NATIONAL GUIDELINES FOR HIV AND AIDS TREATMENT AND CARE IN ADOLESCENTS AND ADULTS

FEDERAL MINISTRY OF HEALTH
ABUJA – NIGERIA

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Foreword

Since the first case of AIDS was reported in Nigeria twenty-one years ago, the Federal Government has in a myriad of ways activated machinery to combat the HIV virus. HIV/AIDS is a major public health problem which has taken its toll on the country, affecting not only the lives of individual men, women and children, but also the future socio-economic development of the nation.

As part of its response, the Nigerian Government in 2002, initiated the National Anti-retroviral Access programme, providing ARVs at minimal cost to 10,000 persons. The country was the first in Africa to do this. Since then, and in collaboration with International partners, the number of people accessing ARVs has risen to over 100,000.

The Guideline for the use of ARVs in Nigeria has been revised to ensure it provides essential, relevant and up-to-date information needed by health workers, not only to understand the course of HIV/AIDS in adults and adolescents, but also to control and manage it.

The Government expects that all those providing care for People Living with HIV or AIDS in Nigeria will strive to attain the standard prescribed in this guideline.

Prof. Eyitayo Lambo
Honourable Minister of Health

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The invaluable and untiring effort of the staff of the National AIDS/STI Control Programme (NASCP) is also appreciated.

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ACRONYMS

AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
ARV	Antiretroviral
CBO	Community based organization
CHEW	Community Health Extension Worker
CHO	Community Health Officer
ELISA	Enzyme Linked Immunosorbent Assay
FBC	Full Blood Count
FBO	Faith-Based Organization
FMOH	Federal Ministry of Health
FGN	Federal Government of Nigeria
GON	Government of Nigeria
HAART	Highly Active Antiretroviral Therapy
HBC	Home-Based Care
HCT	HIV Counselling and Testing
HIV	Human Immunodeficiency Virus
IEC	Information Education Communication
IMAI	Integrated Management of Adolescent and Adult Illness
IMCI	Integrated Management of Childhood Illness
M & E	Monitoring and Evaluation
NACA	National Agency for the Control of AIDS
NASCP	National AIDS/STI Control Program
NGO	Non-governmental Organization
OIs	Opportunistic Infections
PCR	Polymerase Chain Reaction
PEP	Post exposure prophylaxis
PHC	Primary Health Care
PLWHA	People Living With HIV/AIDS
PMTCT	Prevention of Mother-to-Child Transmission
STI	Sexually Transmitted Infections
RAD	Return after Default
TB	Tuberculosis
USAID	United States Agency for International Development

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The first case of HIV/AIDS in Nigeria was reported in 1986. Since then the number of people living with HIV or AIDS (PLWHA) steadily increased and the epidemic moved into a 'generalised' state with an increase in sero prevalence from 1.8% in 1991 to 5.8 in 2001. A slight drop to 5.0% was recorded in 2003 which was sustained in 2005 with a sero prevalence rate of 4.4%. It is estimated that Nigeria has 2.86 million (Sentinel Survey 2005) infected persons, the third highest in the world. Estimates also show a cumulative death of 1.45 million people.

The high burden of the disease with its associated morbidity and mortality despite the concerted efforts of the Federal Government of Nigeria and its international and local partners to combat the disease continues to constitute a major public health concern for the country. The epidemic has impacted all segments of the society, markedly reducing gains in life expectancy which Nigeria had achieved over the past four decades since her independence. It has further weakened and threatened to overwhelm the Nigerian health care system, increased the number of orphans, and increased the cost of achieving set developmental goals by decreasing the size of the workforce, affecting as it does, mainly adults in their most productive years of life (15 – 60 years). The high manpower-intensive sectors of the economy are the most affected; in Nigeria this includes the agricultural, educational and health sectors as well as the rural economy. In summary, the impact of HIV/AIDS on Nigeria's social fabric and on its economic development and well-being continues to be pervasive and, unless controlled, will continue to undermine the quality of life of Nigerians

In response to the challenge of reversal in the gains in development and life expectancy and the fact that about 300,000-700,000 PLWHA were estimated to be in need of treatment based on the sero survey report of 2001, the Federal Government of Nigeria, as part of its care and support strategies initiated the National Antiretroviral Drug Access Programme in 2002 in 25 sites across the country. The goal was to provide access to affordable ARV drugs thereby improving the health and quality of life of PLWHA in Nigeria in order for them to meaningfully contribute to the sustainable development of the Nation. Specifically, the programme was to provide immediate access to ARVs, fully utilize the capacity of the current infrastructure for a coordinated care agenda and develop an environment that would support a broader access to ARVs across the nation through the creation of an enabling environment

for a long-term collaboration between the Nigerian Government and other partners. An ARV Committee was inaugurated to guide the implementation of the programme. This Committee provided technical support for the development of the first ARV Guidelines which was produced by the FMOH in 2004 to equip care givers to manage patients appropriately in all tiers of our health care system.

The Nigerian Government, fully committed to increasing access to treatment, developed a scale-up plan targeting treatment for 1million PLWHAs by 2009 and universal access by 2010. Appreciable progress has been made and there are over 150 ART sites nationwide supported by funds provided by the Global Fund to fight AIDS Tuberculosis and Malaria (GFATM), the World Bank and the President's Emergency Plan for AIDS Relief (PEPFAR) . In addition, Faith based and private organisations are also providing services. In spite of these, there remains a monumental gap to be bridged. In order to bridge this gap, there was a Presidential mandate to place 250,000 PLWHAs on treatment by end of 2006. Concerted efforts are being made to realise this mandate with a new target date of end of 2007.

An increasing challenge today is the need to standardize treatment to ensure the highest quality of care. With current advances in technology and better understanding of the infection, case management of HIV and AIDS will continue to improve and guidelines on HIV and AIDS care and treatment will continue to be subject to regular review as indications emerge from scientific research and advancement. The Nigeria ART Guidelines has been updated based on literature review and relevant local experiences and is meant for the treatment of adults and adolescents. It is hoped that it will provide relevant, simplified but adequate information required for the effective management of our patients.

It is also expected that The Nigeria ART Guidelines will assist in building capacity among clinicians who have the primary responsibility of managing the patients. The use of the Guidelines will prevent or curtail the emergence of drug resistance as a result of inappropriate and irrational use of ARVs.

SECTION 2: VIROLOGY

2.1 Classifications and Structure

The aetiological agents of AIDS have been identified as HIV-1 and HIV-2. These viruses belong to the Lentivirus group of Retroviridae family. The Family Retroviridae of viruses includes three sub-families, Oncovirinae, Lentivirinae and Spumavirinae. All the members of the family contain an enzyme called reverse transcriptase that is used for the synthesis of proviral DNA from the infecting viral RNA. The provirus (also called the complementary or cDNA) integrates itself into the chromosome of the host cell with the aid of additional enzymes encoded by the viral pol gene.

The integration of the viral cDNA into the host cell genome serves as basis for the continuous viral replication characteristic of retroviruses as well as the unconventional (reverse) method of transcription by these groups of viruses than the conventional flow (transcription) of the genetic information from DNA to RNA. This group of Retroviruses are associated with many diseases including rapid and long latency, malignancies, wasting disease, neurological disorders, immunodeficiency as well as long viraemia in the absence of any obvious clinical disease.

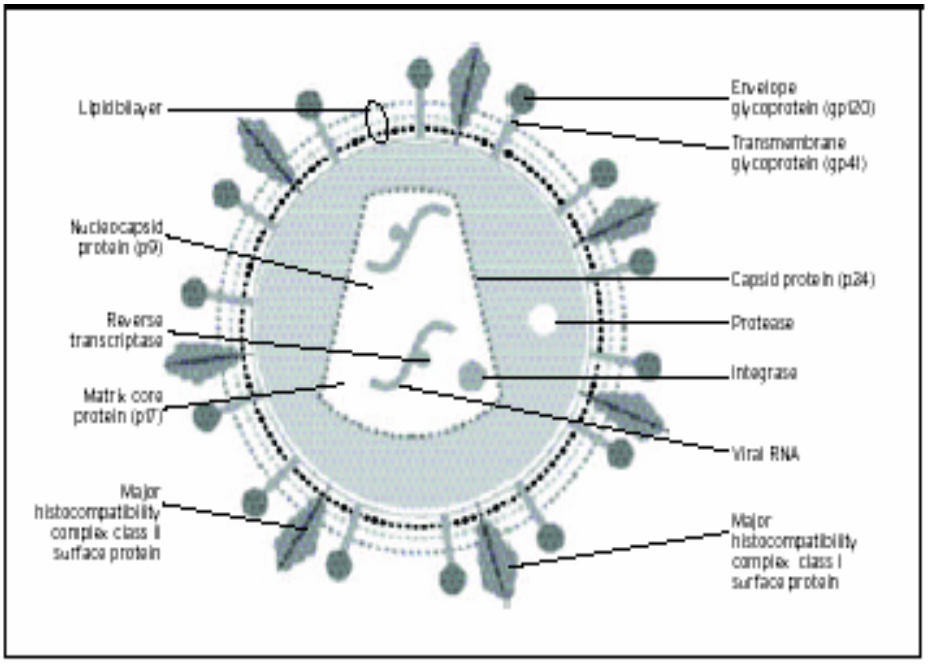
Human immunodeficiency virus like other retroviruses has a positive single stranded RNA. In the mature virus, the genome is diploid, with a 60-70s dimer complex of the two identical positive sense single stranded RNA copies. Electron microscopy studies showed that HIV has a dense, cylindrical core whose structural elements are coded by the gag gene for the protein that encloses the RNA genome. The central core is surrounded or enclosed by an envelope acquired from the surface of the host cell as the virions bud out (Figures 1a&b).

The envelope is made of two glycoproteins with molecular weight of 120,000 and 41,000 (Gp120 and Gp41, respectively) for HIV-1 and 105,000 and 36,000 (Gp 105 and Gp36) for HIV-2. These glycoproteins are trans-membrane proteins, which are found projecting the lipid barrier. The Gp41 is attached to Gp120 and thus appears as small projections on the surface of the virus particle. It is the structure of these small projections and their attaching proteins that appear to be the major difference between HIV-1 and HIV-2. Antibodies to these two sets of proteins (Gp120, Gp41 for HIV-1 and Gp105 and Gp36 for HIV-2) do not usually cross react and thus differentiate serologic response to the two types of the virus.

The HIV proviral genome is approximately 10kb in length with an open reading frame coding for the several viral proteins. The genome is flanked at both ends by long terminal repeat (LTR) sequences that contain regulatory segments for HIV replication. It also comprises the gag, pol and env genes that code for the capsid proteins, the viral enzymes and the internal and external envelope proteins, respectively. In addition to these major genes, an HIV genome has at least five other genes Tat, Rev, Nef, Vif and Vpu/Vpx. Vpu is present in HIV-1 while Vpx is present in HIV-2.

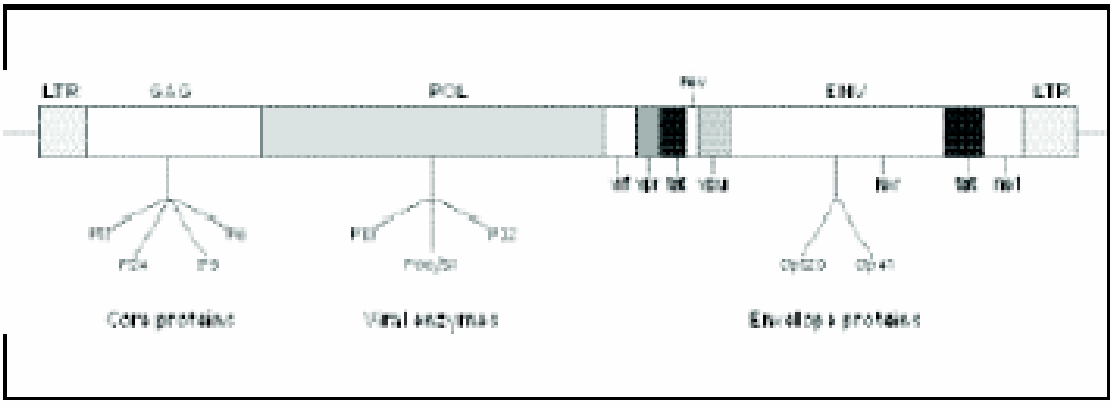
The envelope encloses the core proteins that in nature enclose the virus genome (RNA) and the enzymes (reverse transcriptase, integrase and protease). The core is made up of two proteins of about 18,000 and 24,000 Dalton in size and are usually abbreviated as p18 and p24, respectively. The RNA, the reverse transcriptase, integrase and protease have molecular weights of 66,000(p66), 51,000(p51), 32,000(p32) and 16,000(p16), respectively. The gag precursor p55 gives rise to four smaller proteins p24, p17, p9 and by p6 proteolytic cleavage. The pol precursor protein is cleaved into products consisting of the reverse transcriptase (RT), the protease (PR), and the integrase (IN) proteins. The protease processes the gag and pol polyproteins while the integrase catalyses virus integration. The gag and gag/pol products are usually synthesized in a ratio of about 20:1. The envelope precursor Gp160 is also split into two smaller glycoproteins, Gp120 and Gp41. The p17 core protein provides the matrix (MA) for the viral structure and is vital for the integrity of the virion. The matrix also seems to play a role in the incorporation of env protein into mature virions.

Figure 2.1: Simplified Schematic Structure of HIV



Source: AIDS in Nigeria

Figure 2.2: Genomic structure of a typical HIV-1



In general, the ratio of p25 gag protein to Gp120 is 100:1 while p25 gag protein to polymerase molecule is 10:1. The cleavage of the Gp160 is by cellular enzymes in the Golgi apparatus. The Gp120 forms the external surface (SU) envelope protein and the Gp41, the transmembrane (TM) protein. The virion Gp120 is located on the virus surface and it contains the binding site for the cellular receptor and major neutralizing domain.

However, the external protein and part of p17 have also been reported to be sensitive to neutralizing antibodies.

2.2 Cellular Receptors

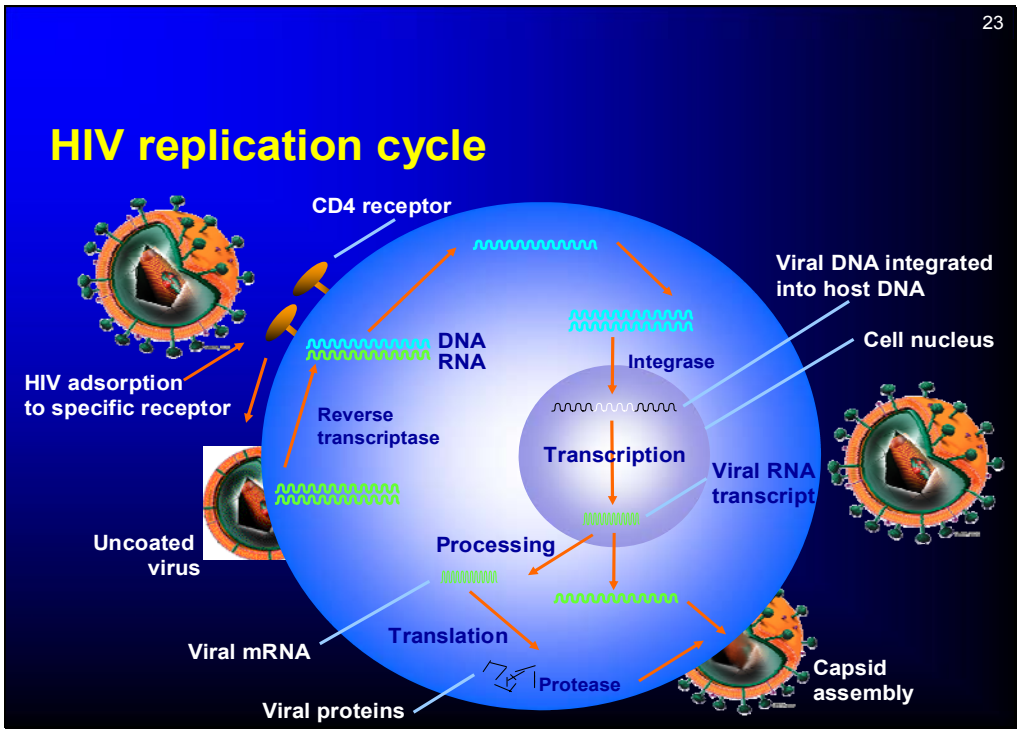
The primary receptor for HIV is the CD4 molecule on the human T-helper cells. However, recent advances in genetics of infectious diseases have shown that human genetic variation might influence susceptibility to pathogenic organisms. Variation in CD4 receptor molecule on T-cell surface may influence the ability of HIV to bind and eventually penetrate the target cell. In addition, attachment to and fusion with the target cells is determined not only by its binding with CD4 molecules, but also other secondary binding sites known as β-chemokine such as CCR5 and CXCR4. There are several reports to show that individuals who are homozygous for a deletion in the CCR5 or CXCR4 gene are less frequently infected with HIV, whereas individuals who are heterozygous for the same mutation become infected but can be protected against rapid progression to disease compared with infected individuals homozygous for the normal CCR5 or CXCR4 gene.

2.3 Replication

Replication of the virus particle begins with attachment of gp120 to the CD4 on the surface of a target cell. Following the gp120-CD4 binding, a structural change allows for the interaction of the V3 loop region in the gp120 with a chemokine receptor, including CCR5 and CXCR4.

The reaction with the co-receptor results in another conformational change in the viral surface glycoprotein, which exposes a fusion domain contained within the envelope trans-membrane glycoprotein. Exposure of the fusion domain results in the insertion of the gp41 into the cellular membrane. Subsequent to the fusion event, the viral core is released into the cytoplasm of the host cell. Once in the cytoplasm, the viral RNA genome is uncoated and reverse transcribed by the virally encoded Reverse Transcriptase (RT) enzyme to generate a double-stranded viral DNA pre integration complex. The double stranded DNA is then transported into the host cell nucleus and, via catalysis by integrase, becomes integrated into the host cell chromosome, where it resides as provirus. Once the viral genome has been integrated into the host cell genome, it can remain in a latent state for many years or can begin the production of new viral RNA. If the host cell is activated, the host cell enzyme RNA polymerase II will transcribe the proviral DNA into messenger RNA (mRNA). The mRNA is then translated into viral proteins that undergo extensive post-translational modifications. The viral RNA becomes the genetic material for the next generation of viruses. Viral RNA and viral proteins assemble at the cell membrane. After proper assembly and processing, new infectious virus particles are released by budding from the cell membrane.

Figure2.3: HIV Replication Cycle



2.4 Variability of HIV Isolates

The human immunodeficiency virus exhibits marked genetic diversity among different isolates. This heterogeneity is distributed throughout the viral genome and most of it is located in the env gene. Based on this variability, HIV has been classified into types 1 and 2. HIV-1 has a global distribution while HIV-2 is limited to West Africa. Nevertheless, HIV-1 is still the predominant type in this sub-region. The 2 sub-types of the virus also vary in their biological characteristics. The rate of transmission (sexually and MTCT) as well as progression to disease of HIV-1 is faster than that of HIV-2.

HIV-1 isolates are classified into subtypes using the nucleotide sequence of the gag, pol and env genes. Subtypes of HIV-1 isolates using the env gene has been based mainly on the third variable region (V3 loop) of the Gp120, known to be important in viral cell type tropism, virus cell-fusion and cytopathology. Based on the nucleotide of the V3 loop of the Gp120, HIV-1 has been classified into three major groups, the group M (major), N (non-M, non-O) and group O (Outlier). The group M virus has been further classified into at least 11 different subtypes (A to K). In addition, recombination of the virus subtypes is a well known

phenomenon and many recombinant forms including the A/G which is the most predominant subtype in West Africa have been identified. In Nigeria, the A/G and the G subtypes are predominant. HIV-2 is classified into 5 subtypes, A-E and recombinant forms have not been identified.

Co-infection or super-infection of an individual by HIV-1 and HIV-2 has been well documented. Infection of an individual with different HIV-1 and HIV-2 subtypes has also been reported.

2.5 Natural History of HIV Infection

The course of HIV infection varies within a population. Nonetheless, a typical infection can be divided into three stages: primary infection, asymptomatic infection, and symptomatic infection, or AIDS. Before the wide spread use of viral load assays, the CD4+ cell count has been used extensively as a surrogate marker for HIV disease progression. In Nigeria, CD4+ cell counts in healthy individuals have been found to range from 324mm^3 to 1160/mm^3 of blood (Audu et al, 2007). In Western countries, the mean value has been reported to be 1,000/mm^3 to 1,100/mm^3. Thus, constant exposure to a number of other pathogens in sub-Saharan Africa may result in an overall less healthy immune system with which to fight HIV infection. Following primary HIV infection, the CD4+ cell count decreases, while HIV RNA rises to high levels. With sufficient exposure to viral antigens, cytotoxic T-lymphocyte responses are generated and the HIV viral load typically declines to an equilibrium known as a virologic “setpoint,” which occurs within 6 to 12 months of initial infection. Once this viral setpoint is reached, the CD4+ cell count may rebound again marginally, although it does not often return to baseline values. Concurrent with these events are clinical manifestations of acute HIV infection in 30% to 60% of people. About half of newly infected people experience flu-like symptoms; the remainder are asymptomatic.

Once infected, humans experience an asymptomatic clinical latency that lasts 2 to 10 years, during which HIV is produced and removed by the immune system, and CD4+ T cells are killed and replaced. During this asymptomatic period, the number of infected circulating CD4+ cells and free virions is relatively low. Moreover, the haematopoietic system is able to replace most T cells that are destroyed, thus keeping the CD4+ cell counts in the normal range (800 to 1200/mm^3 of blood). Later in infection, replicating virus disrupts the follicular dendritic cells’ architecture. Viruses are no longer retained in the lymph nodes; thus, the circulating levels of free virus increase. Eventually, the circulating CD4+ T cell levels fall to

less than 500/mm^3 and opportunistic infections may occasionally occur. During the later stage of infection, the CD4+ cell count declines to below 200/mm^3, a level at which the infected individual is said to have developed immunological AIDS. A number of opportunistic infections—including oral candidiasis and recurrent tuberculosis are common during the early symptomatic phase of AIDS. As the CD4+ cell count declines to an even lower level, additional life-threatening opportunistic infections such as herpes zoster, amoebiasis, and dermatomycoses may occur with increasing frequency. In the later stages of symptomatic HIV infection, the viral load levels rise again.

Quantitative PCR methods, commonly described as viral load assays, have shown that:

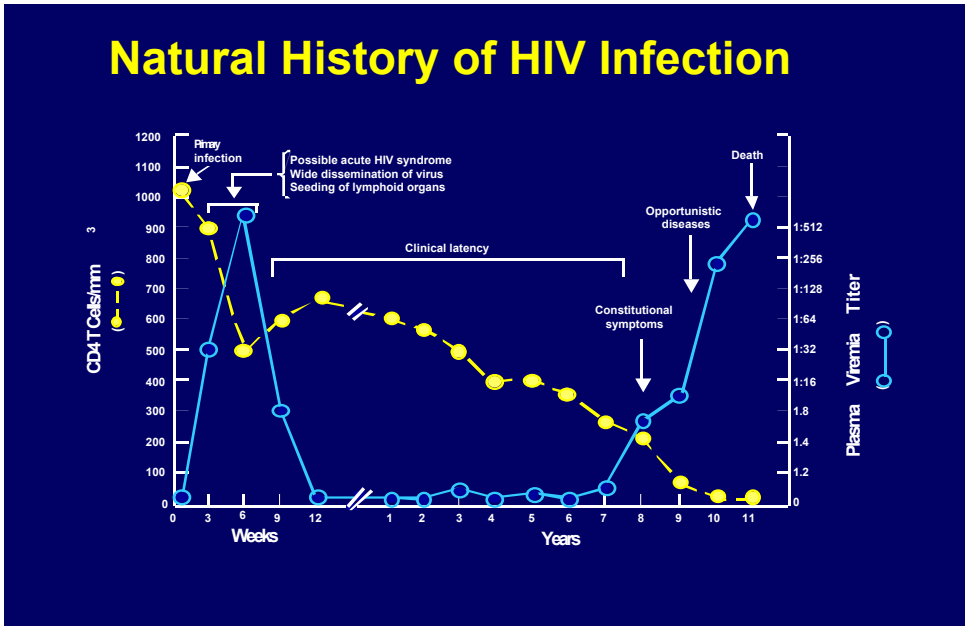
I. Continuous replication of HIV occurs in nearly all infected individuals, although the rates of virus production vary by as much as 70-fold in different individuals;
II. The average half-life of an HIV particle/infected cell in vivo is 2.1 days. Recent reports have suggested an even faster turnover of plasma virus of 28 to 110 per minute;
III. Up to 10^9–10^{10} HIV particles are produced each day; and
IV. An average of $2x10^9$ CD4+ cells are produced each day.

Thus, there is a very dynamic situation in HIV-infected people involving continuous viral replication and destruction and replacement of CD4+ cells. While the CD4+ cell count is a less expensive and less technical measure of HIV disease progression, quantifying the viral load is currently the most direct measurement of the HIV disease process. It has also been used to assess the risk of disease progression and the response to antiretroviral therapy (ART). As the disease progresses, CD4+ cell count declines but may rebound if therapy is efficacious; however, this parameter alone is an incomplete marker for clinical assessment of a patient. Nevertheless, in resource poor settings (which include a large proportion of the most affected countries), the CD4+ cell count is a more affordable and hence more practical yardstick for monitoring disease progression and ART efficacy.

Table 1: CD4 count at varying stages of HIV disease progression

Stage of disease	CD4 cell count
Acute sero-conversion syndrome	> 1000/mm^3 (Value sometimes drops at this stage)
Early disease	> 500/mm^3
Middle-stage disease	200–500/mm^3
Late disease	50–200/mm^3
Advanced disease	< 50/mm^3

Figure 2.4: Dynamics of Virus and CD4+ T lymphocytes Levels Over the Course of an Untreated HIV Infection



SECTION 3: LABORATORY DIAGNOSIS AND HIV COUNSELLING AND TESTING

3.1 Laboratory Diagnosis of HIV Infection

Laboratory diagnosis of HIV infection is based on the demonstration of antibody in plasma or serum, and of virus in the blood. The virus can be demonstrated in the blood with nucleic acid-based tests (PCR for proviral DNA and RT-PCR for plasma viral RNA), culture and p24 antigen assay. With the technology that is available at present, HIV antibodies are detectable within four to six weeks of infection, and within 24 weeks in virtually all infected individuals. However, virus can be detected in plasma at least one week earlier. This period of absent antibody in the presence of virus in plasma is called the "window period".

3.1.1 Antibody Assays

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

- **Rapid Tests**

  Rapid tests are suitable for use in laboratories that have limited facilities and process few samples. They are technically simple to perform, do not require any major equipment, but have a sensitivity and specificity comparable to ELISA. The commonly used rapid antibody tests in laboratories are based on the principles of dot immunoassay, or particle agglutination (e.g. gelatin or latex).

- **Enzyme linked immunosorbent Assay (ELISA)**

  The ELISA procedure is carried out to screen for HIV IgG antibodies in plasma or serum. The principles of ELISA are classified as direct, competitive and sandwich test. The competitive principle is not popular because of the low sensitivity. Antigens derived from HIV grown in human T-lymphocytes or recombinant proteins or synthetic peptides are used to coat beads or microtitre plates.

  To perform an ELISA, the patient's serum is incubated with the antigens on the beads or in the microtitre plates. A conjugate, i.e., enzyme-labelled antibody specific for human immunoglobulin is then added. Detection of the enzyme-labelled antibody is

carried out by the addition of a substrate that produces a colour reaction. ELISA requires a plate washer and an ELISA Reader and printer. It is a suitable test for use in the laboratories where large numbers of samples are tested each time.

- **Western Blot**

  Western blot is the standard confirmatory test for HIV antibody assays. The test utilizes HIV antigens from purified viruses that have been electrophoretically separated and "blotted" (transferred) onto a nitrocellulose paper. The paper is then cut into strips, each containing all the separated HIV antigens. To carry out a Western blot assay, a strip is incubated with the patient's serum. Antibody in the serum binds to the HIV antigens on the strip, and is detected with the aid of a conjugate consisting of labelled anti-human immunoglobulin.

  This assay is very expensive and can under some conditions, produce a relatively large number of indeterminate results. Studies have shown that combinations of ELISAs or rapid assays can provide results as reliable as the Western blot at a much lower cost.

- **Indirect Immunofluorescent Antibody Assay (IFA)**

IFA employs HIV-infected cells (lymphocytes) fixed to the microscope slide. The patient serum is added and reacts (if antibody is present) with the intracellular HIV antigen. After washing the slide, a conjugate consisting of anti-human immunoglobulin labelled with FITC is added, and the reaction is visualized under a fluorescent microscope. IFA has been used to confirm diagnosis in sera producing indeterminate results in Western blot.

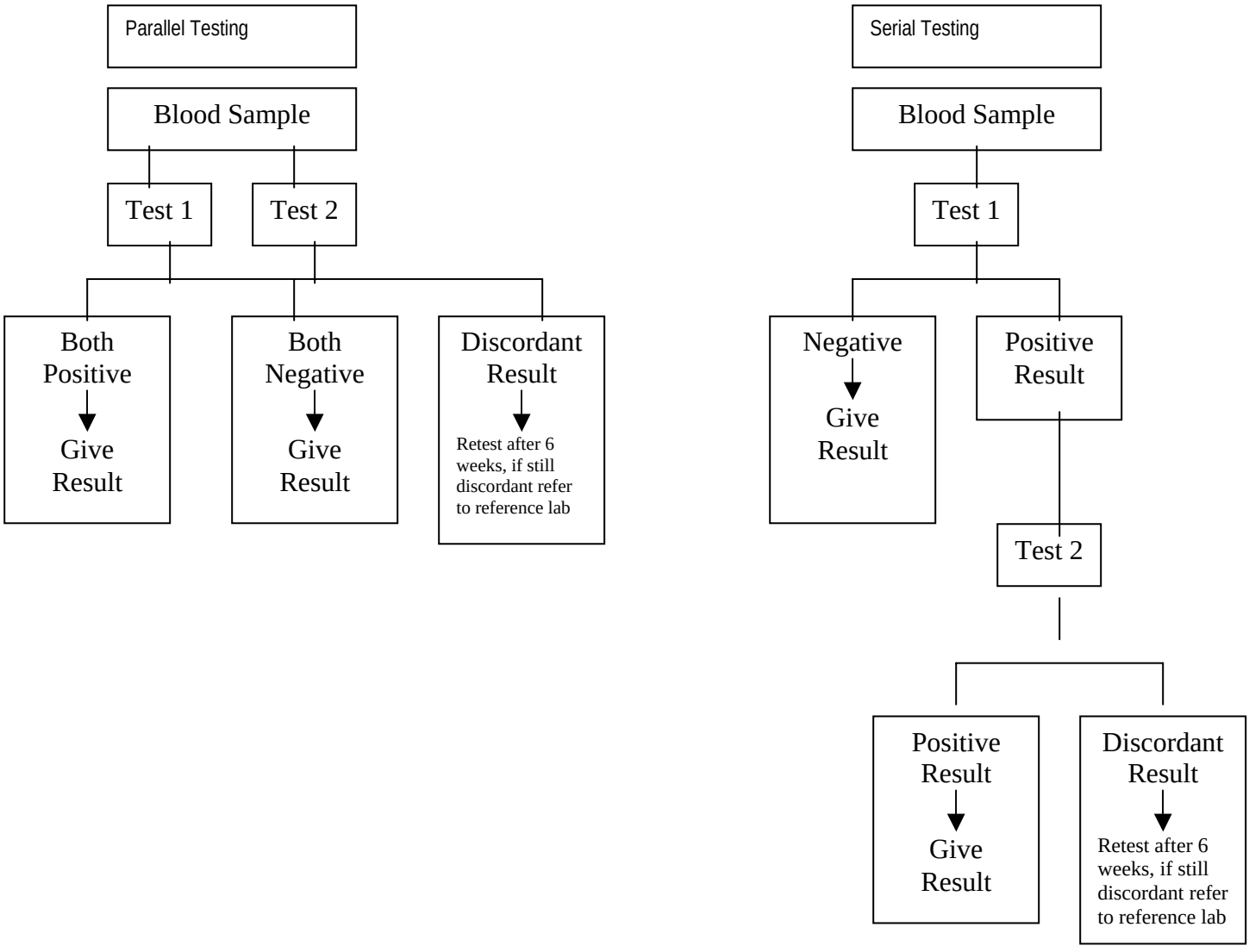
Serial testing refers to the use of 2 screening tests employed sequentially to test for HIV antibody. If the initial screening is negative, no further testing is required. If the initial test is positive, it is followed by one more test. The first test should be the most sensitive test and the second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

Parallel testing involves the use of two screening tests performed simultaneously. Samples reactive to both tests are regarded as positive. However, those with discordant results require further testing. Parallel testing is performed to minimize the chances of false

negative results and to guard against technical errors. It is often used when a very sensitive test is not available for the initial screening, and when the concordance of two tests is to be evaluated.

The WHO in 2004 recommended either a serial or parallel double rapid testing protocol in order to scale up VCT and enhance access to ARV in resource-limited countries as illustrated below:

Figure 3.1 PARALLEL VERSUS SERIAL TESTING ALGORITHM (WHO, 2004)



3.1.2. Nucleic Acid-based Tests

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

- **HIV DNA Polymerase Chain Reaction**

The DNA PCR involves the amplification of specific DNA sequences in the proviral DNA that has been integrated in the host cell. This test is the preferred procedure for diagnosing HIV infection in infants less than 18 months of age. Because of the high sensitivity of the test, false positive results may occur as a result of contamination by minute quantities of extraneous DNA.

- **RT- PCR**

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

3.1.3. Other Tests

These tests are not routinely used for laboratory diagnosis of HIV infection.

- Antigen detection: Detection of p24 antigen is an ELISA-based test. The reliability of the test is in doubt because of specificity and sensitivity problems.

- Virus isolation: HIV is usually isolated in PBMCs. The procedure involves co-cultivating the PBMCs from a patient with those obtained from a healthy donor. HIV isolation in PBMC is quite sensitive and is comparable to DNA PCR in sensitivity.

3.2 National Testing Algorithm

Presently, some laboratories use the serial test algorithm while others use the parallel algorithm. For both algorithms, non-cold chain dependent rapid test kits are recommended for use in areas where cold storage facilities are inadequate. Cold chain-dependent and non-cold dependent kits could be used in places where there is good cold storage. The current interim National testing algorithm recommends parallel testing.

Upon referral, discordant results are resolved at the secondary or tertiary level laboratories with a variety of tests including double parallel rapid tests, OR double parallel ELISA, OR one rapid test and one ELISA and Western blot.

3.3 HIV Counselling and Testing (HCT)

During the past 15 years, the introduction of effective ART and its demonstrated medical benefits has shown the usefulness and importance of expanding HCT services to facilitate early diagnosis and treatment of HIV-infected persons. It has also been shown that early knowledge of HIV infection can result in tremendous public health benefits through decreasing risk behaviours that could transmit HIV to uninfected persons. Furthermore, uninfected persons may benefit from HIV testing if knowing their HIV status assists them in modifying or reducing risk behaviours.

All patients undergoing HIV testing must receive pre- and post-test counselling, and give their consent before the test is performed on their specimens. Post-test counselling should be done irrespective of the test result. Testing may be performed without consent if the patient is unable to give his/her consent and the test result is needed in an emergency to provide medical care.

A high level of confidentiality must be maintained during testing. Careful record keeping is essential to ensure confidentiality.

HCT includes counselling and testing in a variety of settings. Traditional Voluntary Counselling and Testing (VCT), provider-initiated counselling and testing, and opt-out counselling and testing are examples of HCT methods. VCT is a client-initiated approach by an individual to find out his HIV status and in the process receive counselling. Provider-initiated counselling and testing is done based on the recommendation of the care provider to the client. The opt-out approach occurs where HCT is routinely offered with the patient having the option to decline testing and is utilized in the health care setting to capture all patients presenting for other health care services. HCT should be considered whenever there is care provider/patient contact.

3.3.1 Benefits of HCT for the individual include:

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

3.3.2 The benefits of HCT for the public health of the nation include:

- Reduced transmission following increased knowledge of HIV status
- Reduced stigmatization as a result of widespread counselling services
- Improved health and productivity of PLWHA as a result of utilization of care, support, and ART services.

HCT is being rapidly scaled up using innovative, ethical and practical approaches. Services can be provided at free-standing, mobile, primary, secondary, and tertiary facilities. These facilities must meet national minimum standards for HIV testing applicable to their various levels. Category 1 Laboratories will carry out voluntary counselling and testing using rapid kits. In the case of free-standing, mobile, and primary facilities, referral of seropositive individuals to secondary or tertiary facilities for pre-assessment for ART should be done.

SECTION 4: NETWORK AND REFERRAL SYSTEM

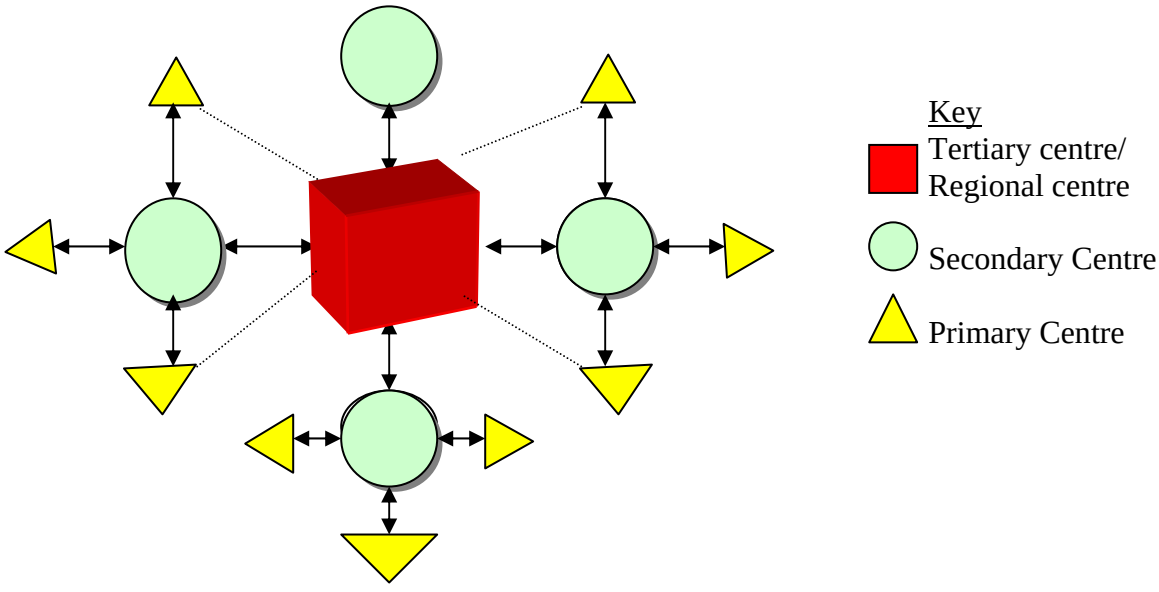
There has been an unprecedented scale up of services in recent times and an accompanying advancement in both technology and protocol for provision of ART services, with an associated need for care services as well as laboratory support to guide treatment of clients. This has created the need to devise appropriate modalities to ensure that available resources are properly leveraged and clients are able to access the complete package of care irrespective of what tier of service they are situated in.

A network model of care has been identified as the most appropriate and cost effective approach to adopt to help achieve this goal in all spheres of HIV programming and services.

4.1 Definition

Referral is the process by which immediate client needs for treatment, care and supportive services are assessed and prioritized, and clients are provided with assistance in accessing services. Referral should also include follow-up efforts necessary to facilitate initial contact with treatment, care and support service providers. Case management is generally characterized by an ongoing relationship with a client that includes comprehensive assessment of medical and psychosocial support needs, development of a formal plan to address needs, substantial assistance in accessing referral services, and monitoring of service delivery. Clients should be referred to services that are responsive to their priority needs.

Figure 4.1 Hub and Spoke Network Model between Levels of Care



4.2 The Hubs

The regional and/or tertiary centres are to serve as the hubs in the model (Fig 4.1). These centres of excellence currently serve as domicile points for specialized services such as laboratory (discordant screening confirmation, hepatitis B and C screening, viral load testing, DNA PCR etc) and care and treatment associated with complications of HIV infection. In the model, the regional and/or tertiary centres will continue to provide these specialized services but will have established linkages with several secondary facilities within a network where patients and or laboratory samples can be referred to for specialized testing and services when the indications for such arise.

4.3 The Spokes

In the model the secondary facilities serve as spokes from the tertiary facilities and at the same time serve as hubs for the primary level of care. They will provide a different level of specialized services like blood chemistries, haematology, microbiology, and chest X-rays. They will also have clearly defined pathways to tertiary centres when further treatment, care and laboratory support is indicated.

With the scale up of HIV services to the primary health care level and private health institutions/faith-based facilities in communities, basic treatment, care and laboratory support will be available to patients and families in their communities. Services that may be provided at this level include HCT, adherence counselling, treatment of opportunistic infections (OIs) and appropriate linkages back to secondary and/or tertiary care services as needed.

The routine referral channel is primary to secondary and secondary to tertiary and vice versa. There may be situations, however, where the primary may refer directly to the tertiary, or the tertiary may refer directly to the primary. This may be the case in certain geographical situations (e.g. closer proximity of primary to tertiary), certain staffing situations (e.g. manpower limitations and clinic capacity), and special laboratory needs (e.g. indeterminate screening results). This is depicted with the broken lines in the figure above.

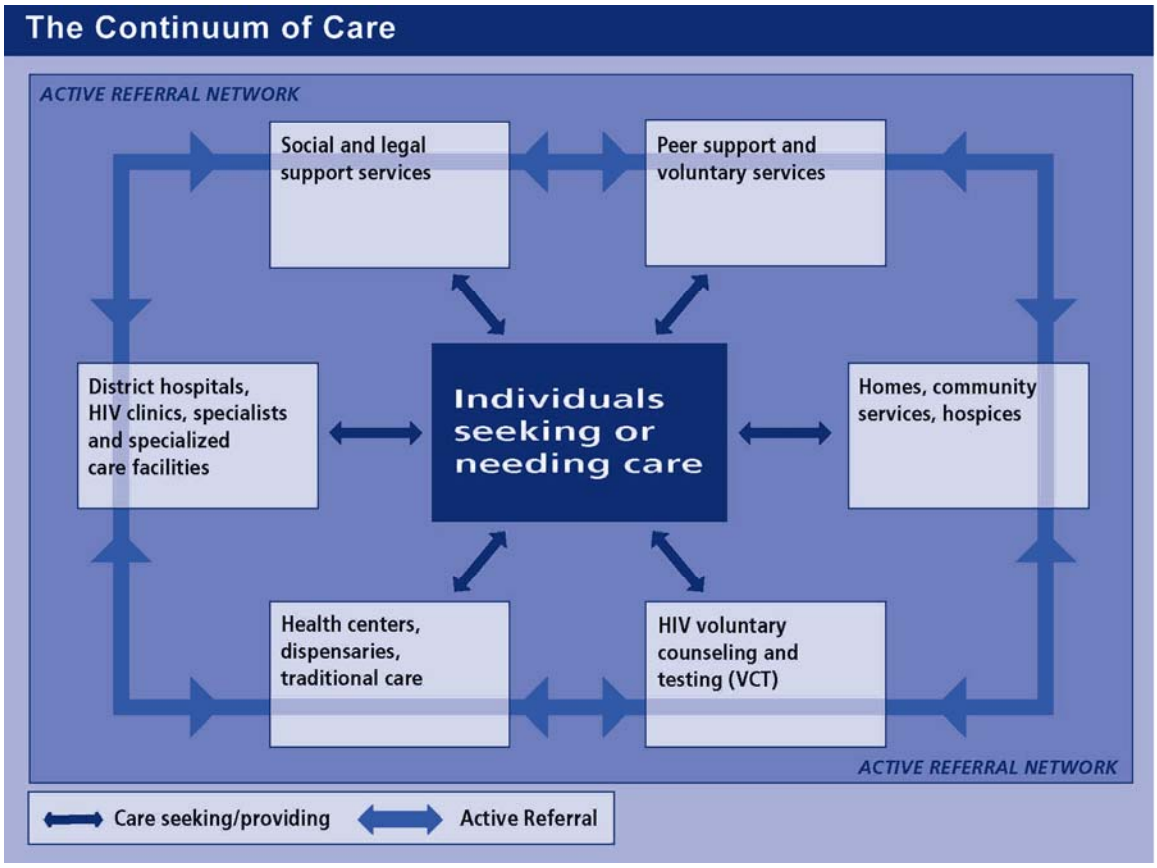
To ensure easy movement of patients and samples along this pathway, strong linkages must be developed between the various levels of care. Clearly defined procedures for referral up or down the levels of care are to be developed to ensure appropriate patient access to

services and decreased loss to follow up. There must be standardized patient referral and tracking tools for proper management.

4.4 Patient Linkages to Support Services within and Outside of the Health Care Setting

The following diagram depicts the variety of services provided to PLWHA and their families by the different caregivers and service providers. The recognition of needed services offers prompt access by PLWHA and their families to these services. It is premised on a functional referral system at all levels of care as described above with linkages and partnerships, requiring the care-providers to have a working knowledge of the locations of other needed resources and services.

Figure 4.2



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

4.5 Typical Referral Needs

Clients should be referred to services that are:

- responsive to their priority needs
- appropriate to their
  - culture,
  - language,
  - spirituality,
  - gender,
  - sexual orientation,
  - age,
  - developmental level

4.5.1 Prevention case management.

This provides prevention counselling, follow up and subsequent referral where necessary for clients with needs that affect their ability to adopt and sustain positive behavioural change with a view to reducing their risk for acquiring and/or transmitting HIV infection. This can be achieved at all levels of care and at the HCT centres.

4.5.2 Medical management services.

This will include provision of medical services for HIV-infected clients for the purposes of:

- Evaluation of immune system function and screening
- Prevention and treatment for opportunistic infections and HIV related conditions
- Early identification of communicable diseases such as TB, STIs, and hepatitis and appropriate referral of such clients for treatment. This will be handled by the primary, secondary and tertiary levels of care.

4.5.3 Partner counselling and referral services (PCRS).

Persons with HIV-positive test results should receive or be referred to services to help them notify their partner(s) regarding their HIV sero-status and how to encourage their spouse to access counselling, testing and referral (CTR) services.

4.5.4 Reproductive health services

Female clients who are pregnant or of childbearing age should receive or be referred for reproductive health services. HIV-infected pregnant women will require the provision of education, prevention counselling and PMTCT services according to national guidelines.

4.5.5 Drug or alcohol prevention and treatment.

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

4.5.6 Mental health services

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

4.5.7 Social/Legal support services

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

4.5.8 Other HIV prevention and support services

Other client needs may be addressed through other HIV prevention and support services such as education materials, support with housing, food, employment, transportation, child care, domestic violence, and legal services. Peer support and voluntary services are essential in this regard. Addressing these needs can help clients access, accept and adhere to medical services offered. It also helps them in the adoption and maintenance of positive attitudinal and behavioural change with a view to reducing the risk for HIV acquisition and transmission.

4.6 Private Sector Involvement

4.6.1 Definition and scope of private sector involvement

The private sector is a dominant stakeholder and includes private health practitioners, FBOs, NGOs, corporations/industries, and individuals. Private sector collaboration is essential because patients access care in both private and public facilities. Services provided by the private sector will cover HCT, PMTCT, ART, Palliative care, training, provision of micro finance, food security, etc. Private sector participants should display the type of services provided within the facility

4.6.2 Criteria for Private Sector participation

Private sector participants should fulfil the following criteria:

- Register service with NASCP
- Adopt a unified M & E plan including use of standardised tools for data collection and data obtained must be reported to the highest national M & E body REGULARLY as prescribed by the coordinating body.
- Promote and display government regulations on exemption from fees relevant to HIV/AIDS
- Be open to regular inspection and visitation by appropriate bodies
- Ensure training and re-training of staff
- Have a minimum package of available services

Table 4.1 Minimum Package of Care and Health Care Level

Primary level	**Secondary level**	**Tertiary level**
• HCT/Haemoglobin (Hb) determination • Treatment of OIs • Psycho-social counselling • HBC • Nutritional support • Palliative care • HIV care (pre-ART) • M & E • Linkage to secondary level	• HCT/Hb determination • E & U, Creatinine • CD 4 count estimation • ART • Treatment of OIs including TB • Training • Adherence counselling • M & E Linkage to tertiary level	• HCT/Hb determination • E & U, Creatinine • CD 4 count estimation • ART • Treatment of OIs including TB • Training • Adherence counselling • M & E Viral load

SECTION 5: ANTIRETROVIRAL THERAPY

5.1 Pre-treatment Evaluation

This includes:

- Complete history and physical examination (always think of Pregnancy, Anaemia, Hepatitis and TB)
- Clinically and Immunological classification of the patient
- Check Laboratory results (FBC with differential, ALT, Creatinine, CD4+ cell count, pregnancy test*)
- Evaluation of nutritional and psychosocial status
- Assessment of readiness for therapy
- Development of patient-specific adherence strategy

* In women of child-bearing age where EFV is being considered

5.2 Criteria for Initiation of ART

Initiation of therapy depends on CD4+ cell count and WHO clinical staging

- WHO Stage IV disease irrespective of CD4+ cell count
- WHO Stage III disease with CD4+ cell counts < 350/mm^3
- WHO Stage I or II disease with CD4+ cell counts ≤ 200/mm^3
- Any WHO Stage with CD4+ cell count 200-350 mm^3 – consider for therapy

5.3 Counselling for ART

There are many patients who know their HIV sero-status through VCT and other testing services but are yet to consider starting ART V. However, when a decision is reached to commence ART, additional counselling is required to address the following issues:

- ARVs do not offer a cure. HIV may be suppressed but is not eradicated from the body
- Use of ARVs is associated with improved quality of life and long term survival
- ARVs need to be taken daily for life to prevent development of resistance and treatment failure

- ARVs, like other medications, are associated with side effects
- Better results are obtained with good adherence to the treatment regimen
- Some patients may fail to respond to treatment and may require changes in their treatment regimen.

These issues should be thoroughly discussed by the counsellor 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.

5.3.1 Counselling for ART in Adolescents

It is not uncommon that children below the age of consent (<18 years) who are sexually active acquire HIV infection and present for care. This situation is different from those children who acquired HIV infection through vertical transmission. The common dilemma is when and how the parents or guardians should be informed. This is more difficult when the child does not want disclosure to parents/guardians but would like to benefit from ART and is willing to have an HIV test.

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 counsellor to discuss with the adolescent about the need to involve the parents/guardians
- Additional counselling time should be given to the adolescent to allow for deep understanding of the implications of ART

5.4 Information for patients before or when starting ART (in the language best understood by the patient)

- Discuss the goal of therapy with the patient emphasising the need to reduce the viral load to an undetectable level
- Emphasise that the chance of being able to achieve this within a six-month period is dependent on adherence to recommended dosage/regimens and instructions such as frequency of intake and dietary advice..
- Discuss common side effects of the ARVs with the patient, emphasising that not all patients will experience such side effects and that many of the side effects may not necessarily result in discontinuation of therapy.

- Highlight the necessity for regular monitoring, particularly to detect toxicities and ensure the efficacy of the regimens.
- Explain that many of the ARVs interact with other medications. The patient should be encouraged to discuss non-prescribed drug intake (including traditional medicines) with his/her care giver before taking them.

5. 5 Classes of ARV

There are 4 classes currently available for treatment .based on the site and mechanism of action. (Table 5.1 – 5.7) Other classes are at various stages of development but are not yet widely available for clinical use.

Different classes and their mechanisms of actions

- Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs) such as nevirapine and efavirenz stop HIV production by binding directly onto the reverse transcriptase enzyme thus preventing the transcription of viral RNA to DNA.
  A recent addition to this class, etravirine is expected to be available for use soon.
- Nucleoside Reverse Transcriptase Inhibitors (NRTIs) incorporate themselves into the DNA of the virus, thereby stopping the building process. The resulting DNA is incomplete and cannot create a new virus.
- Nucleotide Reverse Transcriptase Inhibitors (NtRTIs) act at the same stage of the viral life cycle as the NRTIs, but do not require to be phosphorylated in-vivo for effective antiretroviral activity.
- Protease Inhibitors (PIs) work later in the virus reproduction cycle. They prevent HIV from being successfully assembled and released from the infected CD4+ cell.
- Some of the new classes include the Entry Inhibitors which prevent the virus from gaining access into the cytoplasm of the T-cell. There are 3 categories of these inhibitors:
  - ❖ The chemokine receptors antagonists which bind to CCR5 or CXCR4 on the T cell surface and thereby prevent viral attachment to these co-receptors. This class includes Maraviroc
  - ❖ Attachment inhibitors which inhibit interaction between gp120 and the CD4+ molecule
  - ❖ Fusion inhibitors which bind to viral gp41 and prevent the virus from penetrating the T-cell membrane.

- Newer classes in different stages of development include Integrase Inhibitors which prevent the integration of viral DNA into the T-cell DNA and Maturation Inhibitors which prevent a late stage of processing of the viral GAG protein, thereby interfering with viral assembly

Table 5.1: Classes of ARV drugs

Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs)	Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	Fusion Inhibitors	Protease Inhibitors (PIs)
Zidovudine (ZDV) Didanosine (ddI) Stavudine (d4T) Lamivudine (3TC) Abacavir (ABC) Emtricitabine (FTC) Tenofovir (TDF)	Nevirapine (NVP) Efavirenz (EFV)	Enfuvirtide(T-20)	Saquinavir (SQV) Ritonavir (RTV) {as pharmacoenhancer} Indinavir (IDV) Nelfinavir (NFV) Amprenavir (APV) Lopinavir-ritonavir (LPV/r) Atazanavir (AZV) Tipranavir Fosamprenavir(FPV) Darunavir

Table 5.2: ARVs currently registered with NAFDAC

Class	Drug name	Strength	Manufacturer
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)	Zidovudine (ZDV)	Tabs 300mg	Ranbaxy, Glaxo, Fidson, Sai Mirra, Aurobion
		Caps/tabs 100mg	Glaxo, SmithKline, Ranbaxy, Boeringer
	Lamivudine (3TC)	Caps 150mg	Pharmacare, Ranbaxy, Glaxo, Sai Mirra, Cipla, Emcure, Aurobion, Strides, Hetero, Fidson
	Lamivudine (3TC)	Caps 100mg	Glaxo
	Abacavir (ABC)	Tabs 300mg	M & B, Evans, Ranbaxy, Glaxo
	Tenofovir (TDF)	Tabs 300mg	Patheeneen
	Didanosine (ddI)	Tabs 50mg	Bristol Myers
		Tabs 100mg	Ranbaxy
		Tabs 150mg	Bristol Myers
		Tabs 200mg	Ranbaxy, Bristol Myers
	Stavudine (d4T)	Caps 20mg	Bristol Myers
		Caps/tabs 30mg	Ranbaxy, Cipla, Aurobindo, Strides, Fidson, Bristol Myers
		Caps/tabs 40mg	Pharmacare, Ranbaxy, Cipla, Emcure, Hetero, Aurobindo, Strides, Fidson, Bristol Myers
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	Nevirapine (NVP)	Tabs 200mg	Evans, Cipla, M & B, Ranbaxy, Emcure, Strides, Aurobion, Hetero, Boeringer, Fidson
	Efavirenz (EFV)	Caps 200mg	Janssen (Ranbaxy), Emcure, Hetero, Cipla, Merck
		Caps 600mg	Ranbaxy, Aurobion, Emcure, Hetero, Cipla, Fidson

Class	Drug name	Strength	Manufacturer
Fixed dose combinations (NNRTI/NRTI)	ZDV+3TC+NVP	300mg+150mg+200mg	Cipla, Pharmacare, Ranbaxy, Aurobion, Fidson, Hetero, Plethico
	ZDV+3TC	Tabs 300mg+ 150mg	Drugfield, Evans, Ranbaxy, Meditab, GSK, Cipla, Strides, Aurobion, Emcure, Fidson, Hetero
	3TC+ZDV+EFV	150mg+300mg+600mg	Aurobion
	ABC+ZDV+3TC	Tabs 300mg+300mg+150mg	Ranbaxy, Glaxo
	3TC + ABC	Tabs 80mg+600mg	Glaxo
	TDF + FTC	Tabs 300mg+200mg	Patheon
	d4T+3TC+NVP	Tabs 30mg+150mg+ 200mg	Archy, Cipla, Hetero, Aurobion, Strides, Ranbaxy, Fidson
	d4T+3TC+NVP	Tabs 40mg+150mg+ 200mg	Cipla, Hetero, Strides, Ranbaxy, Fidson, Yangzhou
	d4T+3TC+EFV	Tabs 30mg+150mg+600mg	Ranbaxy, Emcure
	d4T+3TC+EFV	Tabs 40mg+150mg+600mg	Ranbaxy, Emcure, Govt Pharma/Daveon
	d4T+3TC	Tabs 30mg +150mg	Ranbaxy, Cipla, Strides, Fidson
		Tabs 40mg +150mg	Ranbaxy, Cipla, Strides, Fidson
		Tabs 20mg+150mg	Aurobindo
Fixed dose combinations (NRTI/PI)	ZDV+3TC+ Indinavir	Caps 200mg+150mg+40mg	Gosun

5.7 Strengths and usual adult dosing of ARV drugs

Table 5.3 Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

Drug	Strength/Preparation for adults	Adult dosing	Comments
Didanosine (ddI)	25mg, 50mg, 100mg, 150mg, 200mg 250mg 400mg tablets	400mg OD, unless weight is <60kg then 250mg	Antacid containing tablets to be chewed thoroughly, crushed or dispersed in water; tablets should be taken at least 1 hour before food or on an empty stomach
Lamivudine (3TC)	100mg, 150mg tablets	150 mg BD or 300mg OD	May be taken 300mg OD as prescribed by physician
Emtrcitabine (FTC)	200mg	200mg OD	Closely related to 3TC and should not be co-administered with it
Stavudine (d4T)	30mg tablets	30 mg BD,	Not to be used with ZDV. Syrup/suspension needs to be refrigerated and shaken well before use.
Zidovudine (ZDV)	100mg capsule, 300mg tablets	250 – 300 mg BD	Use with caution in the setting of anaemia. Increased toxicity possible when used with other drugs that are associated with bone marrow suppression. Should not be administered in combination with d4T.
Abacavir (ABC)	300 mg tabs	300 mg BD or 600mg OD	Causes hypersensitivity reaction (HSR), which can be fatal; never re-challenge the patient. Educate patient on HSR
Tenofovir (TDF)	300 mg tab	300mg OD	Caution should be taken in renal impairment and renal function (in particular plasma creatinine) should be monitored.

Table 5.4 Non Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Drug	Strength/ Preparation for adults	Adult dosing	Comments
Efavirenz (EFV)	200mg, 600mg capsule	600mg OD or 800mg OD when co-administered with rifampicin in a patient weighing > 60kg	Contraindicated below 3 years of age and in early pregnancy
Nevirapine (NVP)	200mg tablet	200mg BD, always initiate 200mg OD for 2 weeks before giving full dose.	Increase incidence of severe hepatotoxity in women with CD4 count > 250cells/mm^3 and men with CD4 count > 400cells/mm^3. Other common reactions include skin rash.

Table 5.5 Protease Inhibitors (PIs)

Drug	Strength/Preparation for adults	Adult dosing	Comments
Atazanavir (ATV)	100, 150 and 200 mg capsules	300mg boosted with 100mg ritonavir OD	Asymptomatic hyperbilirubinaemia is common. May present with mild jaundice
Darunavir (DRV)	600 mg tabs	600mg with 100mg ritonavir BD	A newer PI effective against many PI resistant mutants
Fosamprenavir (FPV)	700mg film coated tabs	700mg boosted with 100mg ritonavir BD	Life threatening interactions may occur with tricyclic anti depressants. Caution must also be taken in patients with sulphonamide allergy
Indinavir (IDV)	200mg capsule	800mg + 100mg RTV BD	Administer 1 hour before or 2 hours after a meal; may be administered with low-fat, light meal; when given with Didanosine, allow 1 hour between the drugs (antacids in Didanosine reduce absorption of Indinavir)
Lopinavir/ritonavir (LPV/r)	Capsules: 133.3 mg lopinavir and 33.3 mg ritonavir [Heat stable formulation: 200mg LPV/50 mg r]	400mg LPV/100mg r BD	Lopinavir/ritonavir is extensively metabolized by hepatic cytochrome P450 3A. There could potentially be multiple drug interactions. Storage: Oral solution and capsules should be refrigerated, but can be kept at room temperature (up to 25^{o} C) if used within two months. Heat stable formulation that can be stored at room temp. is now available.

Nelfinavir (NFV)	250mg tablet 625mg tabs	1250 mg BD or 750mg TDS	Administer with or after food; powder may be mixed with water, milk, formula feeds or pudding; it should not be mixed with acidic foods or juices owing to its taste
Ritonavir (r, RTV) (with other PIs)	100mg capsule	100mg BD in most cases	Used only to boost other PIs except NFV. Cold chain must be secured for its transportation and storage
Saquinavir (SQV)	200mg gel filled capsule	1000mg + RTV 100mg BD	Administer with or after food
Tipranavir (TPV)	250mg caps	500mg +200mg ritonavir BD	Active against PI resistant HIV and has established efficacy in salvage regimen

5.7 Adverse drug reactions (ADRs) and their management

5.7.1 Drug-specific ADRs

Table 5.6 Common ARV Toxicities and their Management

Antiretroviral Drug	Primary toxicities	Minor toxicities	Monitoring/Management
Zidovudine (ZDV)	Haematological (Anaemia, Neutropenia, thrombocytopenia), myopathy, GI intolerance: Hypersalivation, Nausea and abdominal discomfort	Blue to black discoloration of nails, nausea and headache	For anaemia: • Change to d4T or transfuse • Do not use if Hb < 8.0 g/dl(PCV <24%) For myopathy: Discontinue if CPK rises
Lamivudine (3TC)	Pancreatitis, Liver toxicity Mild peripheral neuropathy	Skin rash, headache	Discontinue if serum amylase elevated. Restart when resolved or change to ABC

Stavudine (d4T)	- Peripheral neuropathy presenting with painful and peripheral sensations in the lower more than in the upper limb - Lactic acidosis with hepatic steatosis. This is worse when d4T is used in combination with ddI. - Peripheral fat atrophy Ascending motor weakness resembling Guillain-Barre syndrome may occur	Insomnia, anxiety, panic attacks	Periodic serum triglycerides should be monitored. Suspicion of lactic acidosis – measure serum lactate and/or anion gap and serum bicarbonate. At first signs of mitochondrial toxicity stavudine should be substituted
Emitricitabine (FTC)	Similar to lamivudine	Occasional hyperpigmentation	
Tenoforvir (TDF)	Nephrotoxicity	Bone demineralisation Occasional GI intolerance	If creatinine clearance declines substitute with a non nephrotoxic drugs such as ABC or adjust dosage. (See section on co-morbidities)
Didanosine (ddI)	Dose-related pancreatitis. Effect is worse when combined with hydroxyurea. Painful Peripheral neuropathy. Effect is worse if combined with d4T. Lactic acidosis (a class adverse effect) may occur.	Abdominal cramps, diarrhoea	Discontinue if neuropathy severe, raised serum amylase and transaminases

Abacavir (ABC)	Life-threatening hypersensitivity may occur in 3-9% of patients Lactic acidosis may also occur with/without hepatic steatosis		Discontinue therapy if hypersensitivity develops. Rechallenge of patient may be fatal – Abacavir should never be used in that individual again
Nevirapine (NVP)	Life-threatening skin rash (Stevens-Johnson syndrome) which occurs in less than 5% of patients and usually within 8 weeks of treatment DRESS syndrome (drug rash, eosinophilia and systemic symptoms) manifesting as fever, athralgia, etc.		Low-dose over first 2 weeks minimizes rash occurrence. If mild or moderate (Grade 1/2) continue cautiously or substitute with EFV. If severe discontinue NVP and permanently if hepatitis confirmed. Do not give as part of ART to women with CD4 >250 or men with CD4 >400 because of increased risk of severe hepatotoxicity.
Efavirenz (EFV)	- Mobiliform rash may appear but usually not life-threatening - CNS side effects occur in about 50% of patients (usually self-limiting) include: - Hallucinations - Insomnia - Abnormal dreams - Somnolence - Amnesia - Abnormal thinking - Confusion - Euphoria	Dizziness,	- Rash in 10% but rarely severe in <1%; CNS symptoms often resolve 2-4 weeks. Potentially teratogenic in primates and humans hence efavirenz should not be used in pregnant women or women who might become pregnant while on therapy.

	For these reasons, EFV is contraindicated in patients who already have psychiatric manifestations, nightmares, rash.		
Lopinavir/Ritonavir (LPV/r)	Diarrhoea, nausea, vomiting and skin rash	Headache, weakness	Diarrhoea rarely severe should be managed with antispasmodics – usually resolves after weeks to months of therapy
Nelfinavir (NFV)	Diarrhoea (seen in 10-30% of patients). Should be managed with agents as Loperamide Fat accumulation Hyperlipidemia and other class effects		- Diarrhoea occurs 10-30% at start of therapy but often resolves on its own. It should be managed with anti-spasmodic agents such as Loperamide.
Indinavir (IDV)	Class effects Class specific events Nephrolithiasis ± haematuria – occurs in 10-28% of patients. - Alopecia in hair-bearing areas	Headache, rash, retinoid-like effects, alopecia	Ensure adequate rehydration (1.5 L/day). Monitor liver enzymes
Saquinavir(SQV)	Class adverse effects	GI Intolerance, headache, increased transaminases	Antiemetic, monitor LFT
Amprenavir (APV)	- Class adverse effects - GIT intolerance (oral paraesthesia in 28% of patients)		Fosamprenavir is related to it and is used as its replacement.

	- Oral solution contains propylene glycol which may precipitate:
	  - Seizures
	  - Stupor
	  - Tachycardia
	  - Hyperosmolality
	  - Lactic acidosis
	  - Renal failure
	  - Haemolysis
	- Oral solution is contraindicated in children below 4 years
	- Oral solution should be changed to capsules as soon as possible		

Fosamprenavir (fAPV)	Class adverse effects	GI Intolerance, Skin rash 19%, increased transaminases	Antiemetic, monitor LFT
Tipranavir (TRV)	increased transaminases, (grade3), Class adverse reactions	GI Intolerance, nausea vomiting and diarrhoea	Antiemetic, monitor LFT
Darunavir(DRV)		GI Intolerance	Dyslipidaemia and raised transaminases appear not to be problem here.
Ritonavir (RTV)	- Class side effects - Perversion of taste - Circum-oral and peripheral paraesthesia - Hepatotoxicity Asthenia		Booster dose rarely causes these problems. With therapeutic dose the drug may have to be withdrawn

5.7.2 Class specific ADRs

Table 5.7 Classes of ARVs and Specific Adverse Drug Reactions

Class	Adverse Reactions
Reverse Transcriptase Inhibitors (NRTI)	- All NRTIs are capable of inhibiting mitochondria DNA polymerase enzyme, therefore all tissues that have DNA can be affected - It causes depression of haemopoiesis (on the bone marrow) leading to anaemia, leucopaenia and thrombocytopaenia, myopathy (muscles), and lypolysis (fat cells) resulting in fat atrophy - Though rare, prolonged usage may also affect myocardial cells resulting in cardiomyopathy - It may affect peripheral neurones, precipitating peripheral neuropathy, hepatic cells leading to hepatitis and the pancreas, causing pancreatitis - Different NRTIs have differing capacity to induce such complications
Protease Inhibitors (PI)	- Fat Redistribution Syndrome (lipodystrophy) Physical components of this include: - Fat accumulation within the abdominal cavity (protease paunch or crix-belly) - Fat accumulation in the upper back (dorso-cervical pad or buffalo hump) - Gynaecomastia in males, and fat accumulation in the breast in females - Fat accumulation in subcutaneous tissue (peripheral lipomatosis) - Peripheral loss of subcutaneous fat (lipoatrophy) thought to be due to RTI component of HAART regimen Biochemical components include: - Hypertriglyceridaemia - Hypercholesterolaemia - Hyperglycaemia (insulin-resistant diabetes) - Hyperinsulinaemia - Low plasma testosterone level

5.8 ARV drug interactions

There are two groups of interactions:

- Non-ARV vs. ARV drug interactions
- ARV vs. ARV drug interactions

As a rule of thumb, most ARVs are metabolised by the Cytochrome P450 3A4 isoenzyme in the liver. Many other drugs are also metabolised by this enzyme and ARVs will either raise or lower these other drug levels and either be increased or decreased themselves by these interactions

5.8.1 Important non-ARV vs. ARV interactions (Table 5.8)

1. **Rifampicin**

- Decreases plasma level of all PIs by at least 75% (except ritonavir, which it decreases by 35%). Therefore its use is contraindicated with all PIs in general. Although limited evidence suggests it may be used along with ritonavir-boosted saquinavir, there are unresolved concerns about the efficacy and hepatic safety of this combination.
- Rifampicin also decreases plasma levels of EFV (25%), and NVP (37%) and DLV (96%). Rifampicin can be used with EFV but the dose of EFV should be increased from 600 mg daily to 800 mg daily. It is not recommended that Rifampicin be used with NVP.

2. **Rifabutin**

A. Effects of Rifabutin on ARVs.

Rifabutin reduces levels of all PIs and NNRTIs by 15 to 35%, except DLV that is reduced by 80%. Therefore, DLV should not be used with Rifabutin.

B. Effects of ARVs on Rifabutin

- Amprenavir (APV) increases Rifabutin levels by 193%, therefore Rifabutin dosage should be reduced to 150 mg daily.
- Indinavir also increases rifabutin so rifabutin dose should be lowered by up to 150 mg daily.
- LPV/r increases Rifabutin level by 300%, therefore Rifabutin should be reduced to 150 mg daily.
- EFV reduces Rifabutin level by 35%, therefore Rifabutin dose should be increased to 450 mg daily.

3. Ketoconazole

A. Effect of Ketoconazole on ARVs

- It increases IDV level by 68%, consequently IDV dosage has to be reduced from 800 mg to 600 mg T.I.D. If used concomitantly
- It increases SQV by 30% but there is no dose adjustment needed when used concomitantly

B. Effects of ARVs on Ketaconazole

- RTV increases its level by 300% therefore the dose of Ketoconazole must not exceed 200 mg daily if it must be used.
- APV increases ketoconazole level by 44% and ketoconazole also increases APV level by 31%. No recommendations for dose adjustment yet.
- NVP decreases its level by 63% and Ketoconazole increases NVP by 15%. The hepatotoxic effect of NVP is increased and Ketoconazole is not effective. The combination is not recommended.
- Fluconazole can be used with PIs and NNRTIs without dose adjustments unlike Ketoconazole).

5.8.2 Important ARV vs. ARV drug interactions

1. **Ritonavir**

- It potentiates or increases plasma levels of NFV by 1.5 times and IDV by up to 5 times. Recommended booster combinations with ritonavir are:
  SQV 1000 mg / RTV 100 mg BD
  APV 600 mg / RTV 100 mg BD
  LPV/r – Co-formulated
  IDV 800 mg /RTV 100 mg BD
- It has no effects on plasma levels of NVP, DLV but increases EFV levels by 21%
- EFV increases RTV levels by 18%

2. Indinavir

- It increases SQV up to 7 times, NFV levels by 80% and APV by 33%.

3. Nelfinavir

- NFV increases IDV by 50%.

4. Amprenavir

- APV decreases IDV by 38% and IDV also increases APV by 33%. There is no dose adjustment when both drugs are used together.

Table 5.8 Common ARV Drug Interactions

DRUG	Potentially Hazardous Interaction	Other Interactions
Didanosine		Antacids present in tablet formulation may affect absorption of other drugs
Efavirenz		Oral Contraceptives, Grapefruit Juice, Indinavir, Lopinavir, Rifampicin, Ritonavir, Saquinavir
Indinavir	Ergotamine, Phenobarbital, Rifampicin	Carbamazepine, Dexamethasone, Efavirenz, Nelfinavir, Nevirapine, Phenytoin, Ritonavir, Saquinavir,
Lamivudine		Sulfamethoxazole+Trimethoprim
Nelfinavir	Oral Contraceptives, Ergotamine, Phenobarbital, Quinidine, Rifampicin	Indinavir, Phenytoin, Ritonavir, Saquinavir,
Nevirapine	Oral Contraceptives, Levonorgestrel, Medroxyprogesterone, Norethisterone, Saquinavir	Indinavir, Lopinavir, Rifampicin
Ritonavir	Amitriptyline, Carbamazepine, Chloral hydrate, Chlorpromazine, Cyclosporin,Clomipramine, Clonazepam, Codeine, Oral Contraceptives,	Nelfinavir

	Dexamethasone, Diazepam, Ergotamine, Erythromycin, Fluconazole, Fludrocortisone, Fluphenazine, Haloperidol, Hydrocortisone, Ibuprofen, Indinavir, Morphine, Nifedipine, Pethidine, Prednisolone, Quinidine, Saquinavir, Theophylline, Verapamil, Warfarin	
Saquinavir	Ergotamine, Nevirapine, Phenobarbital, Rifampicin, Ritonavir	Carbamazepine, Dexamethasone, Efavirenz, Fluconazole, Indinavir, Nelfinavir, Phenytoin,
Stavudine	Zidovudine,	Doxorubicin

5.9 Recommended and Alternative regimens

It is recommended that combinations of drugs from at least two different classes be used so that the drugs can act on at least two different points in the HIV life cycle. Monotherapy or dual therapy is not recommended for treatment as the risks of resistance development are greater .The more the number of sites on the life cycle of the virus the drugs act, the less the likelihood of development of drug resistance. A minimum of three drugs including an NNRTI or a PI, is typically used. Based on availability, accessibility, affordability, efficacy and ease of administration, the following are recommended:

5.9.1. Adults/ adolescents

Preferred first line combinations:

ZDV or TDF Plus
3TC or FTC Plus
EFV or NVP

Other first line options:

ABC or d4T* Plus
3TC or FTC Plus
EFV or NVP

5.9.2 Initiating ARVs in women with prior single dose NVP (sdNVP) exposure

- Wait for 6 months before considering NVP use Or avoid NNRTI (substitute with PI)

5.9.3 Recommendations for Breastfeeding women commencing ARVs

- Women should be questioned regarding breastfeeding before commencing ARVs, otherwise the child will be receiving sub-optimal doses of ART. Should the child become positive, he/she could be resistant to the ARVs

5.9.4 First line recommendations for HIV/TB co-infected patients:

Adults/Adolescents

If on Rifampicin-containing containing regimen:

ZDV or TDF plus
3TC or FTC Plus
EFV (800 mg daily)

If pregnant or intolerant of EFV:

ZDV or d4T Plus
3TC Plus
ABC (triple NRTI)

In selected cases consider:

3TC or FTC plus
ZDV plus
TDF
(triple NRTI)

[1] In patients on Rifampicin based anti-TB combinations avoid the use of Nevirapine and most PIs

[2]Patients on ART who develop TB should have the ARVs reviewed to accommodate the use of Rifampicin in the anti-TB regimen. Nevirapine containing regimen should be substituted with EFV containing regimen.

For patients that cannot tolerate a combination of ART and anti-TB, the ART should be temporarily discontinued (see section 5.15).

Table 5.9 Recommendations For Individuals With TB Disease And HIV Co-Infection:

CD cell count	Recommended regimen	Comments
CD4 <200 /mm^3	Start TB treatment. Start ART as soon as TB treatment is tolerated (between 2 weeks and 2 months)[a]	Recommend ART. EFV is contraindicated in pregnant women or women of child bearing potential without effective contraception.
CD4 200-350 /mm^3	Start TB treatment. Start one of the regimens above after intensive phase.	Consider ART
CD4 >350 /mm^3	Start TB treatment	Defer ART

Note: Timing of ART initiation should be based on clinical judgement in relation to other signs of immunodeficiency. For extrapulmonary TB, ART should be started as soon as TB treatment is tolerated, particularly in patients with severe immunosuppression. For some TB diagnosis that generally respond well to anti TB therapy (i.e lymph node TB, uncomplicated pleural effusion), deferral of ART should be considered (WHO 2006 Guidelines).

5.9.5 Hepatitis B Virus Co-infection

TDF plus
3TC or FTC Plus
EFV or NVP

NVP and PIs should be used with caution in patients with underlying hepatic disease. NVP should not be used for patients with ALT elevations of grade 4 or higher.

The combination of TDF and 3TC or FTC is active against HIV and HBV and reduces the development of HBV resistance to therapy. Dosage of 3TC is as prescribed for treatment of HIV. This differs from treatment of HBV in HIV-negative patient. HBV in an HIV-positive patient should NOT be treated with TDF or 3TC alone or in combination in the absence of HAART.

If TDF and/or 3TC is stopped in an HIV and HBV co infected individual, there may be a flare up of hepatitis.

5.9.6 Hepatitis C Virus Co-infection

No clear guideline for choice of ARV in HCV co-infection. However the following should be noted

a. HCV co-infected patients on PIs have increased risk of raised hepatic transaminases. If the elevation is > 5 times upper limit of normal or 3.5 times the baseline value the PI should be switched
b. NVP should be used with caution in patients with underlying hepatic disease including HCV
c. Ritonavir boosted Tipranavir (TPV/r) is associated with grade 3 to 4 transaminase elevation and should also be used with caution.

5.9.7 Anaemia

Patients with anaemia (Hb < 8g/dl or PCV<24%) should not be initiated on ZDV containing regimen.

Preferred regimen:

TDF or ABC plus
3TC or FTC plus
NVP or EFV or PI (if on second line regimen)

Alternative regimen:

d4T plus
3TC plus
EFV or NVP

•

5.9.8 Renal Failure:

Dosage modifications are recommended for many ARV drugs:

-If serum creatinine is elevated at baseline

-If at any time serum creatinine is increased >1.5-fold above baseline,

Patients with confirmed serum creatinine increases >1.5-fold above baseline should:

- Undergo an evaluation for potential causes of decreased renal function.
- Have serum creatinine monitored more frequently until serum creatinine either stabilizes or decreases to <1.5-fold above baseline.

Many ARV drugs are excreted by the kidney and dosage should be reduced depending on the severity of renal failure.

The degree of renal failure should be determined by estimating creatinine clearance from Cockroft-Gault formula:

For Males > 15yrs, Cr/C = [(140-Age in yrs.) x wt in Kg/ creatinine in mg/dl]/ 72

For Females > 15 yrs, Cr/C =[(140-Age in yrs.) x wt in Kg/ creatinine in mg/dl]/ 72 x 0.85

e.g [(140-38) x 70/(1.8)]/72 = 55ml/min for a 38 year old man with creatinine of 1.8 mg/dl. If serum creatinine is given in µmol/l, convert this to mg/dl by dividing the value by 88.

Table 5.10 Adjustment of Zidovudine Dose in Renal Failure

Available Preparation	Creatinine Clearance ≥ 15 ml /Minute	Patient on Dialysis
ZDV 300mg tabs	One 300mg /PO BD	100mg every 8 hrs
ZDV 100mg caps	Three 100mg /PO BD	100mg every 8 hrs
ZDV Oral Syrup 5mg/ml	300mg (60ml) /PO BD	100mg (20ml) q 8hrs

Table 5. 11 Adjustment of Lamivudine Dose in Renal Failure

Adjustment Of Lamivudine Dose In Renal Failure Available Preparation	Creatinine Clearance ≥ 50 ml /Minute	Creatinine Clearance 30-49 ml /Minute	Creatinine Clearance 15-29 ml /Minute	Creatinine Clearance 5-14 ml /Minute	Patient on Dialysis
150mg tab	One 150mg BD Or Two 150mg OD	One 150mg OD	One 150mg start Then alternate days	One 150mg start Then alternate days	One 150mg start Then alternate days
300mg tab	One 300mg OD	Half 300mg OD			

Table 5.12 Adjustment of Stavudine Dose in Renal Failure

Available Preparation	Creatinine Clearance > 50 ml /Minute		Creatinine Clearance 26-50 ml /Minute		Creatinine Clearance 10-25 ml /Minute		Patient on Dialysis	
	Wt > 60 Kg	Wt < 60 Kg	Wt < 60 Kg	Wt > 60 Kg	Wt < 60 Kg	Wt > 60 Kg	Wt < 60 Kg	Wt > 60 Kg
15	-	2 caps bd	-	1 tab bd		1cap dly		1cap dly
20	2 caps BD	-	1 cap bd	-	1cap dly	-	1cap dly	-
30	-	1 cap bd	-	-	-	-	-	-
40	1 cap BD	-	-	-	-	-	-	-

5.9.8.1 Adjusting TDF Dose

It is better to substitute TDF for a less nephrotoxic drug e.g ABC. If it must be used in patients with HBV co-infection then adopt the guideline below:

Available preparation	Creatinine clearance between 30 and 49 ml/min	Creatinine clearance between 10 and 29 ml/min
	Administer tenofovir every 48 hours	Administer twice a week

5.10 When to substitute or switch ARV

A substitution or switch is necessary under the following conditions:

- Toxicity
- Co-morbidity
- Pregnancy
- Drug interaction
- Treatment Failure

Drug substitution as a response to treatment failure is called Drug switch.

5.10.1 Drug toxicity / Adverse drug reactions

Toxicity is related to:

- Inability to tolerate side effects of the medication and
- Presence of significant organ dysfunction resulting from drug use.

This can be detected clinically (history and clinical examination) and/or through laboratory testing.

5.10.2 How to substitute ARV

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

Table 5.13 Major Potential Toxicities of First-Line ARV Regimens and Recommended Drug Substitutions

Regimen	Toxicity	Drug Substitution
D4T/3TC/NVP	d4T-related neuropathy or pancreatitis	Switch d4T→ TDF
	d4T-related lipoatrophy	Switch d4T →TDF or ABC [(1)]
	NVP-related severe hepatotoxicity	Switch NVP → EFV (except in pregnancy)
	NVP-related severe rash (but not life threatening)	Switch NVP → EFV
	NVP-related life threatening rash (Stevens-Johnson syndrome)	Switch NVP → PI [(2)]
ZDV/3TC/NVP	ZDV-related persistent GI intolerance or severe haematological toxicity	Switch ZDV → d4T or TDF
	NVP-related severe hepatotoxicity	Switch NVP → EFV (except in pregnancy. In this situation switch to NFV, LPV/r or ABC)
	NVP-related severe rash (but not life threatening)	Switch NVP → EFV
	NVP-related life threatening rash (Stevens-Johnson syndrome)	Switch NVP →PI [(2)]
D4T/3TC/EFV	d4T-related neuropathy or pancreatitis	Switch d4T → TDF
	d4T-related lipoatrophy	Switch d4T → ddI, TDF or ABC [(1)]
	EFV-related persistent CNS toxicity	Switch EFV → NVP
ZDV/3TC/EFV	ZDV-related persistent GI intolerance or severe haematological toxicity	Switch ZDV → d4T or TDF
	EFV-related persistent CNS toxicity	Switch EFV → NVP

TDF Containing Regimen	TDF related nephrotoxicity	Switch TDF → ABC or AZT if there is no renal anaemia
[(1)]Withdrawal of d4T does not typically reverse lipoatrophy but may slow its progression. TDF and ABC can be considered as alternatives. [(2)] PI can be LPV/r or SQV/r. IDV/r or NFV can be considered as alternatives (see text).		

Table 5.14 Laboratory Panic Values That May Warrant Switch of ARVs

Laboratory Parameters	The panic Values That May Require ARV Switch
Haematology	
Haemoglobin	< 8 g/dl
Total White Cell Count	< 1,500/mm^3
Absolute Neutrophil Count	< 750/mm^3
Platelets	< 50,000/mm^3
Chemistry	
Sodium	< 122meq/L or > 159 meq/L
Potassium	< 2.4 meq/L or > 6.6 meq/L
Bilirubin	> 2.5 X Upper Limit of Normal
Creatinine	> 3 X Upper Limit of Normal
Glucose	≤ 39 mg/dl or > 251mg/dl in fasting Non-diabetic patients
Liver Function Tests	
AST	5 X Upper Limit of Normal
ALT	5 X Upper Limit of Normal
Alkaline Phosphatase	5 X Upper Limit of Normal
Pancreatic Enzymes	
Amylase	> 2 X Upper Limit of Normal if with symptom
Lipase	> 2 X Upper Limit of Normal if with symptom

Table 5.15: The following combinations of ARVs should be avoided

Regimen	Reasons why it is not recommended
d4T+ ddI	Mitochondrial toxicity is too high. Less efficacious than AZT+3TC in many studies. TAM mutations occur more commonly.
ddI + AZT	ddI needs to be taken on empty stomach but AZT is better tolerated with food. (It is however a potent combination).
ddI+ TDF	Both are purine analogs and may be antagonistic. Combination is relatively toxic because TDF inhibits purine nucleotide phosphorylase – an enzyme that is required for catabolism of ddI - ddI level rises and pancreatic toxicity increases.
TDF+ ABC	Both are purine analogues. Resistance develops very rapidly.
AZT+ d4T	Both are thymidine analogues and are pharmacologically antagonistic.
FTC+3TC	Both are cytidine analogues and are pharmacologically antagonistic.

5.10.4 Pregnancy

Substitution is necessary to remove and replace a drug that is potentially teratogenic.

- The principal drug requiring substitution is EFV which is teratogenic in humans and laboratory animals.
- Care should be exercised in the use of TDF in pregnancy.

5.11 Management of ART failure

Treatment failure can be defined

(1) Virologically as assessed by viral load level

(2) Immunologically using measurement of the CD4 cell counts

(3) Clinically, as assessed by disease progression,

N.B: Clinical disease progression needs to be differentiated from the immune reconstitution syndrome, an entity that can be seen soon after ARV is introduced (See section 6.2).

5.11.1 Virological Failure

- Viral load not suppressed to undetectable levels after 6 months on ART.
- Failure to reduce viral load by at least 2 to 2.5 log $_{10}$ in HIV RNA level after 24 weeks on ART
- A persistent increase in viral load following a period of adequate suppression.

5.11.2 Immunological Failure

- Return of CD4 cell count to pre-therapy baseline level or below
- 50% decline from on-therapy CD4 cell peak level
- Failure to achieve a CD4 cell count increase of 50 to 100 cells/µl per year

NB: The above drop of CD4 cell count should not coincide with other concomitant infections, which can explain transient CD4 cell decrease.

5.11.3 Clinical Failure

- Occurrence of new opportunistic infection or malignancy signifying clinical disease progression.
- Recurrence of opportunistic infection.
- Onset or recurrence of WHO Stage III defining conditions (See Table 1)

5.11.4 Causes of Treatment Failure

- Viral factors
- Non-viral Factors
    1. Host factors – poor adherence, malnutrition, malabsorption,
    2. Choice of initial ART regimen
    3. Drug Interactions

5.12 Management of Treatment Failure

In response to virological treatment failure due to resistance, the three drugs reserved for the first line regimens are replaced with at least two new NRTIs (if possible) with boosted PI, which are available for second line options, provided resistance testing cannot be done. (See second line treatment regimens) Where resistance testing is available, the failing drug may be identified and replaced.

5.13 Recommended Second line options

Adults and adolescents

			In some selected cases	
AZT or d4T plus 3TC or FTC plus NVP or EFV	Should be changed to	TDF or DDI or ABC plus 3TC or FTC Plus PI/r ± AZT	TDF plus ZDV Plus PI/r ± 3TC or FTC	ZDV plus DDI plus PI/r ±3TC or FTC

For patients whose first line regimen did not include NNRTI, EFV or NVP can be considered for second line option

ABC or DDI or TDF plus
3TC or FTC plus
PI/r* *1st preference is LPV/r. This can be replaced with SQV/r, FPV/r, IDV/r or ATV/r) plus NNRTI

All treatment failures at first and second level health facilities should be referred to the nearest tertiary centre. Note that many first-line regimen failures will be recognised only after an extended period of time when the virus has had opportunity to accumulate many NRTI resistance mutations. Thus it must be recognised that the only fully active component of second line therapy may be the protease inhibitor.

5.14 Salvage Therapy (Second line treatment failure)

The choice of salvage therapy is more difficult if genotype of phenotype resistance testing is not readily available. In the event of treatment failure, a comprehensive evaluation of why a patient failed must be performed. For instance, if a patient was non-adherent because the regimen was too complex, it is unlikely that such a patient would respond to an even more complex salvage regimen. This type of patient may require significant in-depth counselling prior to starting a new regimen.

With the currently available drugs in Nigeria options for fully active third line or salvage regimen are limited. It is hoped that newer NRTIs, NNRTIs and PIs which are effective against the mutant viruses shall soon become available. It is also hoped that drugs in new classes, the entry inhibitors, integrase inhibitors and maturation inhibitors shall become available to manage second line failures.

A recent trial showed that tipranavir combined with an optimized background of NRTIs and enfuvirtide can achieve undetectable levels of viral load in almost half of multi-drug

resistant, highly pre-treated patients. Also, darunavir, another novel PI, has shown at least comparable efficacy and better tolerability and safety in similar patients. Along with etravirine, a second-generation NNRTI, and maraviroc, a CCR5 receptor antagonist, these new agents have significantly expanded options for salvaging advanced patients

In light of limited options for salvage therapy at this time, partially active therapy with minimal toxicity may be better than no therapy as this could still maintain the patient in a state of wellbeing.

5.15 Situations When ART may be stopped

From a purely hypothetical and “best medical practice” point of view, a patient should never be advised to stop ARV treatment. However, there are situations where it might be unavoidable.

Such situations include:

- Severe intercurrent illness or major procedure
- Inability to tolerate oral medications
- Severe and unexplained drug toxicity

In these circumstances it is recommended to stop all ARVs simultaneously unless the patient is on an NNRTI because NNRTIs have an extended plasma half life compared with other drugs in the regimen. This will result in monotherapy of NNRTI leading to drug resistance. Thus it is recommended in this situation to continue NRTI for about 2 weeks after stopping NNRTI. This time period is empirical and may be adjusted as more data on the half life of NNRTIs in Africans becomes available.

SECTION 6: PRE-ART AND ART MONITORING AND FOLLOW UP

6.1 Monitoring and Follow-up

The clinician and patient must agree on the schedule for monitoring the progress of disease, and associated care prior to starting ART (baseline assessment) and during ART. Patients who are not yet eligible for ART should undergo clinical assessments and CD4 cell counts every six months. As the clinical or immunological threshold for initiating therapy approaches, these assessments will become more frequent.

Follow-up of patients on antiretroviral therapy continues through-out the patient's lifetime. These visits should be scheduled at a minimum interval of 3-6 months. At treatment initiation (see Table 6.1) or in the event of any treatment change, monitoring should be more frequent.

6.2 Baseline Assessment

The baseline assessment should include:

- Staging of HIV disease.
- Documentation of relevant past medical history
- Documentation of concomitant medication and prior ARV intake, including herbal and traditional medicines.
- Identification of co-existing conditions that may influence the timing of initiation and choice of ART (such as pregnancy, TB, anaemia, hepatitis or major psychiatric illness).
- Weight.
- Assessment of patient's readiness for therapy.

6.3 Assessment during Follow-up

Once therapy has begun, assessment should cover:

- Signs/symptoms of potential drug toxicities.
- Adherence.
- Response to therapy.
- Weight.
- Laboratory monitoring;

Laboratory monitoring tests may differ according to the level of the health care facility (see Table 11.1 for recommended tiered laboratory capabilities) and should be done according to the following schedule.

Table 6.1 Suggested Monitoring Schedule for Patients Starting HAART

	Pre-Treatment (Baseline)	Week 2	Week 4	Week 8	Week 12	Every 12 Weeks	Every 24 Weeks
Physical Exam	X	‡	X	X	X	X	
Adherence Counselling	X	X	X	X	X	*	
HIV-1 RNA	‡						‡
CD4+	X				‡		X
Hb/PCV	X		X[1]		X		X
WBC, Platelets	X	As clinically indicated					
ALT	X		X[2]				X
Creatinine	X						X
Chest X-ray HBsAg, HCV	‡	As clinically indicated					
AST, ALP, FBS, Amylase, Preg test, Lipid profile, U/E, Sputum AFB&m/c/s, Urinalysis	As clinically indicated						

X Essential ‡ Desirable
[1] For patients on AZT [2] Patients on NVP
* Those that are not yet ARV-eligible would require the initial CD4 count and subsequent CD4 at 6 monthly intervals, or more frequently as desirable, in addition to other symptomatically indicated investigations.

SECTION 7: KEY ISSUES IN ART

7.1 Adherence

Adherence to ART is an essential component of individual and programmatic treatment success. Higher levels of drug adherence are associated with improved virological, immunological and clinical outcomes. Adherence rates exceeding 95% are necessary in order to maximize the benefits of ART. Adherence is even more crucial for delaying or avoiding the development of drug resistance and ensuring maximum durability of the first-line ARV regimen. The measures to ensure optimal adherence should be taken before therapy is started, at initiation of therapy and during therapy.

7.2 Before ART is started

The success of any adherence strategy depends on the education of patients before the initiation of ART, an assessment of their understanding of the therapy, and their readiness for treatment. Adherence counselling includes giving basic information on HIV, its manifestations, the benefits and side-effects of ARV medications, how the medications should be taken and the importance of not missing any dose. Peer counsellors and visual materials can be particularly useful in this process. Family support has also been shown to be beneficial in maintaining adherence (see sections 5.3,5.4 and 5.5).

7. 3 At Initiation of ART

Consideration should be given to minimizing the number of pills, reducing the frequency of dosing, avoiding food restrictions, fitting the ARVs into the patient's lifestyle, and involving relatives, friends and/or community members, including peers in supporting the patient's adherence.

7.4 During Therapy

It is essential to continue with adherence counselling. This should involve adherence assessments during every visit, emphasizing of adherence principles to the patient by treatment supporters, and the continuous involvement of relatives, friends, peers and/or community support personnel.

7.5 Measurement of Adherence

Virological success of therapy is strongly dependent on adherence to therapy (Figure 7.1). Adherence in many studies is measured by expressing the number of doses taken as a percentage of the number of doses prescribed. For example if 20 doses are prescribed and 19 doses are taken adherence is 95%. This translates to missing one dose in ten days on a twice daily regimen.

Figure 7.1 Correlation Between Adherence and Virological Success

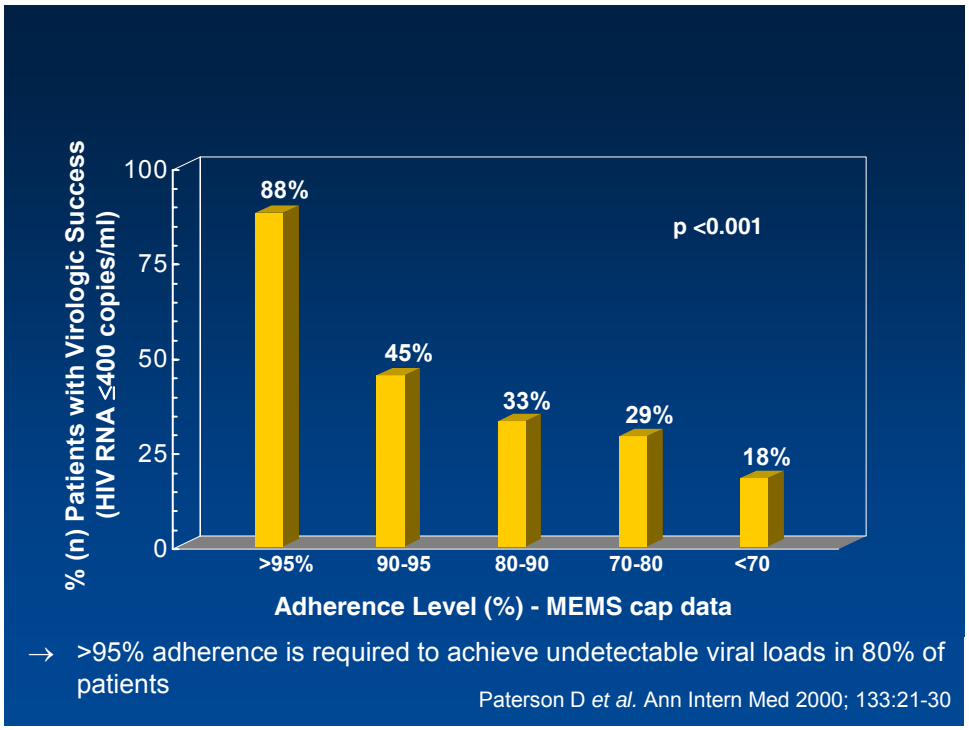


Table 7.1 Factors known to improve Adherence

The following factors have been associated with high adherence rates:

- Medications provided free of charge.
- Family, community members, or treatment-supporter engagement in adherence education.
- Family-based care if more than one family member is HIV-infected
- Continuous and effective adherence counselling
- Knowledge and understanding of the disease
- Drug regimen simplicity e.g. Fixed drug combination (low pill burden)
- Less adverse effects

Table 7.2 Factors Associated With Poor Adherence

- Poor patient-caregiver relationship
- High pill burden
- Forgetfulness
- AIDS Dementia Complex
- Depression
- Lack of patient education
- Inability of patients to identify their medications
- Drug toxicity
- Severe illness.
- Length of treatment
- Complexity of the treatment
- Perceived benefits versus barriers
- Lack of Social support
- Substance abuse
- Self-efficacy regarding adherence
- Cost of treatment and distance to facility

Table 7.3 Strategies for Improving Adherence

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

SECTION 8: UNIVERSAL SAFETY PRECAUTIONS AND POST-EXPOSURE PROPHYLAXIS

8.1 Universal Precautions

All health facilities in the private and public sector should adopt a policy for the prevention of accidental occupational exposure to blood borne pathogens. Since it is not possible for a health worker to know when a patient's body fluids are infectious, standard precautions should be used with all patients in the health care setting, regardless of their infection status. This will also eliminate the contentious issue of some health workers insisting on knowing their clients' HIV status before providing them much needed care, especially when such care is of a surgical nature.

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

- Routine hand washing with soap and water before and after contact with any patient
    - This simple procedure eliminates micro-organisms from the skin
    - Should be carried out as done by surgeons and theatre nurses, i.e. washing and rinsing each arm in turn from the hand to the elbow and preventing flow of water in reverse direction
    - Dry each arm with single-use paper/cloth towel or let hand drip dry from hand to elbow
- Use of barrier precautions
    - Wear disposable gloves to empty bedpans or urinals, clean up spills of blood, vomit, urine, or bowel movements, and to do any invasive procedure such as drawing blood or setting an IV line.
    - Health workers to cover cuts, bruises, and rashes on their bodies with adhesive plaster or bandages
- Safe handling and disposal of sharp instruments and equipment, including needles and syringes
    - Disposable needles and syringes should be used only once
    - Do not recap needles after use

- Discard used disposable needles and syringes in a puncture-resistant container (this could be improvised). This container must be clearly marked as sharps disposal container, even if improvised
- Burn the container in an incinerator or pit.

Health facilities owe their employees the responsibility of providing materials for universal precautions. The minimum materials/equipment that each health facility should provide includes:

- Cake soap (cut into small pieces) or liquid soap from a dispenser
- Soap dishes (with openings to allow water to drain away)
- Running water or a bucket kept full with clean water and a ladle for dipping, if running water is not available
- Single-use towels (paper towels, or cloth towels that wiil be used once and laundered). If not available, hands should be air-dried.
- Materials to educate personnel on susceptibility to HIV infection and means of preventing such.

8.2 Post Exposure Prophylaxis

Post-exposure prophylaxis (PEP) refers to the immediate administration of antiretroviral drugs following exposure of an individual to potentially infectious body fluids in a bid to prevent infection from occurring. The following types of exposures to HIV-infected materials should be considered for post-exposure prophylaxis (PEP):

- Needle-stick injury or injury with a sharp object that has been used on a HIV positive patient
- Mucosal exposure of the mouth or eye by splashing fluids
- Intact skin exposed to a large volume of blood or potentially infectious secretions
- Broken skin exposed to a small volume of blood or secretions

8.2.1 Steps to take following a needle-stick injury or mucosal exposure

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

- Express blood from wound if bleeding
- Wash exposed area thoroughly with soap and water or antiseptic solutions such as polyhexidine, 0.5% sodium hypochlorite, 2% glutaryladehyde, polyvidone iodine, 70% alcohol and 6% hydrogen peroxide if available.
- Rinse eye or mouth, if contaminated, with plenty of water
- Report the injury to a senior member of staff, supervisor or the PEP designated officer
- Ascertain the HIV status of the patient and the exposed health worker after providing appropriate pre-test counselling – the standard rapid HIV antibody tests that are currently used in the VCT programme should be used and the results of the tests obtained as quickly as possible.
- Take antiretroviral drugs recommended for post-exposure prophylaxis immediately – these should be started within 1 hour if possible and at the latest within 72 hours of the exposure (persons presenting after 72 hours of the exposure should also be considered for PEP).

8.2.2 Actions following HIV testing in PEP

Depending on the results of the HIV tests the following actions should be taken:

- If the source patient is HIV negative

  no further PEP is necessary for the exposed health worker UNLESS there is suspicion that the source is newly infected, and in the “window period” of sero-negativity.
- If the exposed health worker is HIV positive
  - no further PEP is necessary
  - the health worker should be referred for further counselling and long-term management

- If the health worker is HIV negative and the source patient is HIV positive,
    - continue antiretroviral for a period of four weeks;
    - repeat health worker‘s HIV test at 3 and 6 months after the initial test.
    - should the health worker seroconvert during this period, provide appropriate care and counselling and refer for expert opinion and long term management.
- If it is not possible to determine the HIV status of the source patient
    - assume that the source patient is positive and proceed according to guidelines above

8.3 Determination of Risk and ARV drugs for PEP

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

8.3.1 Low risk:

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

8.3.2 High Risk:

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

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

Table 8.1 Recommended Drug Combinations for PEP

Recommended 2-Drug Combinations	Recommended 3-Drug Combinations
TDF (300mg once daily) plus 3TC or FTC (300mg once daily) ZDV (300 mg twice daily) plus 3TC (150 mg twice daily) or CBV 450 mg twice daily. d4T (30 mg twice daily) plus 3TC (150 mg twice daily)	Any of the 2-drug combinations plus Protease Inhibitor or EFV. (EFV should be avoided if pregnancy is suspected) Preferred combination is: 2 NRTI plus LPV/RTV (400 mg/100 mg twice daily) or EFV (600 mg once daily) may be used as an alternative if NNRTI resistance is not suspected in source patient NFV (1250 mg twice daily) may also be used. Nevirapine should never be used for PEP as the risks of fatal hepatotoxicity outweigh the risk of HIV infection.

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

Table 8.2 Recommended Schedules of Investigations Following Exposure

Period	Recommended Investigations
Baseline	- Full blood count - Liver function test - Renal function test - HIV screening
Two weeks	- Full blood count - Liver function test - Renal function test
Six weeks	- HIV screening
Three months	- HIV screening
Six months	- HIV screening

8.3.3 Post-sexual exposure prophylaxis

There is not enough evidence to recommend prophylaxis against infection following casual sexual exposure. However, in the event that there has been sexual abuse or rape, it is recommended that the victim be counselled for post-exposure prophylaxis if the victim is negative. If the victim tests positive, the victim should be managed accordingly. It is also important to determine the HIV status of the perpetrator. If this is not possible the perpetrator is assumed to be HIV positive and the victim treated as a case of high-risk exposure. In the event of rape it is important to arrange for on-going counselling and support.

8.4 Minimum requirements for PEP services at health facility level

- A designated PEP officer - there should be a more senior/experienced ART Doctor who can be contacted for guidance when necessary
- ARV drugs and Test kits for PEP – these should be available at all times (24 hours a day/every day of the week)
- Facility PEP Protocol

SECTION 9: MANAGEMENT OF OPPORTUNISTIC INFECTIONS (OIs)

HIV systematically destroys the human immune system, thereby impairing the capacity of the body to fight infectious organisms. At CD4 count below 200 cells/µl most of the opportunistic infections begin to manifest. The effects of these opportunistic infections account for most of the ill health associated with HIV/AIDS and are very useful in grading and staging HIV infection and disease. There is ample evidence that active management of OIs in persons living with HIVAIDS by itself or as an adjunct to HAART greatly reduces the mortality and morbidity associated with HIV infection.

9.1 Symptoms, Signs and Treatment of Opportunistic Infections

The following table gives a comprehensive summary of the symptoms, signs and treatment of common Opportunistic Infections in Nigeria.

Table.9.1 Common OIs Encountered In Nigeria: Symptoms, Signs and Treatment

OI	Causative organism	Symptoms and signs	Diagnosis	Treatment	Interaction with ART
Candida infection. A. Oral thrush	Candida albicans	White painless plaques on the buccal and or pharyngeal mucosa or surface of tongue that is not easily scraped off	Clinical - based on signs. Laboratory - Wet mount microscopy using KOH preparation.	Clotrimazole oral troches 10mg, 5x/day until lesions resolve, usually in 7-14 days. Nystatin 500,000 units (4-6ml) gargled 4-5x/day or pastilles 4-5x/day for 7–10 days Fluconazole 50 – 100mg orally for 14days 1% aqueous solution of gentian violet, local application 2x/day for 7 days	

OI	Causative organism	Symptoms and signs	Diagnosis	Treatment	Interaction with ART
B. Oesophagitis		White patches, in mouth and pharynx, retrosternal pain on swallowing.	Clinical - Presence of thrush, odynophagia; Laboratory CD4 <100cells/mm³; Response to treatment.	Fluconazole 200- 400 mg/day PO for 14-21 days.	
C. Vulvo-vaginal Candidiasis		Vaginal pruritus, erythema and discharge	Clinical; Laboratory - Wet mount microscopy and culture.	Clotrimazole 1% cream 5g/day intravaginally for 7-14 days 100mg vaginal tab/day for 7 -14days Butaconazole 2% cream 5g/day intravaginally for 3 days Fluconazole 150 mg PO stat. For multiple recurrences 150mg wkly	
Tuberculosis A. Pulmonary TB	Mycobacterium tuberculosis	Chronic cough >3 weeks, weight loss, fever, night sweats, haemoptysis	Clinical and Laboratory Send 3 sputum specimen(Collected at following interval: on the spot, early morning and on the spot) for AFB microscopy	Refer TB suspects and patient to DOTS Centre for management Regimen: Category I-(for new cases only) Intensive phase: Two months of RHZE Continuation phase: Six months of EH or Four Months of RH Category II (for Re-	Concurrent administration of NVP and PIs with Rifampicin based anti-TB drugs should be avoided because of adverse drug interactions and severe

			Chest X ray only in AFB sputum Smear negative AFB Culture where necessary and feasible	treatment cases) Intensive phase: Two months of SRHZE AND One Months of RHZE Continuation phase: Five Months of RHZE **Multi-Drug Resistant TB (MDR-TB)** 24 months empirical treatment Intensive phase-6months Km-Cs-Pro-Ofx-Z Continuation phase-18months Cs-Pro-ofx-Z Km-Kanamycin Cs-cycloserin Pro-Prothionamide Ofx-Ofloxacin Z-pyrazinamide	toxicity. Thiacetazone should not be given to HIV +ve individuals. **Hepatic Insufficiency, Drug hypersensitivity, MDR-TB or XDR, refer 2º or 3º facility 2nd line drugs Rifabutin,Cycloserine,Ethionamide,Streptomycin,Capreomycin,Levofloxacin,Gatifloxacin,PAS
B. TB Meningitis		Fever, reduced alertness, headache, meningismus, focal deficits	Clinical; Laboratory - CSF pleocytosis Glucose↓ Protein ↑ Intracranial lesions CSF AFB smear CSF culture	Above regimen x 9 – 12 months + Steroids	

Coccidioidomy-cosis A. Disseminated disease	Coccidiodes immitis	Fever, generalized adenopathy,skin nodules or ulcers, hepatitis, bone/joint lesions, peritonitis	Clinical based on signs and symptoms; Laboratory - Culture, Histology- typical spherules CFT >1:16 titer (or four fold rise) CD4 count <250cells/mm³	Amphotericin B 0.5-1mg/kg/day IV until improvement (500-1000mg usually) Mild disease Fluconazole 400-800mg PO daily	
B. Meningitis		Fever, lethargy, headache, nausea, vomiting	CSF pleocytosis, Glucose < 50mg/dl; Mild protein ↑CSF CFT	Fluconazole 400-800mg/day IV or orally.	
Histoplasmosis	Histoplasma capsulatum	Fever, weight loss, fatigue	Laboratory - Culture of blood, lung secretions, Staining tissue, Capsular polysaccharide in urine, Antigen in BAL fluid.	Initial Amphotericin B IV 0.7mg/kg/day for 3-10 days. Continuation Itraconazole 200mg for 12 weeks Maintenance Itraconazole 200mg orally twice daily or Fluconazole 800mg/day	
Meningitis		Fever, weight loss, fatigue meningismus	Clinical; Lab - Antigen in BAL fluid/CSF	As above	

Oral and genital herpes	Herpes simplex virus types 1 and 2	Recurrent, painful, oral and genital vesicular lesions	Clinical based on signs & symptoms; Laboratory - Tzank smear.	Acyclovir 400mg thrice daily for 7 days, or Famciclovir 500mg orally twice daily for 7days. Valacyclovir 1g orally twice daily 7days Topical antiseptics to avoid secondary bacterial infections. Analgesics.	
Herpes zoster (Shingles)	Varicella zoster	Painful vesicular lesions in a dermatomal distribution	Clinical based on signs and symptoms; Laboratory.	Acyclovir 800 mg four times daily for 7 days, or Famciclovir 500mg orally thrice daily for 7-10days, Valacyclovir 1g orally thrice daily for 7-10 days For post herpetic neuralgia, give NSAIDS, carbamazepine 200 – 400mg daily or amitriptyline 25 – 50mg daily for 1 – 2 weeks or Gabapentin 300-1200mg orally for 1-2 weeks	
Diarrhoea, dysentery	Several possible pathogens: E. hystolitica, Isospora belli, HIV and Cryptosporidi un parvum, Salmonella spp., Shigella,	Frequent watery stools, abdominal cramps bloody stools, fever, nausea and vomiting.	Clinical based on signs and symptoms; Laboratory - Stool microscopy and culture	Rehydrate and treat appropriately. 1. Metronidazole 800mg orally thrice daily for 5-10 days + TMP-SMX 2. Albendazole 400mg twice daily for 5 days to treat strongyloidiasis 3. Ciprofloxacin 500mg twice daily for 5 – 10	Refer intractable cases for specialist care.

	Campylobacter pylori; Campylobacter jejuni, Cyclospora, Microsporidium, Mycobacterium avium complex (MAC), Strongyloides stercoralis			days	
Bacterial pneumonia	Streptococus pneumoniae or Heamophilus influenzae, Stapylococcus aureus, Morazella cattharalis, Klebsiella pneumoniae and Pseudomonas aeruginosa	Fever, chills, cough and pleuritic chest pain fast/difficult breathing.	Clinical based on signs and symptoms; Laboratory - Sputum microscopy and culture	Amoxycillin, Amoxyllin/clavulanic acid, Second generation cephalosporins, TMX/SMP Gentamicin 5mg/kg/day thrice daily for 5-10 days + Ampiclox or Amoxil/clavulanic acid	
Cryptoccocosis					
A. Non-meningeal					
Cryptococcal meningitis	Cryptococcus neoformans	Headache, fever, delirium, neck pain, alert Less common are	Clinical based on signs and symptoms; Intracranial	Fluconazole 400-800 mg/day for 10-12 weeks ± Flucytosine 100mg/kg/day	

		convulsion, visual changes, Stiff neck, Nerve deficits No neurological deficits	pressure Mass effect Laboratory: CSF (India Ink stain) CSF Protein ↑ CSF Culture + Crypt. Antigen + (CSF and Serum) CD4 count < 100cells/mm³ CT scan (normal or ↑ICP)	Maintenance therapy Fluconazole 200mg orally until CD4 >100-200mm³ for 6 months. Amphotericin B IV 0.7mg/kg/day for 14 days	
Pneumocystis pneumonia	Pneumocystis carinii; (jiroveci)	Acute/sub-acute non- productive cough, difficulty in breathing,	Clinical based on signs and symptoms; CXR: interstitial infiltrates, focal infiltrates and mediastinal lymphadenopathy, ground glass appearance, Laboratory: induced sputum or bronchio-alveolar lavage (BAL) for cytology.	Acute: TMP 15mg/kg/day orally or IV for 21 days (3-4 divided doses) TMP 15mg/kg/day + Dapsone 100mg/day for 21 days Pentamidine 4mg/kg/day iv for 21 days; Clindamycin 600mg iv 8hrly or 300-450mg orally four times daily + Primaquine 30mg/day orally for 21 days Severe disease: PO_2 <70mmHg or Central cyanosis add Prednisolone 40mg once daily for 5 days, then reduce to 20mg/day to	

				treatment completion. Prophylaxis: TMP/SMX 960mg/day aerosolised Pentamidine 300mg	
Toxoplasmosis	Toxoplama gondii	Fever, reduced alertness, headache, focal neurological deficits, seizures,	Clinical based on signs and symptoms; Response to empiric therapy. Serology CD4 count <100 cells/mm³, CT scan	Pyrimethamine 200mg loading dose, then 50-100mg/day PO + lecovorin 10-20mg/day + sulfadiazine 1-1.5g four times daily for ≥ 6 weeks Atovaquone 1500mg ± sulfadiazine 1-1.5g orally. Pyrimethamine + Folinic acid + Clindamycin 900-1200mg IV 6-hrly or 300-400mg PO 6hrly for ≥6 weeks Steroids (Dexamethasone) to reduce oedema/mass effect. Prophylaxis: TMP/SMX	
Hepatitis Hepatitis B	Hepatitis B virus (HBV)	Fever, right hypochondrial pain; jaundice.	Clinical based on signs and symptoms; Laboratory: LFTs, HBsAg, HBeAg, anti-HBs, anti-HBe,	IFNα 30 million units/week for 12-24 months. Peg IF Nα 2a 180mcg weekly or	

HBV/HIV co-infection			anti-HBc.	Peg IFNα 2b 1.5µ/kg 3TC 100mg/day Adefovir 10mg daily* Tenofovir (TDF) 300mg qd Emtricitabine(FTC) 200mg qd TDF + FTC (Truvada) Entecavir 0.5 – 1mg qd* Prophylaxis: PEP: HBIg 0.06ml/kg + HBV vaccine x 3 doses; HIV patient: - recombinant HBV vaccine if HBV markers negative. 3TC in HAART 3TC/TDF in HAART TDF/FTC in HAART	*HBV single agents TDF, FTC stoppage may lead to HBV flare **Never use 3TC, TDF, FTC, Truvada alone for HBV treatment in HIV+ patient
Hepatitis C	Hepatitis C virus	Fever, right hypochondrial pain; jaundice.	Clinical based on signs and symptoms; Laboratory: FBC, LFTs, Creatinine, CD4 count,	Presence of fibrosis (F_1 – F_2): CD4 >500 cells/mm³, (contra-indicated in CD4<100 cells/mm³), Initiated in the absence of any active OI.	

			Anti-HCV Elisa HCV RNA Biopsy	HCV RNA checked at 24 weeks of treatment and treatment discontinued. Pegylated Interferon 1.5µg/kg/week sc + Ribavirin 10.6mg/kg/day orally.	Use ZDV,ddI, EFV with Ribavirin with caution due to side effects. Monitor ALT, Blood count
Cytomegalovirus enteritis or colitis CNS CMV	Cytomegalovirus (CMV)	Fever, cramps, watery diarrhoea with or without bloody stools; dysphagia and odynophagia Delirium, lethargy, disorientation, malaise and headache, neck stiffness, photophobia, cranial nerve deficits Visual deterioration, No focal neurological deficits	Clinical based on signs and symptoms; Laboratory - Biopsy: intracellular inclusions Hyponatremia (Adrenalitis) CSF protein ↑ CSF pleocytosis CSF glucose ↓ Biopsy: intracellular inclusions	Gancyclovir 5mg/kg IV twice daily for 2-3 weeks; Foscarnet 40-60mg/kg 8 hrly for 2-3 weeks Retinitis: Same Stop treatment when CD4>150cells/mm³ for 3-6 months.	
Kaposi sarcoma	Human Herpes Virus type8	Brown-black macules, papules, plaques, nodules on skin, lymph nodes, mucous	Clinical based on signs and symptoms; HIV infection with low CD4 count;	Primary treatment is HAART. Interferon to be considered as second line treatment.	

		membranes or any organ of HIV infected individual. risk of malignant transformation.	high viral load. Laboratory: Histology	Other adjunct therapies include: Local: intralesional Vinblastine 0.01-0.02mg/lesion fortnightly for 3. Low dose radiation. Systemic: Adriamycin, Bleomycin, Vincristine or Vinblastine (ABV) Liposomal Daunorubicin 40-60mg/m^2 fortnightly; Liposomal Doxorubicin 10-20mg/m^2 fortnightly	
Scabies	Sarcoptes scabiei	Intense itching, lesions most prominent in interdigital web cleft papular rashes or generalised (Norwegian scabies)	Clinical based on signs and symptoms; Laboratory: Microscopy on KOH preparation of skin scales	20% Benzyl benzoate applied topically for 3 consecutive days. Permethrin cream 5% apply to total body, neck down and wash off after 8 – 14 hours. Repeat after 1 – 2 weeks. All household members should be treated simultaneously even if asymptomatic. Ivermectin 200µg/kg orally, repeated at 2 weeks	Not recommended in uncomplicated cases

Malaria	Plasmodium falciparum	Fever, chills and rigors, malaise, headache, nausea, vomiting	Clinical based on signs and symptoms; Laboratory - detection of malaria parasites in blood film.	Anti-malarials: Artesunate + Amodiaquine or Artemether + Lumefantrine, If complicated use IV Quinine	

9.2 Prophylaxis for Opportunistic Infections in PLWHAs.

There are several treatment regimens for prevention of opportunistic infections in PLWHAs. Isoniazid Preventive Treatment (IPT) for TB and Cotrimoxazole Preventive Treatment (CPT) have been recommended for use in Nigeria.

9.2.I Isoniazid Preventive Therapy (IPT).

Isoniazid Preventive therapy (IPT) is the use of Isoniazid in HIV Positive individuals with latent TB infection in order to prevent the development of active TB disease. Available evidence shows that TB is the most common opportunistic infection and cause of death among PLWHAs and that IPT is effective in preventing it.

IPT is not the treatment for active TB. It is therefore necessary to exclude active TB before commencing a patient on IPT.

9.2.1.1 Steps to Initiating IPT

- Verify/Confirm HIV Status.
- Counsel on TB/HIV interactions.
- Exclude active TB.
    - Ask the patient about Cough, Chest Pain, Fever and Night Sweats.
    - Check for Lymph Node enlargement
    - Do sputum examination

- If smear positive commence short course chemotherapy for TB (DOTS, preferably). Refer patient if necessary.
- Negative sputum results must be confirmed by a medical officer .
- If signs and symptoms absent, do chest X-ray to rule out TB.

- Once the absence of active TB is confirmed, commence IPT.
- Counsel patient on:
  - Treatment adherence
  - Side effects of INH – peripheral neuropathy
  - Immediate recognition and reporting of signs and symptoms of active TB

Dosage of INH for IPT is 5mg/kg/day to a maximum of 300mg/day for 6 months. Dispense on monthly basis.

Monitor side effects. (Ask for side effects and monitor them during monthly visits)

- Peripheral neuropathy - numbness/tingling sensation of extremities (This is the most common side effect.)
- Allergic skin eruptions.
- Jaundice.

If numbness/tingling/burning sensation is present give Pyridoxine 100mg daily. If jaundice develops, discontinue IPT and refer to Medical Doctor for assessment.

If patient develops active TB during the course of IPT, discontinue IPT and commence Anti –TB (DOTS). Refer if necessary.

Review after 2 years.

9.2.2 Cotrimoxazole Preventive Therapy (CPT)

Cotrimoxazole preventive therapy (CPT) is the use of Cotrimoxazole for the prevention of several secondary bacterial and parasitic infections in HIV infected individuals. It helps to improve the quality of life and reduce the rate of death among HIV infected patients.

For a patient to benefit from CPT, he/she must be:

- A PLWA with symptomatic HIV.
- Asymptomatic PLWHA with CD4 count <350 cells/mm³
- A PLWHA with active TB at any CD4 count .
- A Pregnant PLWHA after the first trimester.
- Any child born to an HIV-infected woman should be offered CPT from 6 weeks of age.
- Any child identified as HIV-Positive within the first year of life.
- Be motivated to adhere to treatment.

9.2.2.1 Steps to initiating CPT.

- Verify HIV status.
- Take medical history
- Conduct physical examination.
- Counsel on OIs in HIV infection.
- Treat pre-existing OIs.
- Screen for contraindications to CPT.
  - Known allergy to sulphur-containing drugs e.g. cotrimoxazole and sulphadoxine-pyrimethamine;
  - a pregnant woman in her 1st trimester
  - Kidney or Liver disease.
  - Seriously ill patients.
- Counsel patient on:
  - Drug adherence
  - Side effects of Cotrimoxazole.
    - Skin eruptions, which may be severe (Stevens Johnson syndrome)
    - Nephritis
    - Hepatitis.
    - Anaemia and other signs of bone-marrow suppression
    - Hyperkalaemia

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9.2.2.2 Commence CPT

Dose of Cotrimoxazole (CPT) in Adults
Cotrimoxazole 960mg daily (two single strength tablets, 480mg each) until CD4 count >350 cells/mm³

9.2.2.3 Monitoring and follow-up

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

9.2.2.4 When to discontinue CPT:

- Occurrence of side effects.
- CD4 count >350 cells/mm³ for at least 6 months.

SECTION 10: SUPPORTIVE MANAGEMENT AND PALLIATIVE CARE

10.1 Supportive management

Supportive management is to provide equitable care and support services thereby reducing morbidity and mortality and improving the quality of life of people living with HIV/AIDS.

10.1.1 Nutrition

Good nutrition contributes to the well-being of the person with HIV/AIDS at all stages of the disease and may even prolong life. It is important to have nutritional counselling as soon as the diagnosis of HIV is made and subsequently during clinic visits. On one hand, HIV/AIDS increases the energy requirement while on the other hand, it causes a reduction in food intake. The combination of the two effects increase the demand for balanced nutrition in patients with HIV/AIDS in order to stabilise weight, prevent muscle loss, replace lost nutrients, and allow patients to better deal with medications.

10.1.1.1 Food Choices for People Living With HIV/AIDS

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

10.1.1.2 Strategies for improving and monitoring nutritional status

- Close weight monitoring
- Nutrition education and counselling
- Prompt treatment of OIs (mouth disorders, diarrhoeas etc)
- Nutritional Support (macro- and micronutrient)
- Economic empowerment

10.1.1.3 Indications for therapeutic nutritional support

- Patients with malnutrition (body mass index <17%)
- Inability to eat

10.1.2 Immunisation

Immunisation is an effective way of preventing diseases.

- Patients with HIV infection are at increased risk for a variety of infections that can be prevented by using available vaccine preparations.
- Immunizations should be given as early as possible in the course of HIV infection for optimal effect. Patients with relatively preserved immune function are more likely to have a favourable response to vaccine challenge than those who are significantly immuno-compromised.
- Initiation of combination ART in patients with advanced HIV infection may improve the immunologic response to vaccine preparations.
- In general, live pathogen vaccines, such as yellow fever, mumps, rubella (MMR) and varicella-zoster virus are avoided in HIV-infected adults with low CD4 cell counts. However, killed or inactivated vaccines are considered safe in all patients.
- Influenza and other vaccine preparations have been shown to transiently stimulate HIV replication and increase the viral load. This phenomenon does not appear to have an impact on overall disease progression.

10.1.2.1 Suggestions on immunization for adults/adolescents infected with HIV

- Pneumococcal vaccine may be administered to all HIV-infected patients with CD4 cell count > 200μL. A booster dose is recommended five years after immunization.
- Hepatitis B immunization could be given to patients who have a negative screening serological test for this infection.
- Hepatitis A vaccine could be administered to people who practice anal sex, their partners and to patients with chronic hepatitis C infection.
- Influenza vaccine is important in individuals with historical risk factors for exposure to the virus and the presence of conditions associated with increased morbidity from influenza infection.
- Routine use of hemophilus B vaccine is not recommended, but it should be administered in asplenic patients and to those with history of recurrent hemophilus influenza infection.

Table 10.1 Recommended Immunization Schedule in HIV infected Adults

Immunizations in HIV-infected Adults			
Vaccine	Status	Dose/Regimen	Comments
Pneumococcal vaccine	Recommended	0.5 ml IM	Consider re-vaccination five years after initial dose.
Hepatitis B vaccine	Recommended in selected settings; see comments	Engerix B 20 ug or Recombivax HB 10 ug IM given at 0, 1, and 6 months	Administer to patients without serologic evidence of past or present hepatitis B infection. Vaccinated patients should be tested for HBsAb response after the third dose; non-responders should receive booster injections.
Hepatitis A vaccine	Recommended in selected settings	1 ml IM with re-vaccination in 6 to 12 months	Administer to homosexual or bisexual men and to women who practice receptive anal intercourse. Serologic testing prior to vaccination is not necessary.
Hemophilus influenzae type B vaccine	Consider in selected settings	0.5 ml IM	Administer to asplenic patients and those with history of recurrent hemophilus influenza infection.
Influenza vaccine	Recommended in selected settings	0.5 ml IM annually	Administer to patients at high risk for exposure to or morbidity from influenza. There is evidence that the vaccine may transiently promote HIV replication.
Tetanus toxoid	Same as for patient without HIV infection	0.5 ml IM	Td booster is recommended every 10 years.
Meningococcal Vaccine	Recommended	0.5ml IM	Revaccinate after 3- 5 years

10.2 Palliative Care

Palliative Care is an approach to care that improves the quality of life of patients and their families facing the problems associated with a life-threatening illness, through the prevention and relief of suffering by means of early identification, impeccable assessment and treatment of pain and other problems, physical, psychological, social and spiritual.

10.2.1 Objective of Palliative Care:

- provides relief from pain and other distressing symptoms
- affirms life and regards dying as a normal process
- intends neither to hasten or postpone death
- integrates the psychological and spiritual aspects of patient care
- offers a support system to help the patients live as actively as possible until death
- offers a support system to help the family cope during the patient's illness and in their own bereavement
- enhances the quality of life, and may also positively influence the course of illness

Palliative care is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as Antiretroviral Therapy (ART), cancer chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications.

10.2.3 Dimensions of Palliative Care

Effective HIV/AIDS palliative care for the patient and family consists of the following dimensions:

- Medical/physical aspect: includes pain and symptoms management, OI treatment and prevention, ART including monitoring for toxicity, end-of-life care, basic nursing care, and nutritional support
- Psychological aspect: includes counselling for Voluntary Counselling and Testing (VCT), different mental health and emotions and OI treatment and prevention and ART adherence; support for status disclosure; counselling for coping with stigma and discrimination; bereavement and grief support ; psychiatric manifestations of HIV; and care for caregivers/burnout
- Social/legal/ethics/Human Rights aspect: Includes support for material sustenance such as food; linkage to appropriate community resources; stigma and discrimination

reduction schemes; issues of inheritance; poverty alleviation and income generating activities; rights to care, treatment and support; ensuring confidentiality; informed consent; autonomy; disclosure issues; documentation and management of medical records and decision to forgo therapy

- Spiritual: entails life review and assessment; and spiritual counselling to address hopes, fears, doubts, guilt and other negative feelings; dealing with issues of forgiveness and life-completion tasks; spiritual counselling for end-of–life support including life-review and life-closure and grief and bereavement.

The mix of the care dimensions required by any individual and family depends on the phase of illness and its manifestations.

Palliative care is concerned with anticipating and identifying problems, needs and issues confronting a PLWHA and the family, assessing the scope and impact, and instituting appropriate interventions. Services are needed to deliver care in various settings along the illness continuum.

10.2.4 Common symptoms and their management

The most frequently encountered symptoms and their management are reflected below.

Table 10.2 Common Symptoms Associated With HIV Infection And Possible Disease Specific And Palliative Interventions.

Symptoms		Possible causes	Disease specific Treatment	Palliative Treatment
CONSTITUTIONAL	Fatigue weakness	AIDS OIs Anaemia	HAART Treat specific infections, erythropoietin, transfusion	Psychostimulants (dextroamphetamine)
	Weight loss Anorexia	HIV Malignancy	HAART Chemotherapy Nutritional support, enteral feedings	Testosterone/androgens Recombinant growth hormone

	Fever, sweats	MAC CMV HIV Lymphoma	Azithromycin, ethambutol, ganciclovir, foscarnet, HAART, cytotoxic chemotherapy	NSAIDS (ibuprofen, indomethacin) corticosteroids, anticholinergics(hyoscine) H2 receptor antagonists (cimetidine)
PAIN	Norciceptive • Somatic • Visceral	OIs HIV related malignancy Non specific	Treat specific disease entities	NSAIDS Opiods Corticosteroids
	Neuropathic	HIV related malignancy Neuropathy CMV VZV NRTIs (didanosine, zalcitabine, stavudine and other medications (INH)	Treat specific disease entities HAART Ganciclovir, foscarnet, acyclovir. Change antiretrovirals or offending medication	NSAIDS Opiods and adjuvants Tricyclic antidepressants, (amitryptiline,imipramine) Benzodiazepines, anticonvulsants.

GASTRO-INTESTINAL	Nausea/ vomiting	Oesophageal candidiasis CMV	Fluconazole Ganciclovir, change antiretroviral regimen.	Dopamine antagonist (haloperidol) Prokinetic agents (metoclopromide) Antihistamines, Serotonin inhibitors, proton pump inhibitors (omeprazole) Benzodiazepines
	Diarrhoea	MAC Cryptosporidiosis, CMV Microsporidosis, Other intestinal parasite Bacterial gastroenteritis, Malabsorption	Azithromycin, ethambutol, paromomycin, albendazole, other anti-parasitic agents	Bismuth,methylcellulose, kaolin, diphenoxylate + atropine, loperamide,
	Constipation	Dehydration, malignancy anticholinergics, opioids	Hydration, radiation/ chemotherapy	Softening agents, surfactant laxative, bulk-forming agents Osmotic laxatives (lactulose, sorbitol, saline laxatives (magnesium hydroxide)
RESPIRATORY	Dyspnoea	PCP Bacterial pneumonia Anaemia	TMP/SMX Pentamidine, antibiotics, erythropoetin,	Use fan, open windows, oxygen, opioids, bronchodilators, methylxanthines, benzodiazepines.

		Pleural effusion/mass/obstruction Decreased muscle function	transfusion, drainage/radiation/surgery	
	Cough	PCP, bacterial pneumonia, TB.	Anti-infective agents, therapy as above. Anti-TB chemotherapy.	Cough suppressants (codeine) Decongestants, expectorants.
	Increased secretion (death rattle)	Fluid shifts, ineffective cough, sepsis, pneumonia	Antibiotics	Anticholinergics (atropine, scopalomine) fluid restriction, discontinue IV fluid)
DERMATOLOGIC	Dry skin	Dehydration, end-stage renal disease, end-stage liver disease, Malnutrition	Hydration Dialysis Nutritional support	Emollients +/- salicylates Lubricating ointments

	Pruritus	Fungal infections, end-stage renal disease, end-stage liver disease, dehydration, eosinophilic folliculitis	Antifungals, dialysis Hydration, steroids	Topical agents(menthol, phenol, calamine, doxepin, capsaicin) antihistamines (diphenhydramine) serotonin antagonists
	Decubitius /pressure sores	Poor nutrition Decreased	Nutrition, Increase mobility	Prevent (nutrition, mobility, skin integrity) Wound protection (semi permeable film/ hydrocolloid dressing) Debridement (normal saline, enzymatic agents, alginates)
NEURO-PSYCHIATRIC	Delirium/agitation	Electrolyte imbalances, dehydration, toxoplasmosis, cryptococcal meningitis, sepsis	Correct imbalances, hydration, sulphadiazine, antifungals, antibiotics	Neuroleptics,(haloperidol, chlorpromazine, risperidone). Benzodiazepines(lorazepam)
	dementia	AIDS related dementia	HAART	Psychostimulants, low dose neuroleptics

	Depression	Chronic illness Reactive depression Major depression	Antidepressants Trycyclics, SSRIs, MAO inhibitors	Psychostimulants) dextroamphetamines, pemoline) corticosteroids (prednisone, dexamethasone).

10.3 Care of the Caregiver

In addition to challenging the structures of communities and existing health services, the HIV/AIDS epidemic has also placed significant emotional and psychological burden on health care providers and family members. It is pertinent to enhance care of the care givers to promote their quality of life. These can be achieved through provision of adequate attention to the individuals and groups. Emphasis should be on the provision of education, advocacy, community support services and referral services. In addition, information on type and sources of care available should be widely disseminated.

Commensurate motivation is needed for health workers, community workers and volunteers. This will help personnel to deliver care effectively and efficiently and prevent stress and burnout. In addition, more personnel will be attracted to the service.

SECTION 11: HIV/AIDS Commodity Logistics System

The HIV/AIDS commodity logistics system is essential if the war on the HIV virus is to be won. Securing a dependable, regular supply of HIV test kits, reagents, ARVs and drugs for treatment of opportunistic infections, to service delivery points is pivotal to the success of the treatment programme since any interruption of supplies will endanger the lives of the patients as a result of emergence of drug resistance viruses.

11.1 Key features of Nigerian HIV/AIDS commodities' logistics system

11.1.1 Integrated inventory control system (ARV drugs and HIV test kits, Drugs for treatment of opportunistic infection & other Reagents):-

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The purpose of inventory control system is to ensure uninterrupted supply of commodities and manage ARV drugs so that there are sufficient quantities to meet the needs of clients on treatment. It is aimed at ensuring that facilities maintain appropriate stock levels of ARV drugs and related commodities to avoid shortages and oversupplies. A well-designed and operated inventory control system prevents overstocks, stock-outs, and expiry.

This inventory control system is the forced ordering Maximum/Minimum type meaning every service delivery points are "forced" to order at the end of the Review Period which is 2 months. The maximum stock level is set high enough to guarantee an adequate supply at all times during the ordering cycle, but low enough to prevent overstock and waste. The minimum stock level is set as low as possible but includes a safety margin to prevent stock-outs. The quantity of ARV drugs logistics system is tracked in Months of Stock. This is a measure of how long stocks will last.The stock level in the facility have to be assessed frequently as this will alert the storekeeper in case of the need to place emergency order. The emergency order is done when the stock level of drops to two weeks of stock and it disregard the review period timing .The quantity to order in this instance is calculated to top the stock on hand to the maximum level

11.1.2 Logistics Management Information system (LMIS)

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

The three essential data elements include:

1. Stock on Hand: Describes the quantities of usable stock of ARV drugs available at a particular point in time. Stock-on-hand information guides us when to place an order and how much of each item is in stock. It also guides redistribution decisions. Aggregate data on stock-on-hand is an important input and guide to one of the key and fundamental functions in supply chain management – forecasting and quantification. In addition, a well functioning LMIS provides us information on how long existing stock-on-hand will last.

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

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

In order to collect and report the above mentioned data items, a number of forms were designed for the management of these commodities. The LMIS for the ARV & HIV test Kit's logistics system contains four records and one report. The LMIS forms include: Inventory Control Card, a Daily Consumption Record, and a Record for Returning/Transferring Commodities, a New Patient Regimen Worksheet and the Combined Report: Requisition and Issue Form.

1. Inventory Control Card

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

2. Daily Consumption Record for ARV drugs

   There is a Daily Consumption Record for ARV drugs. This record collects the number of ARV drugs that have been used in the facility over a defined period of time. This information is called the Dispensed-to-user data and is one of the essential data items. The Daily Consumption Record for ARV drugs should be kept with the person(s) who dispenses the ARV drugs.

3. Record for Returning/Transferring Commodities.

   The Record for Returning/Transferring Commodities is used in the event that ARV drugs may be required to be returned to the Central Medical Stores or transferred to another facility at the same level for various reasons ranging from expiry, damage, change in the treatment guidelines, or over-stocking.

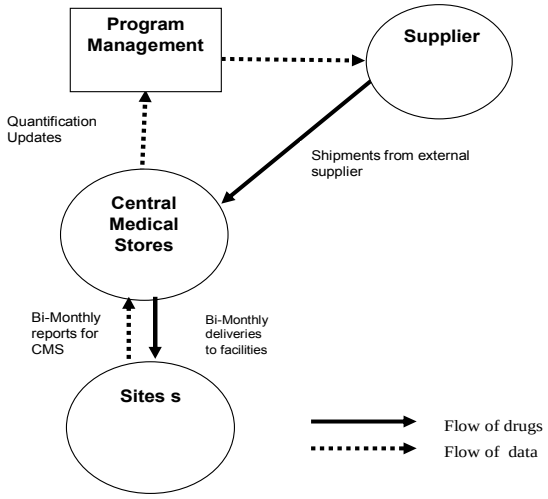
4. Combined Report – Requisition and Issue Form (ARV drugs)

   The Combined Report – Requisition and Issue Form captures all the information that is collected on the Inventory Control Card and the Daily Consumption Record for ARV drugs. The report is used to capture this data, to calculate the facility order quantities, and to monitor whether the facilities are maintaining stock according to plan, i.e. no overstock, shortages, or stock outs. This report is also a transaction record the information on this report is what runs the logistics system. so" No Report – No Commodities"!

11.2 FMOH REPORTING SYSTEM AND COMMODITY SUPPLY PIPELINE

The responsibilities for maintaining appropriate stock levels at the facilities rest on the facilities themselves. Facilities replenishment for consumed stock comes up bi-monthly (Thick Arrow) in response to submission of filed copies of the ordering forms of the Combined Report (Broken Arrows). The reports are directly transmitted to the Central Medical Stores and then to the Logistics Unit in the National Programme where they are analyzed for various decisions – ranging from routine re-supply to strategic decisions such as quantification and forecasting. Feedback on reports is processed by the Logistics Unit and communicated to the treatment sites.

FMOH Distribution System



11.3 Roles and Responsibilities of Logistics personnel in Logistics system

Levels	Personnel	Roles and Responsibilities
Central Level Program level	Logistics officers	❖ Receive, review and analyse summary logistics performance reports (regular updates of stock status reports) ❖ Review and requisition and issue reports and determine which reports sites need supervisory support to ensure regular accurate and timely reporting ❖ Monitor the Central warehouse to ensure that orders are sent o reporting sites timely and efficiently. ❖ Monitor the central Warehouse to ensure good distribution and warehouse management practices ❖ Communicate stock status reports regularly with the PA, FMOH and other relevant stakeholders to ensure that information collected are used for logistics decision making. ❖ Liaise with the PA and PSM providers to perform al relevant supply chain management functions that are geared towards ensuring commodity security Share logistics reports periodically with the Procurement agents and other stakeholders to the programme on the commodities usage, stock levels at the warehouse and service delivery points.
Central warehouse	Warehouse Manager	❖ Supervise the management of the commodities in the warehouse ❖ Approve and document all receipts and issues of commodities Flowing through the pipeline ❖ Monitor the Inventory Control Cards and stock

		levels of commodities ❖ Coordinate the distribution agents ❖ Coordinate all warehouse operations and ensure that all clients t the warehouse derive maximum value for their time ❖ Submit Bi-monthly stock reports to the logistics units
	Store Pharmacist	❖ Receive and issue of commodities ❖ Update inventory control card sever time Commodities are issued or received ❖ Ensure the storage of commodities according to the storage standards ❖ Monitor commodities management in the warehouse
	Store Officer	❖ Ensure the storage of commodities according to the storage standards ❖ Update inventory control cards
Service Delivery Points	Pharmacists/Lab Scientist	❖ Responsible for completing the daily usage forms for al commodities used in the facility. ❖ Responsible for documenting all transaction in the inventory control cars maintained in the unit ❖ Order the commodities from the store ❖ Completes the combined Reports, requisition and issue Forms at the end of review period ❖ Issue the Commodities ❖ Collect the daily usage register from other locations were commodities are dispensed e.g. PMTCT units ❖ Send unusable commodities that must be returned to the Central Medical stores after filing out the record for Returning commodities ❖ Aggregate all usage data from the Daily usage register for commodities and enter in the

		Combined Reports-requisition and Issue Forms and send to the Central Warehouse ❖ Monitor the management of Commodities in the store
	ART Team Leader	❖ Endorse order/requisition to be sent to the central warehouse

11.4 Summary of Logistics System

Distribution System	Two-levels Pull
Maximum/Minimum stock levels	Max 4 MOS/Min 2 MOS
Emergency order point	2 weeks of Stock
Ordering and reporting cycle	Every 2 Months
Lead Time	2weeks
Supply Status	Full supply (Max/Min)

SECTION 12: PROGRAMMATIC MONITORING AND EVALUATION

12.1 Importance of Programmatic Monitoring and Evaluation

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

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

Monitoring and evaluation for the ART programme will be in line with the National Health Management Information System (NHMIS) and feed into the Nigeria National Response Information System (NNRIMS).

12.2 National ART Indicators

Indicators for the National HCT programme include those that measure Coverage, Quality of service, Quantum of Service provided and Outcome. These include the internationally recognized indicators which the country is obligated to report internationally (Table 12.1) and others designed to track service coverage in the country (Table 12.2).

Details on them can be found in the “Monitoring and evaluation framework for the health sector response to HIV and AIDS in Nigeria”.

Table 12.1 ART Programme Outcome Indicators

Code	Indicator Type	Indicator	Periodicity of reporting	Source
ART 1	Input	Core 1: Existence of up-to-date national policies, strategy, and guidelines for ART adult and Paediatric programmes	Every 2 years	Key informant survey
ART 2	Input	Core 2: Percentage of Local Government Areas with at least one health facility providing ART services in-line with national standards [desegregated by adult and Paediatric ART service delivery]	Annual during scale-up, every 2 years thereafter	Record or programme reviews, or health facility survey
ART 3	Input	Core 3: Number of health workers trained on ART delivery in accordance with national or international standards desegregated by (adult and Paediatric ART service delivery)	Annual during scale-up, every 2 years thereafter	Programme records, or health facility surveys
ART 4	Input	Core 4: Percentage of ARV storage and delivery points experiencing stock-outs in the previous 6 months	Annual during scale-up, every 2 years thereafter	Drug tracking system, programme reports
ART 5	Outcome: Coverage	Core 5: Percentage of people with advanced HIV infection receiving ARV combination therapy [desegregated by adult and Paediatric ART service delivery]	Six-monthly during scale-up, annually thereafter	ART PMM/PME MIS

ART 6	Continuation of first-line regimens	Core 6: Continuation of first-line regimens at 6, 12 and 24 months after initiation	Continuous data collection, aggregated on yearly basis	ART PMM/PME MIS
ART 7	Outcome: Survival	Core 7: Survival at 6, 12, 24, 36, etc. months after initiation of treatment	Continuous data collection, aggregated on yearly basis	ART PMM/PME MIS
ART 8	Outcome: Functional status	Core 8: Functional status of HIV positive persons on ART at 6, 12, 24, 36, etc. months after initiation of treatment	Continuous data collection, aggregated on yearly basis	ART PMM/PME MIS

TABLE 12.2 ART Programme Service Coverage Statistics

	Level	Area	Indicator	Recommended method	Frequency of data collection
1	Output	ART programme coverage	Percentage of health facilities with systems and items to provide ART services	Health facility survey with observation component	Annual during scale-up, every 2-4 years thereafter
2	Output	ART programme coverage	# of patients new and cumulatively enrolled in HIV care Program by age and sex	ART PMM/PME MIS	Monthly data collection/Quarterly reports
3	Output	ART programme coverage	# of patients new, currently and cumulatively started on ART i by age and sex	ART PMM/PME MIS	Monthly data collection/Quarterly reports
4	Output	Adherence to treatment	% of clients who with who miss treatment by reasons (Lost, Missed, Dead, Stopped)	ART PMM/PME MIS	Monthly data collection/Quarterly reports
5	Output	Accessibility	# of persons enrolled and eligible but have not started on ARVs (current)	ART PMM/PME MIS	Monthly data collection/Quarterly reports

TABLE 12.2 ART Programme Service Coverage Statistics

	Level	Area	Indicator	Recommended method	Frequency of data collection
6	Output	TB HIV collaboration	# of patients on HIV care/ARVs who were diagnosed with TB and referred for DOTS treatment according to national guidelines this month	ART PMM/PME MIS	Monthly data collection/Quarterly reports
7	M&E		# and % of facilities reporting monthly on ART using PMM/PME tools	ART PMM/PME MIS	Monthly data collection/Quarterly reports

12.3 ART Monitoring Information System (MIS)

The ART Programme shall be monitored through a number of mechanisms including those stated in sources columns in Tables 12.1 and 12.2. A significant number of the indicators will be measured using the ART management information system. This system is made up of 2 intertwined and integrated parts:

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

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

PME provides information on the delivery of care to HIV positive patients as a group. This system should provide data which can be used with other relevant information to routinely

monitor and evaluate the effectiveness, efficiency and acceptability of HIV service provision at health centres, sub-national and national levels.

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

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

12.4 Data Security

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

12.5 Data Collection Instruments[1]:

The tools making up the PMM system include the following:

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

Each of these provides information on individual patients. The care card however acts as a link to the PME system which includes the Care/ART card and other tools that provide data on activities in the ART programme within the health facilities as a group.

[1] Copies of these tools are available in the appendix.
More details of the system can be obtained from the ART MIS guidelines, and the PMM/PME training manuals

The tools that make up the PME include:

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

All these tools were designed through a participatory approach that included stakeholders involved in providing or benefiting from HIV treatment and care for people.

Other tools that will be required in an ART site include the registers required for HIV counselling and testing. These include HCT register, and the HCT laboratory register/worksheet. An adherence register may also be required to be able to report on number of persons that receive adherence counselling.

12.6 Coding System

A standardized system of assigning unique ID numbers to persons enrolling into the ART programme is being carried out to ensure that all patients can be individually tracked and therefore avoid duplicities in counting persons enrolled in the program.

These unique ID numbers will take into consideration the location and name of facilities. The unique codes will be developed in keeping with the codes used in the National Health Information System (NHMIS).

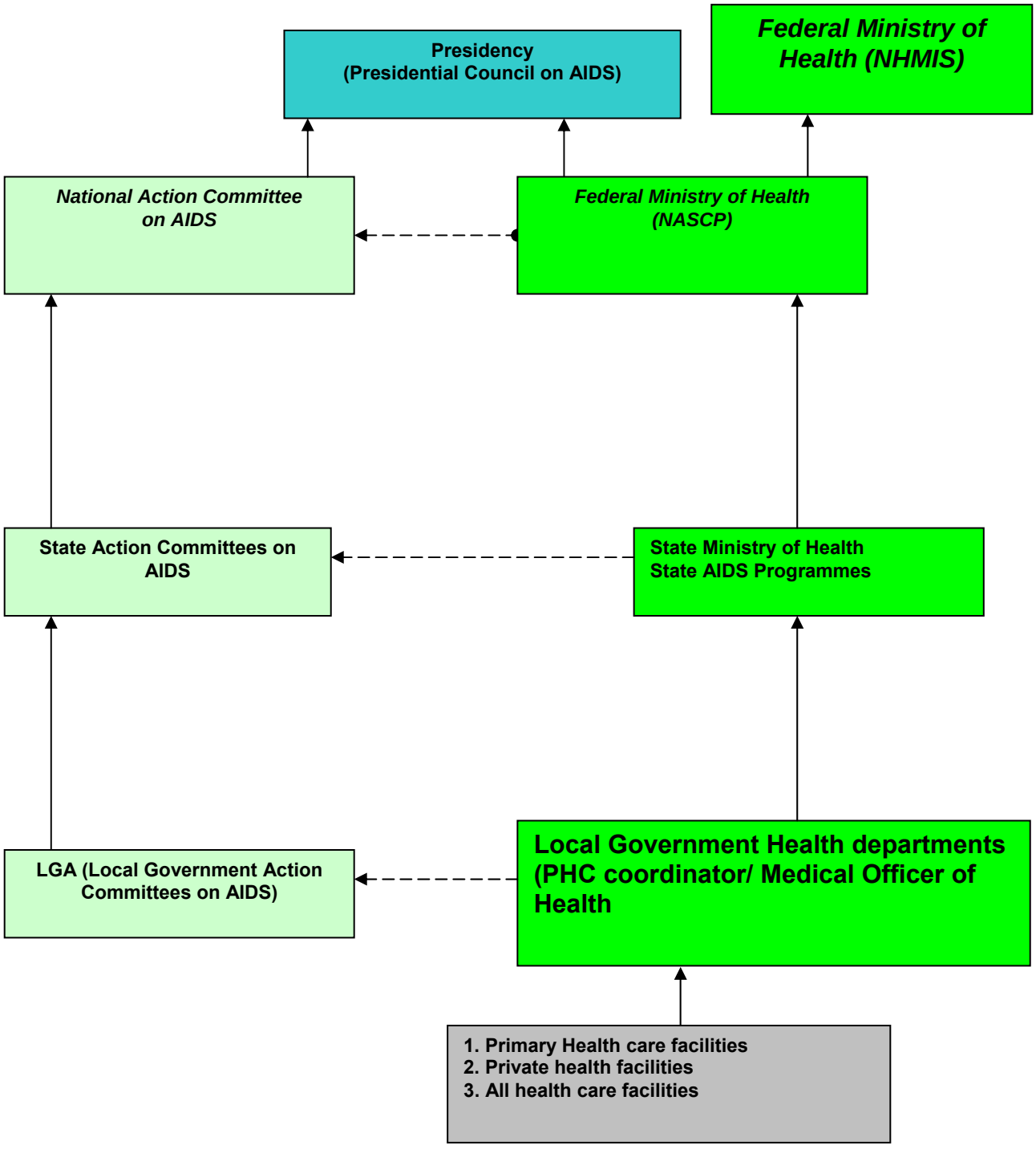
12.7 Data Flow

At each ART site, the ART monthly summary form should be completed and forwarded to the Local Government, where the data are collated and in turn forwarded to the state Ministry of Health. At the state level, all HIV data should be collated, analyzed and forwarded to the NASCP FMOH (see figure 12.1)

The respective health authorities at the various levels will have responsibility for reporting to the HIV and AIDS coordinating authorities at the level (i.e. Primary Health Care coordinator to Local Government Area Action Committee on AIDS; the State AIDS

Programme to the State Action Committees on AIDS; and the National AIDS and STI control Programme report to the National Agency for the Control of AIDS.

Report flow for HIV/AIDS Health sector Service Provision Data



Data Analysis and Reporting: Data collected will be analysed at the national level and findings will contribute to programme planning and implementation. It will also be NACA to fit into the NNRIMS. The FMOH will design feedback mechanisms to ensure that each level of service, the management, partners and stakeholders are informed on a quarterly basis on service statistics of HCT services in the country.

12.8 Quality Assurance:

Staff competency, client satisfaction and adherence to counselling and testing protocols should and will be assessed periodically. Quality assurance measures include the core indicators and examples of selected tools can be found in the annex.

A systematic plan for periodic external data quality checks to be conducted by NASCP/FMOH and other stakeholders will be developed. These checks will include a review of site registers and reporting forms for completeness and accuracy.

12.9 Logistics for M&E for the ART Programme

The FMOH will provide registers and summary forms for all sites delivering HIV care and ART. Guidelines and training materials for proper completion of the registers and forms will also be made available. The FMOH in collaboration with partners and other stakeholders will support training on data collection and reporting.

12.10 Guidelines for the Monthly Summary Form

Table 12.3 Guidelines for filling the Monthly Summary Form

	DATA ELEMENT	HOW TO COLLECT THE DATA
ART 1	Number of Persons cumulatively enrolled into the ART programme for HIV care before this reporting period (month) (disaggregated by age, sex)	This is obtained from the last month's monthly summary report. This reflects what was happening before the month being presently reported. Take the numbers reported in the previous month for ART 3 and insert them here.
ART 2	Number of persons newly enrolled into the ART	This number is obtained from the Pre-ART register, using a tally sheet to divide the clients

	programme for HIV care during the last month (disaggregated by age, sex)	registered during the reporting month into age and sex groups. Once these groups have been obtained they are put under the appropriate subheadings i.e. male 0-14yrs. Male 15yrs and above, females 0-14 yrs & 15yrs and above
ART 3	Number of Persons cumulatively enrolled into the ART programme for HIV care since the beginning of the programme (disaggregated by age, sex)	This is the sum of ART1 and ART2. under each age sex grouping simply add the number of obtained for that group in ART1 and ART 2
ART 4	No of persons eligible for ART but yet to commence ART	This is obtained by going the whole Pre-ART register since the programme began and counting the number of people who are eligible based on the entry in column P23 but are yet to commence ART based on the fact that they have no entries in column P25 (Date ART started). This does not need to be disaggregated by age or sex. Mode of calculation A. Count all persons who are medically eligible (P23) B. Count all persons who have commenced ART (P25) C. Count all person's who have died or transferred out (P21 & P22) ART 4 = A – (B + C)
ART 5	Number of Persons cumulatively started on ART before this reporting period (month)	This is obtained from the last month's monthly summary report. This reflects what was happening before the month being presently reported. Take the numbers reported in the previous month for

		ART 7 and insert them here.
ART 6	Number of persons newly started on ART during the last month	This number is obtained from the ART register. This number is obtained by using a tally sheet and separating the clients that were newly registered for ART in the month into age and sex groups and by source. Once these groups have been obtained they are put under the appropriate subheadings i.e. male 0-14yrs. Male 15yrs and above, non pregnant females 0-14 yrs etc NB: Transfers-in who have already commenced ART are not included in this figure
ART 7	Number of Persons who cumulatively started on ART since the beginning of the programme	This is a summation of the above rows (ART 5 & ART 6) Simply add the 2 columns and put the total in this column. This also does not include transfer in patients because this could lead to double counting.
ART 8	Number of pregnant women who enrol for HIV care this month	This is obtained from the Pre-ART register. The PMTCT link. For the month is studied and all patients with an EDD are counted and desegregated by age.
ART 9	Number of persons cumulatively transferred in for ART from other health facilities	Look through all ART register pages from the inception of the programme till date. Tally all people who were transferred in from other sites. These will be under the line drawn to separate newly enrolled patients from transfer in patients.
ART 10	Number of persons newly transferred into the ART programme for ART from other facilities during the month	This is calculated by simply subtracting the ART 9 obtained this month from the ART 9 obtained in the previous month e.g. ART 10 for November 2006 = ART 9 for November 2006 – ART 9 for October 2006
ART 11	Number of persons who restarted ART therapy after	This is obtained by going through the ART register and counting all patients who in the last month of

	stopping therapy for more than 3 months	prescription have an “RESTART” written in the month of reporting. This “RESTART” should be written in the month of restart alongside the drug regimen
	Drug adherence	
ART 12	Number of persons on due to receive ARVs who had initial adherence counselling this month	This is to be obtained by having a register in the adherence counselling unit which differentiates between initial adherence counselling and other intermittent counselling sessions.
ART 13	Number of persons who did not pick up their ARV regimens in the month	This is obtained by going through the whole ART register. On each page we go through the column that corresponds to the month being reported. We observe all persons who do not have a regimen written against for the month. These are the people who did not pick up their ART regimen in the month. In some circumstances the status of persons will already have been determined. These include deaths, transfer out and Lost to follow-up (dropped). If these are known they should be used to fill the ART 14, 15,16 & 17
ART 14	Number of persons who did not pick up there medication in the past month who have been MISSING from the programme	See ART 13. These are the people who have LOST written in the column for month of reporting
ART 15	Number of persons who did not pick up there medication in the past 3 months who have been LOST TO FOLLOW UP from the programme	See ART 13. These are the people who have LOST in the last 3 months from the period being reported.
ART 16	Number of persons who did	See ART 13

	not pick up there medication in the past month who have died (DEAD)	All persons whose death has been notified should be recorded here.
ART 17	Number of persons who did not pick up there medication in the past month who have STOPPED ART	See ART 13 This includes all persons who are recorded as STOPPED
ART 18	Number of persons who did not pick up there medication in the past month who have TRANSFERRED OUT	See ART 13 This includes all who have TO written in the column
	Laboratory	
ART 19	Number of baseline CD4+ counts for persons who started HIV care during the month being reported on (optional).	Look through all pre-ART register pages of cohorts who started HIV care during the reporting period (previous month). Count the number of CD4+ entries in the CD4 column Enter this into this section For all lab service statistics an alternative is to develop a laboratory register that can provide these figures directly from the laboratory
ART 20	Number of baseline CD4+ counts for persons who started ART during the month being reported on (optional).	Look through all ART register pages of cohorts who started ART during the reporting period (previous month). Simply count the number of tests that were done For all lab service statistics an alternative is to develop a laboratory register that can provide these figures directly from the laboratory
ART 21	Median baseline CD4+ count for persons who started ART during the month being reported on (optional).	Look through all ART register pages of cohorts who started ART during the reporting period (previous month). Take the median CD4 of all patients with available baseline CD4 entered in the CD4 column under Status at start of ART. Enter the median into this section of the summary form

		For all lab service statistics an alternative is to develop a laboratory register that can provide these figures directly from the laboratory
	Opportunistic Infections	
ART 22	Number of persons newly enrolled for HIV care who were screened for TB this month	This is obtained from the Pre ART register. Simply count the number of patients newly enrolled in the month being reported that were screened for TB. This is obtained from the P13 column all persons with “TB” or “2”written in the column of the month
ART 23	Number of persons newly enrolled for HIV care who were placed on INH prophylaxis this month	This is obtained from the Pre ART register. Simply count the number of patients newly enrolled in the month that was placed on INH. This can be calculated by simply counting the number of people with a date in the column “P14”
ART 24	Number of persons newly enrolled for HIV care who were placed on CTX prophylaxis this month	This is obtained from the Pre ART register. Simply count the number of patients newly enrolled in the month who were placed on CTX. This can be calculated by simply counting the number of people with a date in the column “P15”
	ARV Drug Regimens	
	ARV Drug Regimens	This section includes information about the number of persons on 1st-line and 2nd-line ART regimens at the end of the previous month and is sorted by age groups (adults > 14 years versus children) and sex. This information is found in the ART register—tally the regimen codes listed in the column for the last month Even if a patient substituted or switched regimens during the reporting quarter, you will still only count regimen given in the last month. If a patient was changed from 1a to 2b in the month, you will count the patient as 2b

		You will need to tally up the regimen codes by sex and adult/child from all of the ART register pages. After this you will need to determine how many by sex and age and pregnancy status were on first line, second line and both
ART 25	Number of persons currently on 1st-line ART regimens this month	Fill in here only those patient who are on first line regimens
ART 26	Number of persons currently on 2nd line ART regimens this month	Fill in here only those patient who are on second line regimens
ART 27	Number of persons currently on 1st and 2nd line ART regimens this month	Add the above rows together to determine how many patients on either 1st line or 2nd line regimens
ART 28	Number of persons on Salvage drug regimens this month	Fill in here only those on salvage regimens
ART 29	Total number of persons on 1st line, 2nd line and Salvage drug regimens this month	Add the above rows for 1st, 2nd line and salvage regimens together to determine how many patients on either any ART regimen

ANNEX I: LOGISTICS MANAGEMENT NFORMATION SYSTEM FORMS

FACILITY:_____ LGA:_____STATE:_____DATE_____

ART DAILY CONSUMPTION RECORD

		FDC			SINGLE DOSES																
		Adult First Line			Adult First Line							Adult Second Line				Pediatric First Line			Pediatric Second Line		
Serial No.	Pharmacy No.	d4T/3TC/NVP	d4T/3TC/NVP	AZT/3TC (300/150)	Stavudine	Stavduine	Zidovudine	Lamivudine	Nevirapine	Efavirenz	Efavirenz	Didanosine	Abacavir	Ritonavir	Indinavir	Zidovudine	Lamivudine	Nevirapine	Didanosine	Abacavir	Nelfinavir NVF powder 50 mg/g-
1.																					
2.																					
3.																					
4.																					
5.																					
6.																					
7.																					
8.																					
TOTAL QTY DISPENSED- PAGE SUBTOTAL																					
TOTAL (CUMMULATIVE) QTY DISPENSED- ALL PAGES TO DATE THIS MONTH																					
Prepared By Name: Designation: Sign: Date:																					

INVENTORY CONTROL CARD

FACILITY NAME _____ STORE NAME _____

DESCRIPTION OF ITEM

_____

NUMBER OF MONTHS OF STOCK : MAX____ MIN___ SHELF NO._____ BIN NO._____

DATE	VOUCHER NUMBER	RECEIVED FROM/ISSUED TO	QUANTITY			STOCK BALANCE	INITIALS/ SIGN	REMARKS
			RECEIVED	ISSUED	LOSSES/ ADJUSTMENTS			

Record for Returning/Transferring Commodities

Name of facility returning commodities: _____

Sent to: _____

S/N	Product Description	Quantity Returned	Reason for Return

Record Compiled By: _____ Sign: _____ Date: _____

Transfer Approved by:_____ Sign:_____ Date_____

CARRIER

I certify that the above quantities for transfer were received by me except where explained below.

Comments:_____

_____Name of Carrier:

_____

Carrier's Signature:_____ Date:

_____

Receiving Facility

I certify that the above quantities were received by me except where explained below.

Comments: _____

_____

Receiver's Name: _____

Receiver's Signature: _____ Date:

_____

Annex II: MINIMUM REQUIREMENT FOR HIV COUNSELLING & TESTING SERVICE DELIVERY

Stand Alone HCT facilities

Space and equipment

i. Reception area: should be equipped with:

- Desk
- Chairs
- Filing cabinet/s
- IEC materials
- Computer for data entry (if possible)
- Communication gadgets e.g. telephone (if possible)

ii. Waiting area:

- A comfortable sitting facility with a capacity of 5-20 people;
- Open display area for educational materials, including those that explain the HIV testing procedure; and, if possible, audiovisual equipment.

iii. Counselling room(s): (Rapid HIV tests can be conducted in them)

- 3 chairs and a small table
- a washable surface
- sink with running water
- storage space for blood drawing equipment
- “sharps” disposal container
- lockable cupboard, registers and other stationery
- ensure audio and visual privacy

iv. Laboratory:

- a desk and chair
- acid-resistant or formica-surface work bench
- storage space for medical consumables
- lockable storage for test kits that do not need refrigeration
- refrigerator for test kits and/or reagents needing refrigeration
- standard contaminated waste disposal containers, sink with elbow taps and running water (both hot and cold).
- Test kits must be stored according to manufacturers’ specifications.

v. Toilets – Ideally, there should be male, female and staff toilets which must be clean and provided with water.

Staffing

Key staffing areas to be considered are:

- Management
- Technical
- Ancillary

Management

The manager ensures the provision of high quality HCT services. The responsibilities of this position include planning, coordination, supervision and support for staff.

Technical staff

Counsellors

Adequate number of trained counsellors must be provided on the basis of a minimum of 1 counsellor to10 clients/day.

Personnel to perform rapid HIV testing

A Medical Laboratory Scientist/Technician conducts HIV testing where possible. However, in order to support the expansion of HCT services in Nigeria, HCT counsellors and other health workers who have received the requisite training could be authorised to perform rapid HIV tests. Linkages should be established with Medical Laboratory scientists to provide quality assurance.

Data entry personnel

The site should designate personnel for accurate and up to date records of activities of the site. The data will be transmitted to the FMOH through the existing National Health Management Information System (NHMIS) and also meet the reporting needs of the Nigeria National Response and Information Management System (NNRIMS).

Receptionist

The role of the receptionist includes welcoming clients, registering them, collecting user fees if applicable, explaining procedures, providing educational materials and entering data, where applicable.

Ancillary staff

These include general service staff such as cleaners, security guards and drivers. They are responsible for the general upkeep and other duties at the facility.

Integrated HCT facilities

Space and equipment requirements

- Counselling rooms that will ensure privacy during counselling sessions
- Areas for rapid HIV testing must be equipped according to standardised national laboratory guidelines for HIV rapid testing

Reception area should be equipped with:

- Desk
- Chairs
- Filing cabinet/s
- IEC materials
- computer for data entry (if possible)
- communication gadgets e.g. telephone (if possible)

Staffing

Existing staff provide both clinical and HCT services. Additional staff may be required.

Personnel to perform rapid HIV testing

It is desirable that Medical Laboratory Scientists conduct HIV testing where possible. But, in order to support the expansion of HCT service in Nigeria, basic HCT counsellors and other health workers who have received the requisite training could be authorized to perform rapid HIV tests. Linkages

should be established with Medical Laboratory scientists to provide quality assurance

Data Entry Personnel

In integrated facilities personnel should be designated to complete the HCT registers, document activities carried out in the centre as well as ensure data linkage to the M&E framework for Health sector HIV/AIDS response, NHMIS and NNRIMS through data forwarding to the appropriate authorities.

Mobile/Outreach services

Outreach services will be provided from both the integrated and stand alone facilities. Premises from which outreach services are provided should meet the required standards for quality HCT services in the country.

Annex III: PROCESS OF SETTING UP PMTCT SERVICES IN A NEW SITE

The following steps should be followed for setting up PMTCT services in a new site:

- Advocacy to policy makers in the hospital to solicit their support for PMTCT
- Conduct of formative research if no such study has been done in that area, so as to generate data on the knowledge, attitudes, beliefs and practices of health care providers and community members as it relates to HIV/AIDS and PMTCT. The data generated should be used to develop site specific communication interventions. It will also form a baseline for subsequent evaluation of the programme
- Conduct facility assessment to assess the capacity of the health facility to deliver PMTCT services
- Set up site multidisciplinary PMTCT team with clearly defined roles and responsibilities
- Sites should adopt the National SOP which clearly defines roles and roles responsibilities for members of the site PMTCT team
- Conduct or ensure that the appropriate staff of the facility are trained on:
    - HIV counselling and testing
    - PMTCT
    - Infant feeding counselling in the context of HIV and AIDS
    - Monitoring and evaluation
- Establish a sustainable supply system for ARV, HIV test kits, BMS (if possible), record keeping materials and other consumables
- Develop a communication work plan
- Set up a system for monitoring and centres
- Develop an operations research component

The following are the minimum services/requirements that each PMTCT implementing site should provide.

- ANC services to be supervised by a trained health care provider
- The site should have a reasonable flow of ANC attendees per quarter.
- HCT services
- Delivery Services with capacity for elective/emergency caesarean section (or by referral)
- Provisions for care of the new born including ARV prophylaxis
- Infant feeding counselling and support
- Paediatric follow-up and early infant HIV diagnosis (or by referral)
- Immunization services
- Provisions for post-natal services
- Family planning services (or by referral)
- Cervical screening services (or by referral)

Management and coordination of PMTCT Programme

In order to effectively manage and coordinate PMTCT in Nigeria, the following activities and mechanics should be put in place:

- FMOH and Partners should facilitate reporting from the sites to the FMOH and feedback to the sites. All sites should have the national PMTCT registers (ANC, etc)
- The teams in each hospital should comprise members from every relevant department and the roles and responsibilities of members of the team, especially the team leaders at the site should be properly defined.
- The national PMTCT SOP and flow chart should be used to guide the implementation of services at the sites
- HIV Prevention and Control Initiative Group (HIPCIG) should be set up in each implementing institution to consist of core implementers of the ARV and the PMTCT and other HIV-related programmes to ensure better coordination, and enhance the PMTCT Plus strategy. The group should meet regularly, and develop comprehensive plan and implement accordingly.
- NASCP should meet with implementing partners working on PMTCT to determine the process and mechanism for collaboration

ANNEX IV: MINIMUM CRITERIA FOR THE ESTABLISHMENT OF AN ANTIRETROVIRAL TREATMENT CENTRE

Team Leader : To coordinate the HIV and AIDS care and treatment services at the facility. He can be one of the members of the treatment centre.

Counselling services

-Two counselling rooms

-Three counsellors with one being an adherence counsellor and possibly a nurse-counsellor.

Each counselling room is expected to be confidential, well aerated; if available at least an electric fan.

-A table (optional) in each room.

-Two to three comfortable chairs in each room.

-Provision of VCT services.

Laboratory services

There must be a standard of practice (SOP) in place.

Minimum of two laboratory scientists; and cleaners

-A refrigerator.

[Lockable room or cabinet for record storage.

Routine laboratory tests;-

- Heamatological tests: Hb, PCV (manual heamatology)
- Microbiological tests: Routine testing stool and urine, malaria blood smears, HIV diagnostic spot tests; Sputum AFB staining.
- basic serological tests:- HbsAg, VDRL etc.
- Chemistry test: manual biochemistry. Pregnancy testing. Urinalysis, liver function tests, renal function tests (if available)

Pharmacy services

-One pharmacist.

-Two pharmacy assistants/technicians

-A drug/pharmacy shop

-A drug store: - Storage space for one month supply of ARV drugs.

-A refrigerator

-Adequate pharmacy record

-Use of SOPs.

Out patient care services

-Minimum of two medical doctors.

-Minimum of two nurses

-Minimum of two record clerks/data clerks.

-Locked area with limited access for medical records.

-Established medical record system.

-Hospital cleaners

Other important issues

-There must be in place a functional referral system.

-Arrangement for regular training and updates.

-Internal and external quality control mechanism.

ANNEX V: ADMINISTERING TB TREATMENT

TB is curable, provided patients are detected early and treated promptly according to the NTBLCP guidelines. Once a TB patient has been properly classified, the appropriate treatment regimen should be prescribed.

Effective treatment is achieved through DOT (Directly Observed Treatment), which means that the patient swallows the tablets under the supervision of a health worker or designated community member. Therefore the health worker should ascertain the health facility closest to the patient's home and refer if necessary.

Line of Action:
General health worker:

- Complete a 'TB treatment card' (NTBLCP/TB5) and a 'TB appointment card' (NTBLCP/TB6) for every diagnosed patient according to the NTBLCP guidelines
- For smear negative and extra-pulmonary patients, attach the Medial Officer's report to the treatment card.

LGTBLS :
During next visit to facility, enter all diagnosed patients in the 'LGA TB Central Register' (NTBLCP/TB7) according to the NTBLCP guidelines

Treatment Regimen

Information required in order prescribing correct treatment regimen dosages are:

- Pre-treatment weight (this weight is used to determine the dosage required through out the entire treatment)
  - Use the drug table with the weights to determine dosage
- Pregnancy (ask for last menstrual period)
  - Avoid streptomycin in pregnancy
- Age
  - Avoid Ethambuthol for children less than 6 years.

Ask if the patient is taking birth control medications, anti-epileptic medications, corticosteroids, antiretroviral treatment and oral treatment for diabetes or oral anticoagulants. If yes to any of the above refer to the medical officer.

Drugs used within the NTBLCP for TB treatment are☹

R: Rifampicin	H: Isoniazid	E: Ethambuthol
Z: Pyrazinamide	S: Streptomycin	

Two (2) types of treatment regimens are used:

1. Category 1 regimen (Cat. 1)-Adult: (Short course chemotherapy for new cases) (2RHZE/6EH or 4RH)
2. Category 1 regimen (Cat. 1)-Children: (Short course chemotherapy for new cases) (2RHZ/4RH)

3. Category 2 regimen (Cat. 2) Adult: (Retreatment chemotherapy for relapses, failures, RAD and others) (2S/3RHZE/5RHZE OR 5RHE)
4. Category 2 regimen (Cat. 2)Children: (Retreatment chemotherapy for relapses, failures, RAD and others) (2S,6RHZ)

A treatment regimen consists of two phases:

The initial intensive phase of fully supervised daily administration of drugs is 2 months for new cases (Cat. 1) and 3 months for retreatment cases (Cat. 2)

The continuation phase of treatment for new cases (Cat. 1) is 6 months of monthly drug collection by the patient, and is usually self-administered. For retreatment cases, the continuation phase is 5 months and should be supervised daily or thrice weekly.

These drugs could be used as single tablets or in drug combinations.

Treatment regimens when Fixed Dose Combinations (FDC) are used

ADULTS
Category 1 regimen for new cases (adults): 2RHZE/6EH or 4RH

	Pre-treatment weight			
Regimen	> 70 kg	55-70 kg	38-54 kg	30-37 kg
Intensive phase: daily supervised for 2 months Combined tablet of RHZE (150mg + 75mg+400mg+275mg)	5	4	3	2
Continuation phase: daily for 6 months (monthly collection) Combined tablet of EH (400mg + 150mg)	2	2	2	1
*OR Continuation phase: daily supervised for 4 months Combined tablet of RH (150mg + 75mg)	5	4	3	2

Remark: If the patient weighs less than 30 kg, he should be given single tablets.

Category 2 regimen for relapses, failures, RAD and others (adults):

2SRHZE/RHZE/5RHZE

	Pre-treatment weight			
Regimen	> 70 kg	55-70 kg	38-54 kg	30-37 kg
Intensive phase: daily supervised for 3 months Combined tablet of RHZE (150mg + 75mg + 400mg + 275mg)	5	4	3	2
Add in the first two months daily: Streptomycin	1 gram	1 gram	0.75 gram	0.5 gram
Continuation phase: daily intake for 5 months, supervised Combined tablet of RHZE (150mg + 75mg + 400mg + 275mg)	5	4	3	2

i Streptomycin should NOT be given to pregnant women.
ii Patients >45 years should not be given more than 0.75g of streptomycin irrespective of weight

CHILDREN (0-14 YEARS)

Category 1 regimen for new cases (children 0-14 years): 2RHZ/4RH

	Pre-treatment weight			
Regimen	21-29 kg	11-20 kg	5-10 kg	< 5 kg
Intensive phase: daily supervised for 2 months Combined tablet of RHZ (60mg+30mg+150mg)	4	3	2	1
Continuation phase: daily for 4 months (monthly collection) Combined tablet of RH (60mg + 30mg)	4	3	2	1

Children with severe forms of TB (TB meningitis, Diseminated TB, TB Spine, TB pericarditis) should have streptomycin added during Intensive Phase.

Category 2 regimen for relapses, failures, RAD and others (children 0-14 years):

Treatment regimens when non-combined(Single) tablets are used

ADULTS

Category 1 regimen for new cases (adults): 2RHZE/6EH OR 4RH.

Regimen	Pre-treatment weight		
Intensive phase: daily supervised for 2 months	> 55 kg	40 - 55 kg	25-39 kg
(E) Ethambutol 400 mg	3	2	1 ½
(H) Isoniazid 100 mg) (R) Rifampicin 150 mg) combined tablet	4	3	2
(Z) Pyrazinamide 400 mg	4	3	2
Continuation phase: daily for 6 months (monthly collection) (E) Ethambutol 400 mg) (H) Isoniazid 150 mg) combined tablet	2	2	1
OR (R) Rifampicin 150mg) (H) Isoniazid 100mg.) Combined.	4	3	1

Category 2 regimen for relapses, failures, RAD and others (adults):

2SRHZE/RHZE/5(RHE)

Regimen	Pre-treatment weight		
Intensive phase: daily supervised for 3 months	> 55 kg	40 - 55 kg	25-39 kg
(H) Isoniazid 100 mg) (R) Rifampicin 150 mg) combined tablet	4	3	2
(Z) Pyrazinamide 400 mg	4	3	2
(E) Ethambutol 400 mg	3	2	1 ½
Add in the first two months daily: (S) Streptomycin	1 gram	0.75 gram	0.5 gram
Continuation phase: supervised 3 times a week for 5 months			
(R) Rifampicin 150 mg) (H) Isoniazid 75 mg) combined tablet (E) Ethambutol 275 m)	4	3	2

Streptomycin should NOT be given to pregnant women.
Patients >45 years should not be given more than 0.75g of streptomycin irrespective of weight

ART CARD

1. Patient Surname_____ Other names _____ 2.**Unique ID** □□□-□□□-□□□□ 3. Hospital (Unit) No. _____

Including aka/alias

4. Date Confirmed HIV+ test_____ 5. Where_____ HIV 1 2 Ab / PCR 6. Date Enrolled in HIV care _____

7. Date Medically eligible_____ 8.Why eligible: ☐Clinical only ☐CD4/%_____ ☐TLC_____ 9. Clinical stage_____

10. Date ART started_____ 11. Date Transferred in_____ from _____

12a. Date **Start ART 1st-line initial regimen:**_____ 12b. **1st-line initial regimen _____ 12c.At start ART: Weight _____ Function_____ Clinical stage_____**

Substitute within 1st-line:

13. Date New regimen_____ * Why_____ Date New regimen_____ *Why_____

Switch to 2nd-line (or substitute within 2nd-line):

14. Date New regimen_____ *Why_____ Date New regimen_____ *Why_____

Date New regimen_____ *Why_____ Date New regimen_____ *Why_____

15a.Discontinuation category: i. patient transferred Date _____ To where:_____

ii. patient requests withdrawal

iii. patient has died Date _____ **Cause of death _____ HIV related Yes□ No □ Toxicity from ART □ Unknown □**

3mths > 3mths

15b Lost to follow up 1. ☐ ☐ Date ART restarted _____

2. ☐ ☐ Date ART restarted _____

16. Primary source of death information: 1. clinical record 2. Obituary 3. Health care provider 4. Death certificate 5. Relative/friend 6. Other

17. ART treatment interruptions

Stop Lost (circle)	**Date**	*** Why**	**Date if Restart**
Stop Lost			
Stop Lost			
Stop Lost			
Stop Lost			

Codes for 17
Why STOP codes[7]:
1 Toxicity/side effects
2 Pregnancy
3 Treatment failure
4 Poor adherence
5 Illness, hospitalization
6 Drugs out of stock
7 Patient lacks finances
8 Other patient decision
9 Planned Rx interruption
10 Other (specify)

Codes for 13,14
Why SUBSTITUTE or SWITCH codes:
1 Toxicity/side effects
2 Pregnancy
3 Risk of pregnancy
4 Due to new TB
5 New drug available
6 Drug out of stock
7 Other reason (specify)
Reasons for SWITCH to 2nd-line regimen only:
8 Clinical treatment failure
9 Immunologic failure
10 Virologic failure

Unique ID □□□-□□□-□□□□ HIV CARE/ART CARD Patient Name_____

18 Visit Date Check if scheduled. Write in alternate pick-up if ill	**19** Wt	**20** Height	21 * LMP If **P**regnant EDD? PMTCT code.	**22** * **FP/no FP** If FP write method(s)	23 Function **W**ork **A**mb **B**ed	24 WHO clinical stage	25 * TB status	26 * Other SYMPTOMS/ New OIs	**27 ARV drugs** * Adhere/ Why	28 Regimen/Dose dispensed	Cotri-moxazole * 27 Adhere /why	Dose	29 Other drugs Dispensed/ Traditional treatment	30 Duration in months since first starting ART/ since starting current regimen	31 * Potential SIDE EFFECTS	32 CD4	33 VL	34 Hb, RPR, TLC, other lab	35 Consult or, Hospitalise or, Refer or, link	36 Next appt date
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Codes 21,22
Pregnancy//family planning status.
1. On PMTCT
2. Not on PMTCT
3. Family planning
4 Not on family planning

Codes 25
TB status (check on each visit):
1. no signs or symptoms of TB
2. TB suspected and referred for evaluation
3. Currently on INH prophylaxis (IPT)
4. Currently on TB treatment. Record TB card
5. TB suspected and sputum sample sent or record results

Codes 26 New OI or other problems:
1.Herpes Zoster
2.Pneumonia
3. Dementia/**Enceph**
4.Thrush–oral/vaginal
5. Fever
6. Cough
7. Difficult breathing
8.I Immune reconstitution
9. Inflammatory Syndrome
10. Weight loss
11. Urethral discharge
13. Pelvic inflammatory disease

Codes 31 Probable side effects or other problems:
1.Nausea/vomiting
2. Headache
3.Insomnia/bad dreams
4 Fatigue/weakness
5.PV bleeding/discharge
6.Rash
7.FAT changes
8.Anemia
9 Drainage of liquor
10.Stevens **J**ohnson syndrome
12.Diarrhoea
13.Confusion/dizziness
14.Itching
15.Kidney problems
16.Abdominal pain
17.Tingling of extremities
18.Vaginal itching
19.Liver toxities
20.Painful **uterine** contractions

Codes 27,28
ART adherence. Estimate adherence for twice daily ART using the following table, OR:

Poor**3**: Missed ARV in last 3 days
Poor**W**: Missed ARV in last week

Codes 27,28 Adherence	%	Missed doses per month
G(good)	≥ 95%	≤ 3 doses
F(fair)	85-94%	4-8 doses
P(poor)	< 85%	≥ 9 doses

Codes 27,28 Why Poor adherence:
1 Forgot
2 Fell asleep/slept through dose
3 Change in routine/away from home
4 Busy/working/at school
5 Got pregnant
6 Patient moved
7 Ran out of medications
8 Drug stock-out
10 Felt well
11 Felt sick/bad
12 Felt overwhelmed/depressed
13 Did not understand how to take meds
14 Did not want others to know
15 Too many pills
16 Did not want to take meds
17 Afraid of/affected by drug side effects