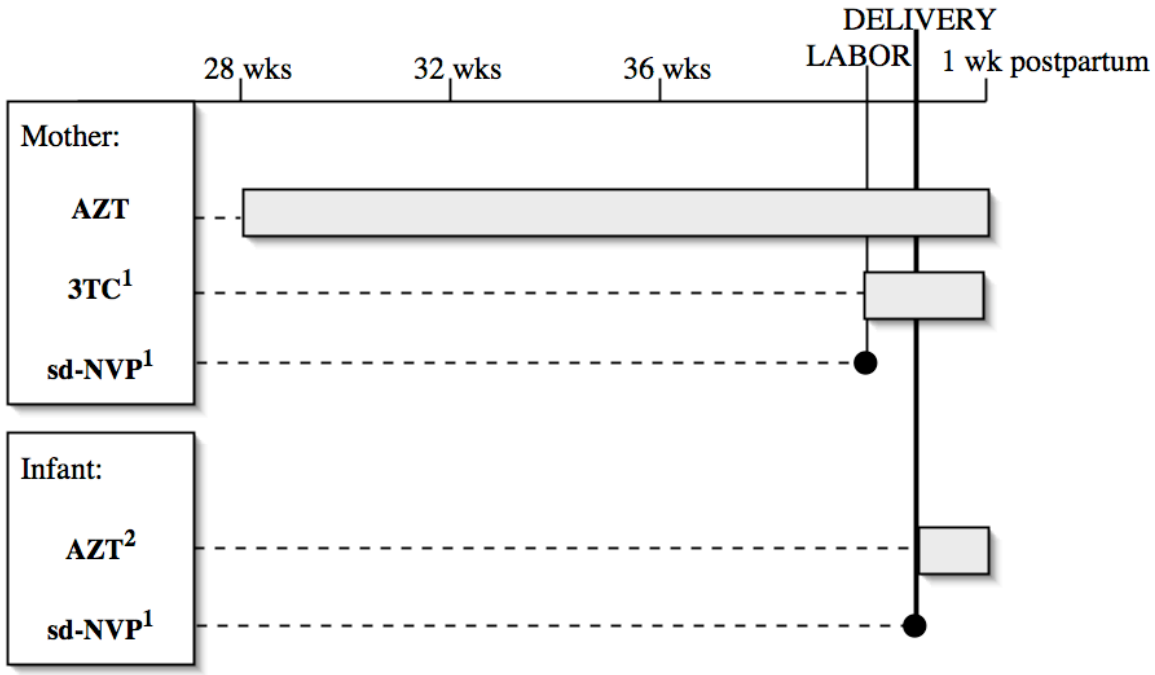
- HIV-2 is less transmissible from mother to child than HIV-1.
  - Only AZT is used as per **Table 13.3** below.
  - Single dose NVP is not used for mother or child. Thus, the mother does not need ARVs postpartum.
  - There is no use of 3TC at onset of labor
  - AZT is discontinued for the mother after delivery

Table 13.2 PMTCT for mothers infected with HIV-2 who are not yet eligible for ART

Patient and Timing	Regimen
Mother Antepartum and Intrapartum Postpartum	 AZT 300 mg twice daily[a] AZT until delivery[b]
Infant	AZT for 7 days[c]

[a] Start at 28 weeks or as soon as possible thereafter.
[b] Dosing at labor: AZT 600mg at onset of labor (or 300mg at onset of labor and thereafter every 3 hours until delivery)
[c] Dosing: AZT 4 mg/kg BID. If mother took AZT for < 4 weeks before delivery, infant should receive AZT for 28 days.

Figure 13.3 Ideal PMTCT regimen for HIV positive mothers not yet eligible for ART and their infants

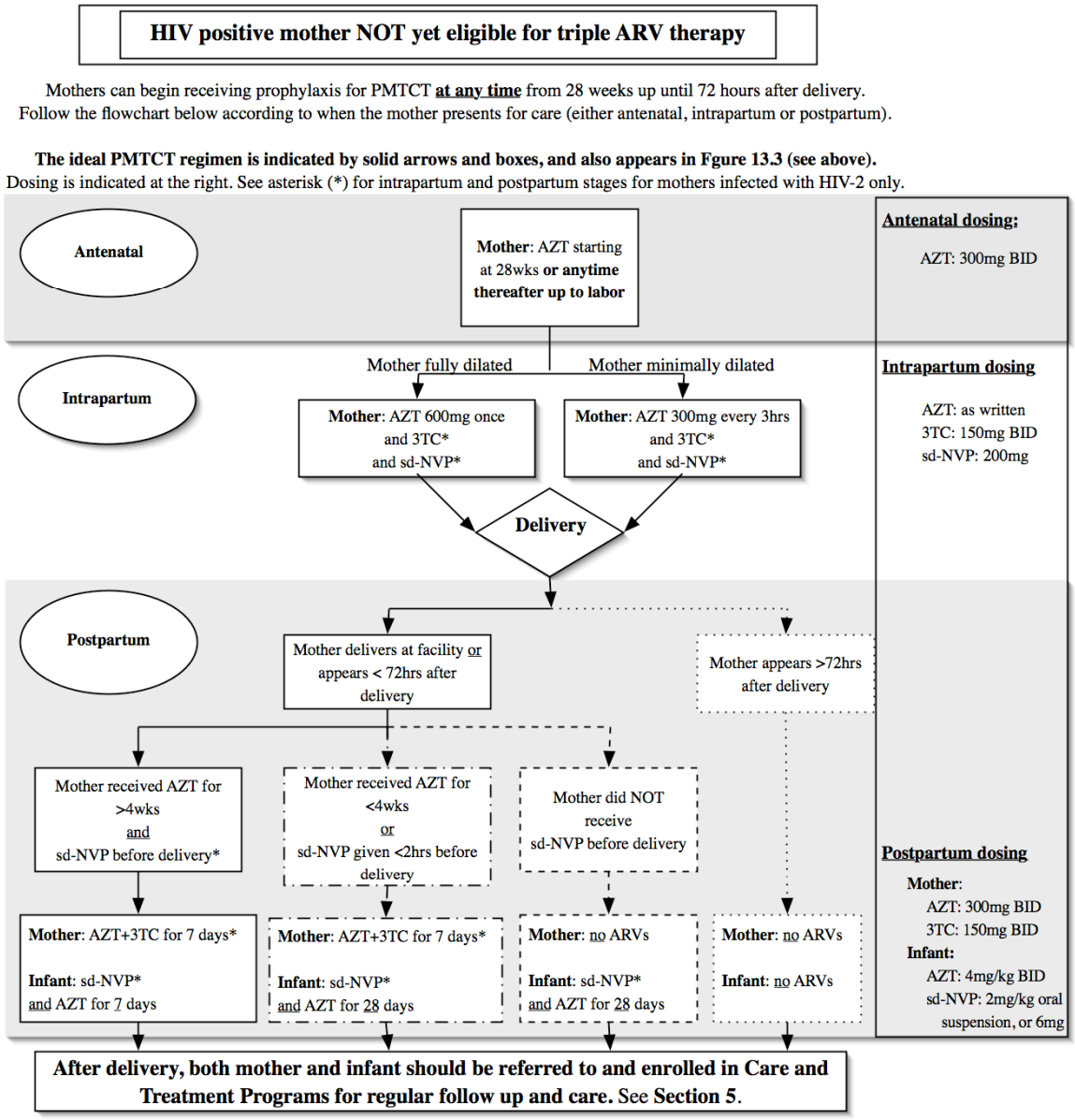


[1]Include for mothers infected with HIV-1 or mothers coinfected with HIV-1/HIV-2 and their infants. Omit for mothers infected only with HIV-2 and their infants. Mothers infected with HIV-2 should **stop** all ARVs after delivery.

[2] If mother was on PMTCT ARVs for <4 weeks continue AZT twice daily for 28 days

Refer to Figure 13.4 (below) for dosing information.

Figure 13.4 Summary of PMTCT for HIV positive mothers not yet eligible for ART



*Omit these ARVs for mothers infected only with HIV-2 and their infants. HIV-2 infected mothers should receive AZT before and during delivery, but should **not receive** sd-NVP or 3TC. After delivery all ARVs should be **discontinued**. Infants born to mothers infected with HIV-2 should **only** receive AZT (no sd-NVP).

13.7 Special notes on PMTCT protocols

13.7.1. Severe anemia (Hb < 8 g/dl)

- **Prior** to commencing ARV prophylaxis, test the mother for anemia. See **Section 12.8.2.1**
- Treat the anemia before commencing AZT.
- Once the Hb >8 g/dl, AZT can safely be used as prophylaxis.
- If started on AZT, obtain Hb at day 0, week 2, 6, and 10 after initiation. If Hb drops <7g/dl after commencing AZT, **stop** AZT. Recommence with standard PMTCT protocol (including AZT) at onset of labor.
- If Hb does not increase to >8g/dl, **do not** give AZT antepartum. Commence prophylactic ARVs at onset of labor (see above, **Figure 13.4**, and follow flowchart beginning with intrapartum ARVs).

13.7.2. Toxicity

There is limited risk of toxicity to the woman or her infant from short-term use of ARVs.

13.7.3. Resistance

Resistance can develop if HIV is treated with only one drug at a time. Giving a single dose of NVP creates an opportunity for resistance to develop—it remains active in the body for up to 7 days after being taken.

To prevent all women receiving the sd-NVP from developing resistance to the NVP, it is essential that she receive 7 days of AZT and 3TC post-partum.

13.7.4. PMTCT in previous pregnancies

The same PMTCT regimens can be used more than once for the same woman.

13.7.5. In the event of shortage of medicines

Providing sd-NVP to mother and infant at time of delivery is not optimal, but is significantly better than providing no care at all.

13.7.6. Deliveries that occur at home

If the provider anticipates that a delivery will occur at home, the woman can be provided with the appropriate medications with *careful* counseling regarding how to take them, how to give them to the infant and *close* follow-up.

13.8 Reducing the risk of MTCT post-partum: infant feeding options

- Mothers should be assisted in choosing the most appropriate method of infant feeding for her circumstances. In Liberia, this will most often be exclusive breastfeeding.
- Triple ART is the most effective means of preventing the transmission of HIV to the infant during breastfeeding. Therefore,
- Mothers who are eligible for ART must be on appropriate therapy (see **Section 6**: Patient assessment for treatment and **Section 12**: Antiretroviral therapy in women of childbearing age and pregnant women);

13.8.1. Counseling and support on HIV and infant feeding

- Before delivery: The mother should be counseled on infant feeding options. This may take one or more sessions. See **Appendix 10** for decision-making tool for infant feeding options.
- Soon after birth: (ideally before discharge from the hospital) Teach the mother how to implement her selected option.
- During routine postnatal care and at every well-child or sick-child attendance: provide follow-up counseling and support
- At any point when the mother plans to change her feeding practice provide appropriate counseling and support.

13.8.2. Infant feeding options

Whichever feeding method is chosen, it should be used exclusively so as to minimize the risk of maternal to child transmission.

- Mixing breastfeeding with forms of replacement feeding increases the child's risk of disease and death.

1. Exclusive breastfeeding
    - **Involves giving infants *only* breast milk and no other liquids or solids—*NOT EVEN WATER*.**
    - Mixing breastfeeding with forms of replacement feeding increases the child's risk of disease and death.
    - **Should be discontinued abruptly when 1) the child is 6 months of age or 2) when it is safe and feasible.**
    - There should be prompt management of breast conditions such as mastitis or cracked/bleeding nipples as these conditions increase risk of HIV transmission. When possible the mother should avoid feeding the child from the affected breast.
    - There should be prompt management of mouth sores or oral thrush in the infant.

2. Exclusive replacement feeding (baby receives only formula milk)
    - Replacement feeding must be culturally *acceptable, feasible, affordable, sustainable and safe (AFASS).* See **Appendix 10**: Decision-making tool for infant feeding options.
    - These criteria may be very hard for a Liberian mother to meet.

Table 13.3 Determining if replacement feeding should be recommended: AFASS

Acceptable: The mother perceives no barrier to replacement feeding. Barriers may stem from cultural or social reasons, or be due to fear of stigma and discrimination.
Feasible: The mother (or family) has adequate time, knowledge, skills and other resources to prepare the replacement food and feed the infant up to 12 times in 24 hours.
Affordable: The mother and family, with support if necessary and available, can pay the cost of purchasing/producing, preparing and using replacement feeding, including all ingredients, fuel, clean water, soap and equipment, without compromising the health and nutrition of the family.
Sustainable: Availability of a continuous and uninterrupted supply, and dependable system of distribution for all ingredients and products needed for safe replacement feeding, for as long as the infant needs it, up to one year of age or longer.
Safe: Replacement foods are correctly and hygienically prepared and stored and fed in nutritionally adequate quantities with clean hands and using clean utensils, preferably by cup.

3. Wet-nursing
    - Having another woman who has tested HIV-negative breastfeed the infant.

4. Expressing and heat-treating breast milk

- Removing the milk from breasts manually or with a pump.
- Put milk in cup or bottle (see below), and immerse in a pot of boiling water for **5 minutes** to kill HIV.
- It may be very difficult for a Liberian mother to do this procedure safely. It requires manual expression of breast milk 3+ times per day and enough fuel to heat it in the water.

The containers used for measuring the milk and feeding the infant should be cleaned with soap and clean water before each use and, should be boiled at an active roll for at least 5 minutes with the cup or bottle completely covered in water.

It is recommended that a mother feed her infant with a cup. Using cups for feeding infants is better than using bottles if they are receiving expressed breast milk, formula or animal milk for several reasons:

- Bottles are harder to clean, so they can be easily contaminated with germs that make the infant sick
- Ear infections are more common with bottle feeding
- Cup-feeding ensures social contact during feeding and adult attention that can help to stimulate or comfort the infant
- Cup-feeding facilitates easier weaning, and can therefore help mothers switch abruptly from giving breast milk to giving replacement foods

It is important to emphasize to women that the infant feeding choice she makes needs to be *exclusive* until the child is 6 months old.

13.8.3. Introduction of complementary foods

- With any feeding method, complementary foods should be introduced to provide an infant with sufficient nutritional balance at **approximately 6 months of age.**
- Milks and liquids that should be avoided and are not suitable for infants include unpasteurised/unboiled animal milk (especially if diluted by an unknown amount), skimmed or low-fat milk powder, sweetened or condensed milk, glucose, custard, thin cereal-based gruels, fruit juice, teas, and sodas.
- Specific guidance and support on ensuring appropriate replacement feeding should be provided to the woman for at least the first two years of the child's life.

SECTION 14: Care and treatment for HIV exposed and HIV positive children

14. Care and treatment for HIV exposed and HIV positive children

14.1 HIV-exposed infants

14.1.1. Goals of care

- Minimize the risk of vertical transmission of HIV
- Recognize HIV infection early using age appropriate test
- Prevent opportunistic infections
- Enroll HIV positive children into ART care early

14.1.2. A plan for comprehensive care of the HIV-exposed infant

- Connecting HIV-exposed infants from obstetrical care/PMTCT to pediatric care is essential.
- HIV-exposed infants need to start CPT at 4-6 weeks (see **Section 9**) since they are at risk of morbidity and mortality regardless of infection status.
- Infants should be seen monthly for the first 6 months then every 3 months.
- Infants with poor growth, failure to thrive or recurrent illnesses should have more frequent close follow-up.

Notes:

- MCH, immunization and under 5 clinics are excellent venues to identify HIV-exposed infants.
- Rapid antibody tests performed on the mother or infant can be used to confirm HIV exposure, enabling these infants to be enrolled into care (See **Section 4**.) Basic care for HIV-exposed infants can be provided in under-5 clinics, pediatric outpatient clinics and in health centers.

14.1.3. Birth

- Arrange postnatal follow-up:
  - **Mothers should be given an appointment for the first postnatal visit at delivery.**
  - Mothers who do not deliver at a health facility should be given appointments at first contact with the healthcare system.
- Record HIV status of the mother on the infant's immunization card in a non-stigmatizing way. (Use identification method employed for the PMTCT-enrolled pregnant women on the infants immunization card.)
- Counsel the mother on the importance of adherence to infant prophylaxis, infant feeding, maternal nutrition and support.
- Immunize the child per National Expanded Program on Immunization (see **Appendix 11**)

14.1.4. Initial visit at 4-6 weeks

Every effort should be made to engage the HIV-exposed infant into care by 6 weeks of age. Review the following at the first postnatal visit:

- History including use of PMTCT, parental concerns, intercurrent illness.
- Nutrition and growth assessment plotting weight, height and head circumference on standard growth charts.
- Developmental assessment using reference provided in **Appendix 12.**
- Targeted physical exam looking for symptoms and signs suggestive of HIV infection. See **Table 7.4** for clinical criteria for presumptive diagnosis of severe HIV infection, for which ART should be initiated.
- Determination of HIV status using appropriate algorithm (see **Section 4**). Caregivers should be counseled on the rationale for infant diagnosis, explain the possible test results, and need for additional tests to definitely determine infection status.
- TB risk assessment
- Cotrimoxazole Preventive Therapy should be provided to all HIV-exposed infants starting at age 4-6 weeks, and continued until HIV infection has been excluded and infant is no longer at risk from breastfeeding (See **Section 9**).
- Immunizations according to the National Expanded Program on Immunization (see **Appendix 11**).
- Counseling on infant feeding, maternal nutrition and support as necessary (**Section 13**).

14.1.5. Follow-up visit schedule for HIV-exposed infants (3 to 18 months)

- HIV-exposed infants who are asymptomatic should be seen monthly until 6 months of age then every 3 months until 18 months of age. HIV-exposed infants who are symptomatic, have poor growth, failure to thrive or recurrent illnesses should have more frequent follow-up.
- HIV-exposed infants should be discharged from care only after they are 12 weeks post cessation of breastfeeding and HIV infection has been excluded.
- This means that the majority of infants will have to be followed until 18 months of age, and CPT continued throughout.
- Children who are determined to be HIV positive should be referred to a center where they can receive HIV care and treatment.
- Children who are determined to be uninfected can be discharged and followed in the under 5 clinics or EPI.

Adherence to care and CPT should be reinforced at each visit (see Section 6.)

Table 14.1 Follow-up visit schedule for HIV-exposed infants*

Age in weeks/ months	At birth	6 wks	10 wks	14 wks	Monthly	6 mos	9 mos	12 mos	15 mos	18 mos
Counseling										
Nutrition counseling and support	√	√	√	√	√	√	√	√	√	√
Adherence counseling	√	√	√	√	√	√	√	√	√	√
Assessment										
History (check for OIs)	√	√	√	√	√	√	√	√	√	√
Physical exam	√	√	√	√	√	√	√	√	√	√
TB Risk Assessment	√	√	√	√	√	√	√	√	√	√
Determination of HIV status		DNA PCR	• Repeat DNA PCR if infant is sick • Or perform rapid antibody test at least 12 weeks after cessation of breastfeeding							Rapid antibody test
Nutrition and growth assessment	√	√	√	√	√	√	√	√	√	√
Developmental assessment	√	√	√	√	√	√	√	√	√	√
Treatment										
Cotrimoxazole Preventive Therapy		√	Continue until HIV is excluded and infant is no longer at risk from breastfeeding							
Immunizations	√	√	√	√			√			

* This is the minimum; children should be seen more frequently if clinically indicated.

After 18 months the child should either be:

- Confirmed HIV positive (see below), in which case s/he should receive continued care and follow up through the Care and Treatment Program, or
- Confirmed negative, in which case ART and/or CPT should be immediately discontinued, and regular childhood care should be provided through the MCH clinic (such as immunizations, see **Appendix 11**).

14.1.6. Determination of HIV status

Infants presenting for the first time at > 9 months of age should have a screening HIV antibody test done first, which, if negative, can exclude HIV positive status. Any positive test should be confirmed with DNA PCR. Any infant with a positive DNA PCR should be referred for staging, care, and treatment. Breastfeeding infants should have repeat testing after complete cessation of breastfeeding (after 6 weeks cessation with PCR or 12 weeks with antibody test). Testing must always be accompanied with counseling of caregivers, explaining the possible test results, need for additional test to definitely determine infection status. Any child who has been determined to be negative but subsequently becomes symptomatic should have repeat diagnostic testing (see **Section 4** for more details.)

Table 14.2 Clinical criteria for presumptive diagnosis of severe HIV disease in infants and children < 18 months of age

A presumptive diagnosis of severe HIV disease should be made if:

- The infant is confirmed HIV antibody positive; *and*
- Diagnosis of any AIDS-indicator condition(s) can be made; *or*
- **The infant is symptomatic with two or more of the following**:
  - Oral thrush[a];
  - Severe pneumonia[b];
  - Severe sepsis[c].

Other factors that support the diagnosis of severe HIV disease in an HIV seropositive infant include:

- Recent HIV-related maternal death; *or* advanced HIV disease in the mother;
- CD4 < 20% in infant.

Confirmation of the diagnosis of HIV infection should be sought as soon as possible.

In these cases, ART should be initiated.

a. Oral thrush: Creamy white to yellow soft small plaques on red or normally colored mucosa which cannot easily be scraped off (pseudomembranous), or red patches on tongue, palate or lining of mouth, usually painful or tender.
b. Severe pneumonia: Cough or difficult breathing in a child with chest indrawing, stridor or any of the IMCI general danger signs; i.e., lethargic or unconscious, not able to drink or breastfeed, vomiting, and presence or history of convulsions during current illness; responding to antibiotics.
c. Severe sepsis: Fever or low body temperature in a young infant with any severe sign such as fast breathing, chest indrawing, bulging fontanelle, lethargy, reduced movement, not feeding or sucking breast milk, convulsions

14.2 HIV positive children

14.2.1. Goals of care for the HIV positive child

- Promote health and well-being
- Prevent disease progression
- Prevent opportunistic infections

14.2.2. A plan for comprehensive care of the HIV positive child

The management of an HIV positive child is best accomplished by integrating HIV services and primary health care. A multidisciplinary, family centered approach to care is effective in engaging children and their families into long-term care. Comprehensive care and support for the HIV positive child should be provided in the same care and treatment center where the parent or caregiver is receiving treatment.

Close regular follow-up is essential since approximately 50% of HIV positive children will die by the second year of life if they remain untreated.

14.2.3. Initial intake visit

Clinical assessment of the HIV positive child should focus on the following:

- History with particular emphasis on previous AIDS defining conditions, history of ARV exposure (PMTCT or previous antiretroviral therapy), family members who are aware of the diagnosis, parental concerns, intercurrent illness.
- TB risk assessment - history of contact and chest X-ray if clinically indicated
- Nutrition and growth assessment - plot weight, height and head circumference on the growth chart
- Developmental assessment (see **Appendix 12**)
- Detailed physical exam looking for symptoms and signs suggestive of severe HIV infection
- Clinical and immunological staging and ART eligibility should be assessed (see **Section 7**)
- Choosing an ART regimen (see **Section 11**)
- Cotrimoxazole Preventive Therapy (CPT) - check eligibility based on clinical stage and/or CD4 if available. Adherence should be reinforced at every visit.
- Immunizations according to the National Expanded Program on Immunization (see **Appendix 11**)
- Nutrition counseling on provision of adequate nutrition, offer support as necessary
- Disclosure of HIV status to the child should be discussed with the caregiver. Disclosure should be introduced early on in a neutral way, and should be tailored to the developmental maturity of the child. It is particularly important that adolescents be informed of their status so they can become active participants in their own care. See Section 6 on adherence and disclosure to children.
- Patient records - complete all pediatric intake forms

14.2.4. Follow-up schedule for HIV positive children

Table 14.3 Follow-up schedule for HIV positive children

Age	Visit interval
0-6 months pre-ART	Monthly
>6 months pre-ART	Every 3 months or more frequently if clinically indicated
On ART	See **Section 15**

14.2.5. Special considerations for children initiating ART

An identifiable adult who is able to administer/supervise medication must be available.

- Demonstrated reliability in the adult caregiver (i.e., has attended three or more scheduled visits to an HIV clinic and the Immunization Record of child is up-to-date).
- The adult caregiver should attend adherence counseling as per usual schedule on behalf of the child.
- Disclosure to another adult living in the same house is encouraged so that there is someone else who can assist with the child's ART.

14.2.6. ARVs for children

A d4T regimen was selected as the preferred first line regimen for children with HIV-1 because of the availability in pediatric fixed dose combinations (see formulary notes and weight band dosing schedules in **Appendices 8** and **9**).

d4T + 3TC + NVP
or
AZT + 3TC + NVP
(if child < 3 kg)

The ARV prescription must be carefully discussed with the caregiver

- **Re-calculate and clearly document dose of medication at each visit (**based on weight band according to WHO 2006 recommendations)**,** total volume of medications required, and prescribe enough medication until next visit (see **Appendix 9** for pediatric dosing).
- **Provide detailed description of drugs,** explain exact dosing schedule to caregiver, instructions should be clearly written on the container. Caregivers should be asked to demonstrate how they give medications regularly during follow-up.
- **Demonstrate use of syringe and cups** to measure medications as appropriate.

SECTION 15: Monitoring of patients on ART

15. Monitoring of patients on ART

15.1 Actions to be taken in the first 6 months: counseling, clinical exams, medication dispensing, and laboratory monitoring

Timely counseling, clinical and laboratory monitoring, and medication refill is essential for care of patients on ART. Providers must collect baseline data on each patient and then follow trends to anticipate and react to problems that occur. Also refer to **Appendix 4**: Schedule of actions for patient visits.

Key actions include:

- "Pre-ARV" sessions: for counseling, baseline assessments and initiation of cotrimoxazole prophylaxis.
- Day 0: Patients should receive a 2 week supply of ARVs .
- Day 14: Patient should return to the clinic for assessment. If there is no adverse reaction s/he can be provided a 4 week supply of ARVs. If adverse reactions are noted, patients should be seen again after 2 weeks for monitoring. Both the 2 and 4 week visits are crucial times to stress adherence and assess for evidence of medication side effects or IRIS.
- Months 1.5, 2.5 and 3.5: Patients should receive a 4 week supply of ARVs at each visit. Continue to stress adherence and assess for evidence of medication side effects or IRIS. Patients should continue to return to clinic every month until the provider is comfortable that (1) the patient is fully participating in his or her care and (2) the patient's clinical and immunological (if CD4 available) condition is stable or improving.
- Month 6.5: Clinical exam and routine laboratory monitoring, including CD4 counts. Most patients will be able to transition to a schedule of clinic visits 3 monthly and laboratory monitoring every 3-6 months. They should receive appropriate supplies of antiretrovirals and prophylactic medicines when required. If stable and adherent, ARVs and other medications can be provided every 2-3 months.

See **Appendix 4**: Schedule of actions for patient visits, and **Tables 15.1** and **15.2** for a detailed schedule of provider activities and interpreting the laboratory results for potential toxicities.

Table 15.1 Schedule of counseling and clinical activities for patients on ART

	Pre-ARV	Day 0	2 weeks	6 weeks	10 weeks	14 weeks	Every 1-3 months after
Counseling							
Adherence counseling	√	√	√	√	√	√	√
Specific discussion of side effects	√	√	√	-	-	-	-
Contraceptive counseling	√	√	See note on **oral contraceptives** below				
History							
Screen for ARV side effects	√	√	√	√	√	√	√
Assess for OIs and STIs (has WHO stage changed?)	√	√	√	√	√	√	√
Physical Exam							
Complete physical exam	√	-	-	-	-	-	-
Focused physical exam*	-	√	√	√	√	√	√
Weight (kg)	√	√	√	√	√	√	√
Height (m)	√						
Treatment							
Cotrimoxazole prophylaxis	√	√	√	√	√	√	√
ARV supply/description	-	2 weeks	1 mo	1 mo	1 mo	1 mo	1-3 mo
Appropriate OI treatment	√	√	√	√	√	√	√
Anemia treatment (if needed) see laboratory scheduling below.	√	√	√	√	√	√	√

Note: Oral contraceptives may be less effective when taken with NVP, EFV, or PI. Women wishing to avoid pregnancy should be advised to use barrier methods (e.g. foam and condoms, diaphragm and foam) in addition to OCP or Depo-Provera.

***Focused physical exam should include**: weight, vital signs, oral cavity, skin, lymph nodes, and chest.

Table 15.2 Laboratory monitoring schedule for adults and adolescents on ART

	First pre-ARV	Day 0	Week 2	Week 6	Week 10	Week 14	6 months & every 6 mo after
Laboratory testing[1]							
Bioline testing (if needed)	√	Bioline testing should only be done if there is no record of type of HIV infection (HIV 1 or HIV 2).[2]					
CD4% + count (if available)[3]	√	-	-	-	-	√	√
Full blood count with diff	√	-	-	-	-	-	√
TLC (if WHO stage 2)	√	-	-	-	-	-	-
Hemoglobin	√	If on **AZT**, obtain Hb at Day 0, week 2, 6, 10 and 14. If abnormal, consider medication change. If all are normal, obtain every 6 mos.					
Liver transaminases (ALT)	√	If patient is **on NVP**, obtain ALT at Day 0, week 2, 6, and 14. If abnormal, consider medication change. If all are normal, obtain every 6 mos.					
Creatinine	√	If on **TDF** obtain creatinine at Day 0, week 2 and 6. If abnormal, consider medication change. If normal, obtain every 6 mos.					
Glucose	-	If on **PIs** obtain glucose at Day 0. If abnormal, consider medication change. If normal, obtain every 6 mos.					
Lipid profile	-	If on **PIs** obtain lipids at Day 0. If abnormal, consider medication change. If normal, obtain every 6 mos.					
Amylase/Lipase	-	If on **ddI** obtain amylase/lipase as clinically indicated.					
Pregnancy test (if needed)	√	-	-	-	-	-	-
Chest x-ray (to rule out TB)	√	-	-	-	-	-	-
Malaria smear	√	-	-	-	-	-	-

[1]The NACP recognizes that all facilities will not be able to perform all of these tests. The above is a recommended schedule.
[2] If patient was diagnosed at another facility, record of a positive HIV test should be checked. If not available, patient should be re-tested to confirm diagnosis.

[3]CD4 testing should be repeated within 3 months if it decreases at any time

15.2 Levels of diagnostic services available

Diagnostic services will be available to support the HIV care and treatment program as below. Equipment to calculate CD4 count and % will be placed at strategic facilities throughout the country. For those facilities without diagnostic services, the NACP will devise a network for sample referral. Samples will also be collected and transported for specialized tests, including DNA PCR.

Table 15.3 Diagnostic services to be available through the basic package of health services

LABORATORY SERVICES	Clinic	Health Center	County Hospital
1. Hematology			
Hemoglobin	√	√	√
Hematocrit			√
Full blood count with differential			√
Blood typing and cross matching			√
Bleeding and clotting times			√
Erythrocyte sedimentation rate (ESR)			√
2. Microscopy			
Malaria parasites	√	√	√
Urine microscopy		√	√
CSF cell count			√
Gram stain for discharges, pus		√	√
Sputum for acid fast bacilli (Ziehl Nielsen stain)	√	√	√
3. Clinical chemistry			
Proteinura & glucosuria	√	√	√
RDT for malaria	√	√	√
Rapid pregnancy test		√	√
Liver function tests			√
Renal function tests			√
Blood glucose			√
Lipid Profile			√
Alkaline phosphatase			√
Electrolytes			√
Serum Amylase			√
4. Serology			
HIV Rapid Tests		√	√
ELISA			√
Rapid Plasmareagin (RPR) test for syphilis		√	√
Hepatitis B			√
Hepatitis C			√
IMAGING SERVICES			
1. X-Ray			
Chest	-	-	√
Abdomen	-	-	√
Skeleton	-	-	√
2. Ultrasound			
Simple portable	-	-	√

15.3 What to expect during the first six months of therapy

The first six months on ART are critical. Clinical and immunological improvement should occur, but are not always apparent. Drug toxicities may appear. Some patients fail to respond as expected or may even exhibit clinical deterioration initially. Complications in the first few weeks following the initiation of ART are seen most commonly when therapy is started in patients with severe immunodeficiency. If a patient with advanced HIV disease does not improve initially, it does not necessarily mean that s/he is not responding to the ART. In fact, patients should be counseled that they will most likely "feel worse" before they start to "feel better."

It takes time for HIV viral replication to be controlled by ART and for the patient's immune system to strengthen. Additionally, as a patient with advanced disease recovers immune function, exacerbation of previously subclinical coexisting infections may occur, resulting in an apparent worsening of disease (see below Immune Reconstitution Inflammatory Syndrome (IRIS)). It is important to allow sufficient time on therapy before judging effectiveness and to consider the possibility of the IRIS in patients with worsening disease in the first few months of ART.

15.4 CD4 recovery

CD4 cell counts should rise following the initiation of therapy in most patients. This trend may continue for many years although the rise may be less rapid if the baseline CD4 count was very low. However, even patients with CD4 counts below 10 cells/mm^3 can achieve an effective CD4 recovery in time, though some patients may never have CD4 counts that exceed 200 cells/mm^3. In a minority of patients with advanced disease and low CD4 counts when therapy is initiated, the CD4 counts may not rise or may fall slightly, even with clinical improvement.

In those who achieve a good response within the 1st 6 months, a subsequent progressive decline in CD4 counts *in the absence of intercurrent illness or poor adherence* indicates immunological failure. The baseline CD4 count and the trend of the CD4 response are needed to best characterize and define immunological failure (see **Table 15.2**).

15.5 Early ARV toxicity

First-line drug toxicities fall into two categories: early (presenting in the first few weeks to months of therapy), and late (see **Section 16**: ARV Treatment Toxicity and Management). Common early and potentially severe toxicities include hypersensitivity to EFV or NVP, which normally occurs within the first few weeks of therapy, and AZT-related anemia and/or neutropenia, which typically present in the first few months of therapy. Acute toxicities, if not identified early, can become life threatening.

Some drug toxicities, especially hepatic and renal toxicity and lactic acidosis, may not be identified early if access to laboratory monitoring is limited. Hypersensitivity reactions may be difficult to distinguish from acute clinical events such as malaria and viral hepatitis and from the many manifestations of IRIS, which can present in the first few months on ART. **Section 16** provides more details on the clinical identification and management of toxicity.

15.6 Immune reconstitution inflammatory syndrome (IRIS)

The immune reconstitution inflammatory syndrome (IRIS) is a spectrum of clinical signs and symptoms resulting from the immune system regaining its ability to mount an inflammatory response. The patient may present with a previously unrecognized opportunistic infection (often TB, PCP, mycobacterium avium complex or cryptococcal disease), a rash, lymphadenopathy, a paradoxical worsening of treatment response several weeks into therapy, or an autoimmune disease such as Graves disease (hyperthyroidism) in the context of immune recovery on ART. Eczema may become worse and viral conditions such as CMV, herpes simplex and herpes zoster may manifest with worsening symptoms.

The occurrence of IRIS means that the patient's immune system is recovering. The syndrome may occur in as many as 1 in 10 patients initiating ART. It is more common in patients who start ART with CD4 counts less than 50 cells/mm^3.

Timing: Typically, IRIS occurs within two to twelve weeks of the initiation of ART, although it may present later.

Risk factors predicting the likelihood of IRIS include:
- Having ever had an opportunistic infection prior to starting ART
- Initiating ART when the CD4 count is below 50 cells/mm^3
- Initiating ART in the setting of a recently diagnosed opportunistic infection

Clinical course:
IRIS may be mild and resolve without treatment. For example, it may involve a temporary elevation of liver enzymes in a patient with HIV/hepatitis B coinfection. Equally, it may be life threatening, as in patients with cryptococcal meningitis, PCP, or tuberculosis.

The development of a new or recurrent OI soon after ART initiation does not indicate treatment failure and is NOT an indication to stop or switch ART.

Management:
- Treat the OI or inflammatory condition. Admission to a hospital may be necessary in some cases.
- Continue ART, if possible.
- Corticosteroids can also be used to decrease inflammation associated with the infection. The best dose and duration of corticosteroid treatment is unclear.

Prescribe:
Prednisolone (or prednisone) at 0.5 mg/kg/day for 5-10 days for moderate to severe cases of IRIS. This is particularly useful with cryptococcal meningitis and ophthalmologic associated IRIS.

ART:
- Where the condition is life threatening and there is no or little response to steroids, ART may need to be temporarily discontinued. This situation is very rare but if it occurs, the same ART regimen should be restarted as soon as possible once the patient has recovered. (See **Section 20**: Interruption or discontinuation of ART.)

SECTION 16: ARV treatment: toxicity and management

16. ARV treatment: toxicity and management

16.1 Managing side effects

Unpleasant side effects such as nausea, headache, malaise, dizziness, nightmares and insomnia are common when starting on ARV drugs and all patients should be warned to expect them. They are distressing but usually tolerable and tend to improve within a few weeks (**See Table 16.1:** Management of common ARV side effects). In these cases, ARVs generally should not need to be stopped. The symptoms can often be successfully treated with anti-emetics, anti-diarrheal medicines, analgesics, neuroleptics, tricyclics, and other medicines.

Table 16.1 Management of common ARV side effects

Side effect	Drugs Responsible	Action to be taken
Anemia	AZT	Measure Hemoglobin Provide iron, folic acid, mebendazole and dietary advice as needed and based upon MCV If anemia is severe and resistant to treatment, substitute another ARV
Confusion, nightmares, somnolence, behavior and/or personality changes	EFV	Rule out other causes of mental status changes Give EFV at bedtime Check appropriate dose/drug administration
Diarrhea	All NRTIs, NNRTIs, and **especially PIs.** Less frequent with d4T, 3TC, FTC, and ABC	Provide ORS for maintenance of hydration ("homemade" or pre-packaged) Loperamide if symptoms are severe
Fatigue	Many of the ARVs	Screening examination and lab assessment to rule out anemia, hepatitis, and lactic acidosis Provide reassurance and continued monitoring
Fever with or without other symptoms	NVP or ABC hypersensitivity reactions; however patients on all ARVs may experience fever	Differential diagnosis includes: Opportunistic Infections; Immune Reconstitution; and ABC or NVP Hypersensitivity
GI intolerance, abdominal discomfort, cramps	All NRTIs, NNRTIs, and **especially PIs.** Less frequent with d4T, 3TC, FTC, and ABC	Rule out more serious adverse events (perform examination and do appropriate lab tests to rule out pancreatitis [amylase, lipase] for patients on d4T, ddI; and hepatitis [ALT, AST] for patients on NVP).
Headache	Many of the ARVs	Rule out anemia. Check for neck stiffness, mental status changes, neurologic deficits. Consider spinal tap if other signs/symptoms present (to rule out Cryptococcal Meningitis). Provide paracetamol
Jaundice (indirect hyperbilirubinemia)	ATV (Atazanavir, a protease inhibitor)	Generally asymptomatic except for icterus. (without ALT elevation) No need for substitution unless demanded by patient for cosmetic reasons (then substitute another PI)
Lipoatrophy and/or Lipodystrophy (detail in **Section 18.3.2**)	All NRTIs (Particularly d4T)	Early Replacement of the suspected ARV drug (e.g., substitute TDF or ABC for d4T). Consider dietary adjustments and physical conditioning exercises.
Nausea, vomiting	All ARVs	Rule out pancreatitis, hepatitis May use promethazine, metaclopramide Dietary modifications (ORS, liquids and bland diet)
Numbness/Tingling in feet	d4T, ddI	Strongly consider replacing with another NRTI which has minimal neurotoxicity (AZT, TDF, or ABC) Add Pyridoxine supplementation (25-50 mg/day), in those on a TB regimen containing isoniazid (INH) Consider symptomatic treatment, e.g. amitriptyline 12.5 to 50mg at bedtime
Rash (mild)	NVP	Rule out severe NVP reaction (monitor clinical status, check ALT) Remove drug that caused the problem if possible. Provide symptomatic treatment, (e.g. hydrocortisone cream, calamine lotion, promethazine, chlorpheniramine, or other antihistamines orally)

16.2 Managing adverse drug reactions

Adverse drug reactions to ARVs are common, ranging from mild to life threatening conditions. Many occur within the first few months, but metabolic toxicities (e.g., lipodystrophy, hyperlipidemia) occur with prolonged use of ARVs. Some toxicities are due to class specific effects while others relate to individual drugs. When diagnosing symptoms in patients early on in the course of ART, opportunistic infections and the immune reconstitution inflammatory syndrome (see **Section 15.6**) must be considered as well as drug toxicity. For instance, hepatitis could be due to immune reconstitution syndrome involving pre-existing hepatitis B infection, or it could be due to NVP toxicity. There must be a balance in managing drug side effects and toxicities—avoiding premature substitution of ARVs during mild to moderate reactions in order to preserve subsequent treatment options, while moving quickly to stop or change ARVs in cases of severe/life threatening toxicity.

16.3 Steps to manage adverse events

1. Evaluate concurrent medications and establish whether the problem is attributable to an ARV drug or to a non-ARV medication taken at the same time.
2. Consider other disease processes. Not all problems that arise during treatment are caused by ARV drugs.
3. Assess the degree/severity of the adverse event, see:
    - **Table 16.2**: ART-related toxicity grading for adults and adolescents;
    - **Table 16.3**: Laboratory grading of adverse events in adults and adolescents;
    - **Table 16.4**: Laboratory grading of adverse events in children; and
    - **Table 16.5**: Grading of ART-related adverse events in children
4. Manage the adverse event according to severity and consider single drug substitutions if necessary (**see Table 16.5**: Toxicities of first line ARVs and single drug substitutions).
5. Stress the maintenance of adherence despite toxicity for mild and moderate reactions.
6. In the event of a severe reaction, stop all ARVs immediately. Determine which drug most likely caused the life threatening reaction, then substitute a new ARV for the drug that caused the problem. ART should be restarted with one new drug and the other two ARVs from the original regimen. See **Section 20**: Interruption or discontinuation of ART, for more detail.

    > Note: If ART regimen contained NVP, the NVP should be stopped two weeks prior to other ARVs **whenever possible**. This is because NVP has a longer half-life than other ARVs, and if stopped at the same time there is an increased risk of developing NVP resistance.

7. All adverse drug reactions should be clearly documented in the patients' records and patient should be told of their allergy and told not to take that drug in the future.

Table 16.2 ART-related toxicity grading for adults and adolescents

Estimating severity grade	
Grade 1	**Mild.** Transient or mild discomfort; no limitation in activity; no medical intervention/therapy required.
Grade 2	**Moderate.** Limitation in activity – some assistance may be needed; no or minimal medical intervention/therapy required. If the patient does not improve on symptomatic therapy, consider single-drug substitutions.
Grade 3	**Severe.** Marked limitation in activity, some assistance usually required; medical intervention/therapy required, hospitalization possible. Substitute a new drug for the one that caused the reaction, without stopping ART.
Grade 4	**Severe life threatening.** Extreme limitation in activity, significant assistance required; significant medical intervention/therapy required, hospitalization or hospice care. Immediately discontinue all ARV drugs, manage the medical event (i.e. symptomatic and supportive therapy) and reintroduce ARV drugs using a modified regimen (i.e. with an ARV substitution for the problem drug) when the patient is stabilized.

Table 16.3 Laboratory grading of adverse events in adults and adolescents

ITEM	GRADE 1 TOXICITY	GRADE 2 TOXICITY	GRADE 3 TOXICITY	GRADE 4 TOXICITY
Hemoglobin	8.0 –9.9g/dL	7.0 –7.9 g/dL	6.5 –6.9 g/dL	<6.5 g/dL
Absolute Neutrophil Count	1,000 – 1,500/mm^3	750-990/mm^3	500–749/mm^3	<500/mm^3
Platelets	75,000-99,000/mm^3	50,000-74,999/mm^3	20,000-49,999/mm^3	< 20,000/mm^3
ALT	1.25 – 2.5 X ULN	2.5 –5 X ULN	5.0 –10 X ULN	>10 X ULN
Bilirubin	1-1.5X ULN	1.5-2.5 X ULN	2.5–5 x ULN	>5 x ULN
Amylase/lipase	1-1.5X ULN	1.5-2 X ULN	2–5 x ULN	> 5x ULN
Triglycerides	200-399mg/dL	400 –750 mg/dL	751-1200mg/dL	>1200mg/dL

ULN = Upper Limit of Normal

Table 16.4 Laboratory grading of adverse events in children

ITEM	GRADE 1 TOXICITY	GRADE 2 TOXICITY	GRADE 3 TOXICITY	GRADE 4 TOXICITY
Hemoglobin [Age >3mo. – <2yr]	9.0 –9.9 g/dL	7.0 –8.9 g/dL	<7.0g/dL	Cardiac failure secondary to anemia
Hemoglobin [Age >2 yr]	10.0 –10.9 g/dL	7.0 –9.9 g/dL	<7.0g/dL	Cardiac failure secondary to anemia
Absolute Neutrophil Count	750-1000/mm^3 0.75-1x10^9/L	500-749/mm^3 0.5-0.749 x10^9/L	250-500/mm^3 0.25-0.5 x10^9/L	<250/mm^3 <0.25x10^9/L
Platelets	100-125 x10^3/mm^3	50-100 x10^3/mm^3	25-50 x10^3/mm^3	<25 x10^3/mm^3
ALT (SGPT) and AST (SGOT)	1.25–2.5 x ULN	2.6–5.0 x ULN	5.1-10.0 x ULN	>10.0 x ULN
Bilirubin (>2wks old)	1.1-1.5 x ULN	1.6-2.5 x ULN	2.6-5.0 x ULN	>5.0 x ULN
Lipase	1.1-1.5 x ULN	1.6-3.0x ULN	3.1-5.0 x ULN	>5.0 x ULN
Cholesterol (fasting, age <18yrs)	170-200 mg/dL	200-300 mg/dL	>300mg/dL	-
Glucose, serum, high (non-fasting)	116-161 mg/dL	161-251 mg/dL	251-500 mg/dL	>500 mg/dL
Glucose, serum, high (fasting)	110-126 mg/dL	126-251 mg/dL	251-500 mg/dL	>500 mg/dL
Lactate	<2.0 x ULN without acidosis	>2.0 x ULN without acidosis	Increased lactate with pH <7.3 without life-threatening consequences, or related condition present	Increased lactate with pH <7.3 with life-threatening consequences (e.g. neurological findings, coma) or related condition present
Triglycerides (fasting)	-	500-751 mg/dL	751-1200mg/dL	>1200mg/dL

ULN = Upper Limit of Normal

Table 16.5 Grading of ART-related adverse events in children

Parameter	Grade 1 (Mild)	Grade 2 (Moderate)	Grade 3 (Severe)	Grade 4 (Severe and life threatening)
Diarrhea ≥ 1 year of age	Transient or intermittent episodes of unformed stools OR increase of ≤ 3 stools over baseline per day.	Persistent episodes of unformed to watery stools or increase of 4 – 6 stools over baseline per day.	Grossly bloody diarrhea or increase of ≥ 7 stools per day or IV fluid replacement indicated.	Life threatening consequences (e.g. hypotensive shock).
< 1 year of age	Liquid stools (more unformed than usual) but usual number of stools.	Liquid stools with increased number of stools or mild dehydration.	Liquid stools with moderate dehydration.	Liquid stools resulting in severe dehydration with aggressive rehydration indicated or hypotensive shock.
Nausea	Transient (< 24 hours) or intermittent nausea with no or minimal interference with oral intake.	Persistent nausea resulting in decreased oral intake for 24 – 48 hours.	Persistent nausea resulting in minimal oral intake for > 48 hours or aggressive rehydration indicated (e.g. IV fluids).	Persistent nausea with no or minimal oral intake resulting in dehydration with aggressive rehydration indicated.
Vomiting	Transient or intermittent vomiting with no or minimal interference with oral intake.	Frequent episodes of vomiting with no or mild dehydration.	Persistent vomiting resulting in orthostatic hypotension or aggressive rehydration indicated (e.g. IV fluids).	Life threatening consequences (e.g. hypotensive shock).
Acute systemic allergic reaction	Localized urticaria (wheals) lasting a few hours.	Localized urticaria with medical intervention indicated or mild angioedema.	Generalized urticaria or angioedema with medical intervention indicated or symptomatic mild bronchospasm.	Acute anaphylaxis or life threatening bronchospasm or laryngeal edema.
Pancreatitis	N/A	Symptomatic and hospitalization not indicated (other than emergency treatment).	Symptomatic and hospitalization not indicated (other than emergency treatment).	Life threatening consequences (e.g. circulatory failure, hemorrhage, sepsis).
Rash	Localized macular rash	Diffuse macular, maculopapular, or morbilliform rash or target lesions.	Diffuse macular, maculopapular, or morbilliform rash with vesicles or limited number of bullae or superficial ulcerations of mucous membrane limited to one site.	Extensive or generalized bullous lesions or Stevens-Johnson syndrome or ulceration of mucous membrane involving two or more distinct mucosal sites or Toxic Epidermal Necrolysis.
Alteration in personality-behavior or in mood	Alteration causing no or minimal interference with usual social & functional activities	Alteration causing greater than minimal interference with usual social & functional activities.	Alteration causing inability to perform usual social & functional activities and intervention indicated.	Behavior potentially harmful to self or others or life threatening consequences.
Altered Mental Status	Changes causing no or minimal interference with usual social & functional activities	Mild lethargy or somnolence causing greater than minimal interference with usual social & functional activities.	Onset of confusion, memory impairment, lethargy, or somnolence causing inability to perform usual social & functional activities.	Onset of delirium, obtundation, or coma.

Table 16.6 Characteristics of available ARVs

Generic Drug	Available Adult and Pediatric preparations	Serious Reactions	Side Effects	Notes for Drug Administration
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)				
Abacavir (ABC)	300mg	Severe Hypersensitivity reaction (5%)	Nausea, vomiting, fever, headache, diarrhea, rash, anorexia	
Didanosine (ddI)	25mg, 50mg, 100mg, 125mg, 150mg, 250mg, 400mg	Pancreatitis, fatty liver disease; optic neuritis, lactic acidosis, hyperuricemia, peripheral neuropathy, electrolyte abnormality	Diarrhea, nausea, vomiting and abdominal pain	Must take on empty stomach (30 mins before or 2 hours after eating). Buffered capsules should be dissolved in a big glass of water. Must take all in one dose (buffering of acid)
Lamivudine (3TC) Side effects with 3TC are usually well tolerated.	150 mg; same dose in combination with AZT. 300mg in combination with TDF		Headache, fatigue, nausea, diarrhea, hair loss, abdominal pain	
Stavudine (d4T)	Capsules of 15, 20, 30 and 40 mg 6 mg, 12mg, 30mg, and 40mg in combination with 3TC and NVP	Peripheral neuropathy, pancreatitis, lactic acidosis, hepatic steatosis.	Headache, GI disturbance, skin rash.	
Zidovudine (AZT, ZDV)	Tablets 300, capsules 100, injections 10mg/ml Also same dose in combination with 3TC	Anemia, neutropenia, lactic acidosis	Headache; Fatigue Nausea; Diarrhea	Don't initiat if Hb <8 g/dl, and discontinue if Hb falls < 7 g/dl
Nucleotide Reverse Transcriptase Inhibitors (NtRTIs)				
Tenofovir (TDF)	300mg cap Same dose in combination with 3TC	Renal failure	Nausea, diarrhea	Avoid use in pregnant women and children, avoid in renal impairment
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)				
Efavirenz (EFV)	100mg, 200mg capsules 50mg, 600mg tablet	Severe CNS side effects, Stevens Johnson Syndrome, Drug-induced hepatitis, teratogenic effect in 1st trimester.	Dizziness, Sleep disturbances, nightmares	Give at bedtime to improve tolerability. Avoid administration with high fat meal
Nevirapine (NVP)	200 mg Same in FDC with AZT and D4T	Muco-cutaneous hypersensitivity reactions; Stevens Johnson Syndrome; Drug-induced hepatitis	Mild skin rash, itching, nausea	Avoid if patient is on rifampicin-based TB therapy.

Generic Drug	Available Adult and Pediatric preparations	Serious Reactions	Side Effects	Notes for Drug Administration
Protease Inhibitors (PIs)				
Lopinavir/Ritonavir (LPV/r, Kaletra©)	400 mg LPV/100mg Ritonavir	Lipid abnormalities and diabetes	Diarrhea, headache, asthenia, nausea and vomiting.	Administer with food. High fat meal can increase absorption If co-administered with ddI, ddI should be taken one hour before or two hours after LPV/r.
Atazanavir/Ritonovir (ATV/r)	300 mg ATV/100mg Ritonavir capsules	Liver function abnormalities, cardiac conduction defect		
Nelfinavir (NFV, Viracept ®)	250 mg tablet.	Lipodystrophy. hyperlipidemia diabetes	Diarrhea, gas, and abdominal pain	Avoid with TB drugs
Fixed Dose Combinations (FDCs)				
AZT+3TC+NVP	300mg/150mg/200mg	See above information on individual drugs		
d4T+3TC+NVP (Triomune)	30mg/150mg/200mg 6mg/30mg/50mg 12mg/60mg/100mg	See above information on individual drugs		
AZT+3TC	300mg/150mg	See above information on individual drugs		
TDF+3TC	300mg/300mg	See above information on individual drugs		
d4T+3TC	30mg/150mg 6mg/30mg 12mg/60mg	See above information on individual drugs		

16.4 Description of specific drug toxicities and management

16.4.1. Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

16.4.1.1. Zidovudine (AZT or ZDV)

Toxicities

Approximately 5-10% of patients taking AZT will experience severe macrocytic **anemia** and/or **granulocytopenia** (low red and white blood cell counts). This toxicity is dose-related and is more common with advanced HIV disease. If a patient has a hemoglobin of <8 g/dl (and the result was confirmed), the provider should treat the anemia before starting AZT. (Note, iron deficiency anemia is microcytic and should be reversible with ferrous sulfate.) AZT can also cause severe granulocytopenia. An Absolute Neutrophil Count below 500 is a definite indication to discontinue AZT and substitute another NRTI (d4T, TDF).

AZT has also been associated with reversible myopathy (about 17% of patients), in which patients will have symptoms of myalgias (**muscles aches**) and proximal weakness (of the hips and shoulders).

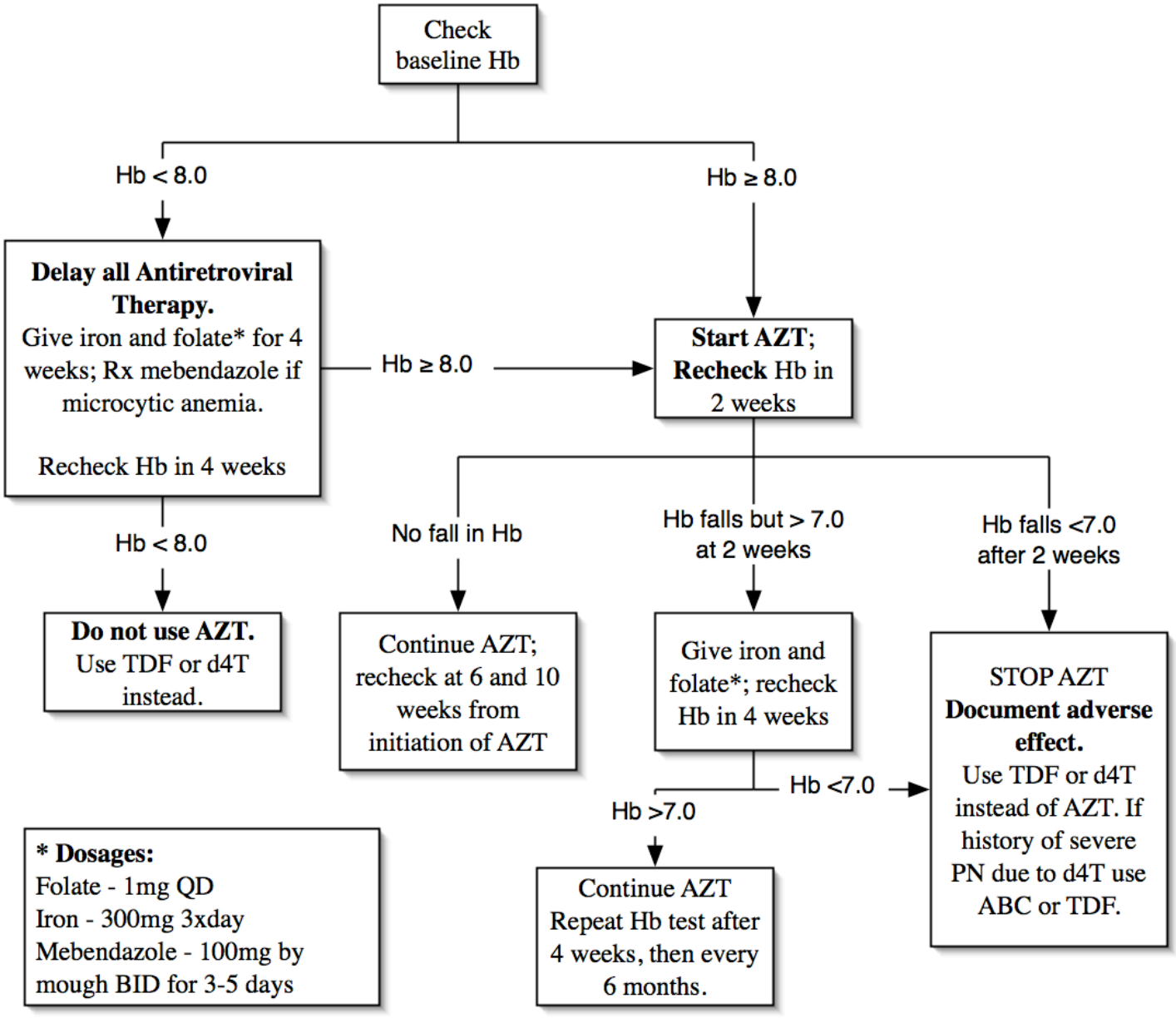
Diagnosis and Management (See **Figure 16.1** for algorithm for AZT toxicity management.)

- The differential diagnosis of anemia is long. In particular, iron deficiency, folic acid deficiency, malaria and hookworm should all be ruled out.

- **If the Hb is > 8 g/dl, AZT can be started but Hb should be rechecked at 2 weeks and monthly thereafter.**
- If the Hb drops but remains >7 g/dl, treat with iron and folate supplements and recheck in 4 weeks.
- If the Hb drops without other known cause <7 g/dl despite treatment for causes of anemia, stop the AZT.
- If myopathy is suspected, check for an increased creatinine phosphokinase (CPK) levels if available. If it is above the limits of normal or if moderate to severe muscle aches persist, stop the AZT.

Figure 16.1 Management of AZT associated anemia

AZT can cause anemia due to bone marrow suppression. Before starting ART, **check patient's hemoglobin**. After initiating AZT**, recheck Hb at 2, 6, 10 and 14 wks**. This is very important, as up to 30% of patients will have a drop in Hb at 4-6 weeks. Usually the drop is minor but a small percent of patients can have a severe drop requiring intensive inpatient management and drug substitution.



16.4.1.2. Lamivudine (3TC)

Generally well tolerated. Patients may experience symptoms noted in **Table 16.1**.

16.4.1.3. Stavudine (d4T)

Toxicities

The primary toxicity of d4T is peripheral neuropathy, which depends on the dose and the duration of treatment. All adult patients should be on low dose (30 mg) of d4T. Neuropathy is more common in patients with advanced AIDS. Other important toxicities of d4T are: lipodystrophy syndrome, pancreatitis (particularly if d4T is administered with ddI, which should be avoided) and lactic acidosis.

Diagnosis and Management:

- Differential diagnosis of peripheral neuropathy includes HIV-associated neuropathy, vitamin deficiency, isoniazid effect, alcoholism, diabetic neuropathy, and others.
- All patients taking isoniazid should be given pyridoxine (Vitamin B6) supplements (25mg QD).
- **If any new symptoms of neuropathy appear after starting d4T, such as numbness, tingling, or burning, it should be discontinued.**
- Replace with AZT, TDF or ABC (see **Table 16.5**).
- The symptoms of peripheral neuropathy usually resolve after discontinuation of d4T. After discontinuation it is not uncommon for the neuropathy to get worse before it gets better. However, **if the medicine is stopped too late, symptoms may not be reversible.**

16.4.1.4. Abacavir (ABC):

Approximately 5% of adults and children receiving ABC develop a **hypersensitivity reaction**. It usually occurs in the first 2-6 weeks of treatment (median onset at 9 days) and is fatal in approximately 3 of every 10,000 people.

Toxicities

Hypersensitivity reaction: The onset is often acute. Typically, a pattern of symptoms builds up over a period of days, often worsening as successive doses are taken.

- Rash is noted in about 70% of all patients and nearly all patients have fever.
- Other common symptoms are: nausea, vomiting, diarrhea, and abdominal pain.
- Less common symptoms include lethargy; muscle or joint pain; headache; numbness of the skin; puffiness of the throat, face, and neck; swollen glands; conjunctivitis; mouth ulcers and low blood pressure.
- Children are more likely to experience rash and gastrointestinal symptoms.

Diagnosis and Management

- If a person who has recently started ABC develops at least two symptoms associated with hypersensitivity, **ABC should be discontinued and not restarted**. If ABC was causing the syndrome, the symptoms will resolve once the drug is stopped.

- Differential diagnosis includes malaria infection and immune reconstitution inflammatory syndrome (IRIS). Ruling out malaria by performing a blood smear is mandatory to avoid stopping the regimen needlessly.
- **Do not restart the patient with abacavir**: anaphylactic reaction and death have been reported from rechallenges.
- All patients should be provided with a warning card that explains how to recognize abacavir hypersensitivity (See **Figure 16.2** below).
- It is extremely important that patients DO NOT STOP OR MISS DOSES ON PURPOSE, and then restart.

Figure 16.2 Abacavir hypersensitivity warning card for patients

If you (or your child) are taking Abacavir (ABC), you need to know some warning signs to watch out for:

- Fever, fatigue, or tiredness
- Pain in your muscles
- Vomiting, stomach pain, or runny stomach
- Throat pain, cough, difficulty in breathing
- Small bumps or red spots on skin, puffy or swollen face and neck

These signs will get worse each time after taking your ARV drugs. If you think that you may have any of the problems listed at the top of this card, you should STOP taking the medicine and VISIT YOUR DOCTOR RIGHT AWAY, especially if this happens in the first 6 weeks of treatment.

DO NOT start taking the medicine again unless your doctor tells you to.

16.4.1.5. Didanosine (ddI)

Toxicities
- ddI commonly causes diarrhea and other gastrointestinal side effects.
- Patients and providers should be alert to signs and symptoms of pancreatitis and peripheral neuropathy. ddI should therefore NEVER be used with d4T, which shares these toxicities.

Management
ddI dose should be reduced to 250mg/day of the enteric coated formulation or 225mg/day of the buffered form when co-administered with TDF.

16.4.2. Nucleotide Reverse Transcriptase Inhibitors (NtRTIs)

16.4.2.1. Tenofovir (TDF)

Toxicities
Tenofovir is generally well tolerated. TDF can be used in situations of mild renal insufficiency, but is contraindicated with moderate and severe renal failure. It should be used cautiously in:
- Regimens that include ddI as TDF can increase ddI's toxicity
- In children under 14 as there is a risk of decreased bone density.

See **Section 18.7**: Kidney and liver disease, for more detailed information.

16.4.3. Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

16.4.3.1. Efavirenz (EFV)

Toxicities

Adverse effects on the **central nervous system** have been reported in 30-50% of patients treated with EFV. These include dizziness, headache, insomnia, depression, impaired concentration, agitation, disturbing dreams, nightmares, and somnolence. EFV has **teratogenic toxicity** (i.e., causes birth defects, especially congenital abnormalities of the CNS, when given in the first trimester). It should not be used in children <3 years old or <10kg.

Management

- The administration of EFV at bedtime can improve tolerance of these side effects.
- Take EFV with food to decrease absorption as side effects usually result from higher drug levels.
- Sleeping agent could be prescribed if non-pharmacotherapeutic techniques don't work.
- Pregnancy should be avoided in women receiving EFV and its use should be avoided particularly during the first trimester.
- Woman of child-bearing age should **not** be placed on EFV unless absolutely necessary, or, can ensure they are using adequate birth control methods.

16.4.3.2. Nevirapine (NVP)

NVP toxicity primarily affects the skin and the liver. Other side effects include nausea, headache, and less commonly fever, and granulocytopenia. All providers must take the risk of liver or skin toxicity very seriously and follow each patient closely in the first few months of treatment.

Interactions with other medicines:

NVP should not be co-administered with:

- Rifampicin: the effectiveness of the NVP is decreased
- Estrogen-based oral contraceptives: the effectiveness of the contraceptive is decreased

Risk factors for liver toxicity

People at increased risk for liver damage from ALT include:

- Those with prior liver damage: baseline elevated transaminases, current or past alcohol abuse, coinfection with hepatitis B and/or C.
- Women with CD4 count >250/mm^3, have an increased risk of developing symptomatic, often rash-associated, nevirapine-related hepatotoxicity, which may be fatal. **Close monitoring of ALT levels, particularly during the first 16 weeks of treatment, is required for this category of patients.**
- Other risk factors: older age, low body mass index

Starting NVP

To decrease the likelihood of a serious reaction:

1) NVP should always be used at a lower (initiating) dose for the first 2 weeks.
2) Look for baseline rashes, check a baseline ALT and ask about symptoms of nausea, vomiting or right upper quadrant pain. It is this baseline that you will

follow over time. *Note: it is possible for the NVP to damage the liver and the ALT to increase, without the patient experiencing any symptoms.*

3) Compare this baseline assessment with a repeat history, physical and ALT check performed at the week 2 visit. If no clinical signs or symptoms of NVP toxicity or allergy appear (new rash, nausea, vomiting, pain or new increase in ALT), the NVP dose can be increased to 2x/day starting at the week 2 visit.
4) Recheck for rash, gastrointestinal symptoms and ALT increases at weeks 6 and 14, and again every 6 months thereafter.
5) Should a rash or ALT increase occur, refer to **Table 16.7** and **Figures 16.3** and **16.4** to grade its severity and determine how to proceed.

Table 16.7 Grading of NVP skin and liver toxicities

	MILD		SEVERE	
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Skin toxicity (rash)	Erythema or pruritis over < 50% of body	Diffuse maculo-papular rash **or** dry desquamation over > 50% of body	Vesiculation **or** Moist desquamation **or** ulceration	Mucous membrane involvement; Stevens-Johnson Syndrome; erythema multiforme
Liver toxicity (ALT)	1.25-2.5x ULN*	>2.5 – 5x ULN	>5.0 – 10x ULN	> 10x ULN

* ULN = Upper Limit of Normal

16.4.3.2.1. **Mild nevirapine toxicity of skin or liver (grade 1 and 2)**

This type of reaction is associated with a rash or mild elevation of ALT is present *without* systemic signs such as body aches, arthralgias (joint aches), myalgias (muscle aches), fever or lymphadenopathy. Treatment interruption is not usually required. See Figures 16.3 and 16.4.

Skin

A mild hypersensitivity **rash** may occur in 1 of every 5 patients on NVP. It is usually erythematous, maculopapular, confluent and most prominent on the body and arms; it may be pruritic. There may be hives and itchiness. The skin should be intact, with no blistering or sloughing of skin, involvement of mucous membranes or angioedema

Liver

There may be grade 1 or 2 level liver enzyme elevations (less than 5x the upper limit of normal).

Management

- Treat with antihistamines, reassure the patient and provide close follow up until resolved.
- If reaction was grade 2, NVP dose escalation should be deferred for up to two weeks or until symptoms resolve.
- If symptoms worsen, this may indicate that the patient has severe hypersensitivity and NVP will need to be stopped immediately. Other medical interventions should be considered, as noted in the next paragraph.
- See **Figures 16.3** and **16.4** for algorithms for NVP management.

16.4.3.2.2. **Severe nevirapine hypersensitivity reaction (grades 3 and 4)**

This type of reaction is associated with a severe rash, large elevation of ALT *and the presence of systemic signs* such as body aches, arthralgias (joint aches), myalgias (muscle aches), fever or lymphadenopathy. Treatment interruption may be required. See **Figures 16.3** and **16.4**.

Skin

A severe **rash** that requires treatment interruption can occur in approximately 1 of every 13 patients on NVP. To qualify as a severe reaction *one or more* of the following should be observed:

- Non-intact skin, with blistering, exfoliative dermatitis, or sloughing of skin
- Erythema, urticaria, desquamation of skin (moist), erythema multiforme (when severe and involving the mucous membranes, known as Stevens-Johnson Syndrome (SJS))
- Anaphylaxis
- Involvement of mucous membranes
- Angioedema
- Cracked/fissured lips

Liver

Liver enzymes are > 5x the upper limit of normal and symptoms may be severe: pain, hepatomegaly, vomiting, nausea.

Management

- Discontinue all three ARVs.
- Admit to the hospital for IV fluids and careful monitoring.
- Begin high dose prednisolone, antihistamines, analgesics.
- All ARVs will be stopped until the patient recovers.
- NVP cannot be restarted. The remaining 2 ARVs will be restarted with a replacement ARV as follows:
    - EFV is preferred if the severe reaction only affected the liver.
    - LPV/r (Kaletra) (or other PI) is preferred if the severe reaction affected the skin (EFV *is not advised*, as the severe reaction may be a class effect[3] (See **Table 16.8**).

[3] Some experts will continue to use EFV in this setting and in small studies rash did not occur. The risk of recurrent rash should be weighed against the disadvantage of moving to second-line PI based treatment early on.

Figure 16.3 Hepatotoxicity and skin toxicity associated with nevirapine (NVP) management during the initiation phase (first 2 weeks)

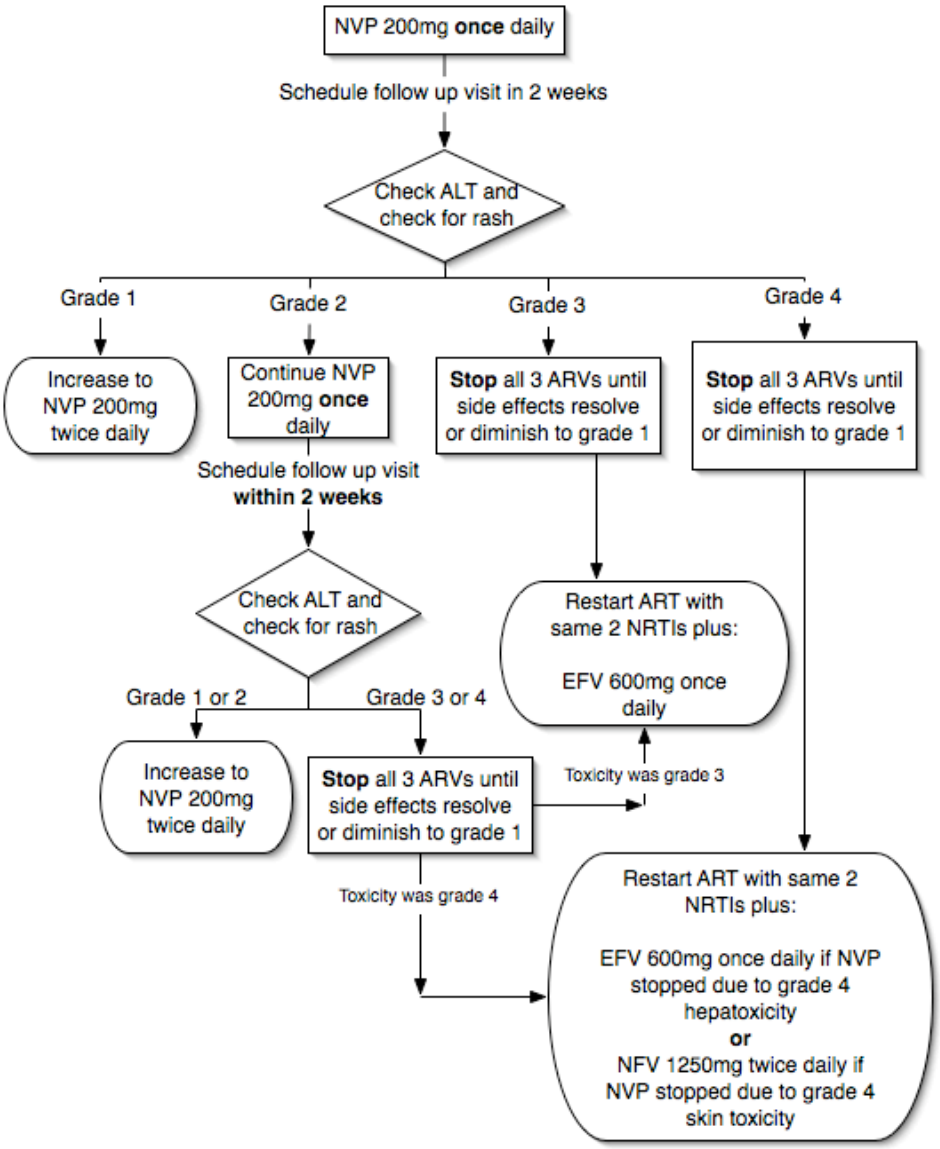
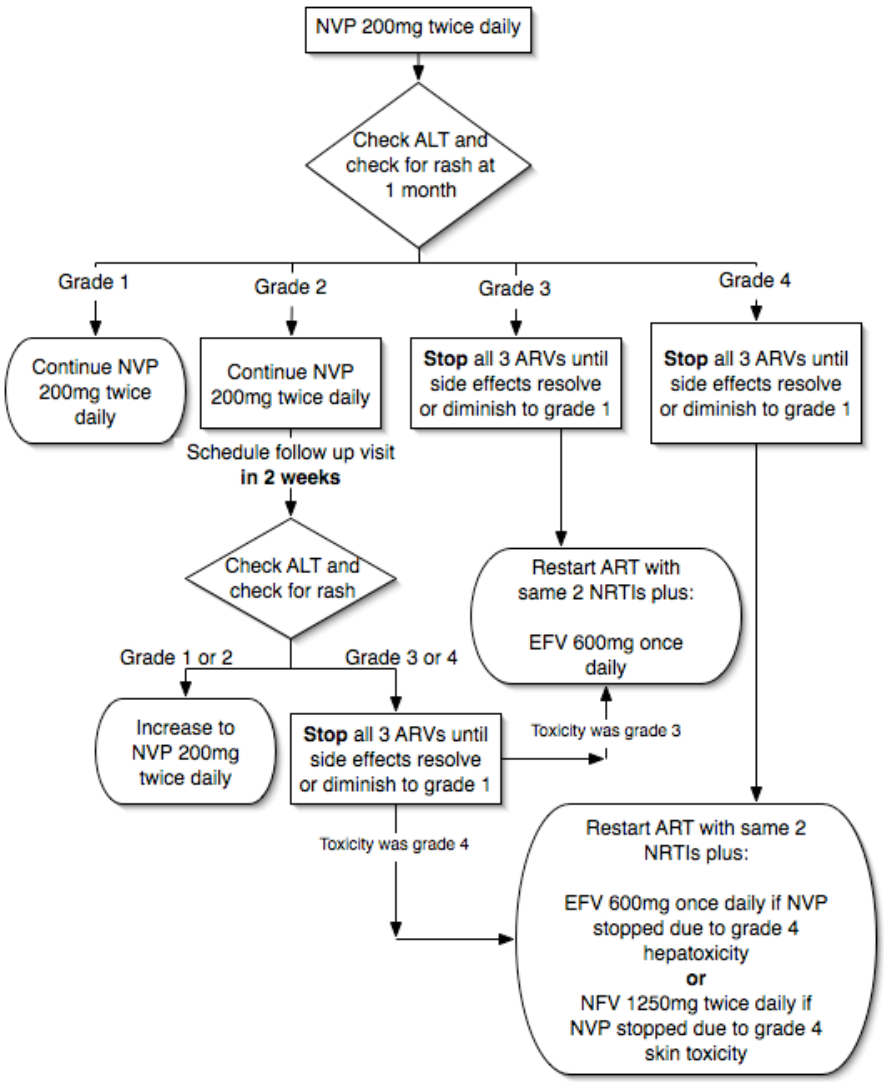


Figure 16.4 Hepatotoxicity and skin toxicity associated with nevirapine (NVP) management after the initiation phase



16.4.4. Protease Inhibitors

16.4.4.1. Lopinavir/Ritonavir (LPV/r, Kaletra ©), Atazanivir/Ritonavir (ATV/r) and Nelfinavir (NFV, Viracept ®)

Diarrhea is the number one most common adverse effect to PIs. Other common side effects include headache, nausea/vomiting, and fatigue. Dosage adjustments are required when co-administered with NNRTIs (NVP or EFV).

Toxicities and Management

Toxicities include insulin resistance, diabetes, hyperlipidemia, lipodystrophy, and increased bleeding in hemophiliacs (see **Section 16.5** for more information).

- Insulin Resistance occurs in up to 40% of patients treated with PIs leading to new-onset diabetes mellitus or exacerbation of pre-existing cases. The median onset time is 60 days after initiation of therapy. Patients receiving PIs should be advised about the warning signs of hyperglycemia, such as polydipsia, polyuria, and polyphagia. Provide supportive therapies (oral hypoglycemic drugs or insulin).
    - In patients with diabetes and patients developing insulin resistance, a non-ritonivir-boosted PI (i.e. NFV) should be used.

- Hyperlipidemia: Elevated triglycerides and/or cholesterol have been reported while on PIs, especially with Ritonavir. Dietary adjustments and exercise along with supportive therapies such as statins and/or fibrates are recommended.

16.5 Metabolic complications and morphological changes: lactic acidosis, lipodystrophy, and insulin resistance

16.5.1. Lactic acidosis

The initial symptoms of **lactic acidosis** are variable. The symptoms may include generalized fatigue and weakness, gastro-intestinal symptoms (nausea, vomiting, diarrhea, abdominal pain, hepatomegaly, anorexia and/or unexplained sudden weight loss), respiratory symptoms (tachypnea or dyspnea) or neurologic symptoms (including motor weakness). Risk factors include female gender, high body mass index, and prolonged NRTI use.

Onset may occur as early as 1 month and as late as 20 months after initiation of ART, particularly any NRTI.

Diagnosis and Management
- If lactic acidosis is suspected, all ARV drugs should be stopped.
- Laboratory findings can include **increased anion gap acidosis**; elevated lactate levels; or elevated aminotransferases (ALT, AST), creatinine phosphokinase (CPK), lactate dehydrogenase (LDH), lipase and amylase levels.
- NRTI drugs less likely to cause lactic acidosis (like ABC, 3TC, TDF, FTC) may be considered but not reintroduced until patient stabilizes.

16.5.2. Lipodystrophy and insulin resistance

Changes in fat distribution are gradual and generally not apparent until months after initiation of therapy. They may result from use of NRTI or PIs. Clinical findings include: central obesity, peripheral fat wasting and lipomas, visceral fat accumulation, dorsocervical fat accumulation ("buffalo hump"), extremity wasting with venous prominence, facial thinning and breast enlargement.

Insulin resistance occurs in up to 40% of patients treated with PIs leading to new-onset diabetes mellitus or exacerbation of pre-existing cases. The median onset time is 60 days after initiation of therapy. Patients receiving PIs should be advised about the warning signs of hyperglycemia, such as polydipsia, polyuria, and polyphagia.

Diagnosis and Management
- If lipodystrophy becomes a serious problem for the patient, a change in regimen can be considered.
- Laboratory findings can include increased lipid and glucose levels (associated with insulin resistance).
- Use insulin or hypoglycemics to treat the insulin resistance/hyperglycemia.
- If available, statins or fibrates can be used to treat hyperlipidemia.
- There is no specific treatment for lipodystrophy. One of the advantages of a regimen of AZT/3TC/ABC is that lipodystrophy is less likely to occur. However, this regimen may be less effective against HIV.

16.6 Recommended single drug substitutions

Table 16.8 Major toxicities of ARVs and recommended single drug substitutions

Drug	Common Associated Toxicity	Suggested Substitute
ABC	Hypersensitivity reaction	AZT or TDF or d4T
AZT	Severe anemia[a] or neutropenia[b] Severe gastrointestinal intolerance[c]	TDF or d4T or ABC
	Lactic acidosis	TDF or ABC[d]
d4T	Lactic acidosis Lipoatrophy/metabolic syndrome[e]	TDF or ABC
	Peripheral neuropathy	AZT or TDF or ABC
TDF	Renal toxicity (renal tubular dysfunction)	AZT or d4T or ABC
EFV	Persistent and severe central nervous system toxicity[f]	NVP[h] (or any PI[i])
	Potential teratogenicity (1st trimester of pregnancy or women not using adequate contraception)	NVP[h] (or any PI[i])
NVP	Hepatitis	EFV[h] (or any PI[i])
	Hypersensitivity reaction	any PI[h,i]
	Severe or life-threatening rash (Stevens-Johnson syndrome) [g]	
ddI	Lactic acidosis, pancreatitis, peripheral neuropathy	TDF
LPV/r	Insulin resistance; diabetes; hyperlipidemia	NFV
ATV/r	Insulin resistance; diabetes; hyperlipidemia	NFV

[a]Exclude malaria in areas of stable malaria; severe anemia (grade 4) is defined as Hb <6.5 g/dl.
[b]Defined as neutrophil cell count <500 cells/mm^3 (grade 4)
[c]Defined as severe, refractory gastrointestinal intolerance that prevents ingestion of ARV drug regimen (e.g. persistent nausea and vomiting).
[d]Reinitiation of ART should not include d4T or AZT in this situation. TDF or ABC is preferred.
[e]Substitution of d4T may not reverse lipoatrophy.
[f]E.g. persistent hallucinations or psychosis.
[g]Severe rash is defined as extensive rash with desquamation, angioedema, or a reaction resembling serum sickness; or a rash with constitutional findings such as fever, oral lesions, blistering, facial edema or conjunctivitis; SJS can be life-threatening. For life-threatening rash, substitution with EFV is not recommended, although this approach has been reported in a small number of patients in Thailand without recurrence of rash.
[h]TDF or ABC may also be substituted for the NNRTI that caused the problem (except in women in the 1st trimester of pregnancy or who may become pregnant, when TDF is contraindicated). Triple NRTI regimens, however, are not recommended.
[i]PI class should be preferentially reserved for second-line therapy as no potent regimens have been identified for recommendation following initial PI failure.

16.7 Reporting adverse drug reactions:

NACP will facilitate data gathering regarding adverse drug reactions through site visits and distribution of appropriate reporting forms. Adverse drug reactions should be reported to NACP at the numbers in the front of this guide if they are severe enough to result in any of the following outcomes:

- A change to the patient's therapy
- Cessation of ARV treatment
- Significant disability
- Death

The following information should be included in the report:

- Age and sex of patient
- Drug history
- Drug suspected of causing the toxicity
- Nature of reaction
- Grade of reaction
- Outcome/new ART regimen

SECTION 17: First-line treatment failure and recommended second-line regimens

17. First-line treatment failure and recommended second-line regimens

Treatment should only be determined to have failed, and the regimen changed from the recommended first-line to the second-line after a minimum of 6 months on therapy. **Do not rush into treatment changes.**

17.1 Assessing treatment failure in adults and adolescents

The decision that treatment has failed should be based on all available evidence: complete clinical assessment and (if available) CD4 count and viral load. OIs that occurred or during the first 6 months should be treated as IRIS and excluded. In particular, **it is vital to investigate adherence** in these circumstances. Poor adherence to treatment is the most common reason for treatment failure. Changing to a second-line regimen will achieve nothing if adherence is not addressed.

Table 17.1 Clinical, CD4 cell count, and virological definitions of treatment failure for adherent patients on a first-line ARV regimen for at least 6 months.

Treatment failure— defined as a combination of the below:	
Clinical failure	• New or recurrent OI, malignancy, pulmonary TB, severe bacterial infections (must distinguish from immune reconstitution syndrome). • New or recurrent WHO Stage 4 condition.[a,b,c] • Significant (>10%) Weight loss after stabilization or gain without other explanation
Immunological (CD4 cell) failure[d]	• Fall of CD4 count to pre-therapy baseline (or below); or • 50 % fall from the on-treatment peak value (if known)[d]; or • CD4 levels do not rise from the baseline after 6 months[e]
Virological Failure	• Plasma viral load above 10,000 copies/ml[f]

a. Current event must be differentiated from the immune reconstitution inflammatory syndrome.
b. Certain WHO clinical Stage 3 conditions (e.g. pulmonary TB, severe bacterial infections) may be an indication of treatment failure and thus require consideration of second-line therapy.
c. Some WHO clinical Stage 4 conditions (lymph node TB, uncomplicated TB pleural disease, esophageal candidiasis, recurrent bacterial pneumonia) may not be indications of treatment failure and thus do not require consideration of second-line therapy.
d. Without concomitant infection to cause transient CD4 cell decrease.
e. If a cut-off value is desired, WHO suggests considering the presence of treatment failure if the CD4 count remains persistently less than 50-100 cells/mm^3 over 6 months (although if less than 50 at baseline, it may take 12 months or more to rise above this level).
f. The optimal viral load value at which ART should be switched has not been defined. However, values of more than 10,000 copies/ml have been associated with subsequent clinical progression and appreciable CD4 cell count decline.

In the complete absence of CD4 testing, the use of clinical definitions listed above should be used to determine if treatment failure has occurred. If CD4 counts are available, they can also be used to determine when not to switch therapy. That is, a patient with a new clinical stage 3 event whose CD4 count is greater than 200 cells/mm^3 should generally not be switched to a new regimen.

17.1.1. TB and other stage 3 and 4 conditions and deferring change in ARV regimens

- TB and recurrent bacterial infections can occur at any CD4 level and do not necessarily indicate treatment failure.
- The response to appropriate therapy should be used to evaluate the need to switch ART.
- The decision to switch ART should be postponed to allow response to therapy where the following conditions are present:
    - Pulmonary TB or extrapulmonary TB (simple lymph node TB, uncomplicated TB pleural disease)
    - Severe and/or recurrent bacterial infections (as stage 3 or 4 events)

17.2 Assessing treatment failure in children

Take note of the following when determining treatment failure in children:

- First check adherence, make sure child has been on therapy for at least 6 months, and adherence has been assessed and found to be adequate.
- When defining treatment failure because of growth failure, ensure that the child is not failing to grow because of inadequate nutrition, and that any intercurrent illnesses have been treated and have resolved.
- Development of TB while on first-line therapy may NOT be an indication of treatment failure. Response to TB treatment should be used to evaluate the need for switching therapy.
- Always consider immune reconstitution inflammatory syndrome (See Section 14).
- CD4% should NOT be measured during an intercurrent infection – but preferably a month after resolution.
- Do NOT use TLC to determine treatment failure.

Table 17.2 Clinical, immunological definitions of treatment failure for adherent children on a first-line ARV regimen for at least 6 months

Treatment failure – defined as a combination of:	
Clinical treatment failure	• Lack of or decline in growth rate in children who show an initial response to treatment (WHO clinical stage 3 or 4– moderate or severe unexplained malnutrition not adequately responding to standard therapy despite adequate nutritional support and without explanation) • Loss of neurodevelopmental milestones or development of HIV encephalopathy • Occurrence of new OI or malignances, or recurrence of infections such as oral candidiasis that is refractory to treatment or esophageal candidiasis
Immunological (CD4 cell) treatment failure	• Development of severe immunodeficiency after initial immune recovery • Development of severe immunodeficiency, confirmed with at least one subsequent CD4 measurement (drop below age appropriate cut-off) • Rapid rate of decline to at or below threshold of severe immunodeficiency

Table 17.3 Management of treatment failure in children

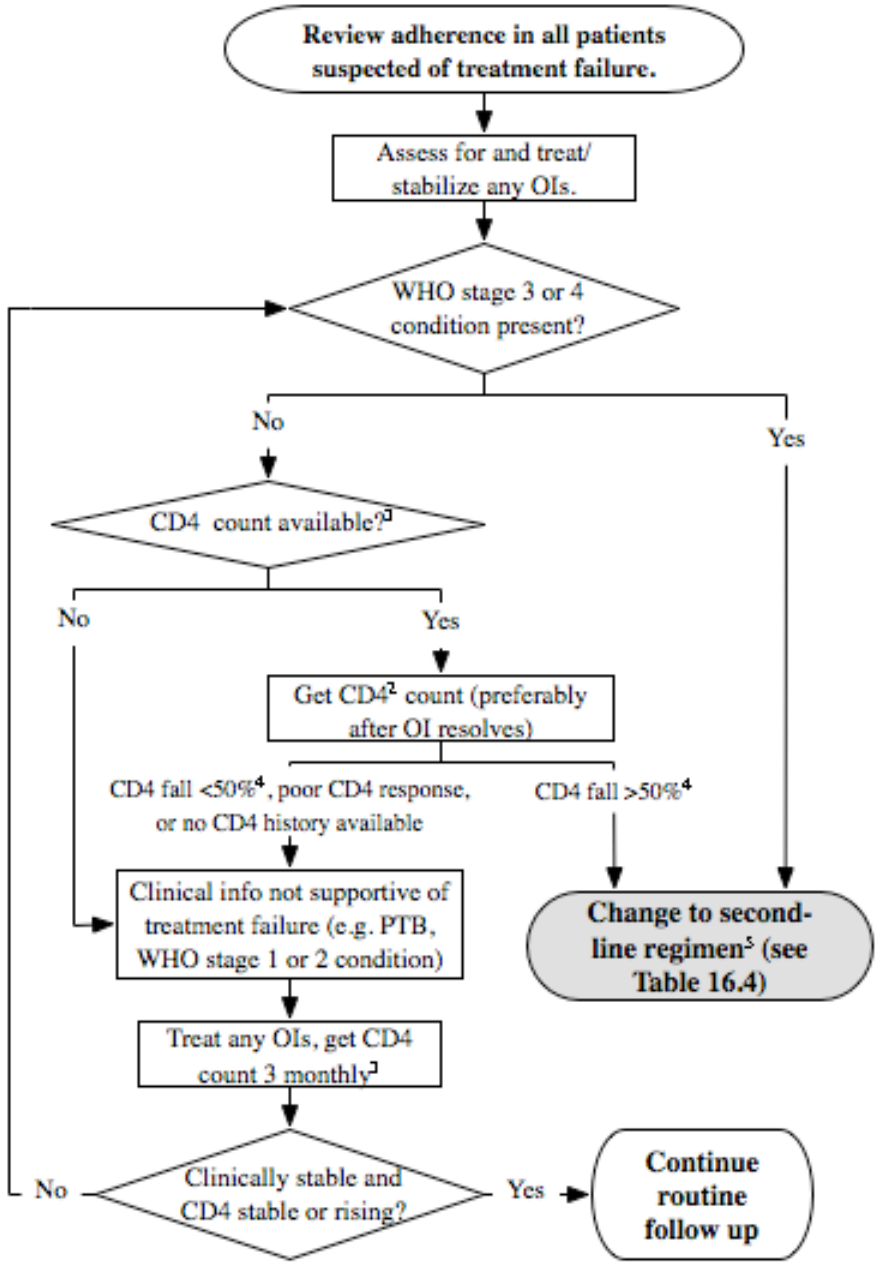
Clinical Stage	Availability of CD4 testing	Management options
New or recurrent Stage 1 and 2 event(s)	No CD4	▪ **Do not switch regimen**
	CD4	▪ Consider switching regimen only if 2 or more values below age-related threshold for severe immunodeficiency* are available ▪ Increase clinical and CD4 follow-up if CD4 approaches age-related threshold for severe immunodeficiency
New or recurrent Stage 3 Event(s)	No CD4	▪ **Consider switching regimen** ▪ If child has pulmonary or lymph node TB, or has severe recurrent presumed bacterial pneumonia, first treat the condition. The need to switch regimen should be decided based on re-evaluation of the child after treatment is complete.
	CD4*	▪ Switching regimen is recommended if CD4 is at or below age-related threshold for severe immunodeficiency,* especially if it has declined after an initial improvement on ART
New or recurrent Stage 4 event(s)	No CD4	▪ **Recommend switching regimen**
	CD4*	▪ Switching is generally recommended but may not be necessary where CD4 is above age-related threshold for severe immunodeficiency*

* Switching should particularly be considered if values are <15% (12-35 months of age), <10% (36-59 months of age), <100 cells/mm^3 (≥5 years of age); use of %CD4 in children less than 5 years of age and absolute CD4 count after 5 years of age is preferred; if serial CD4 values are available, the rate of decline should be taken into consideration.

Figure 17.1 Changing to second-line therapy based on clinical and immunological criteria

SUSPECT TREATMENT FAILURE in a patient on ARVs for >6 months[1] because of:

- Weight loss > 10% (see **Appendix 2** for calculation) and/or
- New or recurrent WHO stage 3 or 4 diseases after period of wellness, and/or
- Falling CD4 count/persistently low CD4 count[2]



[1]OIs in the first 6 months are unlikely to be an indication of ART failure in adherent pts; consider IRIS (see **Section 15.6**.). However, refer to **Section 17.1.1** for cases where treatment of stage 3 and 4 conditions is needed before suspecting treatment failure.
[2]CD4 rise on effective ART averages 100-150/year; poor CD4 response can occur in pts who are otherwise clinically well. Without viral load it can be difficult to determine if they are failing ART.
[3]Many pts may not have had regular CD4 counts done when ART was first initiated; CD4 tests will become increasingly accessible and where possible, should be done in all pts on ART 6 monthly.
[4]For children younger than 5 years of age, refer to CD4 age-related thresholds. See **Section 7**.

17.3 Recommendations for second-line therapy in HIV-1, HIV-2 and HIV-1/2 coinfections in adult, adolescents, and children

The new second line regimen should ideally include at least one drug drawn from a new class. The PI class of drugs is thus preferentially reserved for second-line treatments, preferably supported by one new NRTI or NtRTI along with 3TC. If the patient is infected with HIV-2, a regimen of 2 NRTIs and 1 PI is used for both the first and second lines.

All of the preferred second-line regimens were selected based on efficacy, availability (especially of fixed dose combinations), simplicity of the dosing regimen, toxicity, and cost. 3TC is maintained in second-line regimens because it selects for mutations that lead to a less fit virus, which makes it more susceptible to the other NRTIs.

17.3.1. Choice of protease inhibitors in second-line therapy

- Lopinivir boosted with ritonivir (LPV/r) or atazanivir boosted with ritonivir (ATV/r) are preferred.
- LPV/r exists in a heat-stable fixed dose combination (Kaletra). It is expected that ATV/r will also in the near future.
- If neither is available, Nelfinavir (NFV) can be used. It does not need to be kept cold, but it is not as potent as the boosted PIs and has a higher pill burden.

17.3.2. Choice of NRTIs in second-line therapy

- In general, at least 1 new NRTI should be used for each patient. Typically 3TC is the only NRTI that should be continued in the 2nd line.
- (3TC + TDF) or (ABC + ddI) should be used if d4T or AZT was in the original regimen.
- AZT + 3TC should be used if TDF (but not AZT or d4T) was used in the original regimen.
- ddI dose should be weight-adjusted to reduce risks of toxicity (see below).
- TDF and ddI can be used together, however this combination should be used with caution due to potentially overlapping toxicities. The ddI dose should be reduced to reduce risks of toxicity. (See dose adjustments below.)

Table 17.4 Detailed recommendations for switching to second line ARV regimens in adults and adolescents

		First-line Regimens	Second-Line Regimens[1]	Alternative Second-Line Regimens[1]
HIV-1	Preferred Regimen	AZT + 3TC + NVP [2,3]	TDF + 3TC[4] + PI[3]	ddI + ABC + PI[1]
	Alternative	TDF + 3TC + NVP [2,3]	AZT[5] + 3TC + PI[3]	ddI + ABC + PI[1]
	Second Alternative	d4T + 3TC + NVP [2,3]	TDF + 3TC[4] + PI[3]	ddI + ABC + PI[1]
HIV-2 or **HIV-1/HIV-2** coinfection[1]	Preferred Regimen	AZT + 3TC + PI[1]	TDF + 3TC[4] + PI[3]	ddI + ABC + PI[1]
	Alternative	TDF + 3TC + PI[1]	AZT[5] + 3TC + PI[3]	ddI + ABC + PI[1]
	Second Alternative	d4T + 3TC + PI[1]	TDF + 3TC[4] + PI[3]	ddI + ABC + PI[1]

[1] LPV/r (Kaletra) or ATV/r are recommended as the preferred PI. At the time of this printing, LPV/r is the PI of choice in Liberia due to its lower cost and wider availability. If neither LPV/r nor ATV/r are available, NFV may be used.
[2]EFV can be substituted for NVP in first line regimens, UNLESS patient is pregnant or may become pregnant. EFV may only be used during the 2nd or 3rd trimester. It should be used with caution in women who are not using consistent and effective birth control.
[3]NVP should be given QD for first 2 weeks. If no/mild NVP toxicity, then increase dose to BID.
[4]At the physician's discretion, AZT can be used with 3TC in the second line, creating a four-drug regimen (particularly when an FDC is available).
[5]Or d4T

Table 17.5 Common clinical dosing of ARVs

Drug	Dose [a,b]
NRTIs	
ZDV	300 mg twice daily.
3TC	150 mg twice daily or 300 mg once daily
d4T	30 mg twice daily. Do not coadminister with ddI.
ABC	300 mg twice daily
ddl (EC)	400 mg once daily (250 mg once daily if <60 kg) (250 mg once daily if administered with TDF). Take 1 hour before or 2 hours after eating. NEVER coadminister with d4T.
buffered	300mg once daily dissolved in water
NtRTI	
TDF	300 mg once daily (Note: drug interaction with ddI necessitates dose reduction of latter)
NNRTIs	
NVP	200 mg daily for the first 14 days, then 200 mg twice daily
EFV	600 mg once daily
PIs	
LPV/r	400 mg/ 100 mg twice daily (533mg/ 133 mg twice daily when combined with EFV or NVP)
ATV/r	300 mg/100mg once daily
NFV	1250 mg twice daily

[a] These dosages are in common clinical use. They were selected on the basis of the best available clinical evidence. Dosages that can be given once or twice daily were preferred to enhance adherence. The doses listed are those for individuals with normal renal and hepatic function. See Table 18.7 for adjustments for patients with renal and hepatic dysfunction.
[b] AZT, 3TC, and d4T dosages should be adjusted for the creatinine clearance during renal insufficiency.

Table 17.6 Detailed recommendations for switching to second-line ARV regimens in children

		First-line Regimens		Second-Line Regimens NRTIs	PIs
HIV-1	Preferred Regimen	d4T + 3TC + NVP [1,2]		ABC[4] + ddI +	PI [3]
	Alternative	AZT + 3TC + NVP [1,2]		ABC[4] + ddI +	PI [3]
HIV-2 or HIV-1/HIV-2 coinfection	Preferred Regimen	d4T + 3TC +	PI [3]	ABC[4] + ddI +	PI [3]
	Alternative	AZT + 3TC +	PI [3]	ABC[4] + ddI +	PI [3]

[1]EFV can be substituted for NVP in first line regimens IF child is ≥3 years old AND >10kg.
[2]NVP should be given QD for first 2 weeks. If no/mild NVP toxicity, then increase dose to BID.
[3]Both first-line and second-line regimens for HIV-2 and HIV-1/HIV-2 coinfection, and regimens for second-line HIV-1 infection consist of two NRTIs plus one boosted PI. **LPV/r (Kaletra) is the preferred PI in all cases, whether first- or second-line**. If LPV/r is not available, NFV may be used. ATV/r is not currently licensed for use in children.
[4]If ABC toxicity develops 3TC should be continued in the second-line regimen.

Refer to **Appendices 8** and **9** for all pediatric formulations and dosing.

SECTION 18: Management of HIV in the presence of other diseases: tuberculosis, hepatitis B, disease and liver failure

18. Management of HIV in the presence of other diseases: tuberculosis, hepatitis B, kidney disease and liver failure

18.1 Tuberculosis coinfection

HIV and TB often appear in the same patient. Up to 50% of patients with TB are coinfected with HIV in Africa, so TB diagnosis is a vital entry point for care and treatment services.

18.1.1. TB-HIV co-management

- All HIV positive persons should be routinely screened for TB on initial presentation and during each subsequent visit.
- Coinfection with TB causes more rapid progression of HIV.
- Patients with HIV have higher mortality and morbidity from TB. They have worse and more frequent drug side effects, and higher rates of relapse and recurrence.
- TB in HIV positive patients may cause diagnostic difficulty. There are high rates of sputum negative pulmonary TB and extrapulmonary TB.
- TB is a common and potentially life threatening cause of IRIS (see **Section 15.6**)
- Pulmonary TB is considered to be a WHO stage 3 diagnosis and extrapulmonary TB is WHO stage 4.
- Prompt identification and treatment of TB is a fundamental part of HIV care.
- All patients enrolled in care should be screened symptomatically for TB during each clinical visit.
- All patients should be advised to attend the health care facility if they have a cough for >2 weeks.

All patients should be screened for TB before commencement of ART.

Suspect tuberculosis if one or more of the following are present:

- Cough > 2 weeks that does not improve with normal course of antibiotics
- Other constitutional symptoms such as fever, weight loss, night sweats
- Enlarging or fluctuant lymph nodes
- Other features suggestive of extrapulmonary TB

Any patient with suspected TB should be screened with three sputum smears and a chest x-ray. Lymph node aspirates and examination of CSF (in suspected TB meningitis) can also help with the diagnosis.

TB treatment with DOTS should be started promptly in cases with active TB and HIV. **Priority should be given to anti-TB treatment when there is coinfection with HIV.**

Current Liberian guidelines for TB are as follows:

Adults:

- Intensive phase: 2 months of rifampicin, isoniazid, ethambutol and pyrazinamide, followed by
- Continuation phase: 6 months of isoniazid and ethambutol

Children:

- Intensive Phase: 2 months of rifampicin, pyrazinamide, and isoniazid followed by:
- Continuation phase: 4 months of isoniazid and rifampicin

ART in patients coinfected with TB is complicated by:

- Pill burden and adherence: patients being treated for TB have a large number of pills to swallow each day, especially during the Induction Phase.
- Drug interactions between rifampicin and the NNRTIs (especially NVP) and PIs
- Overlapping toxicities of ARVs and TB treatment regimens (see **Section 18.4**).
- Immune reconstitution inflammatory syndrome (IRIS), which often leads to worsening of symptoms during the early phases of ARV treatment

18.2 Patients who develop TB while on ART

18.2.1. TB develops within the first 6 months of treatment

- Continue with ARV therapy
  - For adults and adolescents, if on NVP switch to EFV
  - For pregnant women on NVP-based ART
    - If in the first trimester switch NVP to ABC; NVP can be restarted 2 weeks after rifampicin has been discontinued.
    - If in the second trimester or above, switch NVP to EFV
    - **NOTE:** Rifampicin has a long half-life and its metabolic effects can persist for up to 2 weeks after discontinuation. Hence, NVP should not be recommenced until 2 weeks after discontinuation of rifampicin.
  - For children
    - If on NVP switch to ABC (if < 3yrs or <10kg) or EFV (if >3yrs and >10kg)
    - Once the child completes anti-TB treatment, they should revert back to the national first-line regimen (switch from ABC back to NVP).
- Where dual treatment is difficult and is likely to affect adherence to either the TB or the ARV treatment, or where toxicity of dual treatment is a problem, consider change or interruption of ART. Resume after completion of anti-TB therapy.
- See **Section 18.5** for returning to original regimens after TB treatment is completed.

Never interrupt TB therapy unless there is serious toxicity **directly attributable** to TB therapy.

18.2.2. TB develops after more than 6 months on treatment

If a patient develops active TB following more than six months of ART, the possibility of treatment failure should be considered. Failure is especially likely if the diagnosis is extrapulmonary tuberculosis or if there are other diseases suggesting advanced immune deficiency (see **Section 17**). If the diagnosis of treatment failure is established, the patient should be managed with the appropriate second-line regimen to be decided by experienced physician (see below). LFTs should be conducted every 2 weeks for at least the first 8 weeks of therapy to determine the risk of added hepatic toxicity. In the absence of evidence for ARV treatment failure, patient should be managed as per **Section 18.2.1** (TB develops within 6 months of treatment) above.

18.3 Patients presenting with TB <u>before commencing ART</u>

If an HIV positive patient who is not on ART presents with TB, the first priority is treating the TB according to the national TB-treatment guidelines. The timing of ARV initiation depends on a balance between avoidance of toxicity and prevention of deterioration of immune function. Initiation should be considered as follows:

Table 18.1 Timing of initiating first line ART in relationship to starting anti-TB therapy for adults and adolescents

CD4 COUNT	TREATMENT RECOMMENDATION	SPECIAL CONSIDERATIONS
NOT available	• Start anti-TB treatment first. • Start ART **as soon as practicable**, preferably between 2 and 8 weeks, especially if there is evidence of extrapulmonary TB or evidence of severe immunosuppression. (Note: some TB diagnoses—lymph node TB or uncomplicated pleural effusions—may respond well to anti-TB therapy and ART can be deferred)	Use an EFV-containing regimen unless contraindicated. (See below.)
CD4 <200/mm^3		
CD4 count 200-350/mm^3	• Start anti-TB treatment first. • Start ART after intensive phase of TB treatment (Start ART earlier if patient is severely ill or if other non-TB stage 3 or 4 events).	Use an NVP-containing regimen unless ART started in intensive phase of TB treatment.
CD4 count >350/mm^3	• Treat TB. • Aim to defer ART until completion of TB treatment but re-evaluate patient at least twice: (1) At end of intensive phase, and (2) At end of TB treatment. If any other Stage 3 or 4 symptoms are noted, start ART.	

Note: Wait until 2 weeks after stopping rifampicin before starting NVP

Table 18.2 Timing of initiating first line ART in relationship to starting anti-TB therapy for children

CHILD'S CLINICAL CONDITION	TREATMENT RECOMMENDATION	SPECIAL CONSIDERATIONS
Stable but ART is needed	Complete 1st 2 months of anti-TB treatment. Start ART in continuation phase.	Use an EFV-containing regimen unless contraindicated.
Advanced HIV Disease; likely to succumb if ART delayed	Start Anti-TB treatment. Start ART in the intensive phase as soon as feasible.	Use an EFV-containing regimen unless contraindicated (see below).

18.4 Treatment recommendations for HIV and TB coinfection

18.4.1. Use of EFV

An EFV containing regimen is the preferred choice in all cases of co-administration of ARVs with rifampicin-containing TB treatment.

- All pre-menopausal women should have a pregnancy test prior to initiation of EFV.
- EFV should be avoided in women in the first trimester of pregnancy and those at risk of pregnancy unless effective contraception is used.
- For women who commence EFV in the 2nd trimester, if treatment with EFV is to continue postpartum, effective contraception should be provided.
- EFV should not be used in children younger than 3 years old or <10kg.

18.4.2. If EFV is contraindicated

In cases where efavirenz is contradicted, (e.g., significant risk of pregnancy, age <3 years old, <10 kg body weight) or the patient does not tolerate it (mental status changes), there are three options:

- **Preferred Option**: Use a triple NRTI regimen (AZT/3TC/ABC, AZT/3TC/TDF or d4T/3TC/ABC)
- Alternative: Use a PI-based regimen e.g., AZT/3TC/ LPV/r (note LPV/r needs to be increased to 4 tablets BID).
- Alternative: NVP may be continued in selected cases, with close clinical and laboratory monitoring (i.e. monthly ALT). The dose of NVP does not need to be changed.

18.4.3. Overlapping toxicities

Avoid using ddI or d4T as they have a high incidence of peripheral neuropathy, as does isoniazid.

All patients on isoniazid should be taking pyridoxine 25 mg daily as prophylaxis against peripheral neuropathy.

If using NVP, be aware that rash, fever and hepatitis can be caused by NVP (and less frequently EFV) and also by pyrazinamide, rifampicin and isoniazid.

18.4.4. Starting ART in patients with TB

1. Start the patient on **pyridoxine, 25 mg QD** (if not already started)
2. Do **pre-emptive counseling:**
    - Treatment of TB while on ART involves taking a large number of tablets which can decrease a patient's ability to adhere to both ARV and TB treatment drugs.
    - When ART is started, TB symptoms may temporarily worsen as a result of immune reconstitution inflammatory syndrome.
3. **Begin antiretroviral treatment**

3.1 For all male TB patients or females who are not of childbearing age, in order of preference, the preferred regimen options in the intensive phase of TB treatment are:

AZT/3TC/EFV
TDF/3TC/EFV
d4T/3TC/EFV

If efavirenz (EFV) is not available or not tolerated the alternative regimen options (in order of preference) are:

AZT/3TC/ABC
AZT/3TC/TDF
d4T/3TC/ABC

PI **at increased dose** or occasionally NVP may be used where there is no alternative. Once TB treatment is complete, switch ABC or PI back to NVP.

3.2 Women of childbearing potential or pregnant women with TB who require ART (see also **Section 12**)

For women with TB starting ART who are:

- In their first trimester of pregnancy, or
- Of childbearing potential and cannot ensure that they will use effective contraception:
  - **Avoid EFV-containing regimens** because of potential congenital deformities

For women with TB who are in the second or third trimester

- Use **an EFV-containing regimen**
- Ensure that effective contraception will be used postpartum if the regimen is continued.
- A change from an EFV-containing to an NVP-containing regimen can be considered when TB treatment has been completed, but must occur cautiously as discussed in the section immediately following.

Recommended regimens for pregnant women with TB who require ART:

If in intensive phase of TB treatment:
(1st trimester) AZT + 3TC + **ABC**
(2nd or 3rd trimester) AZT + 3TC + **EFV**
If in continuation phase of TB treatment:
AZT + 3TC + **NVP**

Table 18.3 Summary of choice of ARV drugs in TB/HIV coinfected ARV-naïve adults and pregnant women

PATIENT CATEGORY	RIFAMPICIN-BASED INTENSIVE PHASE (NVP contraindicated)	NON RIFAMPICIN-BASED CONTINUATION PHASE
Adults & Adolescents	**AZT / 3TC / EFV** 300mg BID/150mg BID/600mg QD	**AZT / 3TC / NVP** 300mg/150mg/200mg BID
Pregnant Women	**AZT/ 3TC / ABC** at any gestation 300mg BID/150mg BID/300mg BID **or** **AZT / 3TC / EFV** if ≥12 weeks gestation 300mg BID/150mg BID/600mg QD	**AZT / 3TC / NVP** 300mg/150mg/200mg BID

3.3 **Children with TB who require ART**

- Start TB treatment first.
- Start ART treatment as soon as possible once TB therapy is established and tolerated.
- To choose the ART treatment:
  - **Avoid NVP-containing regimens**
  - **Do not use EFV-containing regimens** in children < 10kg or < 3 years. Use ABC instead. Once TB treatment is complete, switch ABC back to NVP.

Table 18.4 Summary of choice of ARV drugs in TB/HIV coinfected ARV-naïve children

PATIENT CATEGORY	RIFAMPICIN-BASED INTENSIVE PHASE (NVP contraindicated)	RIFAMPICIN-BASED CONTINUATION PHASE
Children age below 3 years or weight < 10kg*	**AZT / 3TC / ABC**	**AZT/3TC/ABC**
Children age above 3 years and weight >10kg*	**AZT / 3TC / EFV**	**AZT/3TC/EFV**

*See **Appendix 9**: Pediatric dosing guidelines

18.4.5. Choice of ART in patients who develop TB while failing a first-line ART or are on a second-line regimen

- Patients who develop TB on a failing first line regimen need to be changed to second-line ARV drug treatment. However, second-line ART regimens are PI-based, and plasma concentration of PIs is reduced by rifampicin.
- Treatment plan for these patients should quickly be agreed upon with a senior clinician in order to avoid delay in initiating TB treatment.
- While rifabutin is the preferred rifamycin for use in patients on PIs who also need anti-TB treatment, it is currently not widely accessible. Refer to **Table 18.5**.

Table 18.5 ART in patients developing TB while on/needing second-line ART

ART Regimen at TB Diagnosis	If rifabutin not available	If rifabutin available
Failing standard first-line regimen	Continue failing first-line regimen & commence anti-TB treatment. Change to second-line during the continuation phase when rifamycin course completed.	**Start rifabutin-based anti-TB treatment. Switch to second line ARVs as soon as possible.**
Patient on PI-based second-line regimen	Stop all ARVs & start (or continue) 3TC alone and then start anti-TBs. Resume second-line treatment in the continuation phase	**Start rifabutin-based anti-TB treatment. Continue second-line ARV treatment.**

Patients who have previously failed first-line ARV drug treatment should never be given triple nucleoside therapy if they also need concomitant TB treatment.

18.5 Returning to the pre-TB regimen after completion of treatment

As every change to a patient's regimen decreases the likelihood of adherence, returning patients to their pre-TB treatment regimens should be based on the following factors:

- The original substitution was made because of concern for TB medication related toxicities, not because of treatment failure.
- The pre-TB treatment regimen has fewer potential toxicities, is better tolerated, has more efficacy and is in consistent supply.
- The patient has good comprehension of the reasoning for the repeated changes to his/her regimen and has a history of adherence.
- **Wherever possible, patients who were started on triple nucleoside regimen should be changed to a standard regimen once the TB treatment is complete** (because triple NRTI regimes are associated with a lower chance of viral suppression).

18.6 Hepatitis B coinfection

Hepatitis B infection is endemic in Liberia. Progression to advanced liver disease and cirrhosis is faster in patients who are coinfected with HIV.

3TC and TDF are effective against both HIV and Hepatitis B and should be used in combination as part of first line treatment in Hepatitis B/HIV coinfection. Once 3TC and TDF are removed, there is a chance that the Hepatitis B will return.

18.6.1. First-line regimen

TDF + 3TC + EFV

300mg QD/150mg BID/600mg QD

If TDF is not available, use AZT 300mg BID/3TC 150mg BID/EFV 600mg QD.

18.6.2. Second-line regimen

The second-line regimen should include 3TC:

AZT / 3TC / LPV/r 300mg/150mg/ 400/100mg BID

If patient was originally on AZT, switch AZT to:

TDF (300mg QD), **OR** ABC (300mg BID)

18.6.3. Cautions

- Avoid ddI and NVP because of liver toxicity
  - If NVP must be used, ALT should be monitored monthly.
  - NVP should not be used in patients with ALT elevations greater than 10x the upper limit of normal (grade 4) as describe in **Section 16**).

- IRIS may present as a flare-up of Hepatitis B and may be difficult to distinguish from ART-induced hepatotoxicity. Flare-ups present with:
  - Acute rise in ALT
  - Symptoms of acute hepatitis (fatigue, abdominal pain, jaundice)

- Management:
  - ARVs active against Hepatitis B (3TC and TDF) should be continued if the patient can tolerate them.
  - If it is not possible to distinguish a serious Hepatitis B flare-up from a grade 4 ART toxicity, all ARV drugs should be stopped and the patient closely monitored until the clinical condition improves.
  - Once the flare-up resolves, the ARVs can be restarted with close monitoring. If the regime contains NVP it should be replaced with another drug.

18.7 Kidney and liver disease

Patients with impaired kidney or liver function should be assessed and investigated using standard procedures. Assessment of kidney problems should include determination of:

- The cause of the problem:
  - Acute (oliguria, anuria, hematuria, edema, hypertension, HIV-associated nephropathy, focal segmental glomerular nephrosclerosis)
  - Chronic (prolonged symptoms/signs of uremia, edema, broad casts, small kidneys on ultrasound); nephrotic syndrome (proteinuria >3.5g/1.73m^2/day, hypoalbuminemia, edema)
- History of hypertension or diabetes mellitus.
- Drugs used (nephrotoxic drugs as well as those that will need adjustment or discontinuation, see **Table 18.6**)

The severity of renal dysfunction is best measured by the glomerular filtration rate (GFR) or the creatinine clearance. Where this is not possible, the serum creatinine concentration, though less accurate, can be used instead. Below is a rough guide that can be used to determine degree of renal dysfunction.

Table 18.6 Grading renal dysfunction

Grade of Severity of Renal Function	Glomerular Filtration Rate (ml/minute)	Serum Creatinine (µmol/liter)
Mild	20-50	150-300
Moderate	10-20	300-700
Severe	<10	>700

NRTIs may need to be re-dosed in the setting of kidney problems. They are secreted largely unchanged through the kidneys; thus, impairment of renal secretory function impairs NRTI excretion and may require dose adjustment. See **Table 18.7** below.

Table 18.7 ARV drug adjustment in renal and hepatic dysfunction

Drug	Daily Dose	Mild Renal Failure (GFR 20-50)	Moderate Renal Failure (GFR 10-20)	Severe Renal Failure (GFR <10)	Hepatic Dysfunction[1]
AZT	600 mg	Unchanged	Unchanged	300mg QD	Caution
d4T	60 mg	20 mg daily	20 mg daily	15 mg daily	Caution
3TC[1]	300 mg	150mg daily	100 mg daily	50 mg daily	Unchanged
ddI >60/<60kg	400/250 mg	200/125mg daily	125/100mg daily	125/75mg daily	Unchanged
TDF	300 mg	300 mg 48 hourly	Do not use	Do not use	Unchanged
ABC	600 mg	Unchanged	Unchanged	Unchanged	Avoid if severe
PIs	Standard dose	Unchanged	Unchanged	Unchanged	Use with caution (avoid LPV/r in severe liver dx)
NNRTIs	Standard Dose	Unchanged	Unchanged	Unchanged	Avoid NVP in severe liver dx; use EFV with caution

[1]Exclude lactic acidosis as a cause in patients with hepatic dysfunction

SECTION 19: Diagnosis and management of common symptoms in HIV positive people

19. Diagnosis and management of common symptoms in HIV positive people

In symptomatic HIV disease, the cause of morbidity and mortality is most often due to common or opportunistic illnesses that result from HIV-induced immune deterioration. Better management and treatment of these illnesses will result in improvement in the length and quality of life for the HIV positive individual.

The purpose of the tables referenced in section is to provide guidance on identification and management of treatable illness in HIV positive individuals. Complications are grouped by system, with the specific symptoms, investigations, and treatment for the most common OIs listed in greater detail. Treatment is available for most of the opportunistic infections, and there should be prompt management of all other treatable conditions in people with HIV and AIDS.

It should also be noted that both solid and blood cancers are more common in HIV positive patients. In general, they should be managed as in sero-negative individuals.

See **Appendix 13**: Common opportunistic infections, diagnosis, prophylaxis and treatment in adults and adolescents, and **Appendix 14**: Common opportunistic infections, diagnosis, prophylaxis and treatment in children.

SECTION 20: Interruption or discontinuation of ART

20. Interruption or discontinuation of ART

20.1 Interruption of ART

Short-term therapy interruptions[4] is usually a result of:

- Severe life threatening toxicity such as Stevens-Johnson Syndrome or acute fulminant hepatitis (see **Section 16**: ARV treatment: toxicity and management)
- Acute illnesses that preclude oral intake
- TB coinfection when patient cannot tolerate all medications (in this situation every effort should be made to adjust the ART regimen where possible rather than interrupting therapy)
- Severe IRIS syndromes (see **Section 15.6**)
- Repeated and persistently poor adherence

If a short-term interruption is planned, contact a clinician with greater expertise (see contact information at front of these Guidelines) to confirm plan of interrupting ART.

Interruption of ART should always be avoided.

20.2 Discontinuation of ART

Discontinuation of antiretroviral treatment may be considered in case of any of the following conditions:

- Client cannot tolerate side effects and there is no alternative regimen available.
- Client or client's caregiver, in case of children, wishes to stop therapy.
- The patient is dying and can no longer comply.
- Repeated failure to comply with treatment.
- Treatment is failing (defined as above) and there is no alternative regimen available.

  Note: While this is a possible reason for discontinuing therapy, caution should be exercised. There is good evidence that ART provides some clinical benefit even in patients who have developed a strain of virus which is resistant to medications. Drug resistant viruses are less virulent (or "fit") than the wild type, and stopping treatment may encourage the wild type to return in strength (i.e. even failing treatment can slow down progression of disease).

20.3 Follow-up after discontinuation of ART

Clients discontinuing ART for any reason should continue to be followed-up (if they agree to do so) for opportunistic infections. Should they want to restart ARV drugs, a new baseline clinical and biological assessment should be performed as well as a readiness assessment.

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[4] When short-term interruption of therapy is necessary, the provider should be aware that **EFV and NVP have very long half-lives, therefore:**

- Except in the case of acute life threatening toxicity, these medications should be stopped **2 weeks** prior to the discontinuation of the other medications.
- If NVP has been discontinued for more than 2 weeks and it is being reintroduced, it is recommended that initiating dose be used on reintroduction:.
  - 1st 2 weeks: NVP 200 mg once daily
  - If tolerated: increase to NVP 200 mg twice daily

SECTION 21: Palliative and end of life care

21. Palliative and end of life care

21.1 Symptom management

21.1.1. Pain

Determine the site of the pain and grade the severity of the pain.

Adults

- Non-opioids such as aspirin, ibuprofen or paracetamol should be used first.
- Subsequently a mild opioid such as codeine (if available) should be used.
- When these two steps fail, a strong opioid such as morphine (if available) may be used in incrementally increasing dosages to control pain.

See **Table 21.1**: Use of opioids and non-opioid analgesics, below. For management of side effects of morphine and other opioids, see **Table 21.2**.

Children

The principles of pain control in children are similar to those in adults, and in particular important during terminal illness.

- Initially it is advisable to use non-opioids such as paracetamol or non-steroidal anti-inflammatory agents.
- If pain control cannot be achieved with such measures it is essential that children be allowed to be pain free and opioids (e.g. oral morphine) should be used.
- Steroids should also be considered when inflammation is noticed. It is important that care providers and family members work together and keep each other well-informed on new developments.

Table 21.1 Use of opioids and non-opioid analgesics

	Analgesics	Starting dose in adults	Range	Side effects/cautions
Step 1	Non-opioids			
	Paracetamol (also lowers fever)	500mg 2 tablets every 4-6 hours (skip at night or give another analgesic to keep total to <8 tablets/day)	Only 1 tablet may be required in elderly or very ill, or when combined with opioids. Mild pain might be controlled with every 6 hour dosing.	Do not exceed 8 500mg tablets in 24 hours (more can cause serious liver toxicity). People with liver disease should not take >4 tablets/day
	Aspirin (acetylsalicylic acid) (also an anti-inflammatory and lowers fever).	600mg (2 tablets of 300mg) every 4 hours.		Avoid use if gastric problems. Stop if epigastric pain, indigestion, black stools petechiae or bleeding. Do not give to children under 12 years. Avoid if presence of any bleeding
	Ibuprofen (also anti-inflammatory, lowers fever, good for bone pain)	400mg every 6 hours		Max 2400mg per day
Step 2	Opioid for mild to moderate pain (give in addition to aspirin or paracetamol)			
	Codeine (if not available, consider alternating aspirin and paracetamol*)	30mg every 4 hours.	30-60 mg every 4-8 hrs. Max daily dose is 180-240mg due to constipation—switch to morphine.	Give laxative to avoid constipation unless it causes diarrhea.
	Tramadol*	50mg every 6 hours	50-100mg every 6 hours	Drowsiness and/or dizziness.
Step 3	Opioid for moderate to severe pain			
	Oral **morphine** 5 mg/5 ml or 50mg/5 ml Drop into mouth. Can also be given rectally (by syringe).	2.5-5 mg every 4 hours (dose can be increased by 1.5 or doubled after 24 hours if pain persists).	According to need of patient and breathing. **There is NO ceiling dose.**	Give laxative to avoid constipation unless it causes diarrhea.

*Exception: if no codeine or tramadol, aspirin every 4 hours can be alternated with paracetamol every 4 hours – overlap so that one is given every 2 hours.

Table 21.2 Response to side effects of morphine or other opioids

If patient has side effect:	Then manage as follows:
Constipation	• Increase fluids and bulk • Give stool softener (docusate) at time of prescribing plus stimulant (senna) • **Prevent by prophylaxis** (unless diarrhea)
Nausea and/or vomiting	Give and antiemetic (metoclopromide, haloperidol or chlorpromazine). Usually resolves in several days. May need round-the-clock dosing.
Respiratory depression (rare when oral morphine is increased step by step)	• If severe, consider withholding next opioid dose, then halve dose
• Confusion or drowsiness (if due to opioid) • Decrease alertness • Trouble with decisions	Usually occurs at start of treatment or as dose is increased. Usually resolves within a few days. Can occur at end of life with renal failure. Halve dose or increase time between doses, or provide time with less analgesia when patient wants to be more fully alert to make decisions.

If patient has side effect:	Then manage as follows:
Twitching (myoclonus—if severe or bothers patient during waking hours)	If on high dose, consider reducing dose or changing opioids (consult or refer). Re-assess the pain and its treatment.
Somnolence (excessively sleepy)	Extended sleep can be from exhaustion due to pain. If persists for more than 2 days after starting, reduce the dose by half.
Itching	May occur with normal dose. If present for more than a few days and hard to tolerate, give chlorpheniramine.
Urinary retention	Pass urinary catheter if trained—in and out since it usually does not recur.

Reduce morphine when cause of pain is treated (common in HIV/AIDS complications):

- If used only for a short time: stop or rapidly reduce
- If used for weeks—reduce gradually to avoid withdrawal symptoms.

For burning pains; abnormal sensation pains; severe, shooting pains with relatively little pain in between; and pins and needles, give:

- Low dose **amitriptyline** (25mg at night or 12.5 mg BID; some start 12.5 mg QD) – wait 2 weeks for response, then increase gradually to 50 mg at night or 25 mg BID.

21.1.2. Breathlessness

Patients with AIDS often develop severe breathlessness terminally. This may be the result of a severe non-responding lung infection or cancer such as Kaposi's Sarcoma or lymphoma affecting the lungs and pleura. In such patients alleviate dyspnea by propping up the patient and then refer for further management. Morphine may be helpful in this scenario.

21.1.3. Vomiting

Vomiting may lead to poor fluid intake and hence dehydration and therefore it is necessary to correct dehydration. Patient should be encouraged to take small amounts of fluids frequently. Vomiting may be relieved by administering prochlorperazine 5mg orally three times a day or metoclopromide 10mg orally three times a day.

21.1.4. Oral care

Good oral care should always be practiced. This includes regularly brushing the teeth with a soft toothbrush and gargling with mouth wash solutions or weak salt solutions after food. In persons with mouth sores, oral care helps. If the sores are painful patients will not be able to eat or swallow and should be given soft foods and liquid diets. If a specific cause for the ulcers is found these should be treated as described.

21.1.5. Itching

To relieve itching, bath oils or other emollients such as emulsifying ointment may be useful. If a rash is present then antifungal creams will help if the rash is due to a fungal infection or topical steroids will relieve inflamed areas of the skin if a bacterial or viral infection is not present. Orally administered antihistamines, such as, diphenhydramine or hydroxyzine 25mg given at night may reduce the pruritus and allow a relatively more comfortable sleep.

21.2 Comfort

Prevent the development of bedsores by changing the patient's position every 4 hrs and having the patient lie on extra soft material. Avoid prolonged pressure on any one part of the body. Protect areas that have become inflamed because of pressure by avoiding any pressure at all on the area and by applying soothing lotions. Change soiled bed sheets immediately. Massage pressure points such as the heels, elbows, ankles, back and hips frequently. Cover all open sores with a gauze bandage after applying antiseptic cream.

21.3 Terminal care

The main goal of terminal care should be improving the quality of life by removing or alleviating unpleasant symptoms as well as suffering, fear or loneliness. This quality care must be provided wherever the patient is, be it at home or in the hospital. Many patients wish to die at home. As part of the continuum of care, health care providers should extend their services by training and supporting family members to ensure that terminally ill patients at home are well cared for.

All persons with terminal illnesses need end of life care. The patient and the family must have social, emotional, and spiritual support. In palliation the goal is to allow the patient to die with dignity and relieve him/her of distressing symptoms. Palliation also offers support to help the patient live as actively as possible until death, and enables the family to cope with their loved-one's illness and with their own bereavement. The caregiver needs to listen with empathy and should encourage communication within the family. Issues such as family and child support, schooling, and welfare should be discussed.

Spiritual support and discussion with a religious leader may relieve feelings of guilt. The caregiver should be available and should visit regularly. Bereavement counseling should be made available to family members including the children.

21.4 Care of body after death

Care after death is one of the most important aspects of HIV and AIDS care. **Standard precautions stipulate that all people, no matter what they have died from, should be treated the same.**

These precautions should be applied also to people who have died of HIV and AIDS:

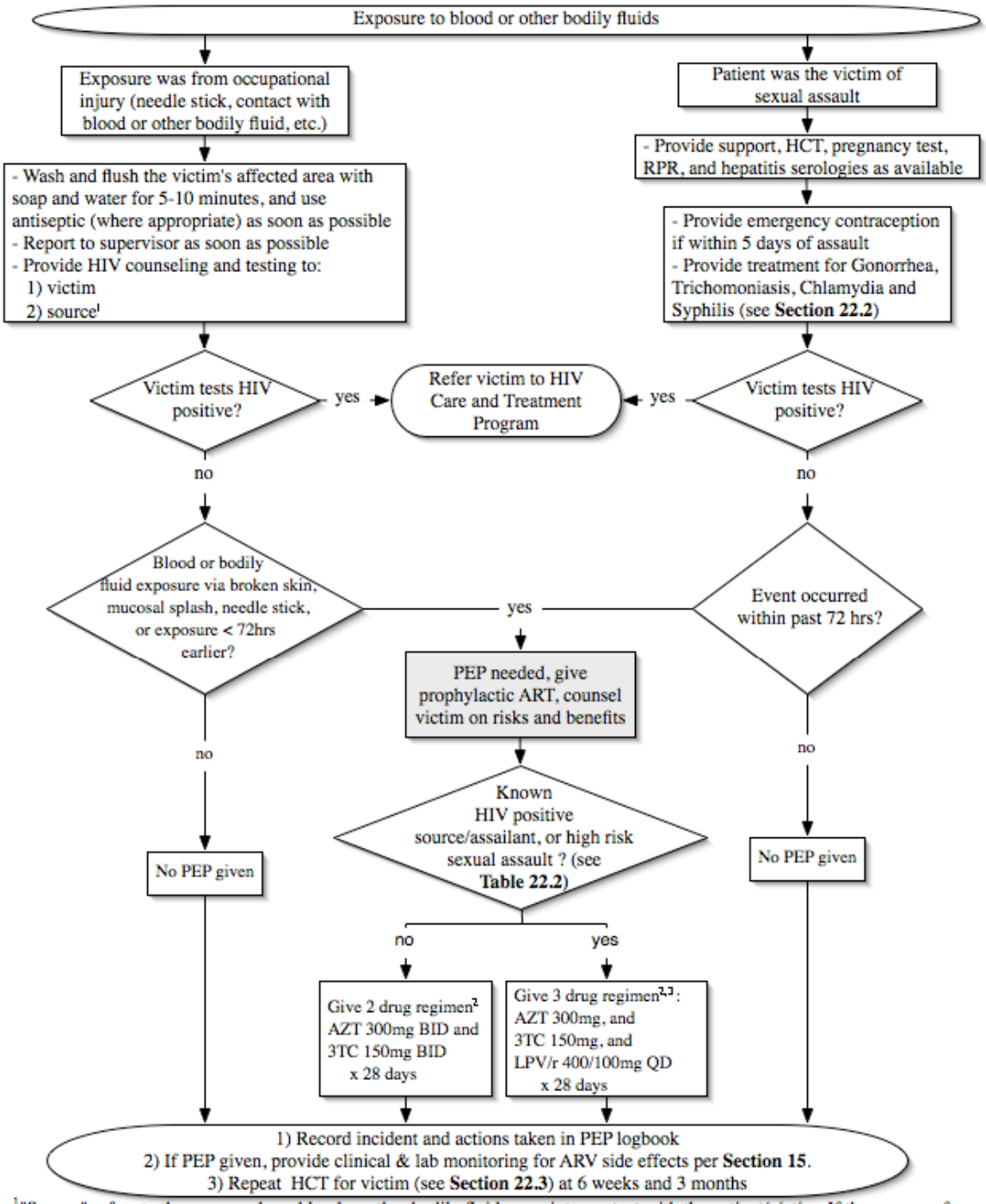
- Avoid contact with any body fluids, use gloves if available.
- Any person with open sores or wounds on his/her hands should not bathe of any bodies without wearing gloves (regardless of known cause of death).
- The body should be bathed with a bleach solution.
- Hands should be washed with soap after any contact with the body.
- If bodies are cared for in a non-mortuary setting, **the body should be buried as soon as possible.**
- Bleach should be used if the body is seeping out fluids; it will kill the virus. However, it is not necessary to cover the body with plastic unless there is need.
- Disposal and care of linen, instruments, and other materials should follow the same procedure of disinfection, sterilization and disposal as discussed in **Section 2**.

SECTION 22: Post-exposure prophylaxis

22. Post-exposure prophylaxis

Post-exposure prophylaxis (PEP) is short-term ARV treatment to reduce the likelihood of HIV infection after potential exposure, either occupationally or through sexual intercourse (rape). Records of all potentially exposed patients should be kept in a PEP logbook by the HIV counselor.

Figure 22.1 Overview of post-exposure prophylaxis (PEP) protocols



[1] "Source" refers to the person whose blood or other bodily fluid came into contact with the patient/victim. If the source refuses HIV testing, testing may still be done; see **Section 4.5.2**.

[2] Check patient/victim Hb before administering AZT; if < 7 g/dl substitute d4T 30mg BID.

[3] If source is failing his/her current ARV regimen, the medications within that regimen should be avoided in the PEP given to the victim.

22.1 Occupational exposure

- The risk of infection from an infected needle is approximately 0.3% (i.e. 3 out of a thousand cases) and approx. 0.03% (3 out of 10,000 cases) for a mucosal splash.
- Prevention of exposure through use of standard universal precautions (see **Section 2**) remains the most effective measure to reduce the risk of transmission.
- These measures are also designed to reduce the risk of transmission of hepatitis viruses B and C: the risk of transmission after percutaneous exposure to these viruses is much higher than for HIV.
- Ideally, all medical workers should be vaccinated against HBV.

22.1.1. Management of potential occupational exposure to HIV

- PEP can reduce infection rates by about 80% if started within 72 hours.
- AZT plus 3TC is the regimen of choice, preferably in a fixed dose combination. d4T can be substituted for AZT if Hb <7g/dl.
- A third drug is used (LPV/r or other PI), in high-risk exposures. Most potential HIV exposures will warrant a two-drug regimen.
- The risk of drug toxicity must be balanced against the risk of infection, which remains low.

22.2 Sexual assault

Rape increases the risk of HIV transmission through sexual intercourse. Sexual violence often results in traumatic lesions of genital mucous membranes, which allow HIV to move more easily from one person to another. Certain additional factors (see **Table 22.1** below) can increase the risk of HIV transmission during sexual assaults.

Post-Exposure Prophylaxis against HIV infection (PEP) should be offered to all survivors. If the victim is HIV positive as a result of the rape, information needs to be provided about all the health services that are available.

Compassion, respect and confidentiality should be offered to all patients, but are particularly important in rape survivors, due to the intense trauma they have suffered. Counseling should be offered as part of post-rape care in addition to emergency contraception, prevention of STIs, and PEP against HIV. PEP is not 100% effective, but the administration of AZT greatly reduces the risk of contracting HIV.

If the patient was a victim of a high-risk assault, choice of **triple therapy** can be considered while emphasizing the importance of good adherence to treatment.

Table 22.1 Risk assessment of HIV transmission after sexual assault

No, or very low risk: no PEP	Standard risk: 2 drug PEP regimen	High risk: 3 drug PEP regimen
Kissing	Vaginal penetration without high risk factor	Multiple assailants and/or multiple penetration
Digital penetration	Oral penetration with ejaculation	Anal penetration
Penetration by means of a foreign object (anywhere)	Unknown act including blood in the mouth, or victim bit or was bitten by the rapist	Menstruation and/or bleeding during intercourse
Ejaculation on intact skin	Ejaculation onto broken skin	STIs in survivor and/or assailant
Condom leak or tear		Wounds, lacerations, or lesions in the survivor's vagina, mouth, and/or anus

Step 1: Assess and treat for life threatening injuries

Step 2: Provide appropriate medications:

- **Emergency contraception**
  - Timing: up to 5 days after the assault.
  - Provide pregnancy test first to confirm that woman was not already pregnant
  - Medicines: Progestin-only pill is the preferred regimen (single dose of 1.5mg levonorgestrel).
  - If the woman should be advised to return for a pregnancy test 2 weeks later to confirm non-pregnancy following the rape, particularly if she is first seen more than 5 days after the assault.

- **Sexually transmitted infections**
  - Assume exposure and treat each infection
    - Gonorrhea: Cefixime 400 mg single dose for patients 12 years of age or older, 8mg/kg for children younger than 12 years.
    - Trichomoniasis: Metronidazole 2 gm single dose or 1 gm orally BID for one day.
    - Chlamydia and Syphilis:
      - Adult: Doxycycline 100 mg BID for 14 days
      - Child: Azithromycin 500 mg once and Benzathine penicillin 2.4 million units IM once

- **Prevention of tetanus**
  - Tetanus prophylaxis should be given unless the survivor has been previously fully vaccinated. Administer tetanus toxoid (TT), which gives active protection
  - Dosing and schedule:
    - 0.5ml per injection, given IM in the mid-lateral part of the thigh or deltoid muscle
    - Second injection 6 weeks later, third injection 6 months after the second, and boosters ever 10 years thereafter

- **HIV post-exposure prophylaxis** (also see **Table 22.2** below)
  - Offer to all victims presenting within 72 hours of rape.
  - First dose of PEP should be given as soon as possible.
  - For most victims **AZT + 3TC** is the recommended regimen, preferably in FDC, BID for 28 days. d4T + 3TC may also be used if AZT is not available or if Hb < 7g/dl.
  - For victims of high-risk assaults (see **Table 22.1** above), a 3-drug regimen of **AZT + 3TC + LPV/r** is recommended, BID for 28 days.

Table 22.2 Recommended PEP regimens and dosing following sexual assault

	Adults and Children >40kg	**Children 20-40kg**	**Children 10-20kg**
2-drug PEP regimen[1]:	AZT: 300 mg, **and** 3TC: 150mg BID	AZT: 2 x 100mg caps **and** 3TC: 1 x 150mg tab BID	AZT: 1 x 100mg caps **and** 3TC: ½ 150mg tab BID
If high risk assault, add third drug:	LPV/r (Kaletra) 400/100mg BID	LPV/r: 2 x 133/33mg caps BID	LPV/r: 1 x 133/33mg cap BID
Duration of PEP regimen:	28 days	28 days	28 days

[1]If victim's Hb < 7g/dl, replace AZT with d4T.

Step 3: Provide or refer for appropriate counseling (i.e. with social worker)

Step 4: Evaluate for criminal investigation

- Forensic documentation
- Sample collection

Step 5: Follow-up

- The victim should be retested for HIV at 6 weeks, and 3 months
- Pregnancy test should be repeated at 2 or 6 weeks, or if a menstrual period is missed.
- Ongoing psycho-social support

22.3 Counseling for all post-exposure patients

- All people presenting to a health facility after potential exposure to HIV should be counseled about the potential risks of HIV infection.
- Parents/guardian of children should be counseled and informed on the risk of HIV infection after sexual assault.
- The following points should be covered in the counseling:
    1. It is important to know the health care worker's/victim's HIV status prior to using any antiretroviral treatment.
    2. Patients should be encouraged to undergo immediate HIV testing.
    3. Initiation of PEP is not recommended more than 72 hrs after exposure.
    4. All patients should be instructed to return at 6 weeks and 3 months post sexual assault for repeat counseling and HIV testing.
    5. Patients should be counseled about the possible risk of infection and the possibility of transmitting infection during sero-conversion.

SECTION 23: Appendices

23. Appendices

Appendix 1 Diagnostic criteria for the staging of HIV-related clinical events in *adults and adolescents*

Clinical event	Clinical Diagnosis	Definitive Diagnosis
CLINICAL STAGE 1		
Asymptomatic	No HIV-related symptoms reported and no signs on examination	Not applicable
Persistent generalized lymphadenopathy	Painless enlarged lymphnodes >1cm, in two or more noncontiguous sites (excluding inguinal), in absence of known cause and persisting for three months or longer	Histology
CLINICAL STAGE 2		
Moderate unexplained weight loss (under 10% of body weight)	Reported unexplained weight loss; in pregnancy, failure to gain weight	Documented weight loss (under 10% of body weight)
Recurrent bacterial upper respiratory tract infections (current event plus one or more in last six months)	Symptom complex, e.g. unilateral face pain with nasal discharge (sinusitis), painful inflamed eardrum (otitis media) or tonsillopharyngitis without features of viral infection (e.g. coryza, cough)	Laboratory studies if available, e.g. culture of suitable body fluid
Herpes Zoster	Painful vesicular rash in dermatomal distribution of a nerve supply does not cross midline	Clinical diagnosis
Angular cheilitis	Splits or cracks at the angle of the mouth not attributable to iron or vitamin deficiency, and usually responding to antifungal treatment	Clinical diagnosis
Recurrent oral ulceration (two or more episodes in last six months)	Aphthous ulceration, typically painful with a halo of inflammation and a yellow- grey pseudomembrane	Clinical diagnosis
Papular pruritic eruption	Papular pruritic lesions, often with marked postinflammatory pigmentation	Clinical diagnosis
Fungal nail infection	Paronychia (painful red and swollen nail bed) or onycholysis (separation of nail from nail bed) of fingernails (white discoloration, especially involving proximal part of nail plate with thickening and separation of nail from nail bed)	Fungal culture of nail/nail plate material
CLINICAL STAGE 3		
Severe unexplained weight loss (more than 10% of body weight)	Unexplained reported weight loss (over 10% of body weight) and visible thinning of face, or waist and extremities with obvious wasting. In pregnancy, weight loss may be masked.	Documented loss of more than 10% of body weight

Clinical event	Clinical Diagnosis	Definitive Diagnosis
CLINICAL STAGE 3 (cont.)		
Unexplained chronic diarrhea for longer than one month	Chronic diarrhea (loose or watery stools three or more times/daily) that is unexplained and non-treatable reported for longer than one month	Three or more stools and observed and documented as unformed, and two or more stool tests reveal no pathogens
Unexplained persistent fever (intermittent or constant and lasting for longer than one month)	Reports of fever or night sweats for more than one month, either intermittent or constant with reported lack of response to antibiotics or antimalarials, without other obvious foci or disease reported or found on examination. Malaria must be excluded in malarious areas.	Documented fever exceeding 37.5° with negative blood culture, negative Ziehl-Nielsen (ZN) stain, negative malaria slide, normal or unchanged chest X-ray (CXR) and no other obvious focus of infection)
Persistent oral candidiasis	Persistent or recurring creamy white curd-like plaques which can be scraped off (pseudomembranoue), or red patches on tongue, palate or lining of mouth, usually painful or tender (erythematous form)	Clinical diagnosis
Oral hairy leukoplakia	Fine white small linear or corrugated lesions on lateral borders of the tongue, which do not scrape off	Clinical diagnosis
Pulmonary tuberculosis (current)	Chronic symptoms (lasting at least two to three weeks): cough, haemoptysis, shortness of breath, chest pain, weight loss, fever, night sweats, PLUS either positive sputum smear OR negative sputum smear AND compatible chest radiograph (including but not restricted to upper lobe infiltrates, cavitation, pulmonary fibrosis and shrinkage. No evidence of extrapulmonary disease.	Isolation of *M. tuberculosis* on sputum culture or histology of lung biopsy (together with compatible symptoms)
Severe bacterial infection (e.g pneumonia, meningitis, empyema, pyomyositis, bone or joint infection, bacterameia, severe pelvic inflammatory disease)	Fever accompanied by specific symptoms or signs that localize infection, and response to appropriate antibiotic	Isolation of bacteria from appropriate clinical specimens (usually sterile sites)
Acute necrotizing ulcerative gingivitis or necrotizing ulcerative periodontitis	Severe pain, ulcerated gingival papillae, loosening of teeth, spontaneous bleeding, bad odor, rapid loss of bone and/or soft tissue	Clinical Diagnosis
Unexplained anemia (below 8g/dl), neutropenia (below 0.5 x 10^9/l) or chronic more than one month) thrombocytopenia (under 50 x 10^9/l)	No presumptive clinical diagnosis	Diagnosed on laboratory testing and not explained by other non-HIV conditions. Not responding to standard therapy with hematinics, antimalarials or anthelmintics as outlined in relevant national treatment guidelines, WHO IMCI guidelines or other relevant guidelines.

Clinical event	Clinical Diagnosis	Definitive Diagnosis
CLINICAL STAGE 4		
HIV Wasting syndrome	Unexplained involuntary weight loss (over 10% of body weight) with obvious wasting or body mass index below 18.8 PLUS EITHER unexplained chronic diarrhea (loose or watery stools three or more times daily) reported for longer than one month OR reports of fever or night sweats for more than one month without other cause and lack of response to antibiotics and or antimalarials. Malaria must be excluded in malarial areas.	Documented weight loss of over 10% of body weight plus two or more unformed stools negative for pathogens or documented temperature exceeding 37.6°C with no other cause of disease , negative blood culture, negative malaria slide, and normal and unchanged CXR.
Pneumocystis pneumonia	Dyspnea on exertion or nonproductive cough of recent onset (within the past three months), tachypnea and fever; AND CXR evidence of diffuse bilateral interstitial infiltrates, AND no evidence of bacterial pneumonia, bilateral crepitations on auscultation with or without reduced air entry.	Cytology or immunofluorescent microscopy of induced sputum or bronchoalveolar lavage (BAL), or histology of lung tissue.
Recurrent bacterial pneumonia	Current episode plus one or more episodes in last six months. Acute onset (under two weeks) of symptoms (e.g. fever, cough, dyspnea, and chest pain) PLUS new consolidation on clinical examination or CXR. Response to antibiotics	Positive culture or antigen test of a compatible organism
Chronic herpes simplex virus (HSV) infection (orolabial, genital or anorectal) of more than one month, or visceral of any duration	Painful progressive anogenital or orolabial ulceration; lesions caused by recurrent HSV infection and reported for more than one month. History of previous episodes. Visceral HSV requires definitive diagnosis.	Positive culture or DNA (by PCR) of HSV or compatible cytology/histology.
Esophageal candidiasis	Recent onset of retrosternal pain or difficulty on swallowing (food or fluids) together with oral candidiasis	Macroscopic appearance at endoscopy or bronchoscopy, or by microscopy/histology.
Extrapulmonary tuberculosis	Systemic illness (e.g. fever, night sweats, weakness and weight loss). Other evidence for extrapulmonary or disseminated TB varies by site: pleural, pericardial, peritoneal involvement, meningitis, mediastinal or abdominal lymphadenopathy or osteitis. Discrete peripheral lymph node *M. tuberculosis* infection is considered a less severe form of extrapulmonary tuberculosis.	*M. tuberculosis* isolation or compatible histology from appropriate site OR radiological evidence of miliary TB (diffuse uniformly distributed small miliary shadows or micronodules on CXR.
Kaposi sarcoma	Typical appearance in skin or oropharnx of persistent, initially flat patches with a pink or blood-bruise color, skin lesions that usually develop into violaceous plaques or nodules.	Macroscopic appearance at endoscopy or bronchoscopy, or by histology.

Clinical event	Clinical Diagnosis	Definitive Diagnosis
CLINICAL STAGE 4 (cont.)		
Cytomegalovirus disease (other than liver, spleen or lymph node)	Retinitis only: may be diagnosed by experienced clinicians. Typical eye lesions on fundoscopic examination; discrete patches of retinal whitening with distinct borders, spreading centrifugally, often following blood vessels, associated with retinal vasculitis, hemorrhage and necrosis.	Compatible histology or CMV demonstrated in CSF by culture or DNA (by PCR)
Central nervous system toxoplasmosis	Recent onset of a focal neurological abnormality or reduced level of consciousness AND response within 10 days to specific therapy	Positive serum toxoplasma antibody AND (if available) single/multiple intracranial mass lesion on neuroimaging (CT or MRI)
HIV encephalopathy	Clinical finding of disabling cognitive and/or motor dysfunction interfering with activities of daily living, progressing over weeks or months in the absence of a concurrent illness or condition, other than HIV infection, which might explain the findings	Diagnosis of exclusion, and, if available, neuroimaging (CT or MRI)
Extrapulmonary cryptoccosis (including meningitis)	Meningitis: usually subacute, fever with increasing severe headache, meningism, confusion, behavioral changes that respond to cryptococcal therapy	Isolation of *Cryptococcus neoformans* from extrapulmonary site or positive cryptococcal antigen test (CRAG) on CSF/blood.
Disseminated non-tuberculosis mycobacteria infection	No presumptive clinical diagnosis	Diagnosis by finding atypical mycobacterial species from stool, blood, body fluid or other body tissue, excluding lung
Progressive multifocal leukoencephalopathy (PML)	No presumptive clinical diagnosis	Progressive neurological disorder (cognitive dysfunction, gait/speech disorder, visual loss, limb weakness and cranial nerve palsies) together with hypodense white matter lesions on neuroimaging or positive polyomavirus JC (JCV) PCR on CSF
Chronic cryptosporidiosis (with diarrhea lasting more than one month)	No presumptive clinical diagnosis	Cysts identified on modified ZN microscopic examination of unformed stool
Chronic isosporiasis	No presumptive clinical diagnosis	Identification of *Isospora*

Appendix 2 Assessing 10% weight loss and BMI

If a patient has lost more than 10% of their baseline body weight then they would be considered WHO Stage 3. If they have lost more than 10% of their body weight and have chronic diarrhea or chronic weakness accompanied by a fever (without an identifiable infectious origin) then they meet requirements for wasting syndrome and would be considered WHO Stage 4 at enrollment and thus eligible for ART.

Remember that most cell phones have calculators built in and may therefore be very useful for these calculations.

To calculate 10% of a person's weight, take their weight and move the decimal to the left by one digit.

Examples:
Patient #1's weight a year ago was 68.5 kg. Now it is 57.2 kg. Has he lost 10% of his body weight?
To calculate the weight loss, subtract the present weight from the original or highest known previous weight:

68.5 - 57.2 = 11.3 kg.

Patient #1 has lost 11.3 kg of body weight.

To calculate 10% of his body weight, we take his previous body weight and move the decimal place over 1 place:

68.5 → 6.85 kg.

11.3 kg is more than 6.85 kg, so Patient #1 has lost more than 10% of his body weight.

Again:
Patient #2 has also lost weight. Her pre-illness weight was 76 kg. Now she weighs 69.8 kg. First calculate her weight loss by subtracting:

76 - 69.8 = 6.2 kg.

Then calculate 10% of her pre-illness weight by shifting the decimal point over by one place:

76 kg → 7.6 kg.

She lost 6.2 kg, which is less than 7.6 kg, so although she has weight loss, it is less than 10% of her body weight. This means she is still in WHO stage 2.

Appendix 2 (cont.) Body Mass Index (BMI)

If a patient's BMI is less than 18, they meet the requirements for severe wasting, a WHO Stage 4 indicator.

Calculating Body Mass Index (BMI):

$$\text{BMI} = \frac{\text{Patient's weight (kg)}}{(\text{Patient's height (m)})^2} = \frac{\text{Patient's weight (kg)}}{(\text{Patient's height (m)}) * (\text{Patient's height (m)})}$$

Remember: $x^2 = x * x$

Example: $3^2 = 3 * 3 = 9$

Example:
Patient weighs 51kg, and is 1.73m tall

$$\text{BMI} = \frac{52}{(1.73)^2} = \frac{52}{(1.73) * (1.73)} = \frac{52}{2.99} = 17.4$$

$17.4 < 18$, therefore patient is WHO Stage 4

Remember that your cell phone probably has a calculator in it, which can be very useful for calculating BMI or 10% weight loss during patient visits.

Appendix 3 Diagnostic criteria for the staging of HIV-related clinical events in *children*

Clinical Event	Clinical Diagnosis	Definitive Diagnosis
CLINICAL STAGE 1		
Asymptomatic	No HIV-related symptoms reported and no clinical signs of examination.	Not applicable
Persistent generalized lymphadenopathy (PGL)	Persistent enlarged lymph nodes >1 cm at two or more contiguous sites(excluding inguinal), without known cause.	Clinical diagnosis
CLINICAL STAGE 2		
Unexplained persistent hepatosplenomegaly	Enlarged liver and spleen without obvious cause.	Clinical diagnosis
Papular pruritic eruptions	Papular pruritic vesicular lesions.	Clinical diagnosis
Fungal nail infections	Fungal paronychia (painful, red and swollen nail bed) or onycholysis (painless separation of the nail from the nail bed). Proximal white subungual onchomychosis is uncommon without immunodeficiency.	Clinical diagnosis
Angular Cheilitis	Splits or cracks on lips at the angles of the mouth without depigmentation, usually responding to antifungal treatment but may recur.	Clinical diagnosis
Lineal gingival erythema (LGE)	Erythematous band that follows the contour of the free gingival line; may be associated with spontaneous bleeding.	Clinical diagnosis
Extensive wart virus infection	Characteristic warty skin lesions; small fleshy grainy bumps, often rough, flat on sole of feet (plantar warts); facial, more than 5% of the body area or disfiguring.	Clinical diagnosis
Extensive molluscum contagiosum infection	Characteristic skin lesions; small flesh-colored, pearly or pink, dome-shaped or umbilicated growths, may be inflamed or red; facial, more than 5% of body area or disfiguring. Giant molluscum may indicate advanced immunodeficiency.	Clinical diagnosis
Recurrent oral ulceration	Current event plus at least one previous episode in past six months. Aphthous ulceration, typically with a halo of inflammation and yellow-grey pseudomembrane.	Clinical diagnosis
Unexplained persistent parotid enlargement	Asymptomatic bilateral swelling that may spontaneously resolve and recur, in absence of other known cause; usually painless.	Clinical Diagnosis
Herpes zoster	Painful rash with fluid-filled blisters, dermatomal distribution, may be hemorrhagic on erythematous background, and may become large and confluent. Does not cross the midline.	Clinical Diagnosis
Recurrent or chronic upper respiratory tract infection (URTI)	Current event with at least one episode in past six months. Symptom complex: fever with unilateral face pain and nasal discharge (sinusitis) or painful swollen eardrum (otitis media), sore throat with productive cough (bronchitis), sore throat (pharyngitis) and barking croup-like cough (laryngotracheal bronchitis TB). Persistent or recurrent ear discharge.	Clinical Diagnosis

Clinical Event	Clinical Diagnosis	Definitive Diagnosis
CLINICAL STAGE 3		
Unexplained moderate malnutrition or wasting	Weight loss: low weight-for-age, up to 2-standard deviations (SDs), not explained by poor or inadequate feeding and/or other infections, and not adequately responding to standard management.	Documented loss of body weight of –2 SDs or >10%, failure to gain weight on standard management and no other cause identified during investigation.
Unexplained persistent diarrhea	Unexplained persistent (14 days or more) diarrhea (loose or watery stool, three or more times daily) not responding to standard treatment.	Stools observed and documented as unformed. Culture and microscopy reveal no pathogens.
Unexplained fever (>37.5 ºC intermittent or constant for longer than one month)	Reports of fever or night sweats for longer than a month, either intermittent or constant, with reported lack of response to antibiotics or antimalarials. No other obvious foci of disease reported or found on examination. Malaria must be excluded in malarial areas.	Documented with fever >37.5 ºC with negative blood culture, negative malaria slide and normal or unchanged CXR, and no other obvious foci of disease.
Oral candidiasis (after 6-8 weeks of life)	Persistent or recurrent creamy white soft small plaques which can be scraped off (pseudomembranous), or red patches on tongue, palate or lining of mouth, usually painfully tender (erythameous form).	Microscopy or culture.
Oral hairy leukoplakia	Fine small linear patches on lateral borders of tongue, generally bilaterally, which do not scrape off	Clinical diagnosis
Acute necrotizing ulcerative gingivitis or stomatitis, or acute necrotizing ulcerative periodontitis	Severe pain, ulcerated gingival papillae, loosening of teeth, spontaneous bleeding, bad odor, and rapid loss of bone and/or soft tissue.	Clinical diagnosis
Lymph node tuberculosis	Non-acute, painless “cold” enlargement of peripheral lymph nodes, localized to one region. May have drained sinuses. Response to standard anti-TB treatment in one month.	Histology or fine needle aspirate for Ziehl Nielsen stain. Culture.
Pulmonary tuberculosis (TB)	Nonspecific symptoms, e.g. chronic cough, fever, night sweats, anorexia and weight loss. In older children, productive cough and hemoptysis. History of contact with adults with smear-positive pulmonary TB. No response to standard broad spectrum antibiotic treatment.	One or more sputum smear positive for acid fast bacilli and/or radiographic abnormalities consistent with active tuberculosis and/or culture positive for mycobacterium.
Severe recurrent bacterial pneumonia	Cough with fast breathing, chest in-drawing, nasal flaring, wheezing and grunting. Crackles or consolidation on auscultation Responds to course of antibiotics. Current episode plus one or more in previous six months.	Isolation of bacteria from appropriate clinical specimens (induced sputum, BAL, lung aspirate).
Symptomatic lymphocytic interstitial pneumonia (LIP)	No presumptive clinical diagnosis.	Chest X ray: bilateral reticulonodular interstitial pulmonary infiltrates present for more than two months with no response to antibiotic treatment and no other pathogen found. Oxygen saturation persistently <90%. May present with cor pulmonale or may have increased exercise-induced fatigue. Characteristic histology.

Clinical Event	Clinical Diagnosis	Definitive Diagnosis
CLINICAL STAGE 3 (cont.)		
Chronic HIV-associated lung disease (including bronchietasis)	History of cough productive of copious amounts of purulent sputum (bronchiectasis only), with or without clubbing, halitosis, and crepitations and/or wheezing on auscultation.	Chest X ray: may show honeycomb appearance (small cysts) and/or persistent areas of opacification and/or widespread lung destruction, with fibrosis and loss of volume.
Unexplained anemia (<8g/dl), or neutropenia (<0.5 x 10^9/L) or chronic thrombocytopenia (<50 X 10^9/L)	No presumptive clinical diagnosis.	Laboratory testing, not explained by other non-HIV conditions, or not responding to standard therapy with hematinics, antimalarials or anthelminthics as outlined in IMCI.
CLINICAL STAGE 4		
Unexplained severe wasting, stunting or severe malnutrition not adequately responding to standard therapy	Persistent weight loss, wasting, stunting or malnutrition not explained by poor or inadequate feeding or other infections and not adequately responding in two weeks to standard therapy. Visible severe wasting of muscles, with or without edema of both feet, and/or weight-for-height of <3 SDs, as defined by WHO IMCI guidelines.	Documented weight for height for age more than 3 SDs from the mean with or without edema.
Pneumocystis Jiroveci Pneumonia (PCP)	Dry cough, progressive difficulty in breathing, cyanosis, tachypnea and fever; chest indrawing or stridor. (Severe or very severe pneumonia as in IMCI.) Usually of rapid onset especially in infants under 6 months of age. Response to high-dose cotrimoxazole +/- prednisolone. CXR: typical bilateral perihilar diffuse infiltrates.	Cytology or immunofluorescent microscopy or induced sputum or broncheoalveolar lavage or histology of long tissue.
Recurrent severe bacterial infection, e.g. empyema, pyomyositis, bone or joint infection, meningitis but excluding pneumonia	Fever accompanied by specific symptoms or signs that localize infection. Responds to antibiotics. Current episode plus one or more in previous six months.	Culture of appropriate clinical specimen.
Chronic herpes simplex infection; (orolabial or cutaneous of more than one month's duration or visceral at any site)	Severe and painful orolabial, genital, or anorectal lesions caused by HSV infection present for more than one month.	Culture and/or histology.
Esophageal Candida (or *Candidiasis* of trachea, bronchi, or lungs).	Difficulty in swallowing, or pain on swallowing (food and fluids). In young children, suspect particularly if oral *Candida* observed and food refusal occurs and/or difficulties/crying when feeding.	Macroscopic appearance at endoscopy, microscopy of specimen from tissue or macroscopic appearance at bronchoscopy or histology.
Extrapulmonary tuberculosis	Systemic illness usually with prolonged fever, night sweats, weight loss. Clinical features of organs involved, e.g. sterile pyuria, pericarditis, ascites, pleural effusion, meningitis, arthritis, orchitis, pericardial or abdominal.	Positive microscopy showing AFB or culture of Mycobacterium tuberculosis from blood or other relevant specimen except sputum or BAL. Biopsy and histology.

Clinical Event	Clinical Diagnosis	Definitive Diagnosis
CLINICAL STAGE 4 (cont.)		
Kaposi's sarcoma	Typical appearance in skin or oropharynx of persistent, initially flat, patches with a pink or blood-bruise color, skin lesions that usually develop into nodules.	Macroscopic appearance or by histology.
Cytomeglovirus retinitis or CMV infection affecting another organ, with onset at age over 1 month.	Retinitis only: may be diagnosed by experienced clinicians: typical eye lesions on fundocopic examination; discrete patches of retinal whitening with distinct borders, spreading centrifugally, often following blood vessels, associated with retinal vasculitis, hemorrhage and necrosis.	Histology or CMV demonstrated in CSF by PCR.
Central Nervous System toxoplasmosis with onset at age over 1 month.	Fever, headache, focal neurological signs, convulsions. Usually responds within 10 days to specific therapy.	Positive serum toxoplasma antibody AND of neuroimaging showing/multiple intracranial mass lesions with mass effect or enhancing with contrast.
Disseminated mycobacteriosis other than tuberculosis	No presumptive clinical diagnosis.	Nonspecific clinical symptoms including progressive weight loss, fever, anemia, night sweats, fatigue or diarrhea; plus culture of atypical mycobacteria species from stool, blood, body fluid or other body tissue, excluding lung.
Chronic cryptosporidiosis (with diarrhea)	No presumptive clinical diagnosis.	Cysts identified on modified ZN stain.
Chronic Isospora	No presumptive clinical diagnosis.	Identification of isospora
Cerebral or B cell non-Hodgkin lymphoma	No presumptive clinical diagnosis.	CNS imaging: histology of relevant specimen.
Progressive multifocal leukoencephalopathy (PML)	No presumptive clinical diagnosis.	Progressive neurological disorder together with white matter lesions on neuroimaging or positive polyomavirus JC (JCF) PCR on CSF.
Symptomatic HIV associated nephropathy	No presumptive clinical diagnosis.	Renal biopsy
Symptomatic HIV associated cardiomyopathy	No presumptive clinical diagnosis.	Cardiomegaly and evidence of poor left ventricular function confirmed by echocardiography.

Appendix 4 Schedule of Actions During Patient Visits

Symptom checklist
The following should be asked at <u>every</u> pre-ART and ART clinic visit: • Fever? • Cough? (Chest pain? Sputum? Blood? How long? Shortness of breath?) • Night sweats? • Fatigue? Weakness? • Weight loss? (How much?) • Diarrhea? (Times a day? Bloody? Mucousy? Watery? Since when?) • Abdominal pain? Swelling? • Eating well? (Pain with swallowing? Nausea? Vomiting? Poor appetite?) • Pain in mouth? (Ulcers? Thrush?) • Headache? (Which area of head? Since when? Severity?) • Visual problems? (Double vision? Blurred vision? Visual field defects?) • Numbness or pain in extremities? (Since when? How disabling?) • Rashes or other skin problems? (Itchy? Painful? Since when? What has been tried? Lumps? Fluid filled or pus-filled?) • STI? (Vaginal discharge or lesion? Penile discharge or genital lesion?) • Sleeping problems? • Urinary problems? • ANYTHING ELSE?

Initial patient assessment and adherence counseling visit (as soon as possible after diagnosis)	

	<u>Counselor</u>
	(repeat post-test counseling and introduce ART, discuss treatment readiness and choice of treatment assistant)
	• Register the patient in the Care and Treatment Program
	  o Issue unique Patient Identification Number and complete intake forms
	• Explore how patient is coping with diagnosis
	• Ask about support systems
	• Explore patient's understanding of HIV
	  o What is HIV
	  o Where does it come from
	  o What does it do in the body
	  o Transmission and basic prevention
	• Explore patient's understanding and expectations of ART
	  o ART is not a cure
	  o ART is a lifelong commitment
	• Discuss importance of adherence (see **Section 6**)
	• Discuss benefits of HIV disclosure, including the benefit of choosing a "treatment assistant" to bring to next visit (see **Section 6**)
	• Distribute condoms (even if partner is HIV positive)

Initial patient assessment and adherence counseling visit (cont.) (as soon as possible after diagnosis)	
	ART clinician **History** • Symptom checklist (see above, ask at every visit) • In particular, screen for TB • Ask if patient has had ART before (possibly a defaulter from previous treatment) • Ask about other clinical conditions, known allergies and medications • Vital signs (BP, P, RR, T, Wt, Ht) **Physical exam** • Complete physical at every visit (at minimum, look in mouth, check conjunctiva, oral cavities, examine lymph nodes, listen to lungs and heart, check abdomen for enlarged liver and other masses, examine genital area, examine skin for rashes) • Calculate BMI [weight in kg divided by height in meters squared (kg/m^2)], if <18 diagnose severe wasting, WHO stage 4 condition • Determine patient's functional status (working, ambulatory, or bedridden) and note on patient card. **Order baseline lab tests** CBC or Hg, Cr, Glucose, ALT, pregnancy test (if appropriate), CD4 and TLC (if available) (see **Table 8.1)** **Diagnosis and Treatment** • Diagnose and treat OIs (see **Section 19**) • Start cotrimoxazole prophylaxis if eligible (see **Section 9**), reinforcing the importance of adherence and discussing possible side effects • Refer for AFBs and CXR if suspect TB • Screen for STIs • Assess for pregnancy if reproductive age female • Start multivitamin if available • Distribute condoms **ASSIGN WHO STAGE (I, II, III, or IV) based on signs and symptoms** • Explain the 4 stages to the patient
	Pharmacy Tech or Pharmacist • Dispense cotrimoxazole if patient is eligible (see **Section 9**) and reinforce the importance of adherence; discuss potential side effects

Based on staging and lab test results, determine patient eligibility for ART (see **Section 7**, Patient assessment for treatment, for details). If eligible, proceed with Pre-ART visit 2 and ART visits as described below.

If patient is not yet eligible for ART but is beginning cotrimoxazole preventive therapy (CPT), schedule Adherence counseling visit 2 for 2 weeks later, then monthly follow up visits (these may become 3 monthly if patient adherence and clinical status remains good).

If patient is not eligible for either ART or CPT, provide counseling on positive living and the importance of adhering to visit schedules. Schedule follow up visit for 3 months (or sooner as necessary, see **Section 8**, Monitoring of adults and children who are not yet eligible for ART, for more details.)

All HIV positive patients should be seen and assessed by a clinician every 3 months, regardless of eligibility for ART or CPT.

Schedule of follow up visits for patients <u>not yet eligible</u> for ART (also refer to **Section 8**: Monitoring of patients not yet eligible for ART):

ADDITIONAL COUNSELING (same day as initial assessment <u>or</u> on next visit)	
	<u>Counselor</u> • Explore how patient is coping with diagnosis • Clarify questions and evaluate patient's understanding and expectations regarding HIV and ART (see key points above from visit 1) • Discuss importance of adherence to both CPT (if necessary) and follow up visits (see **Section 6**) • Provide information on positive living (see **Section 10**) • Explain to treatment assistant his/her role in enhancing adherence
	<u>ART clinician</u> • Review baseline lab results • Assess and treat any OIs • Start cotrimoxazole prophylaxis if eligible (see **Section 9**), reinforcing the importance of adherence and discussing possible side effects • Prescribe 2 weeks CTX • Schedule follow up visit for 2 weeks

FOLLOW UP ADHERENCE COUNSELING (2 weeks after previous visit)	
	<u>Counselor</u> • Explore how patient is coping with diagnosis • Clarify questions and evaluate patient's understanding and expectations regarding HIV and ART (see key points above from visit 1) • Discuss importance of adherence to both CPT (if applicable) and visit schedules (see **Section 6**) • Provide information on positive living (see **Section 10**) • Explain to treatment assistant his/her role in enhancing adherence
	<u>ART Clinician</u> • Assess and treat any OIs • Assess for CTX toxicity and side effects • Prescribe 4 weeks CTX • Schedule follow up visit for 4 weeks

ONGOING FOLLOW UP	
	After determining that the patient is tolerating CPT well and is adhering to therapy, patients may return for CTX refills and clinician evaluation every 3 months. A clinician should evaluate the patient's eligibility for ART every 3 months (including clinical staging, and CD4 count if available). Adherence should be stressed at <u>every visit</u> by <u>all</u> members of the Care and Treatment Program.
	When patients become eligible for ART, they should proceed with pre-ART counseling (see below, and **Figure 5.3**). The number of pre-ART counseling sessions (or the length of time between them) may be decreased at the clinician's discretion, depending upon the patient's history and current clinical status.

Schedule of pre-ART counseling visits for patients eligible for ART (also refer to **Section 15**: Monitoring of patients on ART):

PRE-ART COUNSELING VISIT 2 (2-4 weeks after diagnosis)

Counselor

- Explore how patient is coping with diagnosis
- Clarify questions and evaluate patient's understanding and expectations regarding HIV and ART (see key points above from visit 1)
- Discuss importance of adherence (see **Section 6**)
- Review relationship between adherence and resistance/treatment failure
- Explain to treatment assistant his/her role in enhancing adherence

ART clinician

- Review lab results and explain to the patient
- Review symptom checklist
- Diagnose and treat OIs (see **Section 19**)
- Explore how patient is tolerating cotrimoxazole (side effects? See **Section 9**)
- If mild/no CTX toxicity, prescribe 2 more weeks (see **Section 9**)
- Discuss ARV medications to be started at next visit (see **Sections 11** and **16**)
    - Names and dosing of all ARVs the patient will be taking
    - Side-effects for the ARVs, and how to react if/when they occur
    - With the patient, develop a schedule for taking medications and discuss ways to remember taking every dose (alarms, calendars, pill boxes, etc.)
    - Importance of adherence (see **Section 6**)
- Schedule next visit for 1-2 weeks
- Record keeping

PRE-ART COUNSELING VISIT 3 (which may also be the FIRST ART VISIT) (ART week 0; 3-6 weeks after diagnosis)

Counselor

- Explore how patient is coping with diagnosis
- Answer questions and evaluate patient's understanding and expectations of HIV and ART
- Discuss importance of adherence (see **Section 6**)
- Clarify with treatment assistant his/her role in enhancing adherence
- Determine treatment readiness (if NOT ready, follow up 2 weeks later with another counseling session, and repeat until patient is ready to begin lifelong ART)

ART clinician

- Review lab results
- Review symptom checklist
- Diagnose and treat OIs (see **Section 19**)
- Explore how patient is tolerating cotrimoxazole (side effects?) (see **Section 9**)
- Discuss ARV medications (dosing, side-effects, timing of medications, adherence)
- **IF** ready for treatment, prescribe appropriate medications for 2 weeks
    - See **Section 11.3**: Initiating ART, for a list of all criteria
- If on NVP, prescribe **once a day** dosing for 2 weeks (induction phase)
- Book follow-up appointment in 2 weeks
- Record keeping

Pharmacy Tech or Pharmacist

- Dispense medications
- Carefully review how to take, potential side-effects
- Ask patient to bring pill box or bottle to follow-up appointments (for pill-counting)
- Discuss potential problems (such as travel, job hours etc.) and plan for these

SECOND ART VISIT (2 weeks after first ART visit)	
	Counselor • Any problems with adherence? • Any issues with coping with diagnosis? (eg stigma, discrimination) • Issues with disclosure? • Issues with prevention?
	ART clinician • Assess medication tolerance and side effects • Assess adherence (how many pills missed last week? Last month? Why?) • Symptom checklist • Diagnose and treat OIs (see **Section 19**) • Side effect questions (headache, N/V, diarrhea, skin rashes, bleeding, fast heart beat, abdominal pain, weakness, lack of sleep) • If no/mild NVP reaction (see **Section 16.4.3.2**, and **Figures 16.3** and **16.4** for details), increase dose to QD and discuss change in pills with patient • If no adverse reactions, prescribe 1 month of ARVs • Schedule follow-up in 1 month
	Pharmacy Tech or Pharmacist: • Assess medication tolerance and side effects • Ask how many pills missed last week, last month and count pills • If suspect adherence problems, refer to counselor

3rd, 4th, and 5th ART VISITS (6 wks, 10 wks and 14 wks after initiation)	
	Counselor • Clarify questions and reinforce key adherence messages
	ART clinician • Assess medication tolerance and side effects • Screen adherence • Symptom checklist • Diagnose and treat OIs • Order follow-up lab tests (CBC, ALT) • Prescribe 1 month of ARVs • Schedule follow-up in 1 month
	Pharmacy Tech or Pharmacist • Assess medication tolerance, side effects, adherence and perform pill count

SCHEDULE FOLLOW-UP VISITS EVERY 3 MONTHS

See **Section 11**, Antiretroviral therapy, and **Section 16**, Monitoring of patients on ART, for more details regarding ART.

Appendix 5 Summary of recommended first- and second-line ARV regimens for adults and adolescents

		First-line Regimens	Second-Line Regimens[1]	Alternative Second-Line Regimens[1]
HIV-1	Preferred Regimen	AZT + 3TC + NVP [2,3]	TDF + 3TC[4] + PI[1]	ddI + ABC + PI[1]
	Alternative	TDF + 3TC + NVP [2,3]	AZT[5] + 3TC + PI[1]	ddI + ABC + PI[1]
	Second Alternative	d4T + 3TC + NVP [2,3]	TDF + 3TC[4] + PI[1]	ddI + ABC + PI[1]
HIV-2 or **HIV-1/HIV-2** coinfection[1]	Preferred Regimen	AZT + 3TC + PI[1]	TDF + 3TC[4] + PI[1]	ddI + ABC + PI[1]
	Alternative	TDF + 3TC + PI[1]	AZT[5] + 3TC + PI[1]	ddI + ABC + PI[1]
	Second Alternative	d4T + 3TC + PI[1]	TDF + 3TC[4] + PI[1]	ddI + ABC + PI[1]

[1]LPV/r (Kaletra) or ATV/r are recommended as the preferred PI. At the time of this printing, LPV/r is the PI of choice in Liberia due to its lower cost and wider availability. If neither LPV/r nor ATV/r are available, NFV may be used.
[2]EFV can be substituted for NVP in first line regimens, UNLESS patient is pregnant or may become pregnant. EFV may only be used during the 2nd or 3rd trimester. It should be used with caution in women who are not using consistent and effective birth control.
[3]NVP should be given QD for first 2 weeks. If no/mild NVP toxicity, then increase dose to BID.
[4]At the physician's discretion, AZT can be used with 3TC in the second line, creating a four-drug regimen (particularly when an FDC is available).
[5]Or d4T

Appendix 6 Dosages of antiretroviral drugs for adults and adolescents

Drug class/ drug	Dose [a,b]
Nucleoside RTIs	
Abacavir (ABC)	300 mg twice daily
Didanosine (ddl) enteric coated buffered	400 mg once daily (250 mg once daily if <60 kg) (250 mg once daily if administered with TDF) 300mg once daily dissolved in water
Lamivudine (3TC)	150 mg twice daily or 300 mg once daily
Stavudine (d4T)	30 mg twice daily
Zidovudine (AZT)	300 mg twice daily.
Nucleotide RTI	
Tenofovir (TDF)	300 mg once daily (Note: drug interaction with ddI necessitates dose reduction of latter)
Non-nucleoside RTIs	
Efavirenz (EFV)	600 mg once daily
Nevirapine (NVP)	200 mg daily for the first 14 days, then 200 mg twice daily
Protease inhibitors	
Lopinavir/ ritonavir (LPV/r; Kaletra)	400 mg/ 100 mg twice daily (533mg/ 133 mg twice daily when combined with EFV or NVP)
Atazanavir/ritonavir (ATV/r)	300 mg/100mg once daily
Nelfinavir (NFV)	1250 mg twice daily

[a] These dosages are in common clinical use. The dosages featured in this table were selected on the basis of the best available clinical evidence. Dosages that can be given once daily or twice daily were preferred in order to enhance adherence to therapy. The doses listed are those for individuals with normal renal and hepatic function. Product-specific information should be consulted for dose adjustments that may be indicated with renal or hepatic dysfunction or for potential drug interactions with other HIV and non-HIV medications

[b] AZT, 3TC and d4T dosages should be adjusted for the creatinine clearance during renal insufficiency

Appendix 7 Summary of recommended first- and second-line ARV regimens for children

		First-line Regimens		Second-Line Regimens NRTIs	PIs
HIV-1	Preferred Regimen	d4T + 3TC + NVP [1,2]		ABC[4] + ddI +	PI [3]
	Alternative	AZT + 3TC + NVP [1,2]		ABC[4] + ddI +	PI [3]
HIV-2 or HIV-1/HIV-2 coinfection	Preferred Regimen	d4T + 3TC +	PI [3]	ABC[4] + ddI +	PI [3]
	Alternative	AZT + 3TC +	PI [3]	ABC[4] + ddI +	PI [3]

[1]EFV can be substituted for NVP in first line regimens IF child is ≥3 years old AND >10kg.
[2]NVP should be given QD for first 2 weeks. If no/mild NVP toxicity, then increase dose to BID.
[3]LPV/r (Kaletra) is the preferred PI in all cases, whether first- or second-line. If LPV/r is not available, NFV may be used. ATV/r is not currently licensed for use in children.
[4]If ABC toxicity develops, 3TC should be continued in the second-line regimen.

Refer to **Appendix 9** for all pediatric dosing.

Appendix 8 Pediatric ARV drug formulations, side effects and special instructions for children

Drug / Formulation	Comments	Side Effects
Nucleoside reverse transcriptase		
Abacavir (ABC) Oral solution 20mg/ml Tablet: 300mg	Can be given with food. Tablet can be mixed with small amount of water and taken immediately. Instruct patient on how to recognize and respond to potentially fatal hypersentivity reaction. Patients should not interrupt therapy without consulting their healthcare provider. **DO NOT** rechallenge after hypersensitivity reaction.	**Common**: HA, GI upset and rash. **Less common:** lactic acidosis, hepatomegaly with steatosis. **Life threatening:** potentially fatal hypersensitivity reaction (fatigue, rash, N/V, sore throat, joint and muscle pain, cough, and dyspnea).
Didanosine (ddI) Chewable tablets: 25mg, 50mg, 100mg, 150mg Enteric coated capsules: 200mg, 250mg, 400mg	If tablets are dispersed in water, at least 2 tablets of appropriate strength should be dissolved to ensure adequate buffer. Enteric formulation may be better tolerated.	**Common:** diarrhea, abdominal pain, N/V. **Less common:** increased LFTs, lactic acidosis with hepatomegaly and steatosis, peripheral neuropathy, hyperuricemia. **Life threatening**: pancreatitis which is rare in children.
Lamivudine (3TC) Oral solution 10mg/ml Tablet: 150mg	Can be given with food. Store solution at room temperature (use within one month of opening). Tablet can be mixed with small amount of water and taken immediately. Side effects are rare.	**Common:** HA, nausea, abdominal pain. **Less common:** pancreatitis, neutropenia, increased LFTs. Usually well tolerated.
Stavudine (d4T) Oral solution 1mg/ml Capsules: 15mg 20mg, 30mg, 40mg, FDC 6mg and FDC 12mg	Keep liquid refrigerated. Stable for 30 days. Capsules can be opened and mixed with small amount of food or water. **DO NOT USE WITH AZT.**	**Common:** HA and GI intolerance. **Less common:** peripheral neuropathy, lipoatrophy. **Life threatening:** lactic acidosis with severe hepatomegaly and steatosis.
Zidovudine (AZT, ZDV) Oral solution 10mg/ml Tablet: 300mg Capsule: 300mg	Can be given with food. Syrup is light sensitive, store in a glass jar away from light. Capsule can be opened and contents dispersed or tablet crushed and combined with food or small amount of water. Large volume of syrup not well tolerated in older children. **DO NOT USE WITH d4T.**	**Common:** neutropenia, anemia, granulocyptopenia, macrocytosis, and HA. **Less common:** myositis, myopathy, mitochondrial disease.

Non-nucleoside reverse transcriptase inhibitors		
Efavirenz (EFV) Syrup: 30mg/ml Capsule: 50mg, 100mg, 200mg	Only for children ≥ 3 yrs. Syrup requires higher dose than capsules. Can be given with food (but avoid high fat foods). Capsule can be opened and added to food: to avoid peppery taste mix with sweet food or jam Best given at night time to avoid CNS effects.	**Common:** skin rash, somnolence, insomnia, abnormal dreams, confusion, hallucinations. **Less common:** increased LFTs.
Nevirapine (NVP) Oral solution 10mg/ml Tablet: 200mg	Store at room temperature. Can be given with food. Tablets can be divided and combined with small amount of water or food and immediately administered. Patients should be warned of rash. Do not escalate dose if rash occurs. **For SJS and TEN discontinue drug and do not rechallenge.** Multiple drug interactions.	**Common:** skin rash, HA, nausea, diarrhea. **Less common:** increased LFTs. **Life threatening:** Stevens-Johnson Syndrome, fatal hepatitis.
Protease Inhibitors		
Lopinavir /ritonavir (LPV/r, Kaletra) Oral solution 80mg/ml LPV plus 20mg/ml rit. capsules:133.3mg LPV plus 33.3mg r	Preferable to store capsules and liquid in a refrigerator. Can be stored at room temp 25^0C for 2 months Should be taken with food. Capsules should not be opened or crushed, swallow whole. Liquid has low volume but bitter taste. Tablets require no cold chain; can be used in children on full adult dose.	**Common:** diarrhea, HA, nausea, vomiting,, increase in blood lipids **Less common:** pancreatitis, diabetes, hyperglycemia, hepatic toxicity, fat redistribution.
Nelfinavir (NFV) Powder for oral suspension (mix with liquid): 200 mg per level teaspoon (50mg per1.25 ml scoop) Tablet:250mg	Take with food. Store at room temperature. Crushed tablet preferred even for infants. Drug interactions less than with RTV/PI	**Common:** diarrhea, nausea, vomiting, HA **Less common:** asthenia, abdominal pain, rash, lipodystrophy.
Ritonavir (RTV) Suspension: 80mg/ml Capsule: 100mg	Take with food to increase absorption and reduce GI side effects. Oral solution must be refrigerated. Can be kept at room temperature (25^0C) if used within 30 days. Bitter taste, coat mouth with peanut butter or chocolate milk. If given with ddI there should be 2 hours between taking each drug.	**Common:** N/V, diarrhea, headache, abdominal pain, anorexia **Less Common:** circumoral paraesthesia, increased LFTs, lipodystrophy, elevated cholesterol and triglycerides, hyperglycemia.

Appendix 9 Pediatric dosing of antiretroviral drugs (based on WHO recommendations 2006)

Weight	AZT 10mg/cc syrup or 100mg capsule or 300mg tab	3TC 10mg/cc syrup or 150mg tablet	NVP 10mg/cc syrup or 200mg tab	d4T 1mg/cc syrup or 15mg, 20mg or 30mg cap	EFV 200mg capsule and 50mg capsule	FDC-6: D4T 6/ 3TC 30/ NVP 50	FDC-12: D4T 12/ 3TC 60/ NVP 100	FDC-30: D4T 30mg/ 3TC 150mg/ NVP 200mg	TMP (80mg) – SMX (400mg)
3-3.9 kg 6.6-8.6 lbs	5cc	2cc	5cc	n/a	n/a	1 tab	0.5 tab		2.5cc
4-4.9 kg 8.7-10.8 lbs	6cc	3cc	5cc	n/a	n/a	1 tab	0.5 tab		2.5cc
5-5.9 kg 10.9-13 lbs	6cc	3cc	6cc	6cc	n/a	1 tab	0.5 tab		5cc
6-6.9 kg 13.1-15.2 lbs	7cc	3cc	7cc	7cc	n/a	1.5 tab	1 tab am 0.5 tab pm		5cc
7-7.9 kg 15.3-17.4 lbs	8cc	4cc	8cc	8cc	n/a	1.5 tab	1 tab am 0.5 tab pm		5cc
8-8.9 kg 17.5-19.6 lbs	9cc	4cc	9cc	9cc	n/a	1.5 tab	1 tab am 0.5 tab pm		5cc
9-9.9 kg 19.7-21.8 lbs	10cc or 1 cap	4cc	9cc	10cc	n/a	1.5 tab	1 tab am 0.5 tab pm		5cc
10-10.9 kg 21.9-24.1 lbs	10cc or 1 cap	5cc	10cc	15mg	200mg	2 tab	1 tab	0.5 tab	5cc
11-11.9 kg 24.2-26.3 lbs	10cc or 1 cap	5cc	10cc or 0.5 tab	15mg	200mg	2 tab	1 tab	0.5 tab	5cc
12-13.9 kg 26.4-30.7 lbs	11cc or 1 cap	6 cc or 0.5 tab	11cc or 0.5 tab	15mg	200mg	2 tab	1 tab	0.5 tab	5cc or 0.5 tab
14-16.9 kg 30.8-37.3 lbs	2 cap or 0.5 tab am 1 cap or 0.5 tab pm	0.5 tab	1 tab	20mg	250mg	2.5 tab	1.5 tab am 1 tab pm	1 tab am 0.5 tab pm	10cc or 1 tab
17-19.9 kg 37.4-43.9 lbs	2 cap or 0.5 tab am 1 cap or 0.5 tab pm	0.5 tab	1 tab am 0.5 tab pm	20mg	250mg	2.5 tab	1.5 tab am 1 tab pm	1 tab am 0.5 tab pm	
20-24.9 kg 44-54.9 lbs	2 cap or 0.5 tab	1 tab am 0.5 tab pm	1 tab am 0.5 tab pm	20mg	250mg	3 tab	1.5 tab	1 tab am 0.5 tab pm	
25-29.9 kg 55-65.9 lbs	2 cap or 1 tab am 2 cap or 0.5 tab pm	1 tab	1 tab	30 mg	250mg	4 tab	2 tab	1 tab	

All ARVs are <u>twice a day</u> except EFV and 2 week induction dose of NVP, which are once a day. Dosage is the same for am and pm except where indicated.
Cotrimoxazole (TMP-SMX) is dosed <u>once daily</u>
Efavirenz: There is insufficient data for children <3 years or <10kg so is presently not recommended in this group
FDCs contain NVP so for first two weeks, may use D4T/3TC dual FDC in am or single drugs during that period.
For children < 3kg, calculate dosages based on target dose (see table at end of this appendix)

Appendix 9 (continued): Pediatric dosing of antiretroviral drugs (based on WHO recommendations 2006)

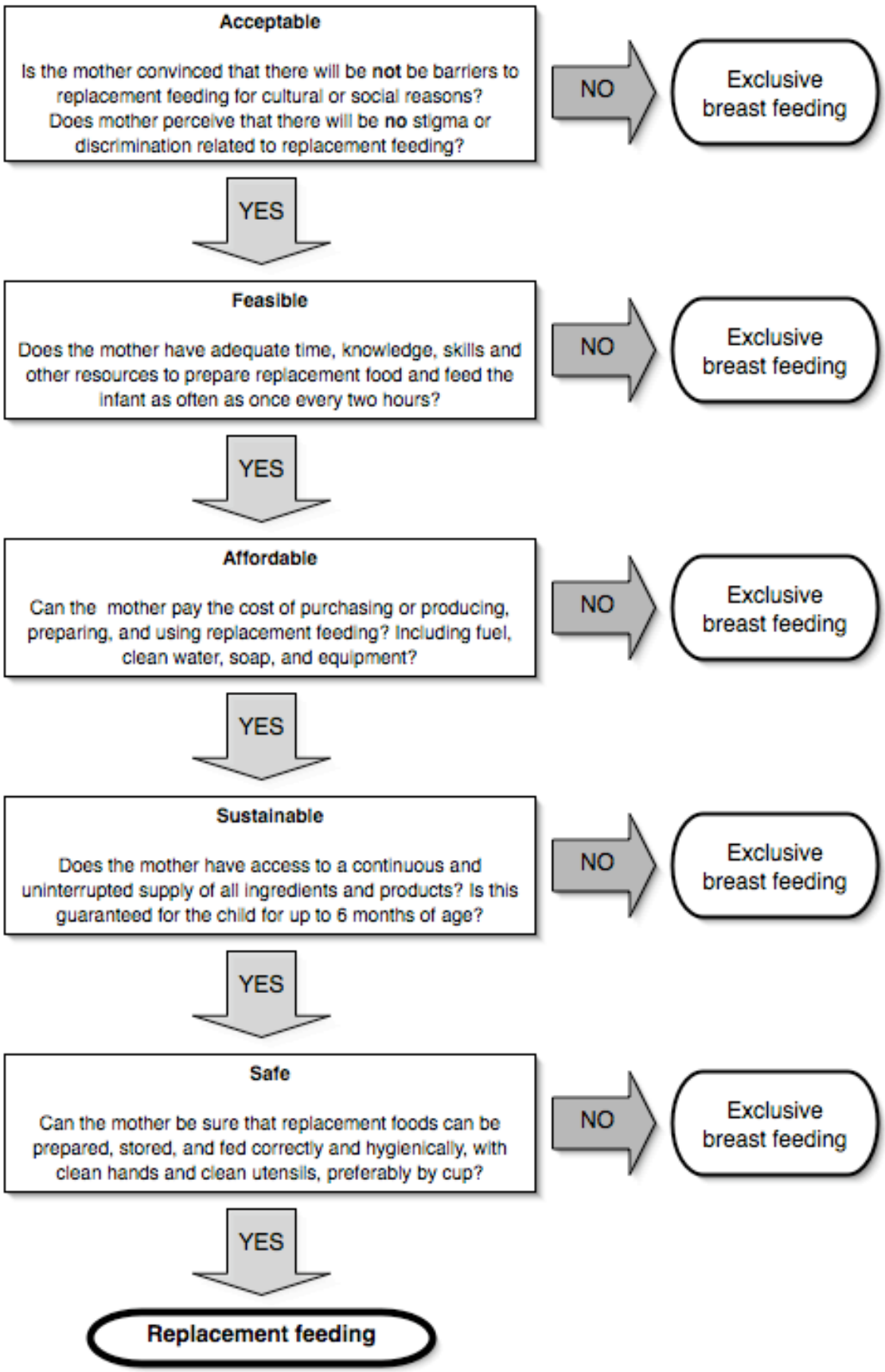
Weight	Abacavir		Didanosine		Lopinavir/ritonavir			Nelfinavir		Ritonavir*	
	8mg/kg/dose TWICE daily		120mg/m^2/dose TWICE daily; use 2 tabs for proper buffering	180-240mg/ m^2/dose ONCE daily	10-16mg/kg/dose TWICE daily			Target dose: <10kg:~75mg/kg/dose 10-19.9kg: 60mg/kg/dose >20kg max dose of 1250mg. TWICE daily		Starting dose 250mg/m^2/ dose TWICE daily	Maintenance dose 250mg/m^2/ dose TWICE daily
	20mg/ml solution	300mg tablets	25, 50, 100mg chewable tablets (not EC caps)	125, 200, 250, 400mg EC caps	80mg LPV/ 20mg RTV. per ml	133mg LPV/ 33mg RIT. capsules	200mg LPV/ 50mg RTV tablets	250mg tablets	625mg tablets	80mg/ml solution	80mg/ ml solution
5-5.9kg 10.9-13 lbs	2ml		25mg+25 mg tabs		1 ml			2 tabs		1 ml	1.5 ml
6-6.9 kg 13.1-15.2 lbs	3ml		25mg+25 mg tabs		1.5 ml			2 tabs		1 ml	2 ml
7-7.9 kg 15.3-17.4lbs	4ml		25mg+25 mg tabs		1.5 ml	1 cap		3 tabs in am 2 tabs in pm		1 ml	2 ml
8-8.9 kg 17.5-19.6 lbs	4ml		25mg+25 mg tabs		2 ml	1 cap		3 tabs		1.5 ml	2 ml
9-9.9 kg 19.7-21.8 lbs	4ml		25mg+25 mg tabs		2 ml	1 cap		3 tabs		1.5 ml	2.5 ml
10-10.9 kg 21.9-24.1 lbs	5ml		50mg+25 mg tabs in am 25mg+25mg tabs in pm	125 mg EC cap	2 ml	1 cap		3 tabs		1.5 ml	2 .5ml
11-11.9 kg 24.2-26.3 lbs	5ml	0.5 tab	50mg+25 mg tabs	125 mg EC cap	2 ml	1 cap		3 tabs		1.5 ml	2.5 ml
12-13.9 kg 24.6-30.7 lbs	6ml	0.5 tab	50mg+25 mg tabs	125 mg EC cap	2 ml	2 caps am 1 cap in pm	1 tab	4 tabs		1.5 ml	3 ml
14-16.9 kg 30.8-37.3 lbs		0.5 tab	50mg+50 mg tabs in am 50mg+25mg tabs in pm	200 mg EC cap	2 ml	2 caps am 1 cap pm	1 tab	4 tabs		2 ml	3 ml
17-19.9 kg 37.4-43.9 lbs		0.5	50mg+50 mg tabs	200 mg EC cap	2.5 ml	2 caps am 1 cap pm	1 tab	5tabs	2 tabs		
20-24.9 kg 44-54.9 lbs		1 tab am 0.5 tab pm	100mg+25 mg tabs	250 mg EC cap	3 ml	2 caps	1tab	5tabs	2 tabs		
25-29.9 kg 55-65.9 lbs		1 tab	100mg+25 mg tabs	250 mg EC cap	3.5 ml	2 caps	2 tabs am 1 tab pm	5tabs	2 tabs		
30-34.9 kg 66-76.9 lbs		1 tab	100mg +25 mg tabs	250 mg EC cap	4 ml	3caps	1tab	5tabs	2 tabs		
35-39.9 kg 77-88 lbs		1 tab	100mg +25 mg tabs	250 mg EC cap	5 ml	3caps	1tab	5tabs	2 tabs		

Appendix 9 (cont.): Pediatric target dosing

For children weighing < 3kg, calculate ARV dosages using body weight or surface area to meet target dosing according to the following table:

Drug and formulation	Target dose
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)	
Zidovudine (AZT) 10mg/ml oral solution, 100mg and 200mg capsules, 300mg tablets	180-240mg/m2/dose, twice daily (up to 300mg)
Lamivudine (3TC) 10 mg/ml oral solution, 150mg tabs	4mg/kg/dose, twice daily (up to 150mg)
Stavudine (d4T) 1 mg/ml oral solution, 15mg, 20mg, 30mg and 40mg capsules	1mg/kg/dose twice daily (up to 30mg)
Abacavir (ABC) 20mg/ml oral solution, 300mg tablets	8 mg/kg/dose twice daily (<16 yrs old)
Didanosine (ddI) 10mg/ml oral solution from powder; 25mg, 50mg, 100mg, 150mg and 200mg chewable tablets; 125mg, 200mg, 250mg and 400mg EC capsules	Age < 3months: 50mg/m^2/dose twice daily Age 3mo-13yrs: 90-120mg/m^2/dose twice daily
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	
Efavirenz (EFV) 30mg/ml, 50mg, 100mg, 200mg capsules, 600mg tablets	19.5 mg/kg/day (syrup) or 15 mg/kg/day (capsule/tablet) NOTE: EFV is not for use in children < 3yrs or <10kg
Nevirapine (NVP) 10mg/ml oral suspension, 200mg tablets	160-200mg/m^2/dose twice daily (after tolerating initiating dose of once daily)
Protease Inhibitors (PIs)	
Nelfinavir (NFV) 50mg per 1.25ml scoop powder for oral suspension; 250mg and 625mg tablets	< 10kg: ~75mg/kg/dose twice daily 10-19.9kg: ~60mg/kg/dose twice daily >20kg max of 1250mg/dose twice daily
Lopinavir/ritonavir (LPV/r) 80mg/ml LPV plus 20mg/ml ritonavir oral solution; 133.3mg/33.3mg capsules, 200mg/50mg tablets	LPV target doses: 5-7.9kg: 16mg/kg/dose twice daily 8-9.9kg: 14mg/kg/dose twice daily 10-13.9kg: 12mg/kg/dose twice daily 14-39.9kg: 10mg/kg/dose twice daily Max of 400mg LPV/100mg ritonavir daily

Appendix 10 Decision making tool for infant feeding options



Appendix 11 National Expanded Program on Immunization schedule

Vaccine	Age					
	Birth	**6 wks**	**10 wks**	**14 wks**	**6 mo.**	**9 mo.**
BCG	X					
Oral Polio	X	X	X	X		
DPT		X	X	X		
Measles						X
In situations where Hepatitis B and Hemophilus Influenza B vaccines are available immunization can be done as per WHO guidelines.						

Appendix 12 Developmental milestones and red flags

Developmental Milestones

Age	Psychosocial	Gross Motor	Fine Motor/Visual	Communication/ Hearing
1 month	- follows faces to the midline	- moves all extremities equally - lifts head when lying on stomach	- opens hands spontaneously	- startled by loud sounds - cries - quiets when fed and comforted
2 months	- follows faces past midline - smiles responsively	- lifts head up 45 degrees when on stomach	- looks at own hand	- makes baby sounds (cooing, squealing, gurgling)
3 months	- recognizes mother - smiles responsively	- supports head for a few seconds when held upright	- opens hands frequently	- responds to voices - laughs
4 months	- follows an object with eyes for 180 degrees - regards own hand - anticipates food on sight	- bears weight on legs - good neck control when pulled to sitting -lifts chest and supports self on elbows when pulled to sit	- brings hands together in midline (clasps hands) - grabs and object (such as a rattle) - reaches for objects	- turns head to sound
6 months	- reaches for familiar people	- rolls from stomach to back or back to stomach - sits with anterior support	- plays with hands by touching them together - sees small objects such as crumbs	- responds to name - babbles
9 months	- indicates wants - waves bye-bye - stranger anxiety	- can sit without support - creeps or crawls on hands and knees	- looks for a toy when it falls from his/her hand - takes a toy in each hand - transfers a toy from one hand to the other	- responds to soft sounds such as whispers
12 months	- has separation anxiety - social interactions intentional and goal-directed	- pulls self up to standing position - walks with support	- points at objects with index finger	- says at least one word - makes “ma-ma” or “da-da” sounds - locates sounds by turning head
15 months	- imitates activities - finds a nearby hidden object	- can take steps by himself - can get to a sitting position from a lying position	- can stack one cube on top of another	- able to say mama and dada to respective parents
18 months	- initiates interactions by calling to adult	- walks without help	- takes off own shoes - feeds self	- says at least 3 words
2 years	- does things to please others - parallel (imitative) play	- runs without falling	- looks at pictures in a book - imitates drawing a vertical line	- combines two different words

Developmental Red Flags

Birth to 3 months	- failure to alert to environmental stimuli - rolling over before 2 months (hypertonia) - persistent fisting at 3 months
4-6 months	- poor head control - failure to smile - failure to reach for objects by 5 months
6-12 months	- no baby sounds or babbling - inability to localize sounds by 10 months
12-24 months	- lack of consonant production - hand dominance prior to 18 months (contralateral weakness) - no imitation of speech and activities by 16 months
Any age	- loss of previously attained milestones

Appendix 13: Common opportunistic infections, diagnosis, prophylaxis and treatment in HIV positive adults - Table of Contents

Appendix 13 Common opportunistic infections, diagnosis, prophylaxis and treatment in HIV positive adults[5]

OI (and associated WHO stage)	Signs/symptoms	Investigations	Prevention/ Prophylaxis	Management	Follow-up/ Comments
General					
Weight loss (3): loss of >10% of baseline body weight **Wasting syndrome (4)**: Loss of > 10% of body weight + chronic diarrhea or chronic weakness + a fever (without an identifiable infectious origin) body weight loss.	-Early satiety -Nausea -Vomiting -Altered sense of taste -Weakness -Fatigue -Odynophagia (pain on swallowing) -Dysphagia (difficulty swallowing) -Poor dentition -Diarrhea -Abdominal pain -Fever	-Look in oropharynx for candida, ulcers, or lesions • Serial measurement of weight -Assess appetite and food availability -Stool exam for parasites -Exclude TB (CXR, sputums if patient has respiratory symptoms)		-Measure and record changes in weight -Treat underlying cause where possible -Nutrition counseling -Increased access to food -High calorie and protein feeds *To calculate 10% of a person's weight, take their weight and move the decimal to the left by one digit.* *Examples:* *(1) 68.5kg→ 6.85kg* *If a 68.5kg patient has lost >6.85 kg, they have lost >10% of their body weight.* *(2) 76kg→7.6kg* *Weight loss >7.6kg would be >10%*	***DIFFERENTIAL DIAGNOSIS:*** • Candidiasis • Esophageal candidiasis • Apthous ulcers • Malignancy • Diminished gastrointestinal uptake (malabsorption, diarrhea) • Intractable vomiting • TB or other chronic infection • Intestinal parasites • Treatment failure and disease progression • Systemic infection • Increased physical activity • No money to buy food

[5] Medical management recommendations are based on Liberian National Drug Service formularies, current as of September, 2007. Alternative regimens are recommended in many cases. If the suggested medicine is not available, please contact a senior clinician or NACP for other recommendations.

OI (and associated WHO stage)	Signs/symptoms	Investigations	Prevention/ Prophylaxis	Management	Follow-up/ Comments
General					
Fever (any stage, if >37.5ºC or 99.5ºF for > 1 month is Stage 3): Fever should never be attributed to HIV alone without every effort being made to eliminate underlying treatable infections. If no features suggesting a diagnosis are present, the minimum investigations noted should be performed.	• Warm to touch • Fast breathing • Chills • Shaking	• Full Blood Count • Blood slide for malaria parasites (Stool microscopy, urinalysis, and blood and urine cultures where available • Chest x-ray • Sputum smear for AFB and sputum cultures where possible		• Broad spectrum antibiotic such as IV chloramphenicol if no cause identified • Paracetamol may be used for symptomatic relief of chronic fever	***DIFFERENTIAL DIAGNOSIS:*** • Multiple infections including primary HIV, malaria, TB, cryptococcosis, toxoplasmosis, PCP, bacterial pneumonia and meningitis, skin infections, etc. • Cancer • Thyroid disease
Persistent Generalized Lymphadenopathy(1):	• Enlarged lymph nodes	• Look for enlarged lymph nodes, note: tenderness, mobility, size, fixed or matted • Chest x-ray • Full blood count • At least six months after initial HIV infection: (1) Aspirate a node with a 21G needle and stain the aspirate for acid-fast bacilli (AFB) (2) Lymph node biopsy for histological diagnosis where available		• Treat any underlying infection including TB. Steroids may be necessary in TB lymphadenitis if nodes are compressing local vessels • Painful nodes or nodes causing compression may be removable by surgery	***DIFFERENTIAL DIAGNOSIS:*** • HIV at any WHO stage • Other viral illness such as CMV • TB lymphadenitis (high index of suspicion if fluctuant or rapidly enlarging) • Kaposi's sarcoma, or lymphomas (high index of suspicion if hard/matted) • Systemic bacterial infection

OI (and associated WHO stage)	Signs/symptoms	Investigations	Prevention/ Prophylaxis	Management	Follow-up/ Comments
Pulmonary and cardiac disease: cough and chest pain					
PCP (3)	Severe shortness of breath, dry non-productive cough, subacute onset (2-3 weeks), CD4 usually <200, lung exam may be normal	▪ Clinical ▪ CXR: ranges from normal to diffuse infiltrates ▪ Low pulse oximetry reading: significant desaturation with only mild exertion ▪ WBC may be normal ▪ LDH may be elevated	▪ Cotrimoxazole 960mg PO QD	▪ Rule out pulmonary TB ▪ Treat immediately if clinical picture is suggestive. ▪ Cotrimoxazole: dose according to trimethoprim component (15-20 mg/kg/d) and then divide total number of pills into 3 or 4 equal doses/day for 21 days. Generally, will give ¼ tablet of cotrimoxazole per kilo per day (if the tab contains 80 mg trimethoprim). *For example: If patient weighs 48kg, 48 kgs x ¼ tablet = 12 tablets daily. Give 3 tabs qid.* ▪ For those allergic to sulphadiazine: use Trimethoprim 12-15mg/kg/day + dapsone 100mg/day for 21 days	▪ If patient is unwell (if oxygen saturation at rest is < 90% or patient is severely short of breath) then admit and give oxygen and prednisone or prednisolone where available. ▪ Prednisone or prednisolone 40mg PO BID x 5 days then Pred 40 mg PO QD x 5 days then 20mg PO QD x 5 days then 10mg PO QD x 5 days

OI (and associated WHO stage)	Signs/symptoms	Investigations	Prevention/ Prophylaxis	Management	Follow-up/ Comments
Pulmonary and cardiac disease: cough and chest pain					
Bacterial PNA (3 if severe, 4 if recurrent) *(most common cause of pneumonia in HIV+ patients)*	Cough, sputum, difficulty breathing, acute onset (<2 weeks), fever, shaking chills, pleuritic chest pain, productive cough with purulent sputum, decreased breath sounds, dullness to percussion	▪ Clinical- ▪ CXR- multiple patterns of consolidation possible, effusion may be present ▪ Elevated WBC	▪ Cotrimoxazole 960mg PO OD	▪ Doxycycline 100mg PO BID x 10-14 days (not if pregnant) OR ▪ Amoxicillin 500mg PO three times/day x 10-14 days OR ▪ Erythromycin 500mg PO QID x 10-14 days	▪ Use agent that is not active against TB (do *NOT use a fluoroquinolone* like Cipro-- these will increase the resistance of the TB) ▪ If no improvement, consider IV 2nd or 3rd generation cephalosporin (cefuroxime or ceftriaxone) or aminoglycoside (gentamicin).
Pulmonary Kaposi's Sarcoma (4)	Non-productive cough, difficulty breathing, fever, wheezing, subacute onset (2+ weeks), mucocutaneous Kaposi's lesions *may* or *may not* be present	• Clinical • CXR often shows bilateral opacities in central or perihilar distribution. Also may show peribrochial cuffing and tram track opacities. • Pleural effusions may be present.		▪ ART ▪ [See comments in Skin section below.]	KS skin lesions *may* or *may not* be present

OI (and associated WHO stage)	Signs/symptoms	Investigations	Prevention/ Prophylaxis	Management	Follow-up/ Comments
Pulmonary and cardiac disease: cough and chest pain					
TB (3 if pulm; 4 if extrapulmonary)	Cough, sputum, hemoptysis, fever, night sweats, weight loss (all for > 2 weeks), rapid breathing Extrapulmonary symptoms: headache, stiff neck, abdominal pain or fullness, back pain	• Sputum for AFB, (this is often negative in HIV patients with TB) • Sputum for culture • CXR: In patients with high CD4 counts typically upper lung zone infiltrates often with cavities. With lower CD4 counts may show more diffuse disease that may be miliary or could be lower and middle lung zone infiltrates.	▪ Isoniazid 300mg PO QD x 6-9 months	▪ INH/RIF/EMB/PZA ▪ Vitamin B6 (to prevent peripheral neuropathy associated with INH)	▪ See Section 17, Management of TB/HIV Coinfection
MAC/Mycobacteria other than TB (4 if disseminated)	Symptoms may vary; cough, malaise, abdominal pain	▪ Culture	▪ Azithromycin 1200mg once weekly if available	▪ Clarithromycin/EMB/ Rifabutin	▪ Usually associated with very low CD4
Other cardiac disease: Pericardial effusion (usually due to TB or MAC KS or pericardial lymphoma); Hypertensive cardiomyopathy; Myocarditis; Cardiac tamponade	Shortness of breath; chest pain; lower extremity edema; poor quality heart sounds; displacement of point of maximal impulse; additional heart sounds	▪ CXR ▪ Pericardiocentisis ▪ Ultrasound of heart		▪ Treat underlying disease and symptoms	

OI (and associated WHO stage)	Signs/symptoms	Investigations	Prevention/ Prophylaxis	Management	Follow-up/ Comments
Central or peripheral nervous system; Mental status changes					
Cerebral malaria	Fever; impairment of consciousness; seizures; coma; focal neurologic signs are unusual; lethargy; variable muscle tone; passive resistance to neck flexion (though less than in bacterial meningitis)	▪ Blood smear ▪ LP to rule out meningitis		▪ Treat according to national malaria guidelines	
Toxoplasmosis (4)	Headache; fever; seizure; focal neurological finding (often asymmetry-such as facial droop, hemiparesis); altered mental status; lethargy	▪ CT scan showing single or multiple ring enhancing lesions, with mass effect, enhancing with contrast ▪ If LP performed, CSF non-specific or normal ▪ Resolution of findings with treatment	▪ Cotrimoxazole 960mg once daily	▪ Pyrimethamine 200mg loading dose x1, then continue for 6 weeks: ▪ *If pt <60kg*: with pyremethamine 50 mg PO QD, sulfadiazine 1 g PO 4 times/day, leucovorin 10-20 mg PO QD ▪ *If pt >60kg*: with pyremethamine 75 mg PO QD, sulfadiazine 1.5 g PO 4 times/day, leucovorin 10-20 mg PO QD OR ▪ Cotrimoxazole (TMP 5-10mg/kg/day) PO for at least 6 weeks ▪ If patient allergic to sulphadiazine, continue pyremethamine and replace sulpha with clindamycin 600mg PO or IV every 6 hours x 6 weeks.	▪ Consider steroids (dexamethasone 4 mg PO or IV q6hours) to decrease edema if not improving in first few days ▪ Need continuous secondary prophylaxis until patient is asymptomatic and CD4 count >200 cells/mm3 for 6 months

OI (and associated WHO stage)	Signs/symptoms	Investigations	Prevention/ Prophylaxis	Management	Follow-up/ Comments
Central or peripheral nervous system; Mental status changes					
Cryptococcal meningitis (4)	Headache, fever, change of mental status, stiff neck, nausea, vomiting, seizure, confusion, personality change	▪ LP: high opening pressure ▪ CSF: positive India ink stain (only ~60% sensitive); absence of lymphocytes		Amphotericin B 0.7mg/kg/day IV x 14 days PLUS Flucytosine 100 mg/kg/day PO x 14 days THEN Fluconazole 400mg/day PO x 8-10 weeks OR Fluconazole 400-800mg/day PO x6-10 weeks PLUS Flucytosine 100 mg/kg/day PO x6-10 weeks	▪ Needs continuous secondary prophylaxis with Fluconazole 200mg per day until CD4 >200 for 6 months/pt asymptomatic ▪ **CAUTION:** A repeat LP may be indicated to control increased intracranial pressure/prevent hernation.
Neurosyphilis	Headache; vertigo; meningeal symptoms; stroke symptoms; personality changes; dementia; cranial nerve symptoms; ataxia; lack of muscle coordination; loss of reflexes; incontinence; shooting pains	• Serum treponemal antibody test • CSF for VDRL, RPR, elevated leukocytes, and elevated protein (Negative CSF VDRL does not rule out neurosyphilis)		▪ Aqueous crystalline Penicillin G 18-24 million Units per day, administered 3-4million IV q4 hours, or continuous infusion, for 10-14 days.	

OI (and associated WHO stage)	Signs/symptoms	Investigations	Prevention/ Prophylaxis	Management	Follow-up/ Comments
Central or peripheral nervous system; Mental status changes					
Peripheral neuropathy	Depressed ankle tendon reflexes; decreased pain and temperature sensation in extremities; constant discomfort and tingling in extremities	▪ EMG ▪ Consider patient's medications		▪ Remove the drugs that caused the problem ▪ If on INH, provide Vitamin B6 as prophylaxis ▪ Amitryptyline, 25 mg, every night	
ARVs can cause central and peripheral neurological toxicities as well				Treat symptomatically with paracetamol, amitriptyline, etc. Consider changing medicine if toxicity is significantly affecting patient's quality of life.	-Efavirenz : exacerbates depression, somnolence, dreams, confusion, and agitation • d4T: Peripheral neuropathy • ddI : Peripheral neuropathy, retinal, optic nerve changes • AZT, TDF, FTC, ATV, INV, SQV: Headache

OI (and associated WHO stage)	Signs/symptoms	Investigations	Prevention/ Prophylaxis	Management	Follow-up/ Comments
Central or peripheral nervous system; Mental status changes					
HIV Encephalopathy/ AIDS Dementia Complex (4)	• Impaired cognitive, motor, behavioral and affective function: including loss of complex decision making and balance, seizures, myoclonus, hallucinations, loss of interest in friends and others and irritability.	LP: mainly to rule out other causes		▪ ART	
AIDS related mania	• Excessive elation; irritability; decreased sleep; increased activity; uninhibited behavior	Differentiate AIDS Related Mania from bipolar disorder (a functional mental disorder)		▪ ART ▪ Mood stabilizing drugs such as carbamazepine (at doses used to treat epilepsy; review dosage within 1-2 weeks as carbamazepine induces liver enzymes and doses of all meds may need to be adjusted; watch for drug interactions)	
Progressive multifocal leukoencephalopathy (4)	• Weakness of the extremities; progressive focal neurological signs without headache or fever; cortical blindness; cerebellar signs; dementia; rare convulsions	LP: mainly to rule out other causes		▪ ART	

OI (and associated WHO stage)	Signs/symptoms	Investigations	Prevention/ Prophylaxis	Management	Follow-up/ Comments
Gastrointestinal: diarrhea, swollen abdomen, painful or difficult swallowing					
AIDS enteropathy	Diarrhea, fever, abdominal pain, cramps, bloating			▪ ART	
Isospora (4)	Profuse watery diarrhea, cramps, bloating, nausea, vomiting, weakness, anorexia, wasting, +/- fever	▪ Stool iodine stain	▪ Cotrimoxazole 960mg PO QD	▪ ART ▪ Cotrimoxazole: 960 mg two times daily for 2 weeks. ▪ Alternative: Pyrimethamine 50-75 mg daily orally PLUS Folinic acid (leucovorin) 5-10 mg daily for 2 weeks	
Giardia	Diarrhea, bulky, foul-smelling stool, flatulence	▪ Stool iodine stain		▪ Metronidazole 400mg PO every 8hrs x 7-10 days	
Cryptosporidium	Acute, subacute, or chronic profuse watery diarrhea, cramps, bloating, nausea, vomiting, some have fever	▪ Stool iodine stain	▪ Cotrimoxazole 960mg PO QD	▪ ART	
Microsporidium	Profuse watery diarrhea, cramps, bloating, nausea, weight loss	▪ Stool iodine stain	▪ Cotrimoxazole 960mg PO QD	▪ ART	
Typhoid (Salmonella) and Shigella infections	Bloody diarrhea, feeling of incomplete defecation	▪ Serum titers		▪ Ciprofloxacin 500mg PO BID x 10 days	

OI (and associated WHO stage)	Signs/symptoms	Investigations	Prevention/ Prophylaxis	Management	Follow-up/ Comments
Gastrointestinal: diarrhea, swollen abdomen, painful or difficult swallowing					
Abdominal TB	Weight loss; abdominal distension; acites; palpable masses; organomegaly	▪ Paracentesis and culture		▪ INH/RIF/EMB/PZA ▪ Vitamin B6	▪ See Section 17, Management of TB/HIV coinfection
Gastrointestinal Kaposi's sarcoma (4)	Abdominal pain; bloody vomiting; melena (dark, tarry stool); persistent diarrhea; abdominal distention due to bowel obstruction; organomegaly; ascites; lymphadenopathy	▪ Paracentesis and culture		▪ ART ▪ [See comments in Skin section below.]	▪ Mucocutaneous KS skin lesions *may* or *may not* be present
Esophageal candidiasis (4)	Difficulty and pain on swallowing, oral thrush	▪ Clinical		▪ Fluconazole 200 mg PO QD x 14-21 days	
Esophageal CMV (4)	Painful, difficult swallowing, fever	▪ Clinical		▪ ART	Usually occurs when CD4< 100
Esophageal Herpes Simplex (4, if lasts for >1 month)	Painful , difficult swallowing, oral ulcers	▪ Clinical		▪ ART ▪ Acyclovir 5-10 mg/kg IV q8 for 2-7 days (or until improves) *or* 400mg PO 5 times/day x 14-21 days	
Apthous ulcers (2)	Painful , difficult swallowing	Clinical: +/- well circumscribed oral lesions with whitish covering, surrounded by a reddish halo		▪ ART ▪ Prednisone or prednisolone 40 mg/day for 10-14 days, then taper: 20 mg/day for 1 week, 10 mg/day for 1 week	

OI (and associated WHO stage)	Signs/symptoms	Investigations	Prevention/ Prophylaxis	Management	Follow-up/ Comments
Gastrointestinal: diarrhea, swollen abdomen, painful or difficult swallowing					
Non-infectious causes of diarrhea: Lactose intolerance, fatty food intolerance, medications such as PIs	Nausea, cramps, bloating, gas			▪ Try to determine cause. ▪ Consider patient's medications ▪ Treat symptoms with loperamide, bismuth salicylate and other anti-diarrheal agents	
Nausea and vomiting (may be associated with medications, depression, brain infections/space-occupying lesions, acute or chronic GI infections, pregnancy, lactic acidosis, etc.)	Nausea, cramps, bloating, gas			▪ Try to determine cause ▪ Consider patient's medications ▪ Treat symptoms with prochlorperazine (5-10 mg PO every 6-8 hours); metoclopramide (5-10 mg PO every 6-8 hours);	• If severe: lorazapam (ativan) 0.025-0.05 mg/kg IV or IM every 8-12 hours
Chronic diarrhea (4) is a severe disease staging criterion; these patients would also qualify for ART.	More than 3 loose stools/day	Stool microscopy and culture		▪ Rehydration: oral and/or IV (if available) ▪ Oral rehydration salts ▪ Treatment of specific organism if isolated, as below ▪ Nutritional advice: avoidance of dairy products, fatty, greasy and gas-inducing foods, increase starchy carbohydrate foods (potatoes, rice, bread, fresh fruits like bananas, oranges)	• Empirical therapy with ciprofloxacin or metronidazole for 7 days followed by empirical therapy with albendazole or mebendazole if symptoms do not resolve • If diarrhea persists loperamide should be used to control symptoms. This may need to be continued long term.

OI (and associated WHO stage)	Signs/symptoms	Investigations	Prevention/ Prophylaxis	Management	Follow-up/ Comments
Head/Neck					
Oral Thrush/ Candidiasis (3, if persistent)	• Whitish or yellowish curd-like plaques than can be scraped off to reveal an erythematous surface • May burn on eating acidic foods	▪ Clinical		▪ Miconazole gel PO 3x/day to mouth OR ▪ Nystatin troches PO 4-5 times a day	▪ If Miconazole or Nystatin are not working use Fluconazole 200mg PO x 1, then 100 mg PO x 10 days ▪ May recur until immune system recovers
Oral hairy leukoplakia (3)	White vertical corrugations on the lateral aspect of the tongue; can not be rubbed off.	▪ Clinical		▪ ART	• Rarely symptomatic and rarely treated
Orolabial HSV (4, if persist > 1 mo)	Vesicles that rupture and then become painful oral or pharyngeal ulcers that crust over	▪ Clinical ▪ Tzanck prep	• Acyclovir	▪ Acyclovir 400mg PO 5 times/day x 7-10 days	
Parotitis	Swelling of parotid gland; pain with mouth movement	▪ Clinical		▪ Amoxicillin 500mg PO TID x 14 days ▪ Pain medication as needed	
Kaposi's sarcoma (4)	Multiple, flat, diffuse or discrete, red, non-removable plaques	▪ Clinical		▪ ART ▪ [See comments in Skin section below.]	KS skin lesions *may* or *may not* be present
Angular cheilitis (2)	Fissures or linear ulcers at the corner of the mouth	▪ Clinical		▪ ART	

OI (and associated WHO stage)	Signs/symptoms	Investigations	Prevention/ Prophylaxis	Management	Follow-up/ Comments
Skin					
Scabies	Itchy rash; burrows and papules may be in webs of fingers, ankles, wrists	▪ Papular rash		▪ Benzyl benzoate applied from the neck down overnight then repeated in 1 week OR ▪ Ivermectin 0.2 mg/kg PO x 1 if available	▪ All clothing and bedclothes must be boiled; family may need treatment
Folliculitis/papular pruritic eruptions (2)	Open sores at hair follicles on face, trunk, extremities. Usually very itchy and often secondarily infected	▪ Papular rash ▪ Burrows and papules may be in webs of fingers, ankles, wrists		▪ Treatment depends on cause. Antihistamines may help with general relief. To cure, can try topical erythromycin or clindamycin, or PO cephalexin 500 mg PO q6h x 10 days. Also can try topical or systemic antifungal agents (ketoconazole, fluconazole), or topical steroids—to be used with caution on face/hands (hydrocortisone)	▪ Often due to S. aureus or yeast. ▪ May reactivate with immune reconstitution
Kaposi Sarcoma (4)	Reddish-purple or hyperpigmented dark flat or raised lesions on the skin or mucous membranes, especially on edematous limbs; skin lesions may be firm, purple to brown-black macules, plaques, papules, or nodules; edema from lymphatic obstruction possible	▪ Clinical		▪ ART ▪ Chemotherapy (e.g. Bleomycin, Thalidomide, Vincristine, etc)	▪ Lesions in oral cavity imply visceral involvement; oral lesions may be purple, red, or blue and may be raised or flat ▪ If mucous membrane or visceral involvement, consider referral to oncology specialists

OI (and associated WHO stage)	Signs/symptoms	Investigations	Prevention/ Prophylaxis	Management	Follow-up/ Comments
Skin					
Herpes Zoster (2)	Vesicles; can be in band-like distribution over dermatome; area around vesicles= red; pain/itchiness may precede vesicles	▪ Clinical ▪ Tzanck prep	•	▪ Acyclovir 800mg PO five times per day x 7-10 days—only useful if given within 72h of onset of rash ▪ **ALERT:** If rash is disseminated or *ophthalmic* nerve is involved give Acyclovir IV 10mg/kg 8 hourly for 7 days, where available. ▪ Bacterial super infection should be treated with penicillin/cloxacillin or erythromycin.	▪ Should follow-up for development of post-herpetic neuralgia ▪ Treat pain with analgesics (opioids are frequently required). Carbamazepine, amitriptyline are useful for post herpetic neuralgia. ▪ *Ophthalmic herpes is a medical emergency*
Molluscum	Umbillicated lesions	▪ Clinical		▪ ART	
Drug reaction	Widespread skin eruptions: morbilliform or maculopapular; appears 10-14 days after initiating a drug; fever; headache; malaise; bllistering skin and mucous membranes; itchiness; may lead to shock and hypotension	▪ Clinical ▪ Check FBC and LFTs for signs of infection or systemic drug reaction		▪ Antihistamines; topical and oral steroids; treatment for any secondary infections; admission to hospital if necessary ▪ Stop the drug that caused the problem if condition is severe. Some drugs (e.g., ABC) should not be restarted if there is any sign of reaction, others (NVP) depend on extent of reaction	

OI (and associated WHO stage)	Signs/symptoms	Investigations	Prevention/ Prophylaxis	Management	Follow-up/ Comments
STIs/Genitourinary					
Vulvovaginal candidiasis	Whitish or yellowish curd-like exudate	▪ Clinical		▪ Clotrimazole topically or as pessary	▪ When topical therapy fails or in cases of severe/life threatening infection use Fluconazole 150-200 mg/day for at least 14 days.
Syphilis	Painless genital lesions, rash	▪ Clinical		▪ Benzathine PCN 2.4 million units IM weekly x 3 weeks	▪ If not responding, give injections weekly x 3 weeks ▪ If neurosyphilis suspected will need aqueous crystalline Penicillin G 3-4 million units Q4 hours IV for 2 weeks
Purulent urethral discharge (Gonorrhea/ Chlamydia)	Burning uretheral discharge	▪ Clinical		▪ Ceftriaxone 250mg IM x 1 PLUS Doxycycline 100mg PO BID x 14 days OR ▪ Ciprofloxin 500mg PO x 1 PLUS Doxycycline 100mg PO BID x 14 days	▪ Should treat all sexual partners as well ▪ Do NOT give doxyycline to pregnant women
Cervical cancer (4)	Vaginal bleeding	▪ PAP smear ▪ Biopsy	▪ HPV vaccine	▪ Coloposcopy ▪ Hysterectomy	
Genital HSV (4, if persist > 1 month)	Painful anal or genital ulcers, may be extensive	▪ Clinical	• Acyclovir 400 mg PO BID	▪ Acyclovir 400mg PO 5 times per day x 10 days ▪ May add topical Acyclovir cream to lesions as well	• *Herpetic lesions at onset of labor is an indication for caesarean section to prevent neonatal herpes.*
HPV/genital warts	Painless, raised fleshy lesions	▪ Clinical ▪ PAP smear	▪ HPV vaccine	▪ Podophyllin 0.5% twice a day to lesions on 3 consecutive days weekly x 4 weeks	▪ Surgical excision or curettage may be needed for extensive disease

OI (and associated WHO stage)	Signs/symptoms	Investigations	Prevention/ Prophylaxis	Management	Follow-up/ Comments
Disseminated/ Systemic					
CMV (4)	General malaise, bloody diarrhea	▪ Clinical		▪ ART ▪ Ganciclovir or Valganciclovir	
Lymphoma (4)	General malaise, swollen lymph nodes, itching, weight loss, fevers	▪ Clinical ▪ Biopsy		▪ Combination chemotherapy	

Appendix 14: Common opportunistic infections, diagnosis, prophylaxis and treatment in children - Table of Contents

Appendix 14 Common opportunistic infections, diagnosis, prophylaxis and treatment in children[6]

OI and associated WHO Stage	Symptoms	Investigations	Management	Follow-up
Weight loss				
Children with HIV infection may be symmetrically small without meeting the criteria for failure to thrive. That is, the child may be below the 5th percentile in both height and weight and yet maintain a steady growth curve. It is important for clinicians to consider HIV infection in a child who is otherwise asymptomatic but is small for age. **Growth faltering** is defined as failure to gain weight or continuous loss of weight for three consecutive months. It is a stage 3 or stage 4 condition. Failure to thrive is easy to diagnose if the child's previous growth rate is known, i.e., if the child has been attending a well baby clinic on a regular basis, has been weighed and measured regularly to fill the growth chart. The cause of failure to thrive in a child with HIV infection is not clearly understood. Growth retardation in HIV positive children may be due to lack of adequate feeding or repeated chronic infections, such as urinary tract infection, diarrhea and pneumonia. Children with failure to thrive may also be severely malnourished. The assessment of the severity of malnutrition may be made by examining the child's weight for age. Severe malnutrition includes kwashiorkor, marasmus and marasmic kwashiorkor. In **kwashiorkor** the child is edematous and the weight falls between 60 and 80% of the normal weight for age. In **marasmus** there is no edema and the weight falls below 60% of the normal weight for age. In **marasmic kwashiorkor** the child has edema and the weight falls below 60% of the normal weight for age. **Growth Charts** Growth charts are used in ART clinics to assess growth and development in children. HIV positive children often do not grow as uninfected children. Growth charts are designed according to age and sex, e.g., girls and boy's birth-20 years and boys and girls 2-20 years. Height, weight, and head circumference must be charted at each visit. These measurements should be connected by a line so that the growth can be easily visualized. Head circumference is also charted and normal ranges are based upon sex and age. Investigations include: Serial measurement of weight; assessment of appetite and food availability; stool exam for parasites; exclude TB (CXR, sputums if patient has respiratory symptoms) and underlying bacterial infections (urinary tract, pneumonia, etc) [Also, refer to information on weight loss in table of adult complications above.]				
PGL (1)	Diffuse lymphadenopathy. Often due to bacterial skin systemic viral infections. Also conditions that cause generalized dermatitis, e.g., eczema, infected scabies and viral infections like infectious mononucleosis as well as tuberculosis, leukemia and lymphoma can cause PGL. Refer to information on PGL in table of adult complications above.			

[6] Medical management recommendations are based on Liberian National Drug Service formularies, current as of September, 2007. Alternative regimens are recommended in many cases. If the suggested medicine is not available, please contact a senior clinician or NACP for other recommendations.

OI and associated WHO Stage	Symptoms	Investigations	Management	Follow-up
Fever (3, if unexplained and persists for > 1 month)	For children, it is essential that serious infections are excluded or treated if necessary-- in an infant under 2 months of age, fever is a sign of severe disease. Children with persistent fever are usually brought in by the mother with the complaint that the child "feels hot". A full history should be taken from the mother and any other symptoms should be elicited. Fever should never be attributed to HIV alone without every effort being made to eliminate underlying treatable infection. *Important signs and symptoms*: Chest signs: High respiratory rate, chest in-drawing, stridor, rhonchi, crepitations, reduced air entry; Other: enlarged lymph nodes; weight loss; bulging fontanelle; dehydration; neck stiffness; hepatosplenomegaly. *Investigations* should include full blood count; blood slide for malaria parasites; stool microscopy, urinalysis, and blood and urine cultures where available; chest x-ray; sputum smear for AFB and sputum cultures where possible. *Treatment*, if no cause identified: broad spectrum antibiotic such as IV chloramphenicol; paracetamol may be used for symptomatic relief of chronic fever			
PULMONARY				
PCP (WHO Stage 4)	Cough, fever, tachypnea, cyanosis	▪ Clinical – high suspicion in infants and pts with low CD4 ▪ CXR if avail, variable, classically bilat alveolar perihilar infiltrates ▪ LDH may be elevated	▪ Cotrimoxazole 5mg/kg PO divided into four equal doses and given QID x 21 days ▪ If severe respiratory distress, Prednisone or prednisolone 2mg/kg/day x 7 days and admit for Ampicillin / Gentamicin and oxygen therapy in addition to Cotrim/Prednisone or prednisolone	▪ Re-assess in 1-3 days depending on severity of respiratory distress ▪ Needs secondary cotrim prophylaxis as per Section 8 ▪ Document suspected cases ▪ If severe respiratory distress, admit (see management) ▪ When there is a high index of suspicion, therapy should be initiated promptly along with treatment for bacterial pneumonia.

OI and associated WHO Stage	Symptoms	Investigations	Management	Follow-up
PULMONARY				
Bacterial pneumonia (3 if recurrent)	Cough, fever, tachypnea, chest in-drawing, cyanosis	▪ CXR if available, usually focal consolidation	▪ Amoxicillin 25-50 mg/kg PO three times/day x 10 days OR ▪ If suspect atypical pneumonia, use Erythromycin 30-50mg/kg/day divided into four equal doses and given QID x 10 days OR ▪ If severe respiratory distress, admit for Ampicillin 200-400 mg IV divided QID / Gentamicin 3-7.5mg IV divided TID and oxygen therapy	▪ Re-assess in 1-3 days depending on severity of respiratory distress ▪ If severe respiratory distress, consider adding prednisone or prednisolone and admitting for IV antibiotics (see management)
Pulmonary TB (3)	Chronic cough and fever (> 3 weeks), lymphadenopathy, night sweats, weight loss	• CXR if available, variable but classically, hilar adenopathy, cavitary lesions, effusion • See Section 17 • Sputum if able to produce	▪ Multivitamins: if malnourished give pyridoxine (B6) ▪ High protein diet ▪ See Section 17	• Steroids (e.g. prednisone or prednisolone 4mg/kg daily for six weeks) are recommended in tuberculosis meningitis, endobronchial TB, miliary TB, massive pleural effusion and TB pericarditis • See Section 17, Management of TB/HIV Coinfection • DOT for initiation phase, if available
Miliary TB (4)	Chronic cough and fever (> 3 weeks), lymphadenopathy, night sweats, weight loss	▪ CXR pattern: miliary pattern (diffuse millet seed pattern)	See Section 17, Management of TB/HIV Coinfection	▪ DOT for Initiation phase, if available

OI and associated WHO Stage	Symptoms	Investigations	Management	Follow-up
PULMONARY				
Lymphoid interstitial pneumonitis (3) / **Chronic lung disease**	Chronic cough (> 3 weeks), generalized lymphadenopathy, hepatosplenomegaly, finger clubbing, parotid enlargement	CXR pattern: ▪ LIP—variable classically, reticulonodular pattern ▪ CLD—variable classically, bronchiectasis, cystic changes, persistent densities	▪ If febrile or acutely symptomatic (worse cough, wheeze, difficulty breathing), give Amoxicillin 25-50 mg/kg PO three times/day x14 days OR ▪ Erythromycin Erythromycin 30-50mg/kg/day divided into four equal doses and given BD or QID x 14 days PLUS ▪ Salbutamol for acute exacerbations: 3-4 puffs every 3-4 hours for resp difficulty ▪ Consider inhaled steroids (Beclomethasone)	▪ If remains symptomatic after multiple courses of antibiotics, rule out TB, then, consider prolonged course of oral steroids (1-2 mg/kg/day) x 2-6 weeks with taper ▪ Always provide symptomatic treatment with oxygen and hydration ▪ Antibiotics are important if bacterial superinfection present. ▪ Always test for and treat anemia ▪ Will resolve with appropriate antiretroviral therapy
Chronic suppurative otitis media (2)	Ear drainage > 14 days	▪ Clinical	▪ Wicking ▪ Chloramphenicol drops to ear x 7 days, although they may or may not be effective ▪ Refer to ENT specialist	▪ Evaluate for hearing loss
HEAD / NECK				
Acute pharyngo-tonsillitis (Stage 2 if recurrent)	Fever, refuses to eat, drooling, red and swollen tonsils and pharynx, may have stridor	▪ Clinical	▪ Amoxicillin 25-50 mg/kg PO three times/day x14 10-14 days	▪ If suspect epiglottis should admit for IV antibiotics

OI and associated WHO Stage	Symptoms	Investigations	Management	Follow-up
HEAD/NECK				
Parotitis	Swelling of parotid gland: "puffy cheeks"; pain with mouth movement; may be associated with generalized lymphadenopathy with or without hepatosplenomegaly and lymphocytic interstitial pneumonitis.	▪ Clinical	▪ ARVs ▪ If superinfection consider 7 day course of clindamycin 20-40 mg divided into 3-4 equal doses given TID or QID	
Periodontal disease	Red gums; bleeding; pain; decreased oral intake; dehydration; ulcerative peridontitis; destruction of gum tissue; visible necrotic bone	▪ Clinical	Medicated oral rinses such as chlorhexidine gluconate 1% oral rinse, 15 ml swished in the mouth for 30 seconds then spit out 2x/day. Patients should be cautioned *not to swallow* the chlorhexidine gluconate rinse and to not eat for 2 hours after the rinse.	If necrotizing, prescribe metronidazole, amoxicillin/clavunate (Augmentin), or clindamycin should be added to the treatment regimen. Refer patients to a dentist Regular brushing and flossing

OI and associated WHO Stage	Symptoms	Investigations	Management	Follow-up
ORAL				
Oral Candidiasis (stage 3 if persists after first 6-8 weeks of life)	White plaques in mouth that do not scrape off; can have erythematous firm with raised red changes on palate and tongue; angular cheilitis may be present	▪ Clinical	▪ Nystatin oral suspension, 100,000 units 6 hourly for 2 weeks, or use cotton wool or a piece of cloth to paint the mouth with nystatin OR ▪ Gentian violet 1% aqueous solution applied 2x/day for 1 week OR ▪ 2% miconazole gel, applied orally 2x/day for 4 weeks OR ▪ Fluconazole 6-12mg/kg daily (max 100 mg) orally for 7-14 days for recurrent refractory oral candidiasis. In cases of suspected esophageal candidiasis extend treatment for 21 days	▪ If breastfeeding, put Clotrimazole on Mother's breast ▪ Common in infants regardless of HIV status. If HIV+, condition is persistent or recurrent and may lead to growth failure as a result of poor feeding. Oral thrush may extend into the esophagus leading to pain on swallowing.
Orolabial Herpes Simplex (stage 4, if persists for > 1 month)	Painful shallow oral or pharyngeal ulcers, may be extensive	▪ Clinical	▪ Acyclovir 25-30 mg/kg PO (max 60mg/kg/d) divided into three equal doses and given every 8 hours x 5-10 days	▪ Recurrent episodes (>6x/year) may be prevented with Acyclovir 10 mg/kg twice a day
Gingivitis	Red swollen gums, may be associated with dental caries and purulent drainage from tooth	▪ Clinical	▪ Amoxicillin 25-50 mg/kg PO three times/day x 7 days	▪ Refer to Dental clinic

OI and associated WHO Stage	Symptoms	Investigations	Management	Follow-up
ORAL				
Acute Necrotizing Ulcerative Gingivitis (3)	Ulcerative gingivitis with soft tissue loss of cheek and gums and loss of teeth	▪ Clinical	▪ Admit to hospital and give Ampicillin 25 mg/kg IV QID PLUS ▪ Gentamicin 2.5 mg/kg IV every 8 hours PLUS ▪ Flagyl 10 mg/kg IV/PO three times a day PLUS ▪ Mouth wash	▪ Dental should be involved for debridement and reconstruction
SKIN				
Herpes Zoster (2)	Painful vesicles; can be in band-like distribution over dermatome	▪ Clinical ▪ Tzanck prep	▪ Acyclovir 20 mg/kg PO four times/day x 7-10 days OR ▪ If severe, give Acyclovir 10 mg/kg IV three times/day until all lesions crusted then switch to PO	▪ Should follow-up in case of development of post-herpetic neuralgia
Varicella (Chickenpox)	Itchy umbilicated papular rash in crops starting on trunk and spreading to arms/legs, fever	▪ Clinical	▪ Acyclovir 20mg/kg PO four times/day x 7-10 days OR ▪ If severe, Acyclovir 10mg/kg IV Q8 x 7days ▪ Panadol ▪ If suspect bacterial superinfection (e.g. skin folliculitis or pneumonia) give antibiotics accordingly	▪ *Make sure to isolate patient away from other immunosuppressed chidren*

OI and associated WHO Stage	Symptoms	Investigations	Management	Follow-up
SKIN				
Impetigo	Erythematous area progressing to honey colored crusts; superficial vesicles and bullae; +/- fever, lymphadenopathy		▪ Cloxacillin 15-25 mg/kg PO four times/day x 7-10 days	▪ Keep lesions clean with soap and water
Tinea corporis (ringworm body)	Round scaly itchy lesions with raised edges on body, may be hypo- or hyperpigmented	▪ Clinical ▪ KOH skin scraping	▪ Clotrimazole cream twice a day for 4-6 weeks	▪ If unresponsive to topical treatment and severe, may need oral Fluconazole or Ketoconazole
Tinea capitis (ringworm scalp)	Round scaly lesions on scalp associated with hair loss	▪ Clinical ▪ KOH skin scraping showing hyphae	▪ Griseofulvin 10-20 mg/kg PO QD x 6 weeks if available OR ▪ Whitfield's Ointment BID x 4 weeks	▪ Longer treatment may be necessary ▪ Monitor LFTs if on concomitant ART and ATT ▪ May need to give Cloxacillin (as per Impetigo) if lesions superinfected
Seborrhea	Greasy scaly rash over scalp, cheeks, arm folds	▪ Clinical	▪ Selenium Sulfide shampoo OR ▪ Hydrocortisone 1% cream BID	
Scabies	Intensely itchy (especially at night); lntraepidermal burrows and vesicles distributed in web spaces of fingers, wrist, elbows, umbilical area, genital area and feet	▪ Clinical ▪ KOH prep skin scraping may show burrow, egg, or mite	▪ Benzyl benzoate applied from the neck down overnight then repeated in 1 week; ▪ Other options: Ivermectin 6gm PO x 1 if available OR Permethrin 5% applied and left on for 8-14 hours and then washed off	▪ All clothing and bedclothes must be boiled; <u>entire family</u> may need treatment
Molluscum (stage 2, if extensive)	Umbillicated lesions	▪ Clinical	▪ Supportive care ▪ ART if qualifies	

OI and associated WHO Stage	Symptoms	Investigations	Management	Follow-up
GENITAL/URINARY				
HPV/genital warts	Painless, raised fleshy lesions	▪ Clinical ▪ PAP smear	▪ Podophyllin 0.5% BID to lesions on 3 consecutive days weekly x 4 weeks	▪ Surgical excision or curettage may be needed for extensive disease
Genital HSV	Painful anal or genital ulcers, may be extensive	▪ Clinical	▪ Acyclovir 25 mg/kg PO 3 times/day x 7 days	
Vaginal discharge (suspected Gonorrhea/ Chlamydia)	Purulent urethral discharge	▪ Wet mount showing pus cells and bacteria	▪ Ceftriaxone 125mg IM x 1 PLUS Doxycycline 100mg PO BID x 14 days OR ▪ Ciprofloxin 500mg PO x 1 PLUS ▪ Doxycycline 100mg PO BID x 14 days	▪ Should suspect abuse if not sexually active ▪ Do <u>not</u>
Candidial dermatitis	Red rash in groin areas with satellite lesions	▪ Clinical ▪ KOH scraping showing hyphae	▪ Clotrimazole cream BID OR ▪ Nystatin cream 4x/day to rash x 2-4wks	▪ Remind caregiver to change nappy frequently and keep skin dry, look for associated oral thrush and treat accordingly
GASTROINTESTINAL (GI)				
Esophagael Candidiasis (4)	Oral thrush and painful or difficult swallowing	▪ Clinical	▪ Fluconazole 6 mg/kg PO on first day, then 3-6 mg/kg QD x 14-21 days	▪ Monitor LFTs if on other hepatotoxic drugs
Acute watery diarrhea	Watery frequent stools without blood	▪ Clinical	▪ ORS hydration	▪ If persistent consider antibiotic or antihelminth treatment like Mebendazole
Dysentery	Bloody frequent stools, abdominal pain, fever, vomiting	▪ Clinical ▪ Stool culture if available	▪ Cotrimoxazole 5 mg/kg divided into four equal doses and given every 6 hrs PLUS ▪ Flagyl 10 mg/kg 3x/day x 7 days PLUS ▪ Zinc administration: >6mo of age: 20mg/day x14 days < 6mo of age: 10mg/day x 14 days CONSIDER Mebendazole 100mg BID x 3 days for worms	▪ Monitor closely for hydration and if severe dehydration admit ▪ If not improving consider Cipro instead of Bactrim

OI and associated WHO Stage	Symptoms	Investigations	Management	Follow-up
GI				
Persistent diarrhea (3, if persists > 14 days)	Chronic diarrhea (>3 loose stools/day for 2 weeks	▪ Stool culture if available ▪ If acute diarrhea, assess hydration status per IMCI guidelines	▪ Management as per "Dysentery" box ▪ If not improving then consider HIV enteropathy (start ART) or malabsorption	▪ Admit if becoming dehydrated
CENTRAL NERVOUS SYSTEM				
Cryptococcal meningitis (4) (less common in children than adults)	Headache, fever, malaise, vomiting CN palsy	▪ Clinical ▪ LP: India Ink, Cryptococcal antigen	▪ Fluconazole 12 mg/kg IV/PO on the first day then 6-12 mg/kg/d divided twice a day PO x 8-10 weeks ▪ If amphotericin B is available start with 0.75-1mg/kg/dose once daily for two weeks, then switch to fluconazole for remaining 8 weeks of treatment	▪ Needs prophylaxis with Fluconazole 3-6 mg/kg/day after completing treatment. Prophylaxis should be continued for life. ▪ Consider repeat LP before switching to prophylaxis to document clearing of CSF ▪ See comments on cryptococcal meningitis in adult section above.
Bacterial meningitis	Fever, vomiting, headache, stiff neck, bulging fontanelle	▪ LP: gram stain and culture ▪ Consider head CT if has any focal neurologic findings (CN palsy, seizure)	▪ Cefotaxime 100 mg/kg IV BID OR ▪ Ceftriaxone 100 mg/kg IV QD OR ▪ Chloramphenicol 25 mg/kg IV/PO four times/day ▪ In newborns, Ampicillin 25 mg/kg IV/IM four times/day PLUS ▪ Gentamicin 7.5mg/kg IV QD ▪ Consider steroids, Prednisone or prednisolone 1-2 mg/kg QD	▪ Consider repeat LP after 1 week treatment to document clearing of CSF ▪ Consider head CT if no improvement or continued fevers

OI and associated WHO Stage	Symptoms	Investigations	Management	Follow-up
CENTRAL NERVOUS SYSTEM				
Seizures			Treatment is aimed at underlying disorder and seizure control through standard anti-epileptic medication **NB:** Drug interactions may be a problem for patients on ART; for those on ART the drug of choice is sodium valproate.	***DIFFERENTIAL DIAGNOSIS:*** • Space-occupying lesions (most often cerebral toxoplamosis or tuberculoma) • Meningitis including cryptococcal meningitis • Metabolic disturbances • No identified cause other than HIV infection
CNS Toxoplasmosis (stage 4, if occurs after 1 month of life)	Headache, seizure, focal neurological finding (e.g. facial droop, hemiparesis)	▪ Clinical ▪ Head CT may show ring-enhancing lesions with edema	▪ Cotrimoxazole (dosing based on TMP component) 10mg/kg/day for at least 6 weeks OR ▪ Pyrimethamine 1 mg/kg BID (max 50mg) PO x 3 days then 0.5 mg/kg BID (max 25mg) PLUS ▪ Sulfadiazine loading dose of 75 mg/kg once, then 150 mg/kg/day divided into 4 equal doses (max 1-1.5g/dose) PLUS ▪ Folinic acid 10mg three times per week ▪ All of above for at least six weeks OR ▪ Cotrimoxazole (dosing based on TMP component) 10mg/kg/day for at least 6 weeks)	▪ Need life-long <u>secondary prophylaxis</u>: Cotrimoxazole 150-750mg/m2/day for all patients with WHO stage 2, 3, or 4 or CD4 <200 cells/mm3. For those allergic to sulpha, give dapsone 25mg/day ▪ Folinic acid necessary to prevent toxicity of sulfadiazine ▪ Dexamethasone IV/IM should be given according to weight where there is evidence of raised intracranial pressure/focal signs.