

HIV Treatment and Care: Antiretroviral Therapy Selection Guidelines

2006

The National AIDS Control Programme
Ministry of Health
Government of Pakistan

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PREFACE

In nearly 30 years of the HIV 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 even 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 antiretrovirals (ARVs) and the necessary supporting laboratory diagnostics required to initiate and monitor ARV therapy, is still beyond Pakistan's resources to provide free to each and every HIV positive person who needs it. This dilemma arises when the demand for HAART exceeds the supply, making it necessary to identify in a fair, transparent and medically acceptable manner which people have a priority.

HAART should be part of a continuum of care: a comprehensive approach that involves voluntary counseling and testing, availability of other social support and preventive services, and prevention of mother-to-child transmission plus pediatric HIV care services.

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, in community mobilization, advocacy and ensure that scarce resources are utilized efficiently.

While this guide primarily addresses "priority setting" in medical and adherence terms for initiating HAART, it also encourages health care providers and PLWHA to build and strengthen 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 managers, and NGOs/CBOs working with HIV/AIDS are encouraged to seek opportunities for addressing gender inequities, enhancing ARV treatment access and ensuring rigorous implementation of standardized and simplified ARV regimens in order to reduce the prevalence of HIV/AIDS in Pakistan.

ACKNOWLEDGEMENTS

The National AIDS Control Program, Ministry of Health is pleased to develop “Antiretroviral Therapy Selection Criteria” to standardize initiation of antiretroviral therapy (HAART) for HIV infected individuals and promote treatment adherence. Though the National AIDS Control Program is working towards scaling up of universal access and availability of antiretroviral therapy (ART), it will be a while before all those who need ART will truly be able to receive it. These guidelines are mainly intended for health care providers to assist them in providing standardized and equitable access to highly active antiretroviral therapy (HAART) based on “scientific evidence” where available and “international best practices” from other resource limited setting in situations where scientific evidence is yet not available. These guidelines also hope to emphasize the difficult choices that policy makers and public health planners must occasionally make when balancing the long term benefits to society against individual benefits.

This document was written by Dr. Ayesha Khan (Infectious Diseases Specialist, NACP) after detailed consultations with a broad range of stakeholders from HIV positive people to international donor agencies. NACP acknowledges the contributions of the Infectious Disease specialists: Dr. Faisal Sultan (Shaukat Khanum Memorial Hospital), Dr. Adnan Khan 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), 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 document.

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 and publications by WHO, UNAIDS, John Snow International and Family Health International on establishing HIV treatment and care centers and scaling up delivery of HAART 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.

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Abbreviations:

AIDS	Acquired Immune Deficiency Syndrome
ANC	Antenatal clinics
ARV	Antiretroviral
HAART	Antiretroviral therapy
CBO	Community based organization
CDC	Centers for Disease Control and Prevention (US)
CO	Community Organization
ddl	Didanosine
EFV	Efavirenz
FHI	Family Health International
FPC	Family planning clinics
HAART	Highly Active Antiretroviral Therapy
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

1. Introduction

HIV/AIDS is a devastating, human crisis that has affected many countries, particularly those in Sub-Saharan Africa. Now 30 years later far from being contained 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 2005, 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 2005. Most alarmingly, many countries in Asia and Eastern Europe are now experiencing rapidly expanding HIV epidemics. 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.

2. Epidemiology of HIV/AIDS in Pakistan

Since the diagnosis of the first HIV/AIDS case in 1987, Pakistan has progressed to 3000+ cases nationwide. However, these numbers are likely a vast underestimation of the actual picture (UNAIDS/NACP 2006 estimates 74000 HIV/AIDS cases, 0.1% prevalence). While heterosexual transmission still remains the predominant mode of spread it is concerning to see rapidly expanding concentrated epidemics (i.e. greater than 5% prevalence) among injection drug users (IDUs) in multiple cities nationwide and transitioning into male and female 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 through bridging populations (i.e clients of sex workers, truckers etc). Lacking accurate information on the size and presence of bridging population, and the

dynamics of sexual networks in the general population men and women it is hard to predict the HIV trajectory.

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.

3. Definitions of Common HIV/AIDS Terminologies

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: Annexe 1).

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 (HAART)

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 HAART and overall disease progression. During effective HAART 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 HAART, 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 HAART 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.

4. Antiretroviral Therapy (HAART) Regimens

ARV Regimens:	
<p>4.1. 1st line:</p> <ul style="list-style-type: none"> • Zidovudine + Lamivudine + Nevirapine (recommended 1st line) <li style="text-align: center;"><i>or</i> • Zidovudine + Lamivudine + Efavirenz <li style="text-align: center;"><i>or</i> • Stavudine + Lamivudine + Nevirapine (recommended 1st line alternate) <li style="text-align: center;"><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>4.2. 2nd line:</p> <ul style="list-style-type: none"> • Tenofovir + Didanosine + Nelfinavir <li style="text-align: center;"><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)

5. Importance of Adherence in HAART

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 (i.e. less than 3 doses missed in a month) to the prescribed dosing schedule is necessary to achieve HAART benefits without resistance development. While clinical (disease stage) and immunological data (CD4) are critical in initiating HAART, patient motivation and actual HAART readiness, and ability to follow the prescribed medical regimen are no less essential for treatment success. The margin for compromising on any of these adherence criteria is costly in terms of risking resistance development and losing lifesaving benefit of HAART for the patient.

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

6. 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 HAART.
- 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.
- HAART 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 HAART will not benefit the patient i.e starting HAART at CD4 counts > 300, or when the patient is not mentally ready to commit to HAART.

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

7. Implications of Non-Adherence

7.1. Medical:

1st line HAART 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 HAART (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 HAART regimens.

7.2. 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.

7.3. Impact on HIV Transmission Dynamics:

HAART reduces the transmission of HIV. However, patients on HAART 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.

8. Rationale for Adherence Criteria Using an Integrated Approach

The number of patients who will be eligible on clinical and immunological basis for HAART initiation is likely to exceed the amount of ARVs available free of cost to PLWHA in Pakistan. Therefore, like many other developing countries 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 medical and adherence criteria to assist health care providers in selecting patients in a fair, transparent, subjective but standardized manner. The adherence criteria may provoke debate and controversy but the general consensus is that such “priority settings” are necessary to maximize benefit of HAART to patients who are most likely to be compliant with treatment and until the time that HAART is more widely available and the risks of resistance development can be adequately mitigated it is an unfortunate reality that we must learn to live with. The eligibility and ineligibility criteria are:

9. Eligibility Criteria

9.1. Medical

- Confirmed HIV positive status (using 2 different tests ELISA, 2 different rapid tests or Western Blot)
- CD4 counts less than 250-300/mm³
- WHO stages 3 or 4 regardless of CD4 count
- Asymptomatic patients (stage 1 or 2) with CD4 less than 250-300/mm³

Adherence

1. Must attend 2- 3 pre-HAART 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-HAART counseling sessions are separate from pre and post test counseling or counseling for other HIV related issues.

9.2. Pediatric Eligibility Criteria

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 HAART initiation, while treatment should be deferred or not initiated in those who meet the medical or adherence ineligibility criteria.

10. Ineligibility Criteria

10.1. Medical

- CD4 cell count greater than 300/mm³
- Asymptomatic patient and WHO stages 1 or 2 (unless CD4 count is less than 300/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 HAART 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 HAART 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 HAART can then become effectively incorporated.

11. 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 HAART initiation
- Patient is not ready to begin HAART or is unwilling to follow the adherence counseling
- Patient cannot keep or follow scheduled clinic visits
- Has a mental condition that should be treated first prior to HAART initiation i.e psychosis or major depression.
- Has an active opportunistic infection that should be treated prior to the initiation of HAART. Example, treatment for pulmonary TB should be initiated and preferably completed prior to HAART initiation. In situations where the CD4 count is very low <50 or patients clinical status requires early initiation of HAART then deferring treatment until after the intensive phase (i.e 2-4 weeks) is recommended.
HAART is never an emergency and should not be started in haste.
- 1st trimester pregnancy (the patient does not medically qualify for HAART initiation and/or is unwilling to initiate HAART at this time). All pregnant HIV positive women should be counseled about transmission risks to their unborn child and referred/linked up to PMTCT programs.
- Active drug user (IDUs) currently in detoxification program and interested to start HAART. IDUs need to complete drug detoxification and drug rehabilitation programs and should be “drug free” for 3 months before initiating HAART. The HIV Treatment and Care center should establish strong referral and contact linkages with NGOs working in IDU harm reduction programs to ensure a holistic approach to care of the HIV+ IDUs.

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 HAART related negative side effects on quality of life and drug related toxicities. Starting HAART 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 HAART demands
- Decreased time on HAART 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 HAART combinations.

12. Entry Points to HIV Treatment and Care Center

Scaling up access to HAART must build on existing medical or public health services and extend their coverage. It also means making the most of synergies between prevention and treatment, recognizing that people are more likely to follow and benefit from prevention advice when they receive comprehensive services. To accomplish this, particularly HAART in the setting of a low prevalence/concentrated epidemic it will be necessary to maximize existing opportunities using a targeted approach 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:

- Targeted Clinical situations where there may be a high suspicion of HIV-related disease (TB services) or where people seeking care have a high likelihood of HIV infection (STI clinics or drug treatment services).
- Through NGOs working with high risk groups for identifying people who are more at risk of HIV and are likely not to use regular care 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.

12.1 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 HIV treatment and care center.
- Sensitize health care providers to actively seek and recognize patients sick with HIV or AIDS in acute medical clinics and hospital wards
- Work with maternal and child health (MCH) and mother-to-child transmission (MTCT) prevention programs.
- Work with pediatric HIV care services
- Link sexually transmitted infection (STI) and HAART services
- Establish linkages with IDU drug rehabilitation programs and harm reduction programs
- Create demand for HIV counseling and testing

12.2 Key Entry Points

Many people using the following services have a higher likelihood of having HIV or HIV-related illness and would benefit from entry into HIV care services:

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 it is unclear what the estimated prevalence of HIV is among TB infected patients and whether performing HIV testing on every TB patient is a cost effective strategy. A large national survey looking at this question is currently planned by the National TB Control Program. .

According to National Guidelines, HIV-TB programs in collaboration need to train workers on risk categorize TB patients for HIV infection and provide appropriate referral to HIV counseling and testing services.

ii) Acute medical services (clinic and hospital ward)

In a similar way to TB services, medical clinics (adult and pediatric) and hospital wards may have a relatively higher proportion of HIV-infected patients than the general population. Medical facilities can therefore serve as an important entry point for HAART services if health care workers are trained to recognize signs/symptoms of HIV or AIDS. 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 HAART 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 HAART. It is likely that with HBC services, the majority will urgently need to start HAART.

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 HAART 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 Pakistan, IDUs are the fastest growing 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 seriously addressed before HAART can be effectively provided to IDUs

- Within NGOs working with IDUs: Increase access to NGO initiated VCT (with informed consent) in harm reduction services, drug detoxification and rehabilitation programs
- Initiate and establish substitution programs to help stabilize IDUs and improve treatment adherence.
- Formulate comprehensive partnerships with IDU-NGOs and HIV care services to work closely together in HAART delivery and monitoring of adherence and complications.

vii) Reaching Out to Socially Marginalized and Vulnerable Groups

The people who most need HIV prevention, treatment and care are most often beyond the reach of health-care services. Poverty, stigma, mistrust of service are 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 street based youth. 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 service delivery programs for sex workers, men who have sex with men, street youth, with testing and counseling, care and treatment programs.
- Work with especially vulnerable young people (e.g. out-of-school, slum-dwelling adolescents) through peer networks and youth-friendly health services.

12.3 Challenges for Using an Integrated Medical and Social Selection Criteria for HAART:

Policy makers and AIDS control programs will have to grapple with the challenges and ethical issues inherent in developing HIV Treatment programs that may not be able to reach all those in need. Yet the realization and risks that the program may not be completely fair cannot be used as an excuse to delay action. Because people may disagree on who should receive HAART, when, how and where this should happen, the guiding principles should be transparent, public, inclusive and revisable based on evidence and lessons learned. They should aim to ensure that decisions on the initiation and implementation of HAART programs are equitable and as transparent as possible, and disseminated clearly among PLWHA to foster their support, even if these PLWHA voice disagreement.

13. Ethical Considerations

In order to promote HAART 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 socially marginalized groups i.e sex workers, IDUs,
- Developing standardized national criteria for ensuring patient confidentiality and the importance of informed consent
- Integration of HIV treatment, care and support within the framework of primary health care services
- Involvement and mobilization of PLWHA in shaping the national HIV response

APPENDIXES

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 ¹
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 Seborrheic dermatitis Fungal nail infections of fingers
CLINICAL STAGE 3
Conditions where a presumptive diagnosis can be made using clinical signs or simple investigations Severe weight loss (>10% presumed or measured body weight) Unexplained chronic diarrhea for longer than one month Unexplained persistent fever (intermittent or constant for longer than 1 month) Oral candidacies 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
Conditions where confirmatory diagnostic testing is necessary Unexplained Anemia (<8gm/dl), neutropenia (<1,000/mm ³) or thrombocytopenia (<50,000/ mm ³) for more than 1 month
CLINICAL STAGE 4
Conditions where a presumptive diagnosis can be made using clinical signs or simple investigations: 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) Esophageal Candidacies Extrapulmonary tuberculosis Kaposi's sarcoma CNS toxoplasmosis HIV encephalopathy
Conditions where confirmatory diagnostic testing is necessary: 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 septicemia 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
<p>Conditions where a presumptive diagnosis can be made using clinical signs or simple investigations</p> <p>Moderate unexplained malnutritionⁱⁱ not adequately responding to standard therapy Unexplained persistent diarrhea (14 days or more) Unexplained persistent fever (intermittent or constant, for longer than 1month) Oral candidacies (outside neonatal period) Oral hairy leukoplakia Acute necrotizing ulcerative gingivitis/periodontitis Pulmonary tuberculosisⁱⁱⁱ Severe recurrent presumed bacterial pneumonia</p> <p>Conditions where confirmatory diagnostic testing is necessary</p> <p>Lymphoid interstitial pneumonitis (LIP) Unexplained Anemia (<8gm/dl), neutropenia (<1,000/mm³) or thrombocytopenia (<50,000/ mm³) for more than 1 month Chronic HIV associated lung disease including bronchiectasis</p>
STAGE 4
<p>Conditions where a presumptive diagnosis can be made using clinical signs or simple investigations:</p> <p>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</p> <p>Conditions where confirmatory diagnostic testing is necessary:</p> <p>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</p>

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 HAART, 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 HAART 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 HAART.

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

Appendix 3:

HIV Treatment and Care Centers

1. Medical OPD, Special Medicine Clinic, Pakistan Institute of Medical Sciences, Islamabad 051-9261170 ext 2213 (Dr. Rizwan Qazi)
2. In door Block, Services Hospital, Karachi 021-9215782 (Dr. Sikander)
3. Infectious Disease Clinic, Services Hospital, Lahore 042- 9200982 (Dr. Arif Nadeem or Dr. Sobia Qazi)
4. OPD, Hyatabad Medical Complex, Peshawar 091- 9217140-6 ext 2160 (Dr. Yasin Khan)
5. OPD, Bolan Medical Complex, Quetta 0300-382-3361 (Dr. Khuda Dad)
6. Infectious Disease clinic, Liaquat National Hospital, Karachi (Dr. Naseem Salahuddin or Dr. Farheen Ali)
7. Infectious Disease clinic, Shaukat Khanum Hospital, Lahore 042- 5945100 ext 2372 (Dr. Faisal Sultan)

Pilot Sites for Prevention of Mother to Child Transmission of HIV Infection Programs

1. MCH, PIMS Hospital, Islamabad (Dr. Ghazala Mahmood)
2. MCH, JPMC, Karachi, (Dr. Shireen Bhutta)
3. Obstetrics-Gynecology Ward, Services Hospital, Lahore (Dr. Rubina Sohail)
4. Obstetrics-Gynecology Ward, Lady Willington Hospital, Lahore (Dr. Ahmad Wasim Yosuf)
5. Obstetrics-Gynecology Ward, Hyatabad Medical Complex, Peshawar, (Dr. Lubna Hassan)

Appendix 4

National and Provincial AIDS Control Programs

National Program Manager
The National AIDS Control Program
NIH, Chak Shehzad
Islamabad
Ph: 051-9255096, 9255367-8

Provincial Program Manager
Sindh AIDS Control Program
II Medical Depot,
Adjacent Jinnah Post Graduate Medical Complex
Karachi
Ph: 021-9203413

Provincial Program Manager
Punjab AIDS Control Program
Directorate General Health Services
Lahore, Punjab
Ph: 042-9200982

Provincial Program Manager
NWFP AIDS Control Program
Khyber Road
Peshawar
Ph: 091-9212263

Provincial Program Manager
Balochistan AIDS Control Program
Western By Pass, Near Fatima Jinnah General and Chest Hospital
Quetta, Balochistan
Ph: 081-2854182

Provincial Program Manager
AJK AIDS Control Program
Directorate General Health Services
Muzaffarabad, AJK
Ph; 058810, 43030

Program Manager
District Headquarters Hospital
Gilgit, Northern areas
Ph: 05811,53690

Appendix 5.

NGO Resources For Health Care Providers and PLWHA:

1. Aahung, Karachi
2. Abbottanains Medical Association, Abottabad
3. AIDS Awareness Society, Lahore
4. AIDs Information and Diagnosis Services (AIDS), Karachi
5. Al-Nijat Welfare Society, Karachi
6. All Women Advancement and Resource Development (AWARD), Peshawar
7. AMAL Human Development Network, Islamabad and Karachi
8. AMAN Welfare Services, Hunza
9. Caritas Pakistan, Lahore
10. Catholic Relief Services (CRS)
11. Community Development Network Forum (CDNF), Larkana
12. DARES Society fro Health Care, Quetta
13. DOST Welfare Foundation, Pesahwar (IDUs)
14. Family Health International, Islamabad
15. Family Planning Association of Pakistan (FPAP)
16. Ghazi Social Welfare Organization, Larkana
17. Greenstar Social Marketing
18. Health Promotion Society
19. Health and Nutrition Development (HAND) Karachi
20. Homeopathic Association of Pakistan (HMAP)
21. Humanitarian Movement International (HMI), DI Khan
22. Infection Control Society, Karachi
23. Kashmir Welfare Society, AJK
24. Legal and Medical AID Trust, Abbottabad
25. Marie Adelaide Rehabilitation Program, Karachi (IDUs)
26. MESSAGE, Lahore
27. Nai Zindigi, Islamabad and Lahore (IDUs)
28. New Light AIDs Control and Awareness Group, Lahore, Karachi and Rawalpindi (PLWHA)
29. Organization for PHAARTicipatory Development (OPD), Gujranwala
30. ORA, Peshawar
31. Pakistan Red Crescent Society
32. Pakistan Society, Karachi (IDUs)
33. Pakistan Village Development Program, Peshawar
34. Park Plus Society, Lahore (PLWHA)
35. Savoir Faire, Lahore
36. Vite-N-Hope
37. UNICEF (The United Nations Childrens Education Fund)

38. UNAIDS (The United Nations Joint Program on HIV/AIDS)
39. WHO (The World Health Organization)
40. World Population Fund (WPF), Islamabad

** This is not a complete list but just some of the NGOs and CBOs working in HIV/AIDS. PLWHA and health care providers are encouraged to seek other available resources in addition to the ones listed above.

Appendix 6.

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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16. Policy Brief: Antiretroviral Therapy and Injecting Drug Users (WHO 2005)
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