



HIV Treatment and Care: Antiretroviral Therapy Selection Guidelines

2006

The National AIDS Control Program
Ministry of Health
Government of Pakistan

ACKNOWLEDGEMENTS

The National AIDS Control Program, Ministry of Health is pleased to develop the national guidelines to standardize the selection criteria to initiate antiretroviral therapy (ART) for HIV infected individuals and strongly promote treatment adherence. Though the National AIDS Control Program is working towards scaling up of universal access and availability of ART, it will be a while before all those who need ART will be able to receive it. These guidelines are mainly intended for health care providers to assist them in providing standardized and equitable access to ART based on “international best practices” used in other resource constrained settings for their patients, and for people affected by HIV/AIDS to understand the tremendous limitations and challenges faced by the National AIDS Control Program in utilizing scarce resources most effectively to combat the HIV epidemic.

NACP is appreciative of the Infectious Disease specialists Dr. Faisal Sultan (Shaukat Khanum Memorial Hospital), Dr. Anita Zaidi (The Aga Khan University Hospital), Dr. Naseem Salahuddin (Liaquat National Hospital), Dr. Maqsood Bhatti (The Aga Khan University Hospital), Dr. Rizwan Qazi (PIMS Hospital), Dr. Farheen Ali (Liaquat National Hospital), Dr. Mahmud Javid (Shifa International Hospital), Dr. Shaukat Bangash (Quaide-Azam Hospital), Dr. Mohammed Aslam (The Aga Khan University Hospital) and Dr. Sobia Qazi (Services Hospital, Lahore), who took time out from their busy schedules to give valuable insights and share their experiences of HIV care in Pakistan and make constructive comments on the overall strategy.

NACP would like to acknowledge that this document has greatly benefited from issues raised by Dr. Samia Hashim (UNAIDS), Ms. Bettina Schunter (UNICEF) and Dr. Amer Raza and without doubt from numerous PLWHA who so generously shared their firsthand experiences. This document has extensively utilized resource materials & publications by WHO, UNAIDS, John Snow International and Family Health International on establishing HIV treatment and care centers and scaling up delivery of ART in resource-constrained settings.

Thanks are also extended to the Global Fund for fighting AIDS, TB and Malaria for their support in funding ARVs for Pakistan. Finally NACP recognizes the firm commitment of the Ministry of Health, Government of Pakistan in establishing comprehensive HIV treatment and care services and providing free ARVs to its HIV positive citizens.

National Program Manager
The National AIDS Control Program

PREFACE

In 20 years of the HIV/AIDS epidemic the world has learned some sobering lessons. We have learned that in HIV, prevention and care are not competing priorities, they are mutually reinforcing strategies. Extending access to treatment in the most resource constrained settings is a priority, because it brings renewed hope and greater mobilization in the response to the epidemic. For the first time, affordable ARV prices, new sources of international funding and growing political commitment by the Government of Pakistan, makes providing treatment and care for Pakistan's HIV positive persons an achievable goal.

Unfortunately, the cost of ARVs and the supporting laboratory diagnostics required to initiate and monitor ARV therapy, is still beyond Pakistan's resources to provide free treatment to everybody who needs it. The dilemma arises when the need for ART exceeds the supply, trying to identify which patients have a priority.

Antiretroviral therapy (ART) should be part of a continuum of care: a comprehensive approach that involves voluntary counseling and testing, availability of other prevention and social support services, and prevention of mother-to-child transmission.

People living with HIV/AIDS (PLWHA) and the medical community both have a crucial role to play in preparing HIV positive people to initiate and continue HIV treatment over the long term. As key beneficiaries of treatment, care and prevention programs PLWHA need to be actively involved in their own health care decisions, participate in community mobilization, advocacy and ensure that scarce resources are utilized efficiently.

While this guide primarily addresses "priority setting" selection criteria for initiating ART, it also encourages health care providers and PLWHA to initiate linkages between HIV treatment and care centers, VCT centers and other community based support organizations to provide comprehensive care services to HIV positive persons and their families. Throughout this guide health care providers, National and provincial AIDS Control Program planners and NGOs/CBOs working with HIV/AIDS are encouraged to seek opportunities for addressing gender inequities, improving ARV treatment access and ensuring rigorous implementation of standardized and simplified ARV regimens in order to reduce the prevalence of HIV/AIDS in Pakistan.

Abbreviations:

| | |
|--------|---|
| AIDS | Acquired Immune Deficiency Syndrome |
| ANC | Antenatal clinics |
| ARV | Antiretroviral |
| ART | Antiretroviral therapy |
| CBO | Community based organization |
| CDC | Centers for Disease Control and Prevention (US) |
| CO | Community Organization |
| ddI | Didanosine |
| EFV | Efavirenz |
| FHI | Family Health International |
| FPC | Family planning clinics |
| HIV | Human Immunodeficiency Virus |
| ID | Infectious Disease specialist |
| IDU | Injection Drug Users |
| NACP | National AIDS Control Program |
| NFV | Nelfinavir |
| NGO | Non-governmental Organization |
| NVP | Nevirapine |
| OI | Opportunistic infection |
| PACP | Provincial AIDS Control Program |
| PEP | Post-exposure Prophylaxis |
| PLWHA | People Living with HIV/AIDS |
| PI | Protease inhibitors |
| PMTCT | Prevention of Mother-Child Transmission of HIV |
| STIs | Sexually Transmitted Infections |
| TB | Tuberculosis |
| TLC | Total Lymphocyte Count |
| WHO | World Health Organization |
| UNAIDS | United Nations Joint Co-sponsored Program on AIDS |
| VCT | Voluntary Counseling and Testing |
| 3TC | Lamivudine |
| d4T | Stavudine |
| ZDV | Zidovudine |

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Introduction

HIV/AIDS is a devastating, human crisis that has affected many countries, particularly those in Sub-Saharan Africa. Now 20 years later far from leveling off the epidemic continues to expand relentlessly destroying people's lives and in many countries causing near complete collapse of public health, economic and social systems.

In 2004, an estimated 40 million people globally were living with HIV, majority of who reside in the developing world. The HIV pandemic has already claimed more than 3 million lives and close to 5 million people acquired the infection in 2004. Most alarmingly, countries in Asia and Eastern Europe are now experiencing the fastest growing HIV epidemics in the world. The large, populous countries of China, India and Indonesia are of special concern. While general prevalence remains low in these countries, it masks the serious and complex epidemics already underway in individual states and provinces.

In many countries formation of national and international partnerships are the key building blocks in effectively containing the epidemic through scaling up of HIV prevention programs, testing and counseling services and expanded access to antiretroviral (ARV) therapy. The scaling up of ARV therapy, if managed properly, can strengthen both HIV prevention programs and the broader health systems. The success in slowing the HIV epidemic will ultimately be determined by the action taken in countries, by governments, civil society, health care providers and partner organizations.

Epidemiology of HIV/AIDS in Pakistan

Since the diagnosis of the first HIV/AIDS case in 1987, Pakistan has progressed to 3000 plus cases nationwide. However, these numbers may be a vast underestimation of the actual picture (UNAIDS/NACP estimates 74000 HIV/AIDS cases, 0.1% prevalence). While heterosexual transmission remains the predominant mode of spread it is concerning to see rapidly developing concentrated epidemics among injection drug users (IDUs) and commercial sex workers.

Epidemiological studies over the past decade have shown that HIV epidemics among high risk groups such as sex workers, men having sex with men (MSM), IDUs and migrant workers may develop independently of each other, depending on the sexual bridges between these populations. However, once HIV is established in these groups it is only a matter of time before the epidemic spreads into the general population. The National AIDS Control Program is aware of the growing challenge of HIV and its implications not only for the health sector but on all aspects of human development. A national strategy focusing on prevention efforts, promoting voluntary counseling and testing, effective behavior change communications, and access to ARVs within the framework of a comprehensive care and support program are the key building blocks in achieving the national goals of containing the HIV epidemic, reducing stigma, and mitigating the social and economic impact of the disease.

Definitions

HIV (Human Immunodeficiency Virus): HIV is caused by a retrovirus that progressively destroys the body's immune system (infection fighting cells) leading to increased risk of infections and certain cancers.

HIV is spread through sexual contact with an infected person, contact or transfusion with infected blood, mother to child transmission, and sharing contaminated needles and syringes. **HIV does not spread through saliva, urine, feces, tears, sweat, insect bites or casual contact (sharing utensils, toilet seats, shaking hands, touching or bedding etc).**

AIDS (Acquired Immune Deficiency Syndrome): AIDS is the most severe form of HIV infection. HIV infected patients are diagnosed with AIDS when their CD4 cells fall below 200 cells/mm³ or when they develop an AIDS defining illness (an illness that is very unusual in someone who is not HIV positive).

CD4 cells: are types of white blood cells that fight infection. They are also called CD4 T cells or CD4 T lymphocytes. A CD4 count is the number of CD4 cells in a sample of blood and helps define the stage of immune defect (i.e mild, moderate or severe). CD4 counts are helpful in determining when to initiate prophylaxis for opportunistic infections (OIs) and antiretroviral therapy (ART)

When HIV enters a person's CD4 cells, it uses the host cells to make copies of itself and continuously infect other CD4 cells. This process destroys the CD4 cells, and the CD4 cell count goes down. As the number of CD4 cells goes down, the immune system weakens and the body loses its ability to fight infections and other diseases (cancer).

HIV Viral load: The amount of HIV in a sample of blood. HIV viral load is used to monitor response to ART and overall disease progression. During effective ART treatment the HIV viral load becomes undetectable in the blood (i.e less than 400 copies/ul or in some cases < 50copies/ul) within 6-8 weeks in majority of the cases. An undetectable viral load does not mean that the person is uninfected or can not transmit the infection to others. An undetectable viral load simply means that the HIV virus is successfully suppressed by the medicines and the person has a less chance of transmitting the infection to other susceptible individuals.

Drug Resistance: HIV can mutate (change form) while a person is taking ART, especially if the person is not adherent to their regimen. This results in HIV infection that cannot be controlled with the usually available anti-retroviral medications. Persons with drug resistant HIV are very difficult to treat since effective/available ART medications no longer work against the infection.

Difference between Treatments versus Cure: HIV treatment should always include 3 drug therapy except for post-exposure prophylaxis (PEP) and preventing mother-child transmission (MTCT). Mono or dual drug therapy is detrimental for the patient and must never be prescribed by the health care provider except for prophylaxis situations i.e PEP and MTCT prevention. Treatment can help people at all stages of HIV disease. ***Although anti-retroviral medications can treat HIV infections, they cannot cure HIV and have to be***

taken life long (forever). HIV therapy is complicated and recommended treatment regimens must be strictly followed by both the patient and health care providers.

Antiretroviral Therapy (ART) Regimens

| <u>ARV Regimens:</u> |
|---|
| <p>1st line:</p> <ul style="list-style-type: none">• Zidovudine + Lamivudine + Nevirapine (recommended 1st line) <i>or</i>• Zidovudine + Lamivudine + Efavirenz <i>or</i>• Stavudine + Lamivudine + Nevirapine (recommended 1st line alternate) <i>or</i>• Stavudine + Lamivudine + Efavirenz <p>Pediatric:</p> <ul style="list-style-type: none">• Zidovudine or Stavudine + Lamivudine + Nevirapine (preferred) or Efavirenz (for children >3 years) |
| <p>2nd line:</p> <ul style="list-style-type: none">• Tenofovir + Didanosine + Nelfinavir <i>or</i>• Tenofovir + Didanosine + Saquinavir/ritonavir or Lopinavir/ritonavir <p>Pediatric:</p> <ul style="list-style-type: none">• Abacavir + Didanosine + Nelfinavir or Lopinavir/ritonavir or Saquinavir/ritonavir (only for children >25kg) |

Importance of Adherence in ART

Adherence to ARV regimens is absolutely essential in order to obtain successful results from treatment and to minimize the emergence of drug resistance. Studies of adherence in the developed world have suggested that >95% adherence to the prescribed dosing schedule is necessary to maximize the benefit of ART. While clinical/immunological data are critical in initiating ART, patient motivation and actual readiness, and ability to follow a complex medical regimen are essential for treatment success.

Pre-treatment counseling emphasizing adherence, ongoing adherence counseling and monitoring of adherence are all part of ensuring that patients rigorously follow their prescribed ARV regimens.

Strategies that Encourage and Support Treatment Adherence

1. Stable living situation
 - The physician and counselor should be aware of the patient's home environment (i.e living at home, HIV disclosure status to close family members/spouse, the number of family members residing at home, relationship to the patient, the general family dynamics)
2. Good social support from family and/or close friends
 - Encourage voluntary disclosure of HIV positive status to supportive family members or close friends.
 - Discuss barriers to disclosing HIV status and assist the patient in overcoming them.
 - Addressing disclosure status at follow up clinic visits to address new issues
3. Identification and involvement of close family member or friend as a "treatment assistant/supporter"
 - Involvement of a "treatment supporter" in all aspects of patient care improves long term treatment success particularly in case of ART.
 - Emphasizing adherence to the treatment supporter as well.
4. Establishing a relationship of trust and rapport between patient, medical care provider and the counselor.
 - The patient should view the counselor as a liaison/patient advocate between him/her and the physician.
 - Patient must clearly understand that all information shared will be strictly confidential.
5. Identification of barriers to treatment adherence and available solutions to overcome them
 - Examples financial concerns, transport issues need to be directly discussed during counseling sessions and in physician visits.
 - Strategies using direct and indirect inquiry into reasons for non-adherence should be used.
6. Development of understanding and insight into his/her disease status and long term commitment to treatment adherence
 - Repeated open discussions with the patient (and family) will assist the patient in developing insight into the disease process.
 - ART should only be started when the patient is ready to accept treatment; do not look only at the medical criteria and do not lose patience. In the long term prematurely initiated ART will not benefit the patient i.e starting ART at CD4 counts > 300, or when the patient is not mentally ready to commit to ART.

7. Assist the patient in setting long term goals
 - Encourage the patient to think about the long term benefit of treatment and not the immediate discomforts (number of pills, side effects, schedule restrictions etc)
 - Directly inquire what the overall expectation and goals with medication are. Expectations should be realistic and clearly understood by the patient and health care providers.

8. Simplify regimens
 - Address complex regimens repeatedly to ensure adherence
 - Develop materials and tools to facilitate patient in long term adherence.

9. Address fears, stigma and other beliefs that may interfere with treatment adherence.
 - These can be culturally sensitive and specific to the local context

10. Promote and encourage enrollment and/or participation in PLWHA support groups.
 - Availability of contact information should be present with the counselor/clinic

11. Improve ways to work with literacy barriers
 - Using easily understandable terms, pictures and symbols to explain meanings.
 - Develop materials for low literacy/no literacy audience

12. Be extra alert for identifying and treating mental illness, especially depression.
 - Depression increases chances of non-adherence

13. Integrate HIV care services into a comprehensive continuum of care approach.
 - Develop linkages with community support systems and NGOs
 - Clearly define the referral chain to the patient and partner NGOs

Implications of Non-Adherence

Medical:

1st line ART regimens are convenient (low number of pills and easier 1-2 times/day dosing), more effective in controlling the HIV infection and generally have less side effects compared to 2nd line regimens. Non-adherence or poor adherence of ART (i.e missing more than 3 doses in a month) leads to development of drug resistance to the current regimen (i.e 1st line) and severely limits the choices and response to other ART regimens.

Financial:

The economic consequences of developing of drug resistance as a result of poor adherence is not just in terms of 2nd line regimen costs but also includes the additional burden for laboratory testing (viral load, CD4, HIV genotyping) and the increased risk of transmission of drug resistant HIV strains into the susceptible population.

Impact on HIV Transmission Dynamics:

ART reduces the transmission of HIV. However, patients on ART who develop drug resistant strains can transmit that drug resistance to other contacts through sexual intercourse, contaminated needles or blood products and through mother-child transmission. For people

infected by drug resistant strains the standard 1st line regimens are not effective and in some cases even the 2nd line regimens may no longer work depending on the degree of resistance present.

Rationale for Selection Criteria Using an Integrated Approach

The number of patients who will be eligible on clinical and immunological basis for ART initiation is likely to exceed the amount of antiretrovirals currently available free of cost to PLWHA in Pakistan. Therefore, like many other developing countries additional adherence criteria have been developed to ensure provision of ARVs to those HIV positive patients who are most likely to follow the prescribed treatment (treatment adherence) and therefore benefit the most from these life saving but demanding antiretroviral regimens.

This integrated approach uses a combination of clinical and adherence criteria to assist health care providers in selecting patients through a subjective but transparent and standardized process. The adherence criteria may provoke debate and controversy but the general consensus is that such “priority settings” are necessary to maximize benefit of ART to patients who are most likely to be compliant with treatment and until the time that ART is more widely available to all those in need. The eligibility and ineligibility criteria are:

Eligibility Criteria

Medical

- Confirmed HIV positive status (using 2 different tests ELISA, 2 different rapid tests or Western Blot)
- CD4 counts less than 200/mm³
- WHO stages 3 or 4 regardless of CD4 count
- Asymptomatic patients (stage 1 or 2) with CD4 less than 200/mm³

Adherence

1. Must attend 2- 3 pre-ART counseling sessions. Attendance is mandatory for a minimum of 2 sessions. Additional counseling sessions may be needed based on the counselor or physicians assessment.

and

Express firm commitment and readiness to following treatment regimen exactly as prescribed and attend the scheduled clinic visits. Patient should inform health care provider immediately of any unexpected adverse events or drug toxicities and/or when stopping the medications.

Note: Pre-Art counseling sessions are separate from pre and post test counseling or counseling for other HIV related issues.

Pediatric Eligibility Criteria

Medical

Medical

- WHO Pediatric Stage 3 or 4
- WHO Pediatric Stage 1 or 2 with CD4 <20% (if younger than 18 months) or CD4 <15% (if older than 18 months)
- Recurrent hospitalizations (>2 admissions/year) for HIV related disease or prolonged hospitalization (>4 weeks)

Adherence

1. An identifiable adult caregiver who is able to administer medication
- and**
2. Demonstrated reliability in adult caregiver i.e has attended 2 or more scheduled counseling sessions.
- and**
3. Caregiver must express firm commitment to follow the treatment regimen and attend the scheduled clinic visits.

Special Note:

Checking the immunization record is a good indicator of reliability of the caregiver. Previous record of adherence to nutritional supplements or other chronic care regimens such as TB drugs may help identify children who are at risk of poor adherence.

The medical and adherence eligibility criteria must be met before ART initiation, while treatment should be deferred or not initiated in those who meet the medical or adherence ineligibility criteria.

Ineligibility Criteria

Medical

- CD4 cell count greater than 200/mm³
- Asymptomatic patient and WHO stages 1 or 2 (unless CD4 count is less than 200/mm³)
- Terminal stage liver disease (decompensated cirrhosis with recurrent ascites needing daily drainage)
- Terminal stage kidney disease (example, on dialysis)
- Terminal stage cardiac disease (Stage IV cardiomyopathy)
- Advanced cancer or any other terminal medical condition (excluding HIV related terminal condition)
- Advanced HIV-related dementia or encephalopathy (these are irreversible conditions even after ART initiation)

Adherence

Active injecting drug users (IDUs)* who are unable to maintain regular clinic appointments and counseling sessions.

Special Note:

Strict adherence to the ARV regimen is the single most important determinant of good clinical outcome. Ineffective utilization of ARVs on non-adherent patients is harmful for the individual's health outcome and promotes the development of drug resistant strains of HIV.

While understanding the limitations of accurately predicting adherence in individual situations (i.e exceptions are always present), nonetheless scientific evidence supports that active IDUs generally have poor or erratic compliance with ART programs without comprehensive supportive services to address the active drug use (i.e substitution and drug rehabilitation programs), lack of stable living situations, psychological (i.e depression) and medical co-morbidities (i.e wound care, Hepatitis B or C co-infections) and poor social support. HIV Care Programs need to closely collaborate with NGOs and Primary Care services to effectively provide necessary services to IDUs.

For HIV positive active IDUs, efforts at the national and civil society level need to focus on development of comprehensive care and support services including substitution programs into which ART can then become effectively incorporated.

Treatment Deferral

A patient is eligible for treatment deferral for the following reasons:

- Patient does not currently meet the medical and/ or adherence criteria for ART initiation
- Patient is not ready to begin ART or is unwilling to follow the adherence counseling

- Patient can not keep or follow scheduled clinic visits
- Has an active opportunistic infection that should be treated prior to the initiation of ART. Example, treatment for pulmonary TB should be initiated and preferably completed prior to ART initiation. In situations where the CD4 count is very low <50 or patients clinical status requires early initiation of ART then deferring treatment until after the intensive phase (i.e 2-4 weeks) is recommended.
ART is never an emergency and should not be started in haste.
- 1st trimester pregnancy (the patient does not medically qualify for ART initiation and/or is unwilling to initiate ART at this time). All pregnant HIV positive women should be counseled about transmission risks to their unborn child and advised to initiate PMTCT regimens as per national guidelines.
- Active drug user (IDUs) currently in detoxification program and interested to start ART. IDUs need to complete drug detoxification and drug rehabilitation programs and should be “drug free” for 3 months before initiating ART. The HTCC should link up with NGOs working with IDUs to ensure a holistic approach to care of the patient.

For patients in the treatment deferral process, initiation and continuation of medications for OIs (as applicable), monitoring of clinical progression of HIV/AIDS, adherence and disease counseling and follow up scheduling on a regular basis, remains very important.

Benefits of Deferred Therapy

- Avoidance of ART related negative side effects on quality of life and drug related toxicities. Starting ART early (i.e CD4 cells >300) is not beneficial for the patient in the long term.
- Preservation of treatment options in the future. Better availability of more potent ARVs in the future.
- Delay in development of drug resistance
- More time for the patient to have greater understanding of ART demands
- Decreased time on ART with reduced chances of treatment fatigue (i.e non-adherence over the long term)
- More time for the development and availability of more potent, less toxic and better studied ART combinations.

Entry Points to HIV Treatment and Care Center

Scaling up access to antiretroviral (ARV) treatment must build on existing clinical or public health services and extend their coverage. It also means making the most of synergies between prevention and care, recognizing that people are more likely to follow prevention advice when they receive comprehensive services. To accomplish this, it will be necessary to utilize existing opportunities i.e *entry points* - for identifying people who could benefit from treatment. Entry points must provide, or facilitate the link to, HIV testing and counseling, the *gateway* to treatment services. Entry points include:

- Clinical situations where there may be a high suspicion of HIV-related disease (acute clinical services, TB services) or where people seeking care have a high likelihood of HIV infection (STI clinics or drug treatment services).
- Community-based opportunities for identifying people within high-prevalence networks who are not using clinic services.

Key Focus Areas...

- **Go** where HIV infection and HIV-related disease is.
- **Find** people who need treatment most.
- **Reach** out to people who do not come to you through PLWHA and community outreach.

HIV Treatment and Care Linkages Checklist

- Strengthen community outreach for voluntary counseling and testing services
- Collaborate with tuberculosis (TB) services to recognize and refer suspected HIV cases for VCT or to the treatment and care center.
- Sensitize health care providers to actively seek patients sick with HIV/AIDS in acute medical clinics and hospital wards
- Work with maternal and child health (MCH) and mother-to-child transmission (MTCT) prevention programs.
- Link sexually transmitted infection (STI) and ART services
- Establish linkages with IDU drug rehabilitation programs
- Generate demand for HIV counseling and testing

Key Entry Points

Many people using the following services are likely to have HIV-related illness and would benefit from ART

i) TB Services

HIV is fuelling the TB epidemic in regions with a high prevalence of HIV (Africa) and is one of the most common causes of morbidity and mortality in HIV-positive adults. In some high-burden countries, more than 70% of TB patients are co-infected with HIV. However, in low

prevalence countries like Pakistan where TB is endemic performing HIV testing on every TB patient would not be cost effective.

According to National Guidelines, TB programs need to risk categorize patients for HIV infection and provide appropriate HIV counseling and testing services. In many localities the TB services can serve as initial entry points to develop, where many patients in immediate need of ART may be found.

ii) **Acute medical services (clinic and hospital ward)**

In a similar way to TB services, medical clinics (adult and pediatric) and hospital wards have a high proportion of HIV-infected patients. Many high-burden countries report bed-occupancy rates in excess of 50% related to HIV. Children's wards are similarly challenged by HIV. Medical facilities can serve as an important entry point for ART services, and it is critical to provide HIV clinical management training to a wider array of physicians and paramedical staff.

iii) **Home-based care**

Home based care is an important aspect of the continuum of care model for HIV management. Many countries have home-based care services, often run by nongovernmental organizations (NGOs) and community-based organizations (CBOs). Usually home-based care is focused on chronically sick, debilitated individuals known to be infected with HIV, and should be an important entry point to ART programs. Rather than focusing on counseling and testing, this entry point needs to speed up the ways that individuals can be clinically evaluated for immediate commencement of ART. It is likely that with HBC services, the majority will urgently need to start ART

iv) **MCH clinics and MTCT Prevention Programs**

While enhancing the prevention of HIV infection in infants, HIV-related care and treatment needs to be extended to HIV-infected women and their families. MCH clinics can serve as an obvious entry point for ART programs. To this effect clinical screening of women for signs of HIV-related disease need to be included, to compliment the provision of testing and counseling and ARVs for prevention of mother-to-child transmission.

v) **Link STI and HIV services**

STIs facilitate the spread of HIV and serve as a marker for infection. Services providing STI care should routinely offer testing and counseling to ensure that STI patients can find out their HIV status and be evaluated for treatment; and informed about HIV treatment and care centers where they can regularly be reviewed for disease progression.

- Scale up HIV counseling and testing within STI services, including private-sector providers.
- Train health care providers providing STI care to clinically screen and better identify and refer persons who might be eligible for antiretroviral treatment.

- Emphasize the provision of youth-friendly services that promote STI symptom recognition and awareness of HIV status.
- Use simple clinical protocols and strengthen capacity of health care workers providing STI services.

vi) **Establish Linkages With Drug Rehabilitation Programs**

In some regions, injecting drug users (IDUs) comprise a significant proportion of infected persons. While the majority may initially be asymptomatic, almost all will eventually require antiretroviral treatment. However the issues of treatment adherence and active injecting drug use need to be taken into account.

- Increase access to both voluntary and health-service-provider-initiated testing and counseling (with informed consent) in drug dependence treatment and harm-reduction facilities with referral linkages.
- Establish collaborations with substance-dependence treatment (including drug substitution) programs to help stabilize IDUs and improve treatment adherence.
- Deliver ART through drug dependence treatment services.

vii) **Reaching Out to Vulnerable Groups**

Many people who need HIV prevention, care and treatment are beyond the reach of health-care services. Poverty, migration, civil unrest, stigma and discrimination are among factors that marginalize people, increase their vulnerability to infection and reduce their access to services. The combined hazards of vulnerability and poor access are often most acute among young people. In order to increase access and uptake of integrated HIV services, 'active' entry points are needed to reach out to marginalized populations that do not seek treatment on their own.

- Integrate existing prevention services for sex workers, men who have sex with men and others with testing and counseling, care and treatment.
- Work with especially vulnerable young people (e.g. out-of-school, slum-dwelling adolescents) through peer networks and youth-friendly health services.
- Work with employers, unions, social services, NGOs, CBOs and FBOs to extend prevention and treatment services to transport and itinerant workers who may be particularly vulnerable and in need of treatment

Challenges for Using an Integrated Medical and Social Selection Criteria for ART:

Policy makers and AIDS control programs will have to grapple with the challenges and ethical issues inherent in developing ART programs that at least for some time ahead, can only reach some of the PLWHA in need. Yet the realization and risks that the program will not be completely fair can not be used as an excuse to delay action. Because people may disagree on who should receive ART, when, how and where this should happen, the guiding principles should be transparent, public, inclusive and revisable. They should aim to ensure that decisions on the initiation and implementation of ART programs are equitable and as

transparent as possible, and disseminated clearly among PLWHA to foster their support, even if these PLWHA voice disagreement.

Ethical Considerations

In order to promote ART scale up that is as effective and fair as possible, policies and procedures should try to ensure that the most marginalized and vulnerable populations have crucial access to HIV treatment and care services. Particular focus needs to be given to

- Equitable access for women and children
- Addressing the barriers to treatment and care and reaching out to marginalized groups i.e sex workers, IDUs,
- Developing standardized national criteria for ensuring patient confidentiality and the importance of informed consent
- Integration of HIV care and support within the framework of primary health care services
- Involvement and mobilization of PLWHA in shaping the national HIV/AIDS policy

Appendix 1:

REVISED WHO CLINICAL STAGING OF HIV FOR ADULTS AND ADOLESCENTS

(For use in those 15 years of age or more with positive HIV antibody test or other laboratory evidence of HIV infection)

| |
|--|
| PRIMARY HIV INFECTION |
| Unrecognized Acute retroviral syndrome ⁱ |
| CLINICAL STAGE 1 |
| Asymptomatic Persistent generalized lymphadenopathy (PGL) |
| CLINICAL STAGE 2 |
| Moderate unexplained weight loss (<10% of presumed or measured body weight) Recurrent upper respiratory tract infections (sinusitis, bronchitis, otitis media, pharyngitis) Herpes zoster Angular cheilitis Recurrent oral ulcerations Papular pruritic eruptions Seborrhic dermatitis Fungal nail infections of fingers |
| CLINICAL STAGE 3 |
| <i>Conditions where a presumptive diagnosis can be made using clinical signs or simple investigations</i> Severe weight loss (>10% presumed or measured body weight) Unexplained chronic diarrhoea for longer than one month Unexplained persistent fever (intermittent or constant for longer than 1 month) Oral candidiasis Oral hairy leukoplakia Pulmonary tuberculosis ¹ (diagnosed in last two years) Severe presumed bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteremia) Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis |
| <i>Conditions where confirmatory diagnostic testing is necessary</i> Unexplained Anemia (<8gm/dl), neutropenia (<1,000/mm ³) or thrombocytopenia (<50,000/ mm ³) for more than 1 month |
| CLINICAL STAGE 4 |
| <i>Conditions where a presumptive diagnosis can be made using clinical signs or simple investigations:</i> HIV wasting syndrome Pneumocystis pneumonia Recurrent severe or radiological bacterial pneumonia Chronic Herpes simplex infection; (orolabial, genital, or anorectal of more than 1 month duration, or visceral of any duration) Oesophageal Candidiasis Extrapulmonary tuberculosis Kaposi's sarcoma CNS toxoplasmosis HIV encephalopathy |
| <i>Conditions where confirmatory diagnostic testing is necessary:</i> Extrapulmonary Cryptococcosis including meningitis Disseminated non-tuberculous mycobacteria infection Progressive multifocal leukoencephalopathy (PML) Candida of trachea, bronchi, or lungs Cryptosporidiosis Isosporiasis Cytomegalovirus infection (retinitis or of an organ other than liver, spleen, or lymph nodes) Any disseminated mycosis (e.g. Histoplasmosis, Coccidiomycosis, Penicilliosis) Recurrent non-typhoidal salmonella septicaemia Lymphoma (Cerebral or B cell non-Hodgkin's) Invasive cervical carcinoma Visceral Leishmaniasis, |

¹ Acute retroviral syndrome : Acute febrile illness 2-4 wks post-exposure often with lymphadenopathy and skin manifestations, pharyngitis.

² TB may occur at any CD4 count, and this must be considered where available. If CD4 is less than 200 it should be considered as a stage 4 event. Diagnosis and treatment of both pulmonary and extrapulmonary TB should be in line with international and national guidelines.

Appendix 2: WHO Classification in Children < 13 years old

(For use in those under 15 years with confirmed laboratory evidence of HIV infection; HIV Antibody where age >18 months, virological or P24 Ag testing for those age <18 months)

| STAGE 1 |
|---|
| Asymptomatic Persistent generalized lymphadenopathy (PGL) |
| STAGE 2 |
| Hepatosplenomegaly Papular pruritic eruptions Seborrhoeic dermatitis Extensive Human papilloma virus infection Extensive Molluscum contagiosum Fungal nail infections Recurrent oral ulcerations Lineal Gingival Erythema (LGE) Angular chelitis Parotid enlargement Herpes zoster Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis,) |
| STAGE 3 |
| Conditions where a presumptive diagnosis can be made using clinical signs or simple investigations Moderate unexplained malnutrition ⁱⁱ not adequately responding to standard therapy Unexplained persistent diarrhoea (14 days or more) Unexplained persistent fever (intermittent or constant, for longer than 1 month) Oral candidiasis (outside neonatal period) Oral hairy leukoplakia Acute necrotizing ulcerative gingivitis/periodontitis Pulmonary tuberculosis ⁱⁱⁱ Severe recurrent presumed bacterial pneumonia |
| Conditions where confirmatory diagnostic testing is necessary Lymphoid interstitial pneumonitis (LIP) Unexplained Anaemia (<8gm/dl), neutropenia (<1,000/mm ³) or thrombocytopenia (<50,000/ mm ³) for more than 1 month Chronic HIV associated lung disease including bronchiectasis |
| STAGE 4 |
| Conditions where a presumptive diagnosis can be made using clinical signs or simple investigations: Unexplained severe wasting or severe malnutrition ^{iv} not adequately responding to standard therapy Pneumocystis pneumonia Recurrent severe presumed bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia) Chronic Herpes simplex infection; (orolabial or cutaneous of more 1 month duration, visceral of any duration) Extrapulmonary tuberculosis Kaposi's sarcoma Oesophageal Candidias CNS Toxoplasmosis (outside the neonatal period) HIV encephalopathy |
| Conditions where confirmatory diagnostic testing is necessary: CMV infection (CMV retinitis or infection of organ other than liver, spleen, or lymph nodes onset at age 1 month or more) Cryptococcal meningitis (or other extrapulmonary disease) Any disseminated endemic mycosis(e.g. extra-pulmonary Histoplasmosis, Coccidiomycosis, Penicilliosis) Cryptosporidiosis Isosporiasis Disseminated non-tuberculous mycobacteria infection Candida of trachea, bronchi or lungs Acquired HIV related rectal fistula Cerebral or B cell non-Hodgkin's Lymphoma Progressive multifocal leukoencephalopathy (PML) HIV related cardiomyopathy or HIV related nephropathy |

Presumptive Stage 4 diagnosis in children less than 18 months

The presumptive diagnosis is designed for use where access to confirmatory diagnostic testing for HIV infection using virological or P24 Antigen for infants and children less than 18 months is not readily available. It is not recommended for use by clinical care providers who are not trained on ART, accredited or certified and experienced in HIV care, and must be accompanied by immediate efforts to confirm the HIV diagnosis with the best nationally or locally available test.

A Presumptive diagnosis of Stage 4 clinical disease should be made if

An infant is HIV antibody positive (ELISA or rapid test), aged under 18 months and symptomatic with two or more of the following:

- +/-oral thrush,
- +/- severe pneumonia,
- +/- severe wasting/malnutrition,
- +/-severe sepsis

CD4 values where available may be used to guide decision making, CD4% below 25 requires ARV treatment

Other factors that support diagnosis of clinical stage 4 HIV infection in an HIV seropositive infant are:

- recent HIV related maternal death
- advanced HIV disease in mother.

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

Explanatory Notes

The clinical staging system for infants and children is designed to:

1. Be used where HIV infection is confirmed by HIV antibody testing in children over 18 months of age, virological or P24 Antigen testing in those < 18 months of age.
2. Provide greater consistency between adult and pediatric staging and harmonize with HIV/AIDS surveillance definitions.
3. Classify disease in a progressive sequence from least to most severe, with each higher clinical stage having a poorer prognosis. Once a stage 3 clinical event has occurred, the prognosis remains that of stage 3 and does not improve, even with resolution of the original condition.
4. Provide simple guidance to assist clinical care providers in when to start, substitute, switch or stop ARV therapy in HIV infected infants and children, or trigger referral as outlined in WHO ART guidelines for a public health approach.
5. Be largely used with reference to CURRENT clinical events, meaning clinical events that have been diagnosed or are being managed at this episode.
6. Be considered in relation to previous clinical events, such as reported TB, severe pneumonia, PCP or other conditions. This is RETROSPECTIVE clinical staging and requires caution. **Note:** Reported history of a stage 3 or stage 4 clinical event should have immediate assessment by, or referral to, HIV care providers able to initiate ARV treatment.

7. Be used to guide clinicians in assessing the response to ARV treatment, particularly where viral load and or CD4 counts/or percent are not widely or easily available. However further evidence is required to determine the significance of staging events once on ART.

¹ Moderate malnutrition: Defined as very low weight for age - up to - 2SD for age http://www.who.int/child-adolescent-health/publications/CHILD_HEALTH/WHO_FCH_CAH_00.1.htm or page4 http://www.who.int/nut/documents/manage_severe_malnutrition_eng.pdf

¹ As for footnote 2. TB is particularly difficult to diagnose in infants and young children.

¹ Severe Malnutrition: Defined as : visible severe wasting or oedema of both feet and weight for height of -3SD Ref: http://www.who.int/child-adolescent-health/publications/CHILD_HEALTH/WHO_FCH_CAH_00.1.htm

Entry Points and Gateways to Access ARVs

Clinical Services:

STI clinics

TB clinics

PMTCT services

Drug treatment and rehabilitation services

Adult and Pediatric In-patient services

Testing Centers

Voluntary counseling and testing centers (VCT)

Hepatitis testing and treatment centers

Blood banks

Community Out-reach Programs

Sex workers

Injection drug users

Migrant workers

Truckers

Other vulnerable populations

Community

Home based care

PLWHA and their networks

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