EUROPE

:

HIV/AIDS Treatment and Care

WHO protocols for CIS countries

Version 1

WORLD HEALTH ORGANIZATION
EUROPE

HIV/AIDS
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ABSTRACT

Lack of access to antiretroviral treatment has been declared by the WHO as a global health emergency, which requires immediate actions. In majority of the CIS countries, where number of PLWHA who need treatment is constantly growing, there is an urgent need to develop a system and algorithm for HIV/AIDS service delivery. This document was developed considering developed health care system of the CIS countries and offers protocols of HIV/AIDS treatment and care, including HAART, for adults and children, treatment of opportunistic infections, palliative care, PMTCT, treatment of HIV/AIDS in IDU, etc.

This document was developed based on the recent WHO recommendations for the countries with limited resources, revised in December 2003 and March 2004 in the framework of the WHO "3 by 5" initiative.

You are keeping the first version of the Protocols in your hand. The Protocols will be revised in the future based on improved data available on HIV/AIDS treatment and care. Check updates on http://www.euro.who.int

HIV/AIDS Treatment and Care protocols were designed as a basis for National Protocol development in the CIS countries.

Keywords

HIV INFECTIONS – prevention and control – diagnosis – drug therapy
ACQUIRED IMMUNODEFICIENCY SYNDROME – prevention and control – diagnosis – drug therapy
COUNSELING
INFANT CARE
ADOLESCENT HEALTH SERVICES
CHILD HEALTH SERVICES
PALLIATIVE CARE
PATIENT CARE PLANNING
COMMONWEALTH OF INDEPENDENT STATES

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ABBREVIATIONS

3TC	lamivudine	**KSHV**	Kaposi's sarcoma herpes virus, also known as HHV 8
ABC	abacavir	**LIP**	lymphocytic interstinal pneumonitis
AFB	acid-faster bacilli	**LFTs**	liver function tests
AIDS	acquired immunodeficiency syndrome	**LPV**	lopinavir
ALT	alanine aminotransferase	**MAC**	mycobacterium avium complex disease
ART	antiretroviral therapy	**MCV**	molluscum contagiosum
ARV	antiretroviral	**MOH**	Ministry of Health
AST	aspirate aminotransferase	**MTCT**	mother-to-child transmission
AZT	zidovudine, also known as ZDV	**MRI**	magnetic resonance imagine
CIS	Commonwealth of Independent States	**NGO**	non-governmental organization
CSF	cerebral spinal fluid	**NFV**	nelfinavir
CMV	cytomegalovirus disease	**NNRTI**	non-nucleoside reverse transcriptase inhibitor
CT	computer tomography	**NRTI**	nucleoside reverse transcriptase inhibitor
d4T	stavudine	**NVP**	nevirapine
ddI	didanosine	**OI**	opportunistic infections related to HIV
DOT	directly observed therapy	**OPC**	oropharyngeal candidiasis
DOTS	DOT strategy	**PEP**	post esposure prophylaxis
DPT	difteria, pertussis, tetanus combined vaccine	**PCP**	pneumocystis carinii pneumonia
DT	difteria and tetanus combined vaccine	**PCR**	polymerase chain reaction
EBV	Epstein Barr Virus	**PGL**	persistent generalized lymphadenopathy
EFV (EFZ)	efaverenz	**PI**	protease inhibitor
ELISA	enzyme-linked immunosorbent assay	**PLWHA**	people living with HIV/AIDS
FBC	full blood count	**PMTCT**	prevention of mother-to-child transmission
FDC	fixed dose combination	**PO**	per os
GI	gastrointestinal infections	**PPD**	purified protein derivative reaction
HAART	highly active antiretroviral therapy	**PPE**	personal protective equipment
HCV	hepatitis C virus	**STI**	sexually transmitted infections
HCW	health care worker	**SQV**	saquinavir
HIV	human immunodeficiency virus	**SW**	sex workers
HHV 8	human herpes virus type 8, also known as KSHV	**TB**	tuberculosis
HPV	human papilloma virus infection	**T&C**	counseling and testing
HSV	herpes simplex virus	**UNAIDS**	United Nations Joint co-sponsored programme on HIV/AIDS
IDV	indinavir	**UNGASS**	United Nations General Assambly Special Session
IDU	injecting drug use	**WB**	Western Blot reaction
IPT	isoniazid preventive therapy	**WBC**	white blood cell
IRS	Immune Reconstitution Syndrome	**WCC**	women's consultation centre
IV	intravenous	**WHO**	World Health Organisation
KS	Kaposi's sarcoma		

Part 1. HIV/AIDS Treatment and Care

I. TESTING AND COUNSELLING (T&C)

1. Policy Statement

In light of increasing access to treatment and care, which depends on knowledge of HIV status, it is time to move beyond a single or rigid model of the provision of HIV testing and counselling. Rather there is need to develop a variety of ethical, innovative, pragmatic and effective methods by which to provide HIV testing and counselling in different settings. Within these settings, HIV testing and counselling should become more normalized and should be offered as standard practice: (a) when requested to assist in the prevention of transmission or acquisition of HIV, (b) where medically indicated in the context of clinical care, and (c) for the prevention of transmission from mothers to children. While the offer of an HIV test may become standard under certain circumstances, it should always be performed with informed consent and under conditions of appropriate confidentiality. The process by which informed consent is obtained will necessarily vary according to service delivery setting, but is acceptable as long as there is sufficient information, understanding, and choice on the part of the one being offered the test.

2. Context of T&C provision

a. The present provision of Testing & Counselling is based in "cabinets of confidence" – the stand-alone community and hospital-based centres offering standard, individualised voluntary counselling and testing and employing ELIZA technology
b. Rapid scaling up of care requires a diversification and expansion of T&C services. Therefore, alternative models of T&C need to be considered for implementation, including:
   - Use of rapid tests in sites situated away from provincial treatment centres and within communities of high prevalence and vulnerability to HIV,
   - Diversification of sites where T&C can be provided. For example, simple/rapid testing is recommended to be situated in those areas where 'capture' of vulnerable populations may be greatest (e.g., STI services, TB services, IDU services) and in non-clinical areas where prevention may be optimised, such as antenatal services.
c. Given the loss of people receiving results and follow-up counselling, care, support and prevention interventions associated with ELISA testing, because of the wait associated with receiving test results, simple/rapid testing should eventually be administered – and results given – by health professionals including physicians, psychologists, social workers, or well trained and skilled feldshers in the sites where patients are most likely to be seen (e.g., community clinics and services).
d. Because of the demands that quality testing and counselling place on health services, quality counselling may be enhanced by active collaboration between established government health services offering testing and counselling and NGOs specialising in HIV/AIDS counselling and psychosocial support. Such collaboration should be encouraged and outcomes reviewed after 6 months.
e. Testing and counselling is free of cost to people being offered and seeking the test for HIV.
f. Activities of the current centres of excellence in HIV counselling and testing should be strengthened and

expanded to include operational monitoring and quality evaluation, and additional training for counsellors and related staff.

g. A national HIV/AIDS counselling network shall be developed as a priority to help ensure quality standards in T&C and in further training of counsellors and health staff. This will require regular group discussions in the form of case conferences, ward rounds, and post-graduate education.
h. With respect to production of ELISA test kits, regulatory authorities are required to systematise quality assurance procedures in the kit manufacturing process.
i. A review of current procedures for maintaining confidentiality in in- and out-patient settings is required, to identify means for improvement in current procedures and recommend improvements. This should be implemented as soon as possible.

2.1. Minimum Standards

a. The Minimum acceptable standard for testing and counselling approaches requires all models of testing and counselling to have the following principles contained in them:
   - HIV testing and counselling should be voluntary.
   - Individuals should have sufficient information, understanding and autonomy to give *informed consent* to testing.
   - Pre-test information should describe the purpose and procedure of HIV testing, and the treatment and support that will be available after testing.
   - There should be appropriate post-test information, counselling and/or referral.
   - Those who test positive should receive counselling and referral to care, support and treatment, where available.
   - HIV test results should be treated confidentially and only those health care workers with a direct role in the management of patients should have access to this information.
b. Counselling on HIV should refer to special issues as necessary arising in the context of specific vulnerable populations, including IDUs, sex workers, prisoners, people with TB/HIV co-infection, and children, etc. T&C should be provided on a priority basis to IDUs, sex workers, prisoners and other vulnerable groups.
c. Outreach initiatives may be necessary to improve access to T&C among 'hard to reach' groups, e.g. IDUs, sex workers, young people.
d. Access to testing and counselling services may be improved by integrating or linking T&C with other services, e.g. harm reduction programmes for IDUs.
e. Access to testing may be improved by identifying and addressing the different needs, expectations, resources and constraints that women and men face in relation to HIV testing and disclosure
   The processes of testing and counselling recommended are illustrated in the attached algorithm (Appendix I-A, Figure 1)

2.2. Training

a. Training in HIV/AIDS and counselling should be included as a module in the training curricula of all physicians, nurses, social workers. This may be done by adapting curricula recommended by WHO and/or other key partners.
b. All counsellors must participate in on-going training and supervision, in the form of case conferences, ward rounds, post-graduate education.

3. Provision of Testing and Counselling

The recommended procedure for implementation of T&C in all settings is illustrated in Figure 1. The recommended algorithm for employing HIV tests is illustrated in Figure 2.

3.1. Pre-test information and/or counselling

a. Wherever possible, the same person should be providing both pre- and post-test counselling for the individual being tested. Where group education is being provided to ensure informed consent for testing, all individuals in the group should have the opportunity for individual, confidential discussion prior to testing should they request it.
b. All individuals who are offered the test have the right to opt out of testing if they do not wish to be tested. All persons opting out should be given essential information on HIV transmission, prevention, and where to seek further HIV-related information, should they desire it subsequently.
c. Pre-test information will be provided by the following staff after they have received training in the key pre-test messages to be shared with individuals, modes of transmission of HIV, modes of prevention of HIV

transmission, and location and types of services for HIV treatment and care and support:

- Cabinet of confidence counselling and testing services health staff
- Physicians
- Nurses
- Social workers
- Counsellors

d. The places for providing group education and for pre-test counselling will include:

- Out-patient services for counselling and testing (e.g., Cabinets of confidence);
- IDU (narcology) services;
- STI services;
- TB services,
- WCC services.

Present cabinets of confidence, out-patients services for testing and counselling, should be maintained and access generally to T&C strengthened by providing alternatives for easy access to T&C in settings managing vulnerable populations. This requires implementation of testing and counselling that employs group education for pre-test education and discussion as an alternative to individualised pre-test discussion in those settings where large numbers of potential testees are seen.

e. Links should be established between hospital services and community-based testing and counselling services so pre-test information and counselling may be provided by specialised testing and counselling services in collaboration with hospital services.

f. Pre-test information training should be provided for, and then can be delivered by: Health staff in treatment services for vulnerable populations (IDU, STI, TB, SW, prisons), including physicians, nurses, social workers. Government health services should be encouraged to collaborate with community-based government and/or non-government HIV services to ensure best possible coverage of counselling issues.

g. Pre-test discussion – whether individual or group-based - shall cover the following issues:

- Risk activities for HIV transmission
- Reasons for testing, including the range of options for post-test care for those found to have HIV
- Understanding of transmission, prevention & testing procedures
- Personal & practical implications of testing
- The process of obtaining informed consent for testing.
- How the results are given to individuals.
- Arrange means for giving the test result.
- Reinforcement of strategies for prevention of transmission
  - Provision of condoms
  - Referral to harm reduction programmes for IDUs (e.g. needle exchange)
- Referral to appropriate services (e.g. people with risky sexual behaviour to STI services, coughing people to TB services)

3.2. Post-test counseling

Post-test counselling should cover the following issues:

3.2.1. If Negative (see attached Appendix I-B for more detail)

- Suggest re-testing in 3 months, if appropriate
- Reinforce strategies for prevention of transmission
- Referral to appropriate services (e.g. people with risky sexual behaviour – to STI services, coughing people – to TB services)

3.2.2. If Positive (see attached Appendix I-B for more detail)

- Check understanding of result
- Conduct risk assessment (Identify immediate concerns, suicidal ideation, social support)
- Reinforce strategies for prevention of transmission
- Discuss medical follow-up
- Refer to appropriate support organisations

3.3. Referrals needed

- Post-test referral procedures should incorporate the following:All those who test positive should be referred to a physician for medical follow-up.

- All those who test positive should be referred for psychosocial support.
- Ideally, post-test counselling with a trained counsellor should be available on-site.
- Those who test positive should also be referred to support groups provided by NGOs.
- Referrals to social workers should be available as required (to those with housing and financial needs and those requiring home care).

3.4. Management of adverse events

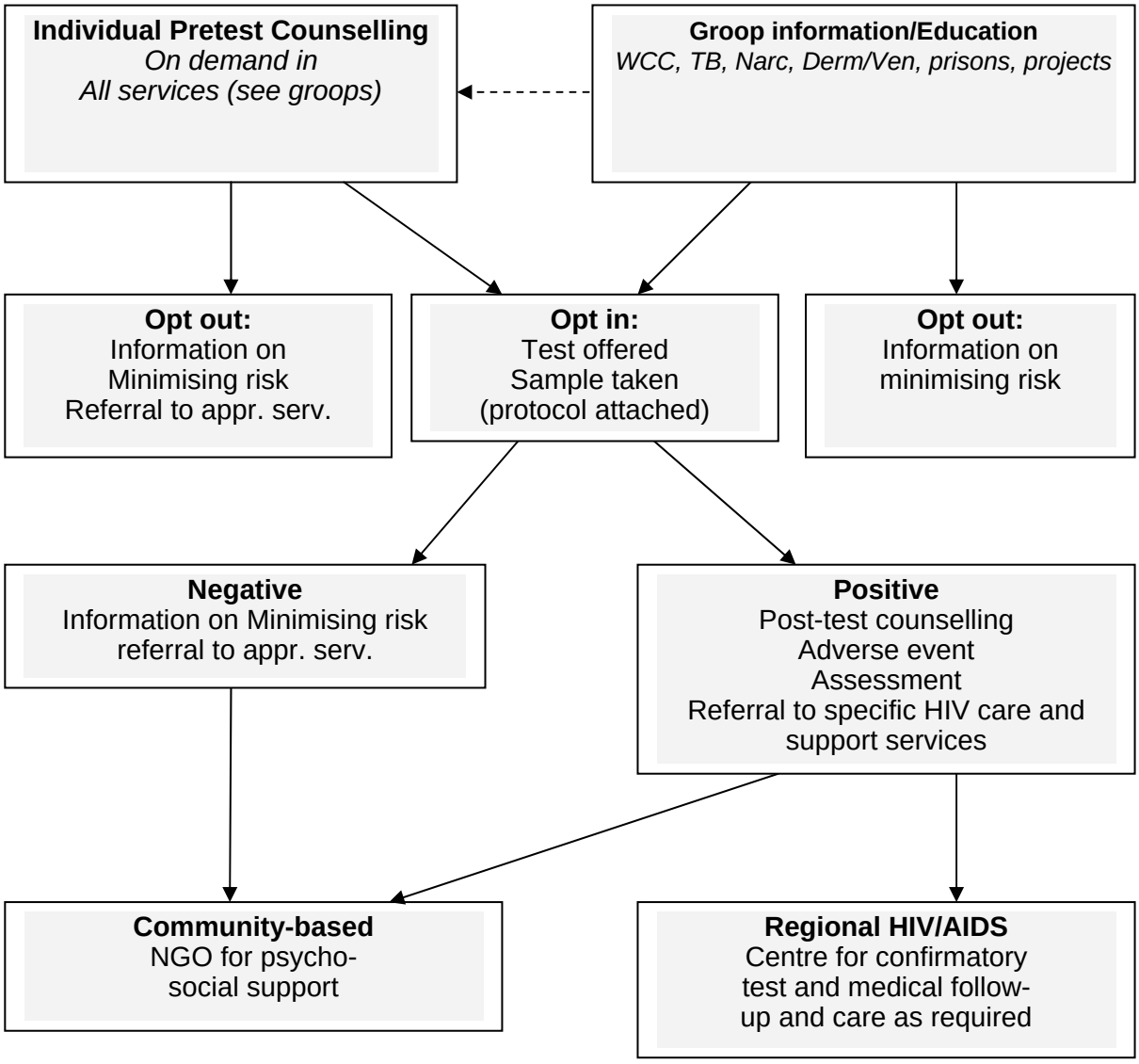
a. Pre-test discussion should aim to identify possible risks of harm (suicide, self-harm, intent to harm others, fears of violence from partners or others). See Appendix I-C: Risk factors for suicide
b. Any such identified risks may affect the decision to test.
c. Anyone identified as being at risk of harm to self or others, who then tests positive should receive assistance. The counsellor should make judgement about the best course: to refer to psychiatric services for assessment or to call for psychiatric assistance.
d. Studies have shown an association in women between being HIV positive and being a victim of gender-based violence. Anyone who fears violence from partners etc. should be referred to appropriate agencies for support, e.g. social workers, women's organisations.

3.5. Monitoring and Evaluation

a. Monitoring and evaluation of the process and content of counselling is a vital requirement for ensuring maintenance of the best possible standards in testing and counselling. The same is true for laboratory-based elements in testing and with provision of consumables.
b. It is recommended that quality of counselling standards be identified as a priority task for the centres of excellence in counselling training, using the document *Tools for evaluating HIV voluntary counselling and testing, UNAIDS, 2000 (UNAIDS/00.09E)* as the basis for this activity.
c. For individual patients, monitoring and evaluation of T&C should include the following issues:
    - Did pre-test discussion take place?
    - Evaluation of pre-test discussion. Were the following areas covered?
        - Risk activities and reasons for testing
        - Understanding of transmission, prevention & testing procedures, meaning of HIV-positive and HIV-negative results & possible implications
        - Capacity to cope with positive result
        - Discussion of potential needs and available support
        - Personal risk reduction plan
        - Follow-up arrangements
        - Referrals to appropriate services
    - Was there sufficient time to think through the issues?
    - Was informed consent freely given?
    - Did the counsellor check understanding and correct any misconceptions?
    - Did post-test discussion take place?
    - Did it cover the following areas:
        - Results given simply & clearly
        - Check understanding
        - Discussion of meaning & implications of result and who to tell
        - Immediate emotional reactions
        - Availability of immediate support
        - Discussion of follow-up care & support
        - Referrals to appropriate services
    - Client satisfaction with the service
        - Was the service conveniently located?
        - How long, on average, are the waiting times?
        - Did the Counsellor show sufficient understanding?
        - Have arrangements been made for follow-up?

APPENDIX I-A.
FIGURE 1: HIV TESTING AND COUNSELLING ALGORITHM

COMMUNITY AWARENESS



APPENDIX I-B.
PROTOCOL FOR TESTING AND COUNSELLING CONTENT AND MANAGEMENT

ACTION	CONTENT
Group pre-test education (to be further refined for application in settings managing WCC, TB, STIs, prisons, and other projects)	• Risk activities and reasons for testing • Understanding of transmission, prevention & testing procedures • Personal & practical implications of testing • The test is voluntary • The test is free of charge • The result is confidential • The process of giving informed consent for testing. • How test results are given. ***Strategies for prevention of HIV transmission*** - condoms - harm reduction programmes for IDUs (e.g. needle exchange) • Available care and support and referral options for those with HIV • Where to receive further discussion and/or counselling if desired
Individual pre-test counselling	• Risk activities and reasons for testing • Understanding of transmission, prevention & the test (e.g., procedures for testing, meaning of possible results, window period) • Personal & practical implications of testing, and their capacity to cope with the results • Identify possible causes of adverse responses to a positive result (suicide, self-harm, intent to harm others, prior history of self-harm and/or psychiatric intervention) • The test is voluntary • The test is free of charge • The process of testing and the result is confidential • The process of giving informed consent for testing. • How test results are given. **Strategies for prevention of HIV transmission, e.g.,** - condoms - harm reduction programmes for IDUs (e.g. needle exchange) • Available care and support and referral options for those with HIV • Referral to STI and/or TB services if appropriate • Where to receive further discussion and/or counselling if desired

ACTION	CONTENT
Obtaining informed consent	• Ensure sufficient time to think through the issues • Check understanding and correct any misconceptions - Specifically ask the client if they agree to be tested - Complete written informed consent form and have it signed by the client (suggested format attached)
Administering the test	• Use format attached for rapid test administration and confirmation (Appendix I-D, Figure 2)
Giving POSITIVE results **NOTE:** This may involve more intensive discussion and follow-up support and counselling, particularly in the early days after a positive diagnosis, than is the case for those found HIV negative. The messages for those found positive and those found negative remain largely similar, but the intensity of follow-up and support will probably be greater for those found positive. For people found HIV positive, the issue of disclosure is extremely important. It requires significant attention and may be the focus of the second post-test session, if this is possible.	• Give result simply and clearly • Allow time for the result to be understood • Check for understanding • Deal with immediate emotional reactions (see adverse events management) • Discuss meaning of the result for the client • Discuss personal, family and social implications of the result • Discuss possible disclosure of the result and when it may happen and with whom – suggest holding back in the immediate term from telling any other than closest contacts (spouse, significant other) • Discuss personal risk-reduction plan and reinforce risk-reduction strategies including options for harm-reduction (needle/syringe exchange, drug substitution), safer sex negotiation, and condom use • Check for immediate support once they have left the service – who will be available at home or nearby? • Discuss who they need to see for follow-up support and care, including referral to appropriate support services (for all positive results, referral to medical services is required) – this may include STI services, TB services, family planning and/or general health services • Review immediate plans, intentions and actions and, where possibly adverse, make appropriate steps • Make an appointment for follow-up counselling with a named counsellor **within 3 days** (sooner if indicated) • Provide risk-reduction supplies if available (condoms, needles, etc)

ACTION	CONTENT
Giving NEGATIVE results **NOTE**: A negative result still requires an emphasis to be made on future risk reduction and avoidance. There may therefore be a need for the counsellor to follow-up with the person who was tested, or to suggest referral to appropriate other services, to reinforce and support risk reduction behaviours and messages.	• Give result simply and clearly • Allow time for the result to be understood • Check for understanding • Deal with immediate emotional reactions (see adverse events management) • Discuss meaning of the result for the client • Discuss personal, family and social implications of the result • Discuss possible disclosure and when it may happen, identify who needs to know and how to tell them • Discuss personal risk-reduction plan, including options for harm-reduction (needle/syringe exchange, drug substitution), safer sex negotiation, and condom use • Discuss follow-up support and care, including referral options/needs, particularly relating to maintenance of risk reduction • Review **immediate** plans, intentions and actions • Make an appointment for follow-up counselling and/or re-testing in 3 months, if appropriate • Provide risk-reduction supplies if available (condoms, needles, etc) • Refer to STI and/or TB services if appropriate
Assessing and managing adverse events	• Use post-test result-giving and counselling session to assess for immediate concerns including possible suicide, depression, anger (violence), and management of partner/family consequences (see suicidal risk table below) • Identify trusted supports in family and social environment • Explain concern about possible adverse event and that further support is needed and will be sought with permission
Referral for follow-up	• All positives require medical referral • All positives require psychosocial referral, e.g., from NGO support organisations, and/or from social workers • Post-test follow-up counselling should be organised on site or as appropriate • Where specific adverse events arise with giving the result, make referrals to appropriate specialisms (e.g., psychiatry, social work)

APPENDIX I-C.
RISK FACTORS FOR SUICIDE

Personal and social:

- Female under 35; Male under 40
- Recent serious health news
- Recent marital separation, divorce, bereavement
- Impending loss of loved-one
- Living alone
- Social isolation
- Lower socioeconomic urban area; resort area
- Financial problems or impoverishment
- Poor physical health

Occupational:

- Recently unemployed or retired
- High-status occupation (doctor, dentist, lawyer); student

Life-events:

- Recent violent quarrel in relationship
- Bereavement; separation
- Loss of job
- Incapacitating terminal illness or diagnosis
- Domestic and social complications of alcohol/drug dependence

Psychiatric status:

- Depression (especially endogenous, chronic, recurrent) and mania
- Alcohol and/or drug dependency
- Organic brain syndromes (especially epilepsy, head injury, early dementia and confusion in the elderly)

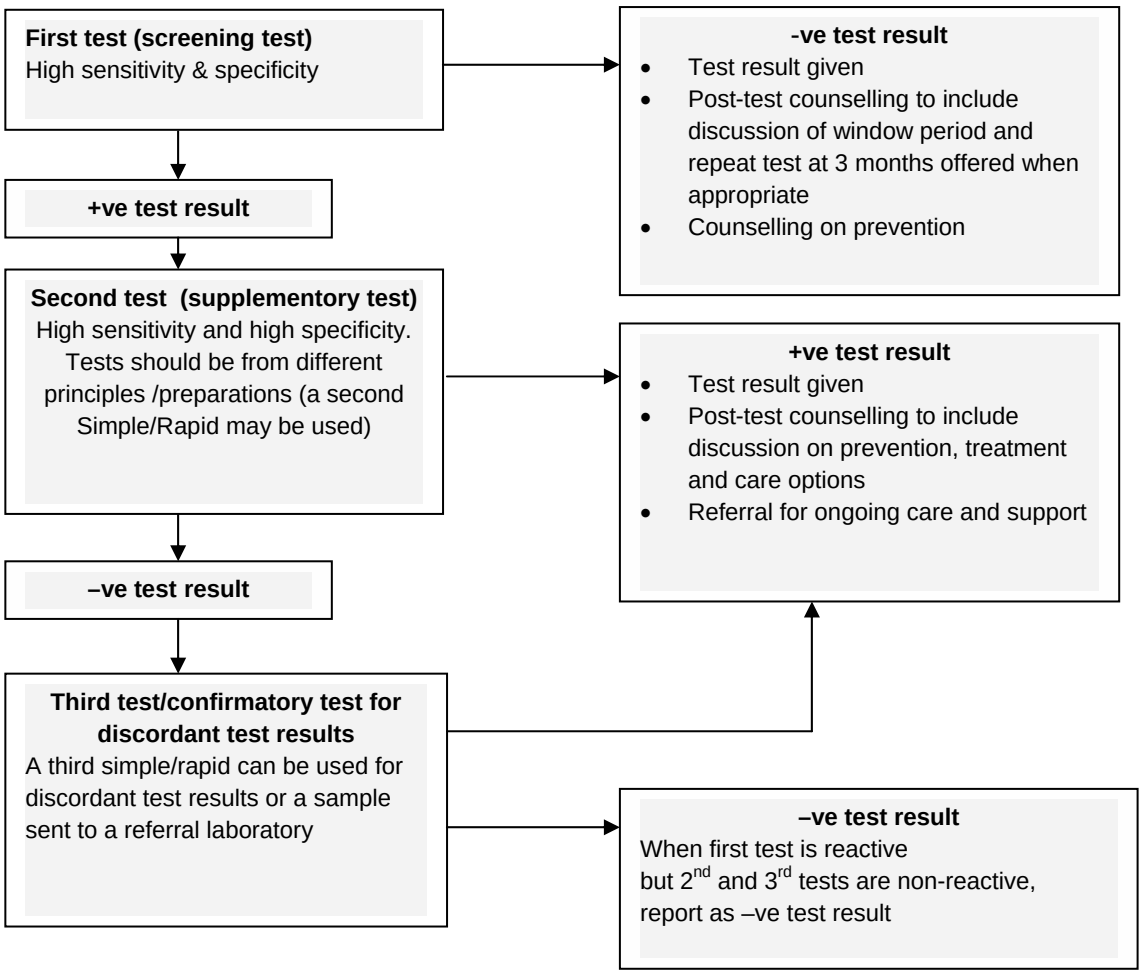
Previous history:

- Prior suicide attempt (especially violent, in past 12 months)
- Previous history of affective disorder
- Family history of affective disorder, suicide, alcoholism

Suicide indications:

- Warnings or talk of suicide
- Preparations (preparing means, making will/insurance, suicide note)

APPENDIX I-D.
FIGURE 2: Algorithm for use of tests and diagnosis of results, including decision-points for supplemental and confirmatory testing



APPENDIX I-E.
CLIENT CONSENT FORM

This is to certify that I the undersigned am _____years old.
I freely and voluntarily came to this service for HIV testing and counselling in order to have an HIV test and hereby request and authorise the Centre to take my blood (or urine or saliva) and test for it.

I verify that the number on the fluid sample matches that on my registration card.

I verify that I have also received information on:

- the aims and procedures of HIV testing,
- on ways of avoiding future potential exposure or transmission of HIV,
- and I have been advised about the next steps depending on whether my HIV status is positive or negative.

I accept that I may elect to receive or not receive the results.

I hereby declare that I will not have any claims against the testing centre, its employees or agents, and all other persons involved in the testing and counselling service arising directly or indirectly out of the test results, including any liability arising from a false positive or false negative result.

I authorise the Centre to perform confirmatory HIV tests on my sample to verify my HIV status at the Centre's discretion.

Client signature or mark: _____

Witness signature:_____

Date: _____

II. ANTIRETROVIRAL THERAPY ADULTS AND ADOLESCENTS

Anti-retroviral treatment has the potential to restore immune function, reduce morbidity and prolong the lives of those infected with HIV. Widespread access to this treatment has previously been available only to economically advantaged populations. The goal of this program is to extend the benefits of this treatment as widely as possible to all those in the CIS who are infected with HIV by using the most cost-effective means possible. Anti-retroviral therapy must be established as a component of an overall program of comprehensive care for those infected with HIV.

1. Policy statement

The ultimate goal of the program is to provide universal and affordable access to anti-retroviral therapy (ART) for all PLWHA who need it.

PRINCIPLES:

- Access to HIV treatment should not be artificially restricted due to political or social constrains. Specifically there should be no categorical exclusion of injection drug users from any level of care. All patients who meet eligibility criteria and want treatment should receive it, including ID-users, sex-business workers and other populations.
- Treatment of the HIV+ patient covers a range of interventions. Patients who are unready or not yet in need of ARV treatment may benefit from OI prophylaxis, attention to other chronic conditions and psychosocial care and services.
- Individualized assessment must be made of each patient's readiness for ARV treatment and a plan to deal with any barriers to adherence developed and implemented.
- Detailed planning of medication procurement and supply is critical for cost-effectiveness and avoiding treatment interruption. Future acquisition of ARVs will be based on WHO pre-qualification and competitive pricing.
- A working referral system should be developed to ensure full access for the HIV-patients to the general healthcare system.
- Patient education and adherence monitoring and promotion are vital, cost effective elements of the program and should be given the highest priority.
- Substance abuse care including substitution treatment may be crucial for the adherence of ID-users to HIV treatment and should be incorporated into AIDS-treatment programs.
- Involvement of PLWHAs as peer educators and outreach workers is important for the effectiveness of the treatment program.

2. Basic evaluation

Initial evaluation of the HIV positive patient must include:

ASSESSMENT	
General health status	+
Presenting symptoms	+
Co-morbidities	+
Mental health and readiness for treatment.	+

Past medical history *(incl. major illnesses (e.g.tuberculosis), hospitalizations and surgeries, the length of time since the diagnosis of HIV-infection, the current medication and symptoms)*	+
Physical examination	+
Gynecologic exam	If necessary
Routine laboratory assessment - Hemoglobin - White blood cell count and differential - Urinalysis - Liver function tests (ALT, AST, bilirubin) - Creatinine Serologic test for syphilis	 + + + + + +
Sputum smear microscopy for AFB (acid-faster bacilli)	
Chest x-ray	+
Pregnancy test	If necessary
CD4 count	+
Other testing should be driven by signs or symptoms.	If necessary

Substance abuse counseling and treatment and mental health services should be offered when indicated.

Education of patients about the nature of their disease, methods to avoid transmitting HIV infection and availability of treatment should be an integral part of initial management.

3. Antiretroviral therapy

3.1. Criteria for starting ART

WHO recommends that HIV infected adolescents and adults should start ARV therapy when they have confirmed HIV infection and one of the following conditions.

Table 1

- **WHO stage IV irrespective of CD4 cell count**
- **WHO stage III disease** (including but not restricted to HIV waisting, chronic diarrhea of unknown etiology, prolonged fever of unknown etiology, pulmonary tuberculesis, recurrent invasive bacterial infections, or recurrent/persistent mucosal candidiasis) **with consideration of using CD4 cell counts < 350/mm^3 to assist decision making ***
- **WHO stage I or II disease with CD4 cell counts = 200\mm^3 ****

* CD4 count advisable to assist with determining need for immediate therapy. For example, pulmonary TB may occur at any CD4 level and other conditions may me mimicked by non HIV etiologies (e.g., chronic diarrhea, prolonged fever)..
** The precise CD4 level above 200/mm3 at which to start ARV treatment has not been established.

References: "Scaling up Antiretroviral Therapy in Resource-Limited Settings". Guidelines for a public health approach. World Health Organization. December 2003.
[SEE ALSO APPENDIX II-A]

3.2. Formulary

The following drugs and formulations are recommended for **first line regimens**:

Three-Drug Fixed Dose Combinations
- ZDV (300mg) + 3TC (150mg) + NVP (200mg)
- d4T (40mg) + 3TC (150mg) + NVP (200mg)
- d4T (30mg) + 3TC (150mg) + NVP (200mg) for patients with body weight less then 60kg

Two-Drug Fixed Dose Combinations (for NVP lead-in dosing or if NVP or EFV must be stopped)
- ZDV (300mg) + 3TC (150 mg)
- d4T (40mg) + 3TC (150mg)
- d4T (30mg) + 3TC (150mg) for patients with body weight less then 60kg

Other drugs:

- EFV (600 mg)[1] once daily
- NVP (200 mg) once daily for 14 days, then 200mg twice daily

The following drugs and formulations are recommended for **second line regimens** (5-10 % of treatment needs in first year)

- TDF (300 mg) once daily
- ABC (300mg) twice daily
- ddI (400mg) once daily
- ddI (250mg) once daily, when co-administered with TDF
- LPV/r (400mg/100mg) twice daily
- SQV/r (1000mg/100mg twice daily)

All drugs and formulations will be considered once pre-qualified by WHO and registered in the countries**.**

3.3. First line ARV regimens and Characteristics which can influence choice

Table 2

ARV regimen	Major Potential Toxities	Usage in women (childbearing age or pregnant)	Usage in TB coinfection*	Availability as Three Drug Fixed Dose combination	Laboratory Monitoring Requirements	Price for least developed countries as June 2003 (US$/year)
ZDV/3TC/NVP	ZDV-related GI intolerance, anemia, and neutropenia NVP-related hepatotoxicity and severe rush	Yes	Yes. In rofampicin-free continuation phase of TB treatment. Use with caution in rifampicin-based regimens*	Yes	Yes	383-418
d4T/3TC/NVP	d4T- related neuropathy, pancreatitis, and lipoatrophy; NVP-related hepatotoxicity and severe rush	Yes	Yes. In rifampicin-free continuation phase of TB treatment. Use with caution in rofampicin-based regimens*	Yes	No	281-358
ZDV/3TC/EFV	ZDV-related GI intolerance, anemia, and neutropenia EFV-related CNS toxicity and potential for teratogenicity	No	Yes, but EFV should not be given to pregnant women or women of childbearing potential, unless effective contraception can be assured	No. EFV not available as part of FDC***. However partial FDC available for ZDV/3TC****	Yes	611-986
d4T/3TC/EFV	d4T- related neuropathy, pancreatitis, and lipoatrophy EFV-related CNS toxicity and potential for teratogenicity	No**	Yes, but EFV should not be given to pregnant women or women of childbearing potential, unless effective contraception can be assured	No. EFV not available as part of FDC***. However partial FDC available for ZDV/3TC****		

* See section IV Protocol on the Management of Opportunistic Infections, Tuberculesis

** See chapter 5.1

***FDC – fixed dose combination

**** These combinations have been not prequalified by WHO, but could be used if assured quality formulations or proven bioequivalence are available.

[1] Consideration should be given to register 600 mg tablets ASAP, if not registered

3.4. Reasons for changing ART in adults and adolescents

ART may need to be changed for either **toxicity** or **treatment failure.**

Table 3.
Major Potential Toxicities or First-line ARV Regimens and recommended Drug Substitution

REGIMEN	TOXICITY	DRUG SUBSTITUTION
ZDV/3TC/NVP	• ZDV-related persistent GI intolerance or severe hematological toxicity	• Switch ZDV → d4T
	• NVP-related severe hepatotoxicity	• Switch NVP → EFV (except pregnancy. If pregnant, switch to NFV, LPV/r or ABC)
	• NVP-related severe rash (but not life threatening)	• Switch NVP → EFV
	• NVP-related life threatening rash (Stevens-Johnson syndrome)	• Switch NVP → PI*
d4T/3TC/NVP	• d4T-related neuropathy or pancreatitis	• Switch d4T → ZDV
	• d4T-related lipoatrophy	• Switch d4T → TDF or ABC
	• NVP-related severe hepatotoxicity	• Switch NVP → EFV
	• NVP-related severe rash (but not life threatening)	• Switch NVP → EFV
	• NVP-related life threatening rash (Stevens-Johnson syndrome)	• Switch NVP → PI*
ZDV/3TC/EFV	• ZDV-related persistent GI intolerance or severe hematological toxicity	• Switch ZDV → d4T
	• EFV-related persistent CNS toxicity	• Switch EFV → NVP
d4T/3TC/EFV	• d4T-related neuropathy or pancreatitis	• Switch d4T → ZDV
	• d4T-related lipoatrophy	• Switch d4T → TDF or ABC**
	• EFV-related persistent CNS toxicity	• Switch EFV → NVP

* PI can be LPV/r or SQV/r. IDV/r or NFV can be considered as alternatives
** Switching off d4T typically does not reverse lipoatrophy but may slow its progression. TDF and ABC can be considered as alternatives, but availability is currently limited in resource-constrained settings. In the absence of TDF or ABC availability, ddI or ZDV are additional alternatives to consider.

Table 4.
Clinical and CD4+ Cell Count Definitions of Treatment Failure in HIV+ Adults and Adolescents

CLINICAL SIGNS OF TREATMENT FAILURE	CD4 CELL CRITERIA FOR TREATMENT FAILURE
• Occurence of new opportunistic infection or malignancy signifying clinical disease progression. This must be differentiated from immune reconstitution syndrome which can occure in the first three months following the initiation of ART* The latter does not signify treatment failure and the opportunistic infection should be treated as usual, without changes in the antiretroviral regimen. • Recurrence of prior opportunistic infection** • Onset or recurrence of WHO Stage III conditions (including but not restricted to HIV wasting, chronic diarrhea of unknown etiology, prolonged fever of inknown etiology, recurrent invasive bacterial infections, or recurrent/persistent mucosal candidiasis)	• Return of CD4 cell to pre-therapy baseline or below without other concomitant infection to explain transient CD4 cell decrease*** • > 50% fall from on therapy CD4 peak level without other concomitant infection to explain transient CD4 cell decrease***

* Immune Reconstitution Syndrome (IRS) is characterized by the appearance of signs and symptoms of an opportunistic disease a few weeks after the start of potent antiretroviral therapy in the setting of advanced immunodeficiency, as an inflammatory response to previously sub-clinical opportunistic infection. It is also possible that this immunological reconstitution may lead to the development of atypical presentations of some opportunistic infections.
** Recurrence of tuberculosis (TB) may not represent HIV disease progression as reinfection may occur. Clinical evaluation necessary.
***If patient is asymptomatic and treatment failure is being defined by CD4 cell criteria alone, consideration should be given to performing a confirmatory CD4 cell count if resources permit.

3.5. Second regimens

Table 5. Recommended second-line regimens in Adults and Adolescents for Treatment Failure on First-line ART

ZDV or d4T + 3TC + NVP or EFV	→	**TDF or ABC + ddI* + LPV/r or SQV/r****

* Dose of ddI should be reduced from 400mg to 250mg when co-administered with TDF
** LPV/r and SQV/r require sequre cold chain. NFV can be considered as an alternative in resource-limited settings without cold chain

[SEE APPENDIX II-**B** FOR MEDICATION DOSING]
[SEE APPENDIX II-**C** FOR DRUG INTERACTIONS]

3.6. Laboratory Monitoring

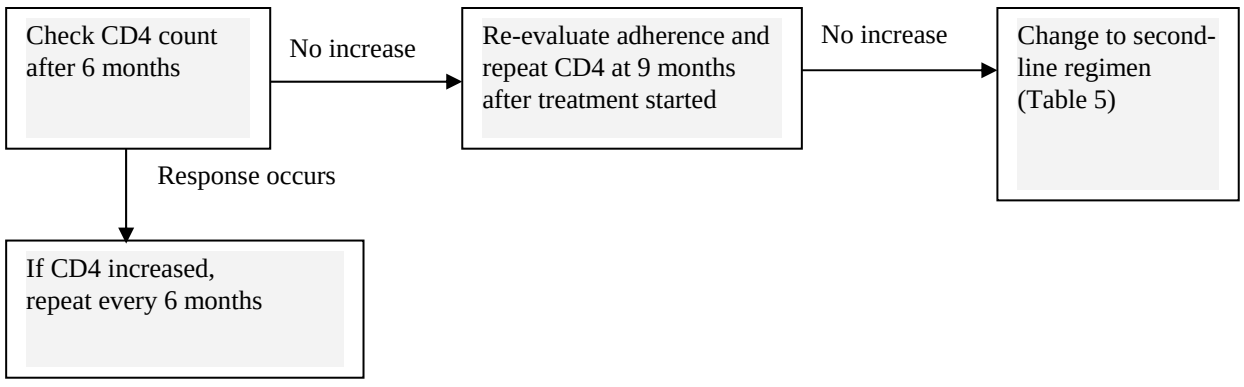
Table 6. Minimum Laboratory Monitoring for Recommended First-Line ARV Regimens

REGIMEN	LABORATORY ASSESSMENT AT BASELINE (PRETHERAPY)	LABORATORY ASSESSMENT ON THERAPY
ZDV/3TC/NVP	Hgb FBC CD4	Symptom directed determination of Hgb, WBC, ALT for toxicity CD4 every 6 months for efficacy
d4T/3TC/NVP	CD4	Symptom directed determination of ALT for toxicity CD4 every 6 months for efficacy
ZDV/3TC/EFV	Pregnancy test Hgb FBC CD4	Symptom directed determination of Hgb, WBC for toxicity CD4 every 6 months for efficacy
d4T/3TC/EFV	Pregnancy test CD4	Symptom directed testing, but none routinely required for toxicity CD4 every 6 months for efficacy

3.7. Treatment effectiveness monitoring

CD4 counts is one of the most useful and reliable ways of assessing whether ARV therapy is effective.

Algorhytm



Although HIV quantitation is an excellent method to measure treatment effect and detect treatment failure it is not a necessity for effective treatment with anti-retrovirals. Since HIV quantitation is still a very expensive technology these protocols have not incorporated it in the initial plan for scaling up access to ART in the CIS countries. Re-assessment of the role of this technology should be made periodically as the program moves forward.

4. Adherence Promotion and Monitoring

High level adherence is critical to the sustained success of anti-retroviral therapy. A widely accepted estimate of the level of adherence necessary to suppress HIV viremia and avoid the development of resistance is 95-100% of prescribed doses. This stands in contrast to other chronic diseases in which 80% adherence is considered acceptable. The requirement for such high level adherence combined with the complexity of antiretroviral therapy makes this treatment a great challenge to almost all patients regardless of background but especially so for those also struggling with other medical or psycho-social difficulties. It is especially important to address adherence before treatment begins for two reasons:

- patients new to treatment are most likely to make errors in the management of medications; and
- lapses in adherence when viral load levels are still high is most likely to lead to selection of drug resistance mutations.

Several recommendations for promoting high level adherence have been derived from experience in many treatment settings although there are few structured or controlled intervention trials in this area of care:

4.1. Assessment of Adherence

Potential adherence barriers should be assessed as part of the pre-treatment evaluation of all patients. This can be done using a formal tool such as a questionnaire or a structured interview or in a less formal discussion with a doctor, nurse or health educator. The critical areas to cover include

- patient knowledge about HIV disease and treatment;
- living situation including privacy,
- safe storage of medications,
- concerns about disclosure of HIV status to household members and colleagues at work;
- daily schedule and eating habits;
- mental health issues and substance abuse issues;
- medical problems and symptoms especially nausea, vomiting and diarrhea;
- other problems and priorities which may conflict with treatment such as economic hardship, child care, legal or immigration problems.

4.2. Preparation for Treatment

A brief period of education and other preparation for adhering to HIV treatment is extremely valuable and almost always possible without unduly delaying treatment. Utilization of peer educators is an especially effective approach. Typically two or three sessions of ½ to 1 hour each are devoted to covering three topics:

- A basic review issues of HIV infection focused on microbial etiology, of immunodeficiency and precautions to prevent transmission;
- A practical review of anti-HIV therapy focusing on the risk of resistance and the need for consistent adherence to potent combination regimens. Details of individual drug side effects, dietary nutrition requirements or restrictions and storage conditions also should be covered. More specific information about the patient's ARV combination (possible side effects, nuitrition and schedule of taking medications etc.)
- A detailed discussion of adherence strategies including specific scenarios addressing what to do if drugs are misplaced, doses are forgotten or side effects prevent taking medication. The experience of a peer educator who has actually experienced the challenges and benefits of therapy is extremely important. Including sharing personal experience of developing adherence to medications.

4.3. Dispensing of medication

Controlled dispensing of antiretroviral medications, especially early in the course of treatment allows frequent patient contact and monitoring of any problems with treatment during this critical phase. At a minimum patients should be assessed after two to four weeks on treatment to ensure that the regimen is being taken properly and well tolerated. More frequent contact is preferable. A successful approach has been to dispense medications in pre-filled multi-chamber pillboxes once a week for the first month then bimonthly or monthly thereafter. At each medication pickup any problems or side effects can be addressed. Most encounters can be very brief and handled by peer educators or other non-physician staff with referral to professionals if needed. An additional benefit of this approach

is that lapses in therapy are detected early and the risk of a patient taking medications erratically for a prolonged period is limited. Therefore patients who fail or drop out of initial therapy are less likely to develop drug resistant viruses.

In certain populations there are may be additional options opportunities to enhance and monitor adherence. Patients who reside in custodial or institutional settings can have treatment administered under direct observation (DOT). Drug users in methadone maintenance can receive partial or full DOT at the same location. DOT antiretroviral therapy can also be administered through needle exchange programs. Where a partial or full DOT approach is used fixed dose combinations and once daily regimens may have particular importance.

The possibility to administer fixed dose combinations (three-in-one or two-in-one) has to be considered in case of DOT approach.

4.4. Ongoing Adherence Monitoring Promotion

Adherence should be reviewed and reinforced at every patient contact. A non-judgemental atmosphere should be promoted so that patients feel free to report lapses in adherence. Many patients overestimate their adherence but self reported non-adherence is almost always accurate. A standardized question method asking patients to report the proportion of medication doses taken correctly during the preceding three days has been widely used. Counting pills remaining in boxes or bottles is another monitoring method. Pill counts or identification of pills that are in their regimen from the pile of different pills (as all of them have different shape and color) may also be useful.

5. ART in special populations

5.1. Women of childbearing potential or who are pregnant

Recommended WHO first-line regimen for this patient subgroup is

(ZDV or d4T) + 3TC + NVP

Important issues to be taken into consideration

- Women who are receiving ART and do not wish to become pregnant should have available to them effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy
- In those women for whom effective contraception can be assured, EFV remains a viable option for the NNRTI component of the regimen
- Women who are receiving ART and become pregnant should continue their treatment with the exception that EFV should be discontinued and replaced by NVP if the woman is in the first or second trimester of pregnancy and EFV has been part of the regimen
- For pregnant women, it might be desirable to initiate ART after the first trimester, although for pregnant women who are severy il, the benefit of early therapy clearly outweighs any potential fetal risk and therapy should be initiated in such cases
- The dual combination of d4T/ddI should be avoided in pregnancy and only used when no other alternatives exist, due to potential increased risk of lactic acidosis with this combination in pregnant women
- Symptomatic NVP-associated hepatic or serious rash toxicity, although uncommon, is more frequent in women than in men, and more likely to be seen in women with higher CD4 cell count (>250/mm^3)
- Until definitive data are available to answer whether single dose NVP prophylaxis does compromise subsequent HAART with NNRTI-based regimens, treatment of women who have previously received single dose NVP prophylaxis or 3TC prophylaxis for prevention of MTCT should be considered eligible for NNRTI-based regimens and not be denied access to life-sustaining therapy.
- When **PI-based option** is preferred to an NNRTI-based regimen during pregnancy, **SQV/r or NFV** are reasonable choices given the safety experience in pregnancy
- If a woman on ARV treatment decides to initiate or continue hormonal contraceptive use, the consistent use of condoms must be recommended for preventing HIV transmission and may also compensate for any possible reduction in the effectiveness of the hormonal contraceptive.

5.2. ART in individuals with active Tuberculosis

HIV is the most potent known risk factor for progression to active tuberculosis (TB) in people with latent *Mycobacterium tuberculosis* infection. HIV also increases the rate of recurrent TB, either due to endogenous reactivation or exogenous re-infection. Increasing TB cases in PLWHA augments the risk of TB transmission to the

general community, whether or not HIV-infected. The level of immunodeficiency at which PLWHA usually develop TB is associated with higher case fatality rates.

Tuberculosis (TB) will be an entry point For a significant proportion of patients eligible for antiretroviral therapy. Antiretroviral therapy is recommended for all patients with TB with a CD4 count < 200cells/mm^3 and should be considered for patients with CD4 < 350 cells/mm^3

Starting ART and its recommended regimens in individuals with active tuberculosis are summarized in Table 7

Table 7.
ART Recommendations for Individuals with Tuberculosis disease and HIV coinfection

CD4 CELL COUNT	RECOMMENDED REGIMEN	COMMENTS
CD4 count <200mm^3	Start TB treatment. Start ART as soon as TB treatment is tolerated (between 2 weeks and 2 months) (1) (ZDV or d4T) +3TC + EFZ (EFV - 600 or 800mg/day) (2,3)	Recommend ART. EFV is contraindicated in pregnant women or women of childbearing potential without effective contraception
CD4 between 200-350mm^3	Start TB treatment. Start one of these regimens after initiation phase (if severely compromised start earlier) (ZDV or d4T) +3TC + EFZ (EFV - 600 or 800mg/day) (2) or In case rifampicin-free continuation phase TB treatment regimen (ZDV or d4T) + 3TC + NVP(3)	Consider ART
CD4 >350mm^3	Start TB treatment	Defer ART(4)
CD4 not available	Start TB treatment	Consider ART(1,5)

1 Timing of ART initiation should be up to clinical judgement based on other signs of immunodeficiency (see Table 1). For extrapulmonary TB, ART should be started as soon as TB treatment is tolerated irrespective of CD4 cell count.

2 Alternatives to the EFV portion of the regimen include SQV/r (400/400 bid os 1600/200 qd in sgc), LPV/RTV (400/400 mg bid) and ABC (300mg bid)

3 NVP (200mg qd for 2 weeks followed by 200mg bid) may be used in place of EFV in absence of other options-NVP containing regimens include d4T/3TC/NVP or ZDV/3TC/NVP

4 Unless non-TB stage IV conditions are present (see Table 1). Otherwise start ART upon completion of TB treatment.

5 If no other signs of immunodeficiency are present and patient is improving on TB treatment, ART should be started upon completion of TB treatment.

6. Referrals for needed care

Referrals may be needed for psychosocial services, management of co-morbid conditions or management of adverse events. As far as possible care of HIV positive patients should be unfragmented with as many primary care services as possible provided at one site. Care of family members should also be coordinated through the primary HIV care provider. Refer to the National Treatment Center to examine 3-rd line ARV treatment options.

7. Follow up schedule

Patients initiating ART should be reevaluated frequently [SEE Table 8.]

Table 8. Patient´s follow up flowchart

Assessment	weeks (ART)						months									
	-4	-2	0	2	4	8	3	4	5	6	7	8	9	10	11	12
Adherence	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
General health status	■		■	■	■	■	■			■						■
Co-morbidities	■		■	■	■	■	■			■						■
Complete history of the disease	■		■	■	■	■	■			■						■
Physical examination	■		■	■	■	■	■			■						■
Routine laboratory assessment • Hemoglobin • White blood cell count and differential • Urinalysis • Liver function tests (ALT, AST, bilirubin) • Creatinine	■		■		■		■			■						■
CD4 count	■									■						■
Gynecologic exam	■									■						■
Sputum smear microscopy for AFB	■															■
Chest x-ray	■															■
Pregnancy test	■															■
Inclusion criteria	■		■													
Other testing should be driven by signs or symptoms.	If necessary															

8. Management of adverse events

Patient education must include information on the common or dangerous adverse events associated with their ART regimens and the steps they should take if they experience such events. Reassurance and symptomatic treatment should be provided and symptomatic medication may be offered for common side effects such as nausea and diarrhea.

9. Program monitoring and evaluation

The proposed program must have a monitoring and evaluation component in order to ensure that programmatic goals are being met. This process should occur on both the level of individual patient care as well as the level of overall program functioning. The number of patients in treatment is one obvious indicator. With regard to individual outcomes, 60-70% of patients starting HAART should have a clinically significant response by 24 weeks of HIV treatment as determined by clinical status (weight gain or resolution of symptoms) or surrogate markers such as CD4.

Important markers of program performance that must be monitored include the number of patients who remain in care and on treatment at 6 month intervals. Severe illness or death in those on ART should be counted. The proportion of missed visits and missed doses of medications are other important performance indicators.

APPENDIX II-A.
WHO staging system for hiv infection and disease in adults and adolescents

Clinical stage I

1. Asymptomatic
2. Generalized lymphadenopathy

Performance scale 1: asymptomatic, normal activity

Clinical stage II

3. Weight loss, <10% of body weight
4. Minor mucocutaneous manifestations (seborrheic dermatitis, prurigo, fungal nail infections, recurrent oral ulcerations, angular cheilitis)
5. Herpes zoster within the last five years
6. Recurrent upper respiratory tract infections (i.e. bacterial sinusitis).

And/or performance scale 2: symptomatic, normal activity

Clinical stage III

7. Weight loss, >10% of body weight
8. Unexplained chronic diarrhoea, >1 month
9. Unexplained prolonged fever (intermittent or constant), >1 month
10. Oral candidiasis (thrush)
11. Oral hairy leukoplakia
12. Pulmonary tuberculosis
13. Severe bacterial infections (i.e. pneumonia, pyomyositis)

And/or performance scale 3: bedridden <50% of the day during the last month

Clinical stage IV

14. HIV wasting syndrome *
15. Pneumocystis carinii pneumonia
16. Toxoplasmosis of the brain
17. Cryptosporidiosis with diarrhoea >1 month
18. Cryptococcosis, extrapulmonary
19. Cytomegalovirus disease of an organ other than liver, spleen or lymph nodes (ex: retinitis)
20. Herpes simplex virus infection, mucocutaneous >1 month, or visceral
21. Progressive multifocal leukoencephalopathy
22. Any disseminated endemic mycosis
23. Candidiasis of oesophagus, trachea, bronchi or lungs
24. Atypical mycobacteriosis, disseminated
25. Non-typhoid Salmonella septicaemia
26. Extrapulmonary tuberculosis
27. Lymphoma
28. Kaposi's sarcoma
29. HIV encephalopathy**

And/or performance scale 4: bedridden >50% of the day during last month

Note: both definitive and presumptive diagnoses are acceptable.

* HIV wasting syndrome: weight loss of >10% of body weight, plus either unexplained chronic diarrhoea (>1 month) or chronic weakness and unexplained prolonged fever (>1 month).

** HIV encephalopathy: clinical findings of disabling cognitive and/or motor dysfunction interfering with activities of daily living, progressing over weeks to months, in the absence of a concurrent illness or condition other than HIV infection which could explain the findings.

APPENDIX II-B.
Antiretroviral dosage regimens for adults and adolescents

("Scaling up Antiretroviral therapy in resource limited settings. Guidelines for a public health approach". WHO, 2003 Revision)

These dosages are in common clinical use. The dosages featured in this table were selected based on the best available clinical evidence and dosages that can be given on a once or twice daily basis were preferred in order to enhance adherence to therapy. The doses listed are those for individuals with normal renal or hepatic function. Product specific information should be consulted for dose adjustments that may be indicated with renal or hepatic disfunction or for potential drug interactions with other HIV and non-HIV medications.

DRUG CLASS/DRUG	DOSE
Nucleoside RTIs (NRTI)	
Zidovudine (AZT)	300 mg BID
Stavudine (d4T)	40 mg BID (30 mg BID if < 60 kg)
Lamivudine (3TC)	150 mg BID or 300mg once daily
Didanosine (ddI)	400 mg x once daily (250 mg once daily if < 60 kg) (250 mg once daily if administered with TDF)
Abacavir (ABC)	300 mg BID
Combivir (AZT+3TC)	(300/150) BID
Nucleotide RTI	
Tenofovir (TDF)	300mg once daily (Note : drug interaction with ddI necessitates dose reduction of latter)
Non-nucleoside RTI (NNRTI)	
Efavirenz (EFV)	600 mg once daily[1]
Nevirapine (NVP)	200 mg once daily for 14 days, then 200 mg BID
Protease inhibitors (PI)	
Nelfinavir (NFV)	1250 mg BID
Indinavir/ritonavir (IDV/r)	800 mg/100 mg BID[2,4]
Lopinavir/ritonavir (LPV/r)	400 mg/100 mg BID (533 mg/133 mg x BID when combined with EFV or NVP)
Saquinavir/ritonavir (SQV/r)	1000 mg/100mg BID or 1600mg/200mg once daily[3,4]

[1] See TB section for specific TB dosing

[2] This dosage regimen is in common clinical use. Other IDV/r dosage regimens that range from 800mg/200mg bid to 400mg/100mg bid are also in clinical use.

[3] Both the hard-gel and soft-gel capsule formulations can be used when SQV is combined with RTV.

[4] Dosage adjustment when combined with an NNRTI is indicated but a formal recommendation can not be made at this time. One consideration is to increase the RTV component to 200mg bid when EFV or NVP is used concomitantly. More drug interaction data are needed.

APPENDIX II-C.
Drug Interactions

1. Drug Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors

	Nevirapine (NVP)	Efavirenz (EFZ)	Indinavir (IDV)	Lopinavir (LPV/r)	Nelfinavir (NFV)	Saquinavir (SQV)
Nevirapine		No effect on NVP EFZ AUC decreased 22% ***Recommendation:*** Standard dosing	NVP increased twofold IDV decreased 28% ***Recommendation:*** Change IDV dose to 1000 mg three times daily No change NVP	No effect on NVP LPV trough decreased 55% ***Recommendation:*** Consider LPV/r 533 mg/ 133 mg twice daily No change NVP	No effect on NVP NFV levels increased 10% ***Recommendation:*** Standard dosing	No effect on NVP SQV decreased 25% ***Recommendation:*** Standard dosing
Efavirenz			No effect on EFZ IDV decreased 31% ***Recommendation:*** Change IDV dose to 1000 mg three times daily No change EFZ	No effect on EFZ LVP AUC decreased 40% ***Recommendation:*** Consider LPV/r 533 mg/ 133 mg twice daily No change EFZ	No effect on EFZ NFV increased 20% ***Recommendation:*** Standard dosing	EFZ decreased 12% SQV decreased 62% ***Recommendation:*** Do not coadminister (SQV/r boosting may be possible)
Indinavir				No effect on LPV IDV AUC and trough increased ***Recommendation:*** Change IDV dose to 600 mg twice daily No change LPV	NFV increased 80% IDV increased 50% ***Recommendation:*** Limited data for IDV 1200 mg twice daily with NFV 1250 mg twice daily	SQV increased fourfold to sevenfold *No effect on IDV* ***Recommendation:*** Insufficient data to provide recommen-dation
Lopinavir					No data	SQV AUC/trough increased ***Recommendation:*** SQV 800 mg twice daily No change LPV/r
Nelfinavir						SQV increased twofold to fivefold NFV increased 20% ***Recommendation:*** Fortovase 1200 mg twice daily No change NFV

Source: ***"Scaling up Antiretroviral Therapy in Resource-Limited Settings". Guidelines for a public health approach. World Health Organization. June, 2002. Appendix 8B***

2. Drug Interactions Involving Non-Nucleoside Reverse Transcriptase Inhibitors And Protease Inhibitors Of Relevance To Poor Countries

	Nevirapine (NVP)	Efavirenz (EFZ)	Indinavir (IDV)	Lopinavir (LPV/r)	Nelfinavir (NFV)	Saquinavir (SQV)
Antifungal						
Ketoconazole	NVP increased 15-30% Ketoconazole decreased 63% ***Recommendation:*** Do not coadminister	No data	IDV increased 68% ***Recommendation:*** Change IDV to 600 mg three times daily	Lopinavir (LPV/r) LPV decreased 13% Ketoconazole increased threefold ***Recommendation:*** None	No dose adjustment	Saquinavir (SQV) SQV increased threefold ***Recommendation:*** Standard dosing
Antimycobacterials						
Rifampin	NVP decreased 37% ***Recommendation:*** Use with caution only if no alternatives available	EFZ decreased 25-33% ***Recommendation:*** Consider EFZ 800 mg daily	IDV decreased 89% ***Recommendation:*** Do not coadminister	LPV AUCdecreased 75% ***Recommendation:*** Do not coadminister	NFV decreased 82% ***Recommendation:*** Do not coadminister	SQV decreased 84% when given without RTV ***Recommendation:*** If using SQV/RTV rifampin can be used at 600 mg/day or two or three times weekly
Rifabutin	NVP decreased 16% ***Recommendation:*** Standard dosing	EFZ unchanged Rifabutin decreased 35% ***Recommendation:*** Increase rifabutin dose to 450-600 mg daily (or 600 mg two or three times weekly); EFZ no change	IDV decreased 32% Rifabutin increased twofold ***Recommendation:*** Decrease rifabutin dose to 150 mg daily (or 300 mg two or three times weekly); IDV dose change to 1000 mg three times daily	Rifabutin AUC increased threefold ***Recommendation:*** Decrease rifabutin dose to 150 mg daily; LPV/r no change	NFV decreased 32% Rifabutin increased twofold ***Recommendation:*** Decrease rifabutin dose to 150 mg daily (or 300 mg two or three times weekly); NFV dose increase to 1000 mg three times daily	SQV decreased 40% (RTV increases rifabutin levels fourfold) ***Recommendation:*** If using SQV/RTV, use rifabutin 150 mg two or three times weekly
Clarithromycin	NVP increased 26% Clarithromycin decreased 30% ***Recommendation:*** Standard dosing	EFZ unchanged Clarithromycin decreased 39% ***Recommendation:*** Do not coadminister	Clarithromycin increased 53% ***Recommendation:*** Standard dosing	No data	No data	Clarithromycin increased 45% SQV increased 177% ***Recommendation:*** Standard dosing
Oral contraceptives	Estradiol decreased 20% ***Recommendation:*** Use alternative or additional methods	Estradiol increased 37%; no data on other components ***Recommendation:*** Use alternative or additional methods	When used with RTV: estradiol decreased ***Recommendation:*** Use alternative or additional methods	Estradiol decreased 42% ***Recommendation:*** Use alternative or additional methods	Estradiol decreased 47%; norethindrone decreased 18% ***Recommendation:*** Use alternative or additional methods	When used with RTV: estradiol decreased ***Recommendation:*** Use alternative or additional methods
Methadone	Methadone decreased significantly ***Recommendation:*** Opioid withdrawal reported; may require increase in methadone dose	Methadone decreased significantly ***Recommendation:*** Opioid withdrawal reported; may require increase in methadone dose	No change but there may be a decrease if given with low-dose RTV ***Recommendation:*** When IDV is given with low-dose RTV: opioid withdrawal possible; may require increase in methadone dose	Methadone AUC decreased 53% ***Recommendation:*** Opioid withdrawal possible; may require increase in methadone dose	May decrease methadone levels ***Recommendation:*** Opioid withdrawal possible; may require increase in methadone dose	No data but may decrease if given with low-dose RTV ***Recommendation:*** When given with low-dose RTV: opioid withdrawal possible; may require increase in methadone dose

	Nevirapine (NVP)	Efavirenz (EFZ)	Indinavir (IDV)	Lopinavir (LPV/r)	Nelfinavir (NFV)	Saquinavir (SQV)
Anticonvulsant						
Phenobarbital	Unknown	Unknown	Unknown	Unknown but may decrease LPV levels substantially ***Recommendation:*** Monitor anticonvulsant levels	Unknown but may decrease NFV levels substantially ***Recommendation:*** Monitor anticonvulsant levels	Unknown but may decrease SQV levels substantially ***Recommendation:*** Monitor anticonvulsant levels
Lipid-lowering agents						
Simvastatin, Lovastatin, Atorvastatin, Pravastatin	No data	No data	Potential for large increase in statin levels (except pravastatin) ***Recommendation:*** Do not coadminister except pravastatin; no dose adjustment	Potential for large increase in statin levels ***Recommendation:*** Do not coadminister	Potential for large increase in statin levels ***Recommendation:*** Do not coadminister	Potential for large increase in statin levels ***Recommendation:*** Do not coadminister
Additional drugs that should NOT be coadministered						
	Herbs: St. John's wort, garlic supplements	***Antihistamine:*** astemizole, terfenadine ***Gastrointestinal:*** cisapride ***Psychotropic:*** midazolam, triazolam ***Ergot alkaloids:*** dihydroergotamine, ergotamine ***Herbs:*** St. John's wort, garlic supplements	***Antihistamine:*** astemizole, terfenadine ***Gastrointestinal:*** cisapride ***Psychotropic:*** midazolam, triazolam ***Ergot alkaloids:*** dihydroergotamine, ergotamine ***Herbs:*** St. John's wort, garlic supplements When IDV is used with low-dose RTV: ***Cardiac:*** flecainide, propafenone ***Neuroleptic:*** pimozide	***Antihistamine:*** astemizole, terfenadine **Gastrointestinal**: cisapride ***Psychotropic:*** midazolam, triazolam ***Ergot alkaloids:*** dihydroergotamine, ergotamine ***Herbs:*** St. John's wort, garlic supplements ***Cardiac:*** flecainide, propafenone ***Neuroleptic:*** pimozide	***Antihistamine:*** Astemizole, terfenadine ***Gastrointestinal:*** cisapride ***Psychotropic:*** midazolam, triazolam ***Ergot alkaloids:*** dihydroergotamine, ergotamine ***Herbs:*** St. John's wort, garlic supplements	***Antihistamine:*** astemizole, terfenadine *Gastrointestinal:* cisapride ***Psychotropic:*** midazolam, triazolam *Ergot alkaloids:* dihydroergotamine, ergotamine ***Herbs***: St. John's wort, garlic supplements When SQV is used with low-dose RTV: ***Cardiac:*** flecainide, propafenone ***Neuroleptic:*** pimozide
Miscellaneous	Can induce glucosteroid metabolism, resulting in lower serum steroid levels Efavirenz (EFZ)	Monitor warfarin if used concomitantly	Grapefruit juice decreases IDV by 26%.	-	-	Grapefruit juice increases SQV levels Dexamethasone decreases SQV levels

Source*: "Scaling up Antiretroviral Therapy in Resource-Limited Settings". Guidelines for a public health approach. World Health Organization. June, 2002.Appendix 8C*

III. HIV Care and Treatment for Injection Drug Users

Introduction

Substance abuse has profound consequences for health and health care. Injection drug use exposes the user to a variety of blood-borne infectious complications including HIV. In some areas such as the former Soviet countries this is the major risk factor for HIV transmission. Prevention efforts using educational and harm reduction strategies have had success in controlling the spread of HIV among injection drug users but the absence of HIV care and especially anti-retroviral therapy has undermined these efforts in many areas.

Based on the experience of other countries (i.e. Brazil) the most effective response to the epidemic should consists of both components, prevention and treatment for all those who need it. Thus, it is crucial for countries with the fastest developing HIV-epidemic fueled by injecting drug-use to respond immediately to the needs of these vulnerable population with both preventive and treatment services.

The present opportunity to make HIV care including anti-retroviral therapy widely available in CIS countries can bring many hard to reach drug users into care for the first time and enhance both their own health and the effectiveness of educational and harm reduction prevention programs. Special attention must be paid, however, to delivering treatment services in ways that maximize the participation of all those who need care.

Where comprehensive HIV care has been provided to drug users in an accessible and non-judgmental way the ability to attract and retain high proportions of patients in effective treatment regimens has been apparent. In particular the combination of HIV care with social and psychological services as well as substance abuse services including harm reduction, detoxification and substitution therapy has been most successful.

1. Organization of medical care

1.1. General Principles

It is often difficult to adequately coordinate medical services for HIV-infected IDUs, who commonly have a variety of medical problems. Successful programs delivering medical care (including HIV/AIDS-care) to active ID-users have identified certain important principles:

1.1.1. Care must be accessible.

The services should be located in places that are accessible by the client and situated in facilities that are part of the general healthcare infrastructure.

1.1.2. Care should be comprehensive.

The maximum possible number of the most-needed services should be available at one location. Necessary services such as gynecology and family planning are most efficiently delivered if they can be accessed at the same site as HIV care. Social services, counseling and education should be integrated in the medical care setting. Substance abuse or psychiatric services may be vital ingredients in a successful management plan for many ID users.

1.1.3.Care should be offered to patients at any level they are able to utilize.

Injection drug users newly diagnosed with HIV are sometimes difficult to engage in comprehensive care.

Feelings of denial, anger and guilt may overwhelm them. It is important to offer care at whatever level of intensity the patient can handle so as not to drive him or her away entirely. This may mean starting with very simple interventions like OI prophylaxis and advancing to more complex care including anti-retroviral therapy later. Education and counseling, especially utilizing peer group members can be very helpful in this situation.

1.1.4.Outreach strategies are a vital component of HIV care.

Successful treatment programs for stigmatized diseases like HIV/AIDS especially in marginalized groups like ID users have developed effective outreach strategies to bring potential patients into the treatment system and to retain patients in care. The most effective programs have formed strong links with community-based organizations representing or serving the affected groups and have utilized peer educators and counselors drawn from these groups.

1.2. Models of Comprehensive Care for Injection Drug Users

A number of current models are employed to provide primary medical care for HIV patients who are in addiction treatment. One model is to provide medical care by referral of patients to a nearby HIV clinic. This approach may be most effective for patients who are stable, but it may be less appropriate for more complex patients, such as those actively using drugs, who may have minimal or strained relationships with health care providers. Also, IDUs often require ongoing adjunctive care for coexisting psychiatric problems. Untreated behavioral problems can interfere with medical care. Drug users may have difficulty keeping appointments, and may be fearful of or ambivalent about medical care. Medical staff in HIV or primary care clinics may not be fully equipped to manage the psychiatric and substance use problems that can interfere with adherence to medical care. If the medical clinic is conveniently and closely situated, however, the referral model can work effectively.

A second model of primary medical care for HIV-infected drug users consists of establishing a substance abuse treatment component at an AIDS clinic. This model would allow HIV-infected IDUs to obtain methadone or other treatment for substance use disorders on-site in a primary care HIV medical clinic. One limitation of this model, however, is the difficulty of responding to the regulatory requirements for methadone treatment.

A third model is to provide on-site primary medical care for IDUs in an addiction treatment facility, such as a methadone maintenance treatment program. The methadone treatment setting is efficient for providing medical services in a "one-stop shopping" approach. Referral of patients to off-site primary care clinics can sometimes result in patients failing to reach medical care. Continued primary medical care for IDUs with HIV infection is critical.

1.3. Linkage to Harm Reduction (HR) programs

Many countries where the HIV epidemic is fueled by injecting drug use have experience providing HR services to members of vulnerable groups, including ID-users. Also, HR programs have prepared a pool of trained staff (social workers, counselors and outreach workers) that has access to the community and are able to work in a non-judgement and trustful manner. Although HR programs have focused mainly on prevention activities there are some promising examples of using HR sites for providing laboratory service for clients (St. Petersburg, Russia) and for PMTCT services in Roma ID-using community (Uzhgorod, Ukraine.) Harm reduction programs offer important assests for HIV care. They have experience reaching and communicating with IDUs and have established credibility and trust. HR programs should be involved in planning HIV treatment for IDUs and should be invited to participate in the outreach to potential patients for testing, treatment and in maintaining follow-up with patients who drop out of care. HR programs may be useful in specific treatment activities such as delivering medications in a DOT system.

1.4. Education and peer-support groups

Support group or educational programs should be established or incorporated into the overall HIV treatment program for IDU. Former drug users often have unique effectivness in educating and motivating current users to take steps to access effective care. Peer educators have proven very effective in several HIV treatment adherence promotion programs.

1.5. Methadone Maintenance as part of HIV-service structure

Where substitution therapy is available or contemplated consideration should be given to offering HIV care and dispensing HIV medication at the same site where substitution therapy is delivered. This approach can achieve maximal levels of treatment supervision which should enhance efficacy and reduce the risk of HIV drug resistance. In addition co-location of these services facilitates management of the important drug-drug interactions with between methadone and HIV medications (see ANNEX 1).

2. Anti-retroviral therapy

2.1. General considerations

There are widely held opinions that injection drug users are poor candidates for anti-retroviral therapy (ART). This is usually based on the perception that drug using behavior will prevent adherence to the treatment regimen or that the medical complications of drug use such as Hepatitis C infection will make drug users intolerant to ART. Although these limitations are indeed a problem for many patients, extensive experience and numerous publications have documented that individualized HIV care for injection drug users is often highly successful. The key to effective treatment is careful assessment and education of the patient leading to development of an individualized treatment plan to maximize adherence. Some authorities have taken the position that injection drug users must demonstrate prolonged abstinence before they should begin ART. This approach is unnecessary and has adverse effects on the credibility of the treatment program. While abstinence is desirable for several reasons it is often impossible to achieve especially in the setting of a recently-diagnosed life-threatening illness. Although abstinence should be encouraged, drug users must understand that a harm-reduction approach to both substance abuse and to ART can be very successful. If drug users are able to keep medical care appointments and adhere to a schedule for taking medications they are likely to have a successful response to ART even though not fully abstinent. In a non-judgmental care environment any relapse or ongoing substance abuse can be addressed as a problem needing additional attention rather than as a moral failing which jeopardizes their care entirely.

2.2. Criteria for Initiating Treatment

Clinical and immunological criteria for initiating HAART in substance using patients do not differ from general recommendations Timing of the initiation of antiretroviral therapy is a critical matter for all patients, perhaps especially for injection drug users. Making sure that patients are well informed, motivated to begin and have had all potential barriers to successful adherence assessed and addressed is crucial. It is far better to briefly delay the initiation of treatment in all but the most critically ill patients to carry out these steps than to invite the risk of treatment failure and drug resistance. In a well organized program with trained staff to carry out these functions the process of preparing patients for ART can be done over several weeks. If severe problems are identified which are likely to make treatment unsuccessful the patient and care provider must make a judgment about the risks and benefits of delaying treatment while addressing these problems. If well-informed most patients will accept the idea that better preparation whether it involves establishing a more stable living situation or obtaining treatment for substance abuse or a psychiatric problem, will greatly improve their chances of success once they begin ART. In cases that are disputed there should be a mechanism in each center for alternative evaluation of the case by one or more methods: peer counselor, patient advocate, or medical second opinion.

2.3. Choice of regimen

The clinical and immunological criteria for initiating HAART in substance dependent patients do not differ from general recommendations. Therefore, injecting drug users who are eligible for ART should be ensured access to this life saving therapy. Special considerations for this population include dealing prospectively with life style instability which challenges drug adherence and accounting for the potential drug interactions of ARV's with agents such as methadone. Development of programs which integrate care of drug dependence including drug substitution therapy) and HIV is encouraged. In such settings, approaches such as directly observed therapy can be implemented. Once daily ARV regimens are being intensively explored in this arena and lend themselves to such approaches. The number of ARVs which are approved or being investigated for once daily use is progressively expanding and includes 3TC, FTC, ddI, d4T, TDF, ABC, EFV, SQV/r, LPV/r and ATV.

Co-administration of methadone with EFV, NVP or RTV in HIV infected individuals with a history of injecting drug use resulted in decreased plasma levels of methadone and signs of opiate withdrawal. Patients should be monitored for signs of withdrawal and their methadone.

2.4. Medication Administration

Attention should be paid to the process of dispensing antiretroviral therapy and providing ongoing supervision. As a rule small amounts of medicine should be dispensed at frequent intervals when a patient begins treatment. This approach has two benefits: Frequent visits to pick up medication provides an opportunity to detect and address adherence problems before they lead to drug resistance; and if there are disruptions in treatment the amount of medication available to be misused by the patient is limited therefore also limiting the potential for resistance to develop. While true DOT is desirable for some patients it is usually impractical. It may become more feasible with once daily regimens. Substance abuse treatment facilities are strategically appealing sites for trials of this approach. Existing harm reduction programs should be evaluated for the possibility of integrating DOT strategies at needle-

exchange points and other outreach sites.

Several other approaches should be available at treatment centers including:

- Dispensing of medications in pre-filled pill boxes, initially on a weekly basis then every two or 4 weeks;
- Dispensing of one dose of medication five days per week at Methadone Maintenance Treatment Program sites with the other doses self-administered.
- Dispensing on a weekly or more frequent basis at needle exchange or other harm reduction sites.

2.5. ART in patients with hepatopathy

Co-infection with Hepatitis C is common in HIV + IDU. Chronic active infection with Hepatitis B and alcoholic liver disease are also frequent. The resultant hepatopathy may increase the risk of liver toxicity and impair the metabolism of some anti-retroviral agents.

Despite the common association between hepatotoxicity and antiretroviral agents, almost 90% of HIV+ patients, regardless of whether they are co-infected by hepatitis viruses, will tolerate ART treatment without severe liver toxicity.

Among the nucleoside analogues, hepatotoxicity has been more commonly reported with AZT, ddI or d4T in the form of liver enlargement, liver enzyme abnormalities and/or lactic acidosis. Abacavir or 3TC have also been involved but at a lesser degree. Among the non-nucleoside reverse transcriptase inhibitors (NNRTI) hepatic toxicity has been associated with efavirenz but appears more frequent and severe with nevirapine. The protease inhibitors are often associated with mild hepatotoxicity. Ritonavir, especially if administered at full doses as a single PI is significantly more hepatotoxic than the others. Unlike the hepatotoxicity associated with NNRTIs which turns up during the first weeks of therapy in most cases, that associated with PIs can appear at any time during the treatment.

In managing these patients it is helpful to classify them according to the degree of liver damage. In chronic hepatitis without signs of hepatocellular insufficiency the usual ART doses are used but there may be a greater risk of hepatic toxicity. Nucleoside analogues and efavirenz appear slightly better tolerated than nevirapine or PIs.

In patients with cirrhosis or severe hepatic insufficiency impaired hepatic metabolism may increase the risk of lactic acidosis with nucleosides but dose reduction is only advised for zidovudine. Efavirenz can be administered at full doses in patients with liver insufficiency but nevirapine should be avoided if possible. PI dosing is difficult in patients with decompensated liver disease. If drug level monitoring is available this is helpful for adjusting doses but usually a trial and error approach is the only option.

3. Managing Methadone in HIV infected patients

3.1. Medication dose adjustments for patients on methadone

Methadone is extensively metabolized by cytochrome enzymes, and the methadone level may decrease when methadone is used together with cytochrome inducers such as carbamazepine and rifampin -- necessitating higher doses. Conversely, methadone levels could be raised by cytochrome inhibitors. In turn, methadone inhibits the metabolism of zidovudine (AZT) and can elevate AZT levels.

It is essential to note that additional analgesics are needed to treat acute or chronic pain in the HIV-infected drug user who is on methadone maintenance treatment, because patients do not obtain adequate pain relief from their usual daily dose of methadone, to which they have become tolerant.

Pharmacologic interactions may produce either changes in methadone concentrations, or changes in concentrations of the antiretroviral agents being used. Studies suggest that nevirapine, efavirenz, and ritonavir decrease methadone concentrations through induction of the cytochrome P450 system (principally CYP 3A4), and produce clinically significant opiate withdrawal in some patients. Signs and symptoms of methadone withdrawal typically occur 4-8 days after starting a new drug and include chills, sweating, piloerection, nausea, diarrhea, abdominal cramping, rhinorrhea and lacrimation, myalgias, tremulousness, and anxiety. Precipitating opiate withdrawal may trigger relapse of heroin use, distrust of medical providers, and unwillingness to take antiretroviral therapy. Frequent, open communication between HIV provider, patient, and methadone maintenance staff is prudent when new antiretroviral therapy is initiated. But usually an immediate and a substantial increase in methadone dose is not appropriate because the increase in methadone dose required is not as great as might be expected from the pharmacokinetic data. Medical assessments should be done frequently for such patients to monitor withdrawal symptoms, increasing methadone dose in increments of 10mgs from day 8-10 onwards.

Alterations in antiretroviral concentrations, especially NRTIs, may result when administered with methadone. At present 2 potentially relevant interactions have been described. First, zidovudine concentrations are increased approximately 40% when administered with methadone. No empiric dose reduction is currently recommended, but signs of zidovudine toxicity should be closely monitored. Second, didanosine concentrations have been found to be reduced approximately 60% when administered with methadone. This may lead to didanosine underexposure,

incomplete viral suppression, and the development of resistance. Of note, these pharmacologic data are based on the buffered-tablet formulation of didanosine, given twice daily. There are no data on the powder or enteric-coated capsule formulations. Until more information is available, use of the buffered tablet didanosine formulations in methadone recipients should be avoided if other options exist.

4. Other Considerations

4.1. Bacterial infections

A striking feature of HIV disease in IDUs is the frequent occurrence of bacterial infections, especially skin infections, pneumonia, endocarditis, and sepsis. Bacterial pneumonia tends to be an earlier (CD4+ cell count 200-400 cells/mm) and more common manifestation of HIV infection in this group of patients than in others. Trimethoprim-sulfa prophylaxis for pneumocystis pneumonia appears to provide some protection from bacterial pneumonia as well.

Education about preventing infection at injecting sites is emphasized in harm reduction programs and should be incorporated in HIV care an treatment programs as well. In addition it is desirable for these programs to offer care for skin and injection site infections since this is a service frequently needed and difficult to obtain. Provision of care for such problems is likely to enhance the treatment program's credibility and outreach efforts among drug users.

4.2. PMTCT and family planning

Access to family planning and PMTCT services should be an integrated part of the continuum of medical care for ID-users. Information about existing choices and services available should be provided to female patients as part of the initial evaluation.

A peer consultant,(a women/mother with HIV, who is trained in pre- and post-test counseling and basics of PMTCT) can play a crucial role in providing follow up for the pregnant women, ensuring adherence to the ARV regimen for PMTCT, and motivating the women and her child to stay within the healthcare system during the postnatal period.

Taking into consideration the fact that majority of women are coming directly in labor and thus miss antenatal care, the staff of the maternity houses should have access to quality rapid-test kits (qualified by WHO, 2002) and the emergency ARV regimen (Nevirapine-based.) See also Protocol on Prevention of HIV infection in infants ans young children (PMTCT).

4.3. Treatment of chronic hepatitis

The management of patients with chronic hepatitis B or C and HIV is evolving rapidly. Use of agents active against both HIV and Hepatitis B such as lamivudine (3TC) and tenofovir (TDF) is suggested for patients with this coinfection. Current standard of care for Hepatitis C is provision of pegylated alpha-interferon with ribavirin but results of treatment are poorer, with no more than one-third having a sustained response to therapy. Case selection is therefore challenging and determination of the extent of liver damage via liver biopsy is very useful. Excessive alcohol consumption has a very deleterious effect on the course of liver disease in these patients so counseling and alcohol treatment should be emphasized. Generally patients with CD4 below 200 (350)??? should become stabilized on effective ART before consideration is given to treatment for Hepatitis C. If the CD4 count is above 350 in ART-naïve patients this may be the best time to initiate HCV treatment since interactions with ART can be avoided. Contraindications to therapy of HCV infection should be evaluated including coexistent psychiatric disorders such as depression which may be exacerbated by interferon. Hematologic disorders especially anemia may be exacerbated by ribavirin.

If Hepatitis C treatment must be combined with HIV treatment there are several additional considerations. Because of potential interactions between ribavirin and NRTIs enhancing the possibility of lactic acidosis may be enhanced. In addition the possibility that HCV therapy side effects may destabilize a successful ART response should be realized.

APPENDIX III-A.
Interactions Between Antiretrovirals and Methadone

ANTIRETROVIRAL AGENT	EFFECT ON METHADONE	EFFECT ON ANTIRETROVIRAL AGENT	COMMENT
NRTIs			
Zidovudine	None	↑AUC by 40%	Watch for nausea, vomiting, asthenia, headache, and bone marrow suppression in recipients. If methadone trough levels are normal, suspect that problem is zidovudine toxicity rather than methadone withdrawal.
Didanosine	None	↓AUC by 60%	This has only been studied with twice-daily administration of the buffered tablets and was hypothesized to be due to reduced bioavailability of didanosine in the setting of slower transit through the acidic environment of the stomach in patients taking methadone. Additionally, there was great interindividual variability in didanosine pharmacokinetic data. The effects of methadone on didanosine powder or enteric-coated tablet formulations are unknown.
Zalcitabine	Unknown	Unknown	
Stavudine	None	↓AUC by 18%	Decreased stavudine concentrations probably not clinically significant.
Lamivudine	None	None	No known interactions.
Abacavir	↑clearance by 23%	↓peak by 34% ↑time to peak	Data sparse, risk of opiate withdrawal low.
NNRTIs			
Nevirapine	↓AUC 46%, withdrawal reported	Unknown	In a case series of chronic methadone recipients initiating nevirapine, 50%-100% increases in the daily methadone doses were required to treat opiate withdrawal. Withdrawal symptoms generally occurred between 4 and 8 days after starting nevirapine.
Efavirenz	↓levels	Unknown	See nevirapine.
PROTEASE INHIBITORS			
Indinavir	None	None	Studies limited, but no reported interactions.
Ritonavir	↓levels 35%-50%	None	Studies limited. Observe closely for signs of methadone withdrawal.
Saquinavir	None	None	Studies limited, but no reported interactions.
Nelfinavir	↓levels 29%-47%	None reported	Clinical withdrawal was not reported in studies in which decreased methadone concentrations were reported.
Amprenavir	Unknown	Unknown	
Lopinavir/ritonavir	Unknown	Unknown	Methadone withdrawal possible from low-dose ritonavir.

IV. Protocol on the Management of Opportunistic Infections (OI)

1. Policy

Management of opportunistic infections (OIs) is considered an essential element of the comprehensive HIV/AIDS care agenda. Providers should have basic equipment for diagnostic procedures as well as proper medication for treatment. Their acquisition should be covered by national and international funding programs. Prevention, treatment and care should be provided at all levels of the health care system, in accordance to the capacity and facilities of each individual level of care. Patient referral and consultation of specialists in related sections of the health care system assures quality. To ensure that all HIV-infected individuals in need of treatment will receive optimal care, regional AIDS-centres as per order of the MOH, will coordinate and supervise cooperation among all institutions involved

2. Principles

- Management of OIs will receive equal funding opportunities as other components of comprehensive HIV/AIDS care.
- Partners, such as non-governmental organizations (NGOs), will be encouraged to support and cooperate with the public health system. They will be involved in the management of OIs, providing services in accordance with the national standards.
- ***All*** patients with OIs (including ID-users, sex workers, prisoners and other populations) will have access to treatment. The decision of whom to treat will be entirely based on medical considerations.No patient will be denied treatment because of political or social reasons.Special efforts will be undertaken to provide prophylactic treatment of OIs to those who could benefit from such treatment.
- Treatment for other diseases and comorbidities will not be withheld at any stage of the disease. This includes methadone substitution for IDUs.
- Regional AIDS centres will monitor cooperation among the institutios involved in order to ensure optimal standard of care.

3. Initial evaluation

- Any patient presenting with signs and symptoms will be syndromically managed (and referred for HIV testing when indicated).
- An HIV -infected patient with symptoms not responding or deteriorating to routine first line regimen (will be checked against the list of most common OIs in the country and managed accordingly. The patient with OIs different from the list of common OIs will be referred to the next higher level of care.
- HIV-related infections and illnesses include the following:

Table 1. HIV-related infections and illnesses

BACTERIAL INFECTIONS	FUNGAL INFECTIONS	VIRAL INFECTIONS	PARASITIC INFECTIONS	OTHER ILLNESSES
▪ **Tuberculosis** ▪ **Bacterial respiratory infections** ▪ **Bacterial enteric infections** ▪ **Atypical mycobacteriosis** ▪ **Bartonellosis**	▪ **Candidiasis** ▪ **Cryptococcosis** ▪ **Histoplasmosis** ▪ **Pneumocystis pneumonia** ▪ **Coccidioidomycosis**	**Herpes simplex virus disease** **Varicella zoster virus disease** **Cytomegalovirus disease** **Human herpes virus type 8 infection** **Human papilloma virus infection**	▪ **Toxoplasmosis** ▪ **Cryptosporidiosis** ▪ **Microsporidiosis** ▪ **Isosporiasis** ▪ **Leishmaniasis**	▪ **Kaposi's sarcoma** ▪ **Non-Hodgkins lymphoma** ▪ **Cervical cancer** ▪ **Encephalopathy** ▪ **Vacuolar myelopathy** ▪ **Progressive multi-focal leukoencephalopathy**

- The most common OIs in one of the CIS countries, Ukraine, include the following (regularly updated):
  - TB
  - Bacterial infections
  - PCP
  - Herpes infections (including Herpes Zoster, CMV, HSV-1/2)
  - Candidiasis
  - Cryptococcus meningitis
  - Toxoplasmosis
- Less frequent opportunistic infections and cancers: include the following (regularly updated):
  - MAC (Mycobacterium avium complex disease)
  - KS (Kaposi sarcoma)

Table 2. Initial evaluation of Person living with HIV/AIDS in need of management of OIs

ASSESSMENT	
History: General health status Current symptoms Co-morbidities and current medication Mental health, including drug use Past medical history (*incl. major illnesses (e.g. TB), hospitalizations and surgeries, the length of time since the diagnosis of HIV-infection,*	+ + + + +
Physical examination	+
Gynecologic exam	+
Laboratory assessment - Hemoglobin - White blood cell count and differential - Urinalysis - Liver function tests (ALT, AST, bilirubin) - Creatinine - HIV test - CD4 count	 + + + + + if not performed if not known
Sputum smear microscopy	Ar indication
Chest x-ray	At indication
Pregnancy test	At indication
Other tests	At indication

The assessment should result in a staging of the HIV infection and identification of co-morbidities and conditions.

Specific diagnostic proceedings will be discussed under the detailed OI subsections.

Prophylaxis and treatment, referral and follow-up:

Prophylaxis and treatment will be provided in accordance with the specific protocols for the different OIs and HIV-related illnesses, described below. Referral and follow-up will be undertaken as indicated in the specific protocols.

Table 3

PATHOGEN	INDICATION	FIRST CHOICE	ALTERNATIVES
Pneumocystis carinii	CD4+ count <200/µl or Oropharyngeal candidiasis	TMP-SMZ, 1 double strengh tablet po QD	TMP-SMZ, 1 single strengh tablet po. QD TMP-SMZ, 1 double strengh tablet po. TIW Dapsone, 50mg po BID or 100mg po QD
M. tuberculosis	PPD reaction ≥5mm or contact with case of active tuberculosis	Isoniazid, 300mg po plus pyridoxine 50mg po QD for 9 months	Rifampin, 600mg po QD for 4 months
Toxoplasma gondii	CD4+ count < 100/µl	TMP-SMZ, 1 double strengh tablet po QD	TMP-SMZ, 1 single strengh tablet po. QD Dapsone, 50mg po QD plus pyrimethamine, 50mg po QW plus leucovorin, 25mg po QW
M. avium complex	CD4+ count < 50/µl	Azithromycin, 1200mg po QW	Clarithromycin, 500mg po BID
Cryptococcus neoformans	CD4+ count < 50/µl	Fluconazole, 100-200mg po QD	

4. Opportunistic infections and other HIV-related illnesses

4.1. Tuberculosis

WHO estimated in 2001 that there were 484,000 new TB cases in Europe, representing 6% of the global TB burden. The Russian Federation had the 9th highest burden of TB in the world. Within European region, TB incidence varies enormously, from 5/100,000 in Sweden to 181/100,000 in Kazakhstan. High rates of TB are associated with socioeconomic crisis, health system weaknesses, HIV and multidrug-resistant TB epidemics, and poor TB control interventions among vulnerable populations. Recent analysis shows that 2.6% of all new TB cases that occurred in Europe in 2000 were attributable to HIV co-infection. In the Russian Federation, 1% of all new TB cases were estimated HIV-positive and 35% adult AIDS have died from TB. In Ukraine, estimated proportion of people co-infected with TB and HIV is 5%. TB is a significant cause of all HIV-related mortality.

TB should always be considered in immunosuppressed persons. HIV is the most potent known risk factor for progression to active TB in people with latent *Mycobacterium tuberculosis* infection. HIV also increases the rate of recurrent TB, either due to endogenous reactivation or exogenous re-infection. Increasing TB cases in PLWHA augments the risk of TB transmission to the general community, whether or not HIV-infected. The level of immunodeficiency at which PLWHA usually develop TB is associated with higher case fatality rates.

The National TB Programme should implement DOTS, the WHO internationally-recommended strategy to control TB, whether or not patients are co-infected with HIV.

Diagnosis

As HIV infection progresses, CD4 lymphocytes decline in number and function. The immune system is less able to prevent the growth and local spread of M. tuberculosis. Disseminated and extrapulmonary disease is more common. Sputum should always be examined for the presence of acid-fast bacilli (AFBs). Latent TB is diagnosed on the finding of a positive tuberculin skin test in the absence of clinical or radiological evidence of TB. Any patient with suspected TB should be examined by a TB specialist and referred to the TB clinic when needed.

4.1.1. Adult pulmonary TB

Even in HIV-infected patients, pulmonary TB is still the commonest form of TB. The presentation depends on the degree of immunosuppression. Table 1 show how the clinical picture, sputum smear result and chest X-ray appearance often differ in early and late HIV infection.

Table 4

FEATURES OF PULMONARY TB	STAGE OF HIV INFECTION	
	EARLY	LATE
Clinical picture	Often resembles post-primary TB	Often resembles primary TB
Sputum smear result	Often positive	Often negative
Chest X-ray appearance	Often cavities (may be normal)	Often infiltrates with no cavities (may be normal)

Reported case rates of smear-negative pulmonary TB have increased in association with the TB/HIV co-epidemic. There is a lack of a widely available "gold standard" diagnostic test for smear-negative pulmonary TB. It is often difficult to distinguish other HIV-related pulmonary diseases from pulmonary TB. The extent of over-diagnosis of smear-negative pulmonary TB is therefore uncertain. It is important to follow recommended diagnostic guidelines as closely as possible and to ensure good quality control of sputum smear microscopy in order to diagnose smear-negative pulmonary TB as accurately as possible.

4.1.2. Adult extrapulmonary TB

The commonest forms of adult extra-pulmonary TB are pleural effusion, lymphadenopathy, pericardial and meningeal disease, and haematogenous (disseminated)/miliary.

Please see "ART Recommendations for Individuals with Tuberculosis disease and HIV coinfection" in table 7, page 26.

4.1.3. Childhood TB

The most frequent presentation of childhood TB is extrapulmonary TB (most commonly intrathoracic). Pulmonary TB is usually smear-negative. As in adults, the natural history of TB in a child infected with HIV depends on the stage of HIV disease. Early in HIV infection, when immunity is good, the signs of TB are similar to those in a child without HIV infection. As HIV infection progresses and immunity declines, dissemination of TB becomes more common. Tuberculous meningitis, miliary TB, and widespread tuberculous lymphadenopathy occur. The current diagnostic approach to childhood TB is even more limited in HIV-infected patients. In the absence of improved diagnostic methods, the diagnosis of childhood TB still rests largely on careful clinical assessment and growth monitoring, chest X-ray, tuberculin test and a positive family history of TB.

Treatment

Treatment will be provided by the TB specialist according to national guidelines.

The most effective treatment of all persons with TB, whether or not co-infected with HIV, consists of standard TB treatment regimens recommended by WHO. HIV-infected TB patients respond well to treatment with standard TB treatment regimens. However, the case fatality rate is higher among TB patients who are HIV-infected.

The same criteria determine diagnostic categories for TB patients irrespective of HIV status. Thus, HIV-infected new TB patients receive Category I anti-TB treatment if they have smear-positive pulmonary TB, smear-negative pulmonary TB with extensive parenchymal involvement, or severe forms of extrapulmonary TB. TB treatment should always be rifampicin based. HIV infection is associated with an increased risk of adverse drug reactions to many antituberculosis drugs.

Isoniazid preventive therapy

Isoniazid preventive therapy (IPT) decreases the risk of progression of recent, and of reactivation of latent, *M tuberculosis* infection. The condition of active TB must be excluded before starting IPT. IPT is recommended in PLWHA with PPD reaction >= 5 mm or contact with a case of active TB. Isoniazid 5mg/Kg (300mg) is given daily for 9 months in associaition with pyridoxine 25mg daily. Alternative regimen with rifampicin is not recommended.

4.2. Respiratory infections

Introduction

Lower respiratory tract infections are the most common recurrent infections in PLWHA. They are usually life threatening and are caused by bacteria, viruses and fungi.

Early in the course of HIV infection patients may present with bacterial pneumonias which respond readily to antibiotics. Patients with HIV infection appear to be particularly prone to infections with encapsulated organisms such as S. pneumonae and H. influenzae. Later, and with the onset of immune suppression, patients may develop opportunistic pulmonary infections. The most important of which is pulmonary TB. As cell mediated immunity deteriorates patients may develop life threatening opportunistic infections such as PCP and severe fungal and viral pneumonias. Table 5 summarises the respiratory illnesses associated with HIV infection.

Table 5

RESPIRATORY ILLNESSES IN PERSONS WITH HIV INFECTION AND AIDS	
Bacterial infections: Pneumococcal pneumonia H. influenzae pneumoniae Klebsiella pneumonia Staphylococcal pneumonia M. tuberculosis pneumoniae MAC pneumonia *Possible complications:* ▪ Lung abscess ▪ Empyema ▪ Pleural effusion ▪ Pericardial effusion ▪ Pneumothorax	**Viral infections:** Cytomegalovirus Herpes simplex virus *Possible complications:* Lymphocytic interstitial pneumonitis **Fungal infections:** Pneumocystis pneumonia Cryptococcosis Histoplasmosis Aspergillosis **Other conditions:** Kaposi's sarcoma Lymphoma

4.2.1. Bacterial respiratory infections

Bacterial lower respiratory tract infections are common in the general population. They are more frequent and more severe in immunosuppressed persons with HIV infection. Pneumonia caused by *Streptococcus pneumonia* is the most common lower respiratory tract infection. Other causes of bacterial pneumonia in persons with HIV infection are shown in Table 5. Patients with bacterial pneumonia present with cough and fever and they often have chest pain, difficulty in breathing and tachypnoea. Chest x-rays may show classical lobar pneumonia, bronchopneumonia or atypical or no infiltrates.

Diagnosis

The diagnosis of pneumonia is usually made on clinical grounds and chest x-ray. Radiologic changes on the chest x-ray may reveal lobar consolidation, patchy consolidation, diffuse lung infiltrates or atypical changes including cavitatory disease.

Treatment

If the patient is not severely ill, treatment can be provided at home, according to the tables below:

Table 6

FIRST LINE TREATMENT				
ANTIBIOTIC	**DOSE**	**FREQUENCY**	**ROUTE**	**DURATION**
Amoxycillin (Use Augmentin if chance of Penicillin/Ampicillin resistance)	500–1000 mg	every 8 hours	PO	7 days resolves
OR				
Erythromycin	500mg	every 6 hours	PO	7 days
OR				
Clarithromycin	500mg	every 12 hours	PO	7 days
OR				
Doxicyclin	100mg	every 12 hours	PO	7 days

If patients do not respond to first line treatment over a period of 72 hours, the patient will be referred to the hospital and second line treatment will be prescribed as indicated below. Patients may also require oxygen.

Severely ill patients should be referred for admission immediately.

Table 7

SECOND LINE TREATMENT				
ANTIBIOTIC	**DOSE**	**FREQUENCY**	**ROUTE**	**DURATION**
Ceftriaxone plus Erithromycin	2g 500mg	Once dayly Every 6 hours	IV	7 days
OR				
Ampicilin plus sulbactam plus Erithromycin	1500mg 500mg	Every eight hours Every 6 hours	IV	7 days
OR				
Chloramphenicol (only if other drugs are not avaiable)	12.5 mg (base) per kg of body weight	Every six hours	IV	7 days

If patients do not respond to this treatment, consider *Pneumocystis* pneumonia or TB as possible diagnosis.

4.2.2. Pneumocystis pneumonia

Pneumocystis pneumonia (PCP) is a common HIV-associated opportunistic infection. It is caused by the fungus *Pneumocystis jiroveci* (previously known as *Pneumocystis carinii).* Patients usually present with cough, shortness of breath and fever. Occasionally patients with PCP have no chest signs. Often patients with PCP have features of respiratory failure such as shortness of breath and cyanosis. Symptoms may be very severe and an attack of PCP may lead to death if not treated early and effectively.

Diagnosis

The diagnosis is often made on clinical grounds when a febrile patient with HIV infection presents with respiratory distress with or without cyanosis. The patient may have a nonproductive cough but the main feature is shortness of breath with minimal or absent chest signs on physical examination. The classic chest x-ray appearance of a ground glass opacification in the lower zones of both lung fields may not always be present. There may be evidence of patchy infiltrates in both lung fields mimicking bacterial Pneumonia or Tuberculosis. A considerable proportion of patients with confirmed PcP have no changes at all on chest X-ray. The diagnosis is confirmed upon the finding of cysts of *Pneumocystis* in sputum or in bronchial lavage aspirate. If the diagnosis can not be established due to the lack of bronchoskopy deteriorating pulmonary function tests can be used as an indicator of PcP and treatment should be started immidiately.

Treatment

Patients should be admitted to hospital for management. Supportive therapy including intravenous fluids and oxygen may be necessary. Details of treatment are given in the tables below:

Table 8

PCP FIRST LINE TREATMENT				
ANTIMICROBIAL AGENT	**DOSE**	**FREQUENCY**	**ROUTE**	**DURATION**
Cotrimoxazole (Sulphamethoxazole/trimethoprim)	1600mg/320mg	Every 6 hours	PO/IV	21 days

PCP SECOND LINE TREATMENT				
ANTIMICROBIAL AGENT	**DOSE**	**FREQUENCY**	**ROUTE**	**DURATION**
Clindamycin plus Primaquine	600mg 15 – 30 mg	Every 8 hours Once dayly	PO/IV PO	21 days
OR				
Pentamidine	4 mg/kg IV daily. Dose reduction to 2 mg/kg after 14 days of treatment	Once daily	IV	21 days

Severely ill patients will require prednisolone 80mg PO daily for 2 weeks.

Secondary chemoprophylaxis

After successfully treating the acute episode of pneumocystis pneumonia it is necessary to continue secondary prophylaxis with trimethoprim 160mg/sulphamethoxazole 800mg PO OD on a long-term basis. Prophylaxis may be discontined when the patient's CD4 count remains stable > 200/µl for at least three months.

4.2.3. Other causes of pneumonia in immunosuppressed persons

Other causes of pneumonia include fungal and viral infections. These are difficult to diagnose without sophisticated laboratory facilities and are difficult to treat. Viral pneumonias may be caused by herpes simplex virus, varicella zoster virus, and cytomegalovirus. In addition to PCP, other fungal causes of pneumonia include *Histoplasma capsulatum*, *Cryptococcus neoformans* and *Aspergillus*. However, it should be remembered that tuberculosis is probably the most common infection amongst immunosuppressed persons with HIV infection in the CIS countries.

Diagnosis

TB and pneumonia caused by viruses, fungi or protozoa should be suspected in persons with pneumonia which fails to respond to standard treatment. However making a specific diagnosis of fungal and other infections requires sophisticated laboratory tests.

Treatment

Treatment will depend on the cause.

4.2.4. Atypical mycobacteriosis

Mycobacterium avium complex disease (MAC) is less common than some other OIs. It presents with fever, weight loss, night sweats, diarrhoea, and wasting. Organisms may be found in the blood and excreta of infected persons.

Diagnosis

Blood cultures on special media are the cornerstone of the diagnosis of MAC infection. In most symptomatic patients, the intensity of mycobacteremia is such that most or all blood cultures are positive. Because the liver and bone marrow are often involved in disseminated MAC infection, the bacteria may be visible in acid-fast-stained biopsy samples from these sites. Presumptive diagnosis by examination of a biopsied liver specimen saves time..

Treatment

Table 9. Atypical mycobacteriosis

FIRST LINE TREATMENT				
ANTIBIOTIC	**DOSE**	**FREQUENCY**	**ROUTE**	**DURATION**
Clarithromycin	500mg-1000mg	BID	PO	lifelong
PLUS				
Ethambutol	15mg/kg	OD	PO	lifelong
PLUS				
Rifabutin	300-600mg/	OD	PO	lifelong
OTHER DRUGS ACTIVE AGAINST MACA				
ANTIBIOTIC	**DOSE**	**FREQUENCY**	**ROUTE**	**DURATION**
Azithromycin	600mg	OD	PO	
Ciprofloxacin				
Amikacin				
Rifampin				

4.3. Gastrointestinal infections (GI)

Gastrointestinal infections (GI) problems in persons with HIV infection may be the result of direct infection of the GI tract by HIV, or the result of bacterial, fungal, viral, protozoal or parasitic infection. Some of the problems may arise from atrophy of the intestinal villi which commonly leads to malabsorption. The most common GI problem encountered is diarrhoea which could be acute, acute-on-chronic or chronic. In persons with AIDS, diarrhoea is persistent or chronic. Chronic diarrhoea is defined as passing 3 or more liquid stools daily for 14 days or more. The passing of bloody or blood stained stools occurs in persons with shigellosis or amoebic dysentery.

Other common GI problems in persons with HIV infection include, poor appetite, nausea and vomiting, and progressive loss of weight.

Diarrhoea is an important cause of death among persons with HIV infection. Acute diarrhoea unless properly treated leads to dehydration, while chronic or persistent diarrhoea leads to malabsorption, malnutrition and secondary systemic infections. These contribute to the mortality associated with diarrhoea in these patients.

Table 10 summarises the clinical features and treatment of some of the commoner gastrointestinal infections seen in immunosuppressed persons with HIV infection.

Table 10. Gastrointestinal infections commonly encountered in persons with HIV infection

PATHOGEN	CLINICAL FEATURES	TREATMENT
Non-typhoid salmonelloses	Fever, abdominal pain, diarrhoea with or without blood, weight loss, anorexia, hepatosplenomegaly. Diagnosis on blood or stool culture	Ciprofloxacin 500mg PO BID for > 2 weeks Then maintenance for several months
Shigelloses	Fever, abdominal pain, bloody diarrhoea. Diagnosis on blood or stool culture	Ciprofloxacin 500mg PO BID for 5 days, OR Nalidixic acid 500mg PO QID for 5 days, OR Sulphamethoxazole/trimethoprim 800mg/160mg PO BID for 5 days
Cryptosporidiosis	Watery diarrhoea, loss of appetite, afebrile. Diagnosis on stool microscopy.	Paromomycin 1g PO BID PLUS Azithromycin 600mg PO OD for 4 weeks, then paromycin alone for 8 weeks
Microsporidiosis	Watery diarrhoea, loss of appetite, afebrile. Diagnosis on stool microscopy.	Albendazole 400mg PO BID for 4 weeks Mebendazole 500 mg PO TID (The efficacy of Albendazole is established only for infections involving Septata intestinalis – 10-20% of cases)

4.3.1. Chronic diarrhoea in adults

Adults with chronic diarrhoea complain of passing loose stools frequently over 14 days. During the course of the illness the patient may have episodes of acute diarrhoea as well. The stool does not usually contain blood except if there is concomitant dysentery. The patient usually also has a poor appetite and weight loss. The patient may be dehydrated, anaemic and wasted. Adults with chronic diarrhoea often have skin and hair changes of malnutrition and may have hypopigmentation of the lips, while the nails may be darkly pigmented. They may also have oral thrush, hairy leukoplakia and lymph node enlargement.

An assessment of the state of hydration is essential in the management of persons with chronic diarrhoea. Features of dehydration are summarised in Table 11.

Table 11. Clinical assessment of dehydration in adults

CLINICAL FEATURES	DEHYDRATION		
	MILD	MODERATE	SEVERE
General condition	Weak	Weak	Restless, irritable, cold, sweaty, peripheral cyanosis
Pulse	Normal	Slight tachycardia	Rapid, feeble
Respiration	Normal	Normal	Deep and rapid
Skin elasticity	Normal	Pinch retracts slowly	Pinch retracts very slowly
Eyes	Normal	Sunken	Deeply sunken
Mucous membranes	Slightly dry	Dry	Very dry
Urine flow	Normal amount; urine dark	Reduced amount; dark amber in colour	No urine; bladder is empty

Details on the management of chronic diarrhoea are provided in table 12.

Table 12. Management diarrhoea

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
General	• Increase fluid intake, to prevent dehydration • Use ORS if large volume of diarrhea • Suggest a supportive diet	• Encourage plenty of fluids to replace lost water • Increase frequency of small amounts of food intake Special care for rectal area: • After the person has passed stool, clean with toilet paper or soft tissue paper • Wash the anal area 3 times a day with soap and water • If the sick person feels pain when passing the stool, apply Vaseline around the anal area • Seek help of a trained health worker for any of the following: o Vomiting with fever o Blood in stools o Diarrhea for more than 5 days o Increasing weakness patient o Broken skin around the rectal area
Give constipating drugs, unless blood in stool or fever or child less than 5 or elderly	**Loperamide** 4 mg stat than 2 mg after each stool OR codeine or morphine (if approved by MOH)	
If local tenderness:	Suggest local anesthetic ointment or petroleum jelly	
If incontinent:	Use petroleum jelly to protect perianal skin	

4.4. Candidiasis

Thrush is caused by the fungus *Candida albicans*. The organism colonizes most body cavities and generally produces no symptoms at all. The gastrointestinal tract of both men and women, and the genital tract in women are the sites most commonly colonized by the fungus. Up to one third of all normal women carry *C. albicans* in the vagina.

The common manifestations of thrush (candidiasis) are vulvovaginal and oral infection. Women with vaginal candidiasis may develop a vaginal discharge and vulvovaginal pruritus. Men with genital thrush will develop balanitis or balanoposthitis and will complain of a subpreputial discharge and itchiness of the penis and foreskin. Oral candidiasis leads to inflammation of the mucosal surface together with the appearance of adherent white plaques. Elsewhere in the body *C. albicans* can infect the skin and cause pruritic dermatitis. Depending on the level of immune suppression oral infection may extend to involve the oesophagus. Bronchial and disseminated infection are rare. In persons with immune suppression for whatever reason, thrush occurs commonly.

Clinical aspects

Oral thrush includes infection of the buccal mucosa, tongue, oropharynx, gums and the hard and soft palate. Patients may have no symptoms at all or may complain of a burning sensation in the mouth when eating food. Some patients may complain of white patches in the mouth. If the thrush has extended into the oesophagus then patients may complain of pain on swallowing food, retrosternal pain and excessive salivation. Candidiasis occurs more commonly under certain circumstances as shown in Box 1.

Box 1: Conditions in which candidiasis occurs more frequently

- **Healthy pregnant women and healthy women on oral contraceptives.**
- **Healthy neonates especially pre-terms.**
- **Persons receiving prolonged courses of broad-spectrum antibiotics.**
- **Persons receiving steroids systemically.**
- **Persons with diabetes mellitus.**
- **Persons who have congenital or acquired immune deficiencies.**
- **Persons suffering from a chronic debilitating condition.**
- **Severely malnourished persons.**
- **Persons with cancer and those receiving chemotherapy or radiotherapy.**

Examination of the oral cavity may reveal redness and inflammation of the mucosa and patches of white plaques. Inflammation may be seen on the palate, the throat, the gums, the tongue and the inside of the cheeks. When the tongue is affected it may be smooth and red and the papillae normally found on the tongue may be absent. This should not be confused with white flakes of loose particles of food commonly found in people with poor oral hygiene. The latter is easily removed with a spatula while oral candidiasis plaques are adherent

and not easy to scrape.

Oropharyngeal candidiasis (OPC) is believed to occur at least once in the lifetime of all HIV-infected patients. This does not lead to death but can cause pain and painful swallowing and interferes with alimentation. The symptoms of oesophageal candidiasis are difficulty in swallowing and pain in the chest that increases with swallowing. Disseminated candidiasis causes fever and symptoms in the organs affected by the disease (for example, blindness when it affects the eyes).

Principles of diagnostic of candidiasis:

1. Direct vizualization
2. Lack of clinical signs
3. Resistance to or worsening with antibacterial therapy

Endoscopy

Diagnosis

The diagnosis of oropharyngeal candidiasis is made on clinical grounds. The diagnosis may be confirmed by direct visualization and microscopic examination of material obtained from lesions. In other sites the diagnosis is made by histologic examination of tissue biopsies.

Treatment

Localized disease is treated first with relatively inexpensive topical drugs such as nystatin, miconazole, or clotrimazole. In patients with disseminated candidiasis and in those in whom topical therapy has failed, systemic antifungal agents such as ketoconazole, fluconazole, itraconazole, or amphotericin B may be given.

Table 13. Oral candidiasis

ANTIFUNGAL AGENT	DOSE	FREQUENCY	ROUTE	DURATION
FIRST LINE TREATMENT				
Myconazole	Buccal tablets	Once a day	Gum patch	7 days
OR				
Fluconazole	100mg	BID	PO	7 days
SECOND LINE TREATMENT				
Ketokonazole	200-400 mg	OD	PO	7 days
OR				
Amphotericine B	0,3-0,5 mg/kg/day up to 50mg	OD Infuse over a period of 2 to six hours	IV	7 days

Table 14. Vaginal candidiasis

ANTIFUNGAL AGENT	DOSE	FREQUENCY	ROUTE	DURATION
FIRST LINE				
Fluconazole	100 mg	Single dose	PO	Once
Clotrimazole	500 mg	Single dose	Vaginal	Once
SECOND LINE				
Ketoconazole	200 mg	BID	PO	3 days
Ketoconazole	200 mg	OD	PO	7 days
MAINTAINING THERAPY OF RECURRENT CANDIDIASIS				
Nystatin	2000-4000 mg	BID	PO	10 days
OR				
Fluconazole	50-200 mg	Once a day	PO	Every day
SECOND LINE				
Ketokonazole	200mg	Once a day	PO	
Amphoterecine B	0,0001 gr/kg/day	BID	IV	
Intraconazole	100 mg	Once a day	PO	

Table 15. Oesophageal candidiasis & dissiminated candidiasis

OESOPHAGEAL/SYSTEMIC CANDIDIASIS				
ANTIFUNGAL AGENT	**DOSE**	**FREQUENCY**	**ROUTE**	**DURATION**
FIRST LINE TREATMENT				
Ketokonazole	200-400 mg	BID	PO	21 days
OR				
Fluconazole (more effective than ketoconazole)	200-400 mg	Once a day	PO/IV	14-21 days followed by:
Fluconazole	50 mg	Once a day	PO	
SECOND LINE TREATMENT				
Amphotericine B	0,3-0,5 mg/kg	OD	IV	10-14 days
Then maintaing therapy with Ketokonazole, Fluconazole or Intraconazole 14-21 days				
OR				
Itraconazole	200-400mg	OD	PO	2-3 weeks

Long term maintenance treatment with fluconazole 100mg OD PO, or itraconazole 100mg OD PO, or ketoconazole 200mg OD PO, may be necessary for persons who have been treated for candidial oesophagitis. If the patient fails to respond to this treatment the diagnosis of CMV or herpes simplex virus oesophagitis should be considered and the patient should be referred for oesophagoscopy.

4.5. Cryptococcal meningitis

Systemic mycoses such as cryptococcosis probably cause up to 10% of all HIV-associated deaths worldwide. Cryptococcosis most often appears as meningitis, and occasionally as pulmonary or disseminated disease. Cryptococcal meningitis is a common systemic fungal infection in HIV-infected persons. Patients usually present with headache, fever, neck stiffness, cranial nerve palsies and may be comatose. However often signs of meningeal inflammation including fever and neck stiffness may not occur. Without treatment, life expectancy is probably less than a month.

Diagnosis

Cryptococcosis is relatively easy to diagnose. The centrifuged deposit of the cerebrospinal fluid is examined microscopically after a drop of India ink is added. The yeasts are seen as organisms surrounded by a thick capsule. The CSF may be cultured for cryptococci. The cryptococcal antigen test is useful in assessing patients for cryptococcosis and may be performed on serum and on cerebrospinal fluid.

Treatment

The treatment of cryptococcal meningitis is summarised in the tables below.

Table 16. Cryptococcal meningitis

ANTIFUNGAL AGENT	DOSE	FREQUENCY	ROUTE	DURATION
FIRST LINE REGIMEN				
Amphotericin B Plus 5-flucytisine	0.7 –1.0 mg/kg 100 mg./kg/day	OD	IV/PO	14 days
THEN				
Fluconazole	400 mg	OD	PO	at least10 weeks
THEN				
Fluconazole	200-400 mg	OD	PO	lifelong
SECOND LINE REGIMEN				
Amphotericin B Plus 5-flucytsine	0,7-1,0mg/kg 100mg/kg	OD	IV/PO	6 to 10 weeks
OR				
Amphotericin B	0,7-1,0mg/kg	OD	IV	6 to 10 weeks
OR				
Fluconazole	400-800mg	OD	PO	10-12 weeks
THEN				
Fluconazole	200-400 mg	OD	PO	lifelong

Secondary chemoprophylaxis or maintenance therapy: Fluconazole, 200-400mg PO

Lifelong secondary chemoprophylaxis is necessary and this may be achieved with fluconazole 200mg orally daily for life. Alternate long term secondary prophylaxis may be achieved with itraconazole 200mg orally once daily for life.

4.6. Other oral lesions

In persons with HIV infection a large number of oral lesions may be found. Some of these are described in Table 17.

Table 17. Oral lesions found more commonly in PLWHA

CONDITION	DESCRIPTION	MANAGEMENT
Gingivitis	Gingivitis is inflammation of the gums. The gums are usually swollen and red and tend to bleed easily.	Metronidazole 400 mg orally twice daily for 7 days, or Erythromycin 500 mg orally 4 times a day for 7 days
Pyorrhoea	Pyorrhea is an accumulation of pus in the gingival margin around the teeth.	The treatment of pyorrhea is to advise on oral hygiene, i.e., to gargle the mouth with warm salty water after every meal and to brush the teeth twice daily.
Periodontitis	This is a painful condition in which there is rapid loss of bone and soft tissue supporting the teeth. Teeth become loose and fall off and there is bleeding from the gums. Ulceration may also occur	Local debridement, chlorhexidine mouth washes. It is also necessary to treat with amoxycillin 500mg PO TID or metronidazole 200mg PO TID for 5 days
Aphthous ulcers	Aphthous ulcers are painful punched out ulcers on the mucosal surface. They are usually covered in a purulent exudate and tend to bleed when touched.	Aphthous ulcers may be treated with oral hygiene and with topical steroids.
Stomatitis	Stomatitis means inflammation of the mucosa of the oral cavity. It is often associated with poor oral hygiene and bacterial invasion with anaerobic bacteria.	The treatment of stomatitis to advise on oral hygiene, i.e., salt water gargles and brushing teeth.
Cheilitis	Inflammation and redness of the lips leading eventually to pallor of the lips is commonly seen in persons with more advanced immunosuppression	No specific treatment is available. Patients should be given vitamins A, B and C and should be advised on oral hygiene.
Secondary syphilis	Lesions of secondary syphilis that may be found on the buccal mucosa include moist papules and snail track ulcers. Also found are condylomata lata at the angles of the mouth and around the nostrils. During the course of secondary syphilis all serological tests for syphilis are positive.	Patients should be treated with benzathine penicillin 2.4 million units by intramuscular injection, alternatively doxycycline 100mg is given orally twice daily for 14 days or erythromycin 500mg orally 4 times a day for 14 days.

4.7. Kaposi's sarcoma

Kaposi's sarcoma is caused by the human herpes virus type 8 (HHV8), also known as the Kaposi's sarcoma herpes virus (KSHV). In HIV associated immunosuppression Kaposi's sarcoma is more aggressive, disseminated and more rapidly progressive when compared with endemic disease found in non-HIV-infected persons. Lesions may be found anywhere on the body and on any mucosal surface. Skin lesions are hyperpigmented, blue or purplish papules or nodules and are associated with lymphoedema. Lesions are commonly found on the palate, the gastrointestinal

tract, lungs or lymph nodes.

Oral lesions of Kaposi's sarcoma may be found on the hard palate and occasionally on the tongue, throat, tonsils and gums. The lesions are papules that are purple in colour and are usually painless. Sometimes lesions may be large and pedunculated.

Pulmonary lesions are infiltrative and often lead to respiratory failure. In persons with pulmonary infiltrative Kaposi's sarcoma the outcome is poor and there is a high mortality.

Diagnosis

The diagnosis of Kaposi's sarcoma is made on clinical suspicion and is confirmed by histological examination of tissue obtained by biopsy. The condition may be confused with bacillary angiomatosis (Bartonellosis), an infective condition seen in persons with HIV/AIDS.

Treatment

Treatment of Kaposi's sarcoma should be performed by an oncologist . Kaposi's sarcoma is a cancer and treatment is with radiotherapy if lesions are localized and with combination cytotoxic chemotherapy for generalised disease. Cytotoxic drug combinations that have been used with varying degrees of success include Liposomal doxorubicin, bleomycin, vincristine, daunorubicin, vinblastine and etoposide. Unfortunately remission is difficult to achieve and relapses occur commonly. Localised lesions may be surgically excised or treated with liquid nitrogen, laser therapy or radiation. Intralesional injection with bleomycin has also been shown to be effective.

Any patient suspected of KS should examined by an oncologist and be referred to the oncology clinic when needed.

4.8. Cervical cancer

Cervical cancer is a common cancer of women throughout the world accounting for about 30% of all cancers and 80% of all gynaecologic cancers. The mean age of cervical cancer diagnosis is about 38 years. It is a common cause of death among women. There has been an increase in the incidence of cervical cancer in the past 15 years. The cancer is most prevalent in women who have multiple partners or in those monogamous women whose partners have multiple partners. Human papilloma virus (HPV) infection is the leading aetiologic agent in the development of premalignant and malignant lower genital tract disease including cervical cancer. The incidence of cervical dysplasia is increased in HIV-infected women.

HIV positive women

It is recommended that a gynaecologic evaluation with pelvic examination and Pap smear at the time of diagnosis in HIV-infected women be performed. The examination and Pap smear should be repeated at six months and then annually.

Any patient suspected of cervical cancer should examined by a gynaecologist/oncologist and be referred to the gynaecologist/oncologist clinic when needed.

4.9. Other cancers

Lymphoma, including non-Hodgkins lymphoma, intracranial lymphoma and Burkitt-type lymphoma, and squamous cell carcinoma are more commonly found in immunosuppressed persons with HIV infection.

4.9.1. Non-Hodgkin's Lymphoma

Non-Hodgkins lymphoma occurs fairly commonly in persons with immunosuppression from HIV. It is thought that Ebstein Barr Virus (EBV) plays a role in the pathogenesis of this disease. EBV has been found in biopsy specimens of lymph nodes obtained from persons with non-Hodgkin lymphoma. For non-Hodgkin lymphomas the EPOCH regimen that includes etoposide, prednisolone, vincristine, cyclophosphamide and daunorubicin together with ART has been shown to be effective.

4.9.2. Burkitt-type lymphoma in HIV infected persons

Burkitt-type lymphomas are associated with HIV infection and may occur before advanced immunosuppression sets in. This tumour is associated with EBV. The diagnosis of Burkitt-type lymphoma is made on careful examination of lymph node and tumour biopsies. Burkitt-type lymphoma is managed as for other lymphomas.

Diagnosis

The diagnosis is made on histological examination of biopsied material.

Treatment

For non-Hodgkins lymphoma the EPOCH regimen that includes etoposide, prednisolone, vincristine, cyclophosphamide and daunorubicin together with ART has been shown to be effective. For intracranial lymphoma

cranial radiation together with cytotoxic chemotherapy and steroids are advised.

Any patient suspected of cancer should examined by an oncologist and be referred to the oncologist clinic when needed.

4.10. Neurologic infections

Invasion of the nervous system by HIV leads to encephalopathy, myelopathy and peripheral neuropathy. Numerous neurologic syndromes have been ascribed to HIV including, cerebral atrophy and degeneration, AIDS dementia complex, cerebellar atrophy, vacuolar myelopathy, facial nerve paralysis, Guillain Barre syndrome and painful sensory and motor peripheral neuropathy. A number of opportunistic infections including bacterial, viral and fungal infections, also affect the central nervous system.

For Cryptococcal Menigitis, please referre to the section on fungal infections.

4.10.1. Toxoplasmosis

This disease, though fairly frequently encountered in PLWHA in industrialized nations, is diagnosed infrequently in developing countries. This is probably the result of the lack of diagnostic facilities in developing countries. The infection leads to the development of multiple cystic lesions in the brain. In HIV-infected persons toxoplasmosis mainly appears as encephalitis or as disseminated disease. Patients with cerebral toxoplasmosis usually present with headache and focal neurologic signs such as monoparesis, hemiparesis and focal fits. Features of raised intracranial pressure may also be present.

Diagnosis

Toxoplasmosis may be suspected by the clinical findings Patients may present with altered mental status, fever, seizures, headaches, and focal neurologic findings, including motor deficits, cranial nerve palsies, movement disorders, dysmetria, visual-field loss, and aphasia. Patients who present with evidence of diffuse cortical dysfunction develop evidence of focal neurologic disease as the infection progresses.

CT or MRI scans of the brain may reveal multiple ring enhancing lesions. Serologic tests for toxoplasma antibody (IgG) may help in establishing the diagnosis in the absence of neuroimaging techinques. Most patients with cerebral toxoplasmosis have serologic evidence of prior infection with Toxoplasma gondii. If toxoplasmosis is suspected, patients should be given a trial of therapy, and only if they do not respond to this therapy within a few daysa brain biopsy should be considered. The diagnosis can be confirmed by histologic examination of tissue obtained by brain biopsy.

Treatment

Treatment is summarised in the tables below:

Table 18. Toxoplasmosis

DRUG	DOSE	FREQUENCY	ROUTE	DURATION
Pyrimethamine	200mg	Single (loading dose)	PO	Single dose
THEN				
Pyrimethamine	25-50mg	TID	PO	6-8 weeks
PLUS				
Folinic acid	15mg	OD	PO	6-8 weeks
PLUS				
Sulphadiazine	1g	Every six hours	PO	6-8 weeks

Instead of sulphadiazine in this regimen, the following may be used:

- Clindamycin 600mg every six hours IV/PO for 6 weeks then 300-450mg QID PO for life, OR
- Azithromycin 1200mg OD PO for 6 weeks then 600mg OD PO for life, OR
- Clarithromycin 1g BID PO for 6 weeks then 500mg BID PO for life, OR
- Atovaquone 750mg QID PO for 6 weeks then 750mg BID PO for life

4.10.2. Herpes simplex virus

Herpes simplex virus (HSV) infection is commonly encountered in clinical practice. It usually presents with vesicles and painful superficial sores around the mouth, nose, lips and genitals. Following an initial attack of herpes simplex infection recurrences occur frequently. In immunosuppressed persons the infection may be extensive and persistent and may become disseminated. Dissemination may lead to infection of the lungs, the oesophagus, and the brain. Herpes simplex virus may also cause meningoencephalitis and meningitis.

Diagnosis

The diagnosis of herpes simplex virus infection is usually made on the typical clinical presentation. It is often difficult to make a diagnosis of disseminated herpes and special laboratory tests, such as viral culture, radioimmunoblot assay and fluorescent and monoclonal antibody tests, may be necessary. Herpes simplex encephalitis leads to the development of multiple lesions in different parts of the brain and typical changes may be seen on CT scan studies of the brain.

Treatment

Treatment is summarised below:

Table 19. Herpes simplex virus mild infection

ANTIVIRAL AGENT	DOSE	FREQUENCY	ROUTE	DURATION
FIRST LINE TREATMENT				
Aciclovir	400mg	TID	PO	7-10 days
OR				
Famciclovir	250mg	TID	PO	7-10 days
OR				
Valaciclovir	1g	BID	PO	7-10 days

Table 20. Herpes simplex virus recurrences

ANTIVIRAL AGENT	DOSE	FREQUENCY	ROUTE	DURATION
FIRST LINE TREATMENT				
Aciclovir	800mg	5 times per day	PO	7-10 days
OR				
Famciclovir	500mg	BID	PO	7-10 days
OR				
Valaciclovir	1g	BID	PO	7-10 days

Table 21. Herpes simplex virus severe infection

ANTIVIRAL AGENT	DOSE	FREQUENCY	ROUTE	DURATION
FIRST LINE TREATMENT				
Aciclovir	10mg/kg	every 8 hours	IV	7-10 days
OR				
Valaciclovir	1g	BID	PO	7-10 days

Table 22. Herpes virus severe and visceral infection

ANTIVIRAL AGENT	DOSE	FREQUENCY	ROUTE	DURATION
FIRST LINE TREATMENT				
Aciclovir	10mg/kg	every 8 hours	IV	14-21 days
SECOND LINE TREATMENT				
Foscarnet (suspected resistance to aciclovir)	40 mg/kg	every 8 to 12 hours	IV	14 days

4.10.3. Herpes zoster

Herpes virus varicella zoster often causes disseminated infection after initial exposure. In children initial infection results in the development of chicken pox, though most persons that become infected develop no symptoms and signs of infection. The virus lays dormant in the paraspinal ganglia for years. However, with immune suppression from whatever cause, the virus replicates and produces lesions along the length of a cutaneous nerve in a dermatomal distribution. Dissemination can also occur at this time with involvement of skin, nervous system, lungs and mucous membranes. In immune suppressed persons zoster is often multidermatomal in distribution and is persistent and extensive. It is associated with severe pain and debility.

Diagnosis

The diagnosis is usually made on clinical grounds.

Treatment

Treatment is summarised in the tables below:

Table 23. Dermatomal zoster

ANTIVIRAL AGENT	DOSE	FREQUENCY	ROUTE	DURATION
FIRST LINE TREATMENT				
Aciclovir	800mg	5 times a day	PO	7-10 days or until lesions crust
OR				
Famciclovir	500mg	TID	PO	7-10 days

Table 24. Disseminated, visceral, ophthalmic zoster

ANTIVIRAL AGENT	DOSE	FREQUENCY	ROUTE	DURATION
FIRST LINE TREATMENT				
Aciclovir	10mg/kg	every 8 hours	IV	7-10 days
OR				
Famciclovir	500mg	TID	PO	7-10 days
SECOND LINE TREATMENT				
Foscarnet	60mg/kg or 40 mg/kg	Q12h Q8h	IV	7-10 days

Post-herpetic neuralgia is a common and serious debilitating problem. It causes severe pain in a dermatomal distribution usually at the site of the lesions. Pain control is often necessary and be achieved with Non-Steroid Anti-Inflammatory Drugs (NSAID). If pain control is not achieved, amitryptiline, cabamazepine or phenytoin may be tried.

4.10.4. Cytomegalovirus infection (CMV)

Cytomegalovirus may affect multiple systems and organs in the body in immunosuppressed individuals. Symptoms include fever and diarrhoea from CMV colitis, dyspnoea from CMV pneumonitis, and blindness caused by CMV retinitis. CMV infection can lead to the appearance of painful ulcers in the mouth resulting in difficulty in eating.

Diagnosis

The making of a diagnosis requires costly tests, such as, tissue biopsies and DNA hybridization studies and sophisticated equipment.

Treatment

CMV GI disease, neurologic disease and retinitis:

Table 25. CMV GI disease, neurologic disease and retinitis

ANTIVIRAL AGENT	DOSE	FREQUENCY	ROUTE	DURATION
Ganciclovir	5mg/kg	BID	IV	2-3 weeks

Long term treatment with ganciclovir 5mg/kg given IV daily may be necessary.

Table 26. CMV GI disease and neurologic disease

ANTIVIRAL AGENT	DOSE	FREQUENCY	ROUTE	DURATION
SECOND LINE TREATMENT				
Foscarnet	90mg/kg	BID	IV	3 weeks

Long term treatment with foscarnet 90mg/kg given IV daily may be necessary.

4.10.4.1. CMV retinitis:

Table 27. CMV retinitis

ANTIVIRAL AGENT	DOSE	FREQUENCY	ROUTE	DURATION
SECOND LINE TREATMENT				
Ganciclovir intraocular implant				
PLUS				
Valganciclovir	900mg	BID	PO	21 days

Long term treatment with valganciclovir 900mg OD PO may be given after successful treatment.

4.10.5. Epstein Barr Virus-related conditions

Infection with Epstein Barr Virus, a herpes virus, occurs commonly in persons with HIV infection as well as in persons without HIV infection. Patients with HIV have increased amounts of EBV in their oropharyngeal secretions and have higher EBV antibody titres than HIV-seronegative persons. EBV is thought to cause a number of conditions including,

- Oral hairy leukoplakia
- Lymphocytic interstitial pneumonitis (LIP)
- Non-Hodgkins lymphoma (see cancers)
- Burkitt-type lymphoma (see cancers)
- Nasopharyngeal carcinoma

Oral Hairy Leukoplakia

Oral hairy leukoplakia occurs in HIV-infected patients as well as in some immunosuppressed transplant recipients. It presents as raised, white, corrugated lesions of the oral mucosa, especially on the lateral aspect of the tongue. It is a non-malignant lesion of epithelial cells.

It is commonly mistaken for oral candidiasis with which it is commonly found. No specific treatment is available for the condition. Patients are generally advised on good oral hygiene.

Lymphocytic Interstitial pneumonitis (LIP)

Lymphocytic interstitial pneumonitis (LIP) occurs primarily in children, but it also occurs in adults infected with HIV. It is characterized by diffuse interstitial pulmonary infiltrates that may be confused with tuberculosis or PCP. However patients with LIP often do not have signs of severe respiratory illness. No specific treatment is available for LIP.

4.11. Viral Hepatitis

Viral hepatitis is one of the most common co-morbidities of injecting drug use. Co-infection with HIV and Hepatitis C Virus (HCV) is common in CIS.

`http://www.aidsmap.com/news/newsdisplay2.asp?newsId=2107`

HIV-positive patients who are coinfected with hepatitis C virus (HCV) are less likely to discontinue anti-HIV therapy because of liver toxicities if they first receive six months of anti-HCV treatment, according to a small Italian study published in the June 1st edition of the Journal of Acquired Immune Deficiency Syndromes.

4.12. Histoplasmosis

This infection is caused by *Histoplasma capsulatum*, a fungus that can cause an acute or chronic illness. Infection occurs by inhalation of spores. This is an uncommon condition. The outcome of exposure depends on immune status of host as well as size of inoculum. Intact cell mediated immunity is essential for preventing its dissemination. The acute illness is influenza-like with fever, anorexia, arthralgia, myalgia, dry cough and chest pain. Dissemination occurs soon after initial infection in immunosuppressed patients who develop weight loss, oral and skin lesions, chest symptoms, and liver, spleen and lymph node enlargement. Oral lesions may appear as punched-out, necrotic ulcers. There may be perforation of the palate and extensive soft tissue destruction.

Diagnosis

The diagnosis is made on clinical grounds and is confirmed on fungal cultures or histological examination of biopsied tissues. A chest x-ray in the acute illness may show hilar lymphadenopathy, scattered infiltrates and lower lobe nodules. Blood and skin tests have been developed for the diagnosis of histoplasmosis but these are not widely available.

Treatment

Acute histoplasmosis is self-limiting with normal immunity and does not require treatment. In immunosuppressed patients it may be treated as follows:

Table 28. Histoplasmosis

ANTIFUNGAL AGENT	DOSE	FREQUENCY	ROUTE	DURATION
Amphotericin B	0.7-1mg/kg	OD	IV	10 days

This is followed by long term treatment with itraconazole 200mg BID PO, or

- Fluconazole 200mg BID PO, or
- Amphotericin B 1mg/kg IV weekly
- Alternative regimen: Itraconazole 200 mg TID PO x 3 days then 200 mg PO BID x 12 weeks (plus dietary considerations: meal plus acidic drink)

4.13. Skin conditions

4.13.1. Fungal skin and nail infections

4.13.1.1. Dermatomycosis

Fungal skin rashes (dermatomycoses) occur commonly in HIV infected and non-HIV-infected individuals. The rash is usually itchy and dry and on examination scales of dead skin are visible. The lesions may be found anywhere on the body.

Diagnosis

On examination of skin scrapes microscopically fungal elements may be found.

Treatment

Topical applications of antifungal ointments and creams will usually clear the lesions. The following may be used for treating dermatomycoses:

Table 29-30. Dermatomycosis

ANTIFUNGAL PREPARATION	DOSE	FREQUENCY	ROUTE	DURATION
FIRST LINE TREATMENT				
Topical miconazole		TID	Topical	21 days
OR				
Topical clotrimazole		TID	Topical	21 days
SECOND LINE TREATMENT				
Ketoconazole	200mg	OD	PO	1-3 months
OR				
Itraconazole	100mg	OD	PO	1-3 months

4.13.1.2. Onychomycosis

Nails may also become infected with fungi and the infection results in distortion and destruction of the nails (onychomycosis).

Diagnosis

The diagnosis is usually made on clinical findings. Microscopic examination of KOH preparations of subungual material may reveal fungal elements.

Treatment

Table 31. Onychomycosis

ANTIFUNGAL PREPARATION	DOSE		FREQUENCY	ROUTE	DURATION
FIRST LINE TREATMENT					
Terbinafine	250mg	OD	PO	6 weeks for fingers OR 12 weeks for toes	
OR					
Itraconazole	200mg	BID	PO	For 1 week each month for 2 months (fingers) and for 3-4 months (toes)	

4.13.2 Molluscum contagiosum

Molluscum contagiosum is a superficial skin infection caused by the Molluscum contagiosum virus (MCV). The virus invades the skin causing the appearance of firm, flesh-coloured, papules measuring 2-5 mm in diameter. The lesions contain a white sebaceous material. The papules can occur anywhere on the body and often remain unchanged for many months, after which they disappear. The infection is spread through close body contact and may occur through sharing. The infection is also sexually transmissible. The incubation period varies from several weeks to several months. Shaving or scratching may cause the infection to spread. The infection occurs more commonly in persons immunosuppressed with HIV infection and in this situation the lesions are more widespread, more persistent, much larger than those found in non-HIV-infected persons and are more difficult to treat.

Diagnosis

The diagnosis is based on the typical appearance of the bumps. No diagnostic test for this virus is available.

Treatment

The goal of treatment is to remove the soft center, after which the papule resolves. Therefore each lesion needs to be treated individually. Various methods are available for the destruction of the lesion including:

- Curettage
- Chemical destruction with concentrated phenol
- Cryotherapy
- Electrocautery

It is known that the in persons with HIV infection, antiretroviral therapy helps in healing the infection and recently an anti-viral agent called cidofovir, which is also a potent antiretroviral agent has been shown to be effective in treating molluscum contagiosum.

4.13.3. Seborrhoeic dermatitis

Seborrhoeic dermatitis is a common presenting feature in persons with HIV infection. It is probably caused by a fungus known as *Pityrosporum ovale* (also known as *Malasezia furfur*). The rash appears commonly on the face, around the nostrils, the nasolabial folds, eyebrows, scalp, chest, axillae, the upper trunk and the genital area. The rash is erythematous and scaly and in persons with HIV infection may be extensive, persistent and recurrent.

Diagnosis

The diagnosis is made on clinical grounds and may be confirmed by finding fungal elements on microscopic examination of skin scrapes.

Treatment

Frequent skin washing to remove scales is advised and shampooing with selenium sulphide shampoo is effective. Topical applications of 1% hydrocortisone are probably the most effective. Ketoconazole 2% cream has also been shown to be effective.

4.13.4. Scabies

Scabies is caused by the mite *Sarcoptes scabei*. The female mite burrows into the skin and the burrows appear as raised lines up to several centimetres long. The mite deposits eggs in the burrows and then migrates to other sites of the body. The eggs hatch out and develop into adult mites which mate and more eggs are deposited in new burrows.

Clinical features

When a person is infested with scabies mites for the first time, there is usually little evidence of infestation for the first month (range 2 to 6 weeks). After this time and in subsequent infestations, people usually become sensitised to mites and symptoms generally occur within 1 to 4 days. Mites burrowing under the skin cause a rash, which is most frequently found on the hands, particularly the web spaces between the fingers, the folds of the wrist, elbow or knee, the ulna margins of the forearms, the penis, the breast and the shoulder blades. Burrows and mites may be few in number and difficult to find in some cases. Commonly there is severe itching, especially at night and frequently over much of the body, including areas where no mites are living. A more severe form of scabies that is more common among immunocompromised persons is called Norwegian scabies, characterized by vesicles and formation of thick crusts over the skin, accompanied by abundant mites but only slight itching. Complications due to infestation are usually caused by secondary bacterial infections from scratching.

Diagnosis

The diagnosis is usually made on finding the rash and burrows. Skin scrapes may reveal mites or ova on microscopic examination.

Treatment

Several lotions are available to treat scabies. The treatment of choice is the topical use of 1% gammabenzene hexachloride applied to the whole body from the neck down and washed off after 24 hours in adults and 8 hours in children. A single application is sufficient.

Permethrin 1% or Lindane 1% applications are also useful and both are applied in the same manner, i.e., apply to affected areas and wash off after 8 hours. These agents should not be used during pregnancy and lactation and in children.

Ivermectin in a single oral dose of 200mg is an alternative drug that is effective for crusted scabies in immunocompromised persons.

All clothes, bedding, and towels should be washed in hot water, and dried and ironed. All members of the household and sexual partners should also be treated.

4.13.5, Staphylococcal folliculitis

Folliculitis is a skin infection localized to the hair follicle. In HIV-infected persons a pustular perifolliculitis occurs commonly. Lesions are small (less than 5mm in diameter), multiple, erythematous follicles that may have a centre of pus. Lesions are itchy and are often found in clusters. Usually the condition is caused by *Staphylococcus aureus* though other organisms may also cause the infection.

Diagnosis

Diagnosis is made on clinical findings

Treatment

Treatment is with antibiotics such as cephalexin or cloxacillin 500mg PO QID for 7-21 days.

4.14. Persistent generalised lymphadenopathy in adults with HIV infection

The commonest clinical manifestation of HIV infection is symmetric generalised lymph node enlargement. Enlarged lymph nodes are generally painless, firm, mobile and rubbery and are most easily palpated in the neck, submental area, the axillae and in the groins (Box 2). The patient may or may not have other associated symptoms of HIV infection.

Box 2: Definition of PGL

Persistent generalised lymphadenopathy (PGL) is defined as the presence for more than one month of lymph nodes measuring more than 1 cm in diameter in more than one area of the body excluding the groins

It is important to palpate specifically for lymph nodes in the following areas:

- Anterior and posterior triangles of the neck
- Submental area
- Suboccipital area
- Anterior and posterior auricular areas
- Both axillae
- Epitrochlear areas
- Both inguinal regions – all persons, HIV infected or not, often have enlarged lymph nodes in these sites

Persons with PGL caused by HIV infection may have other features of HIV infection, including, oral thrush, oral hairy leukoplakia, pruritic skin rash, hyperpigmented nails, oral or genital herpes, involuntary weight loss, unexplained fever.

Generalised lymphadenopathy may be caused by a number of conditions other than HIV infection including, tuberculosis, leukaemias, lymphomas, Kaposi's sarcoma, syphilis, cytomegalovirus, toxoplasmosis, Epstein-Barr virus, cryptococcosis, histoplasmosis, and septic skin conditions, bubonic plague, and hepatitis B virus infection.

Generalised lymphadenopathy is a very common feature of HIV infection and in most cases the lymph node histology only reveals "reactive hyperplasia" or "follicular hyperplasia". A lymph node biopsy is necessary to establish a cause (See Box 3).

Box 3: Criteria for performing a lymph node biopsy

A patient with PGL should be referred for a lymph node biopsy if he/she has any of the following:

- **Lymph nodes are asymmetrically enlarged**
- **There is massive enlargement of lymph nodes, i.e., at least one lymph node measures more than 3 cm in diameter**
- **Lymph nodes are getting bigger over a period of observation**
- **There is evidence of TB on chest x-ray**
- **There is evidence of enlargement of hilar lymph nodes on chest x-ray**
- **There is evidence of Kaposi's sarcoma elsewhere in the body**

4.15. Fever in persons with HIV infection

Fever occurs as a result of infection, inflammation or malignancy. In persons with HIV infection fever may be the only clinical presentation of the infection. Hence it is important to keep in mind the diagnosis of HIV infection when managing a patient who presents with persistent fever for which a cause is not immediately obvious. Persistent fever in adults is defined as a body temperature of more than 38°C lasting for more than two weeks.

In patients with HIV/AIDS, persistent fever may be accompanied by features of the possible underlying cause, e.g., pneumonia, TB, gastrointestinal infection, or lymphoma. In adults with persistent fever the following factors may suggest the presence of HIV infection:

- Patient gives history of having engaged in unsafe sexual behaviour previously.
- Patient's partner is known to have HIV infection.
- Patient is a parent of a child known to have HIV infection.
- Patient has other features suggestive of HIV infection, such as PGL, oral or genital thrush, oral hairy leukoplakia, pruritic skin rash, oral or genital herpes, involuntary weight loss, darkening of the nails (melanonychia), hypopigmentation of the lips, and, thinning and straightening of the hair.

4.16. Weight loss in adults with HIV infection

HIV infection is a common cause of weight loss. The syndrome of severe involuntary weight loss in a person with HIV infection is known as "HIV associated wasting syndrome", or, "slim disease". The cause of the wasting is not fully understood. Possible causes of weight loss in patients with HIV/AIDS include, chronic and recurrent infections, chronic diarrhoea, malabsorption, HIV induced myopathy and poor appetite. None of these factors have been substantiated as the exact cause of the severe weight loss.

Definition

Severe weight loss is defined as involuntary weight loss of greater than 10% body weight.

Clinical features in adults

The patient may complain of involuntary weight loss, loss of appetite with or without fever and diarrhoea. Patients with HIV-associated wasting disease are ill and emaciated and may be feverish and dehydrated. Oral candidiasis is commonly found in such patients. The patient may have other features of AIDS including features of neurologic involvement such as encephalopathy and AIDS dementia complex.

Dietary considerations

PLWHA should take a balanced diet high in calories and protein. The diet should be made calorie rich by adding oil and sugar to the staple starch base of potatoes or rice. Protein rich foods include: milk and milk products such as cheese or sour milk, eggs, beans, meat, fish, and soya beans. Fat containing foods include: vegetable oil and fish. Patients should also take vegetables and fruits that are easily available: cabbage, onions, garlic, root beet, carrots, peas, pumpkin and apple, apricot. These provide essential minerals and vitamins.

For patients with severe stomatitis and difficulty in chewing or swallowing the food should be made into a palatable liquid, paste or porridge. Patients should feed frequently throughout the day. Very ill patients may be given a high-energy supplement made up at home by adding sugar (50g) and cooking oil (20ml) to 500 ml of milk. This

high-energy milk could be further fortified by beating up one egg into the mixture if eggs are available and are tolerated. An adult should drink 500 ml of high-energy milk daily until he is able to take a full normal diet. The patient is fed this four to six times a day. Multivitamins that include vitamins A, B and C should be given once daily to all patients.

Nutritional support for HIV-positive asymptomatic persons

All HIV-infected persons should receive nutrition counselling as part of the management plan of persons with HIV infection. Counselling should include information on locally available foods and diets. HIV-positive individuals should increase their energy intake to 40kcal/kg/day and their protein intake to take 5g/kg/day. These increases may be achieved by taking high-energy high-protein snacks such as a cup-full of yoghurt, fish with bread, and milk, two or three times a day. Multivitamins that include vitamins A, B and C should be given in a once daily dose to all patients.

Nutritional support for symptomatic HIV-positive persons

HIV-positive persons experiencing weight loss should be provided with nutritional counselling and support. Often the weight loss is due to periodic bouts of infections and therefore such persons should be examined carefully and treated adequately if infection is found. In addition individuals should be educated and counselled regarding increasing their energy and protein intake during and after a bout of illness. All patients should be educated on the dangers of smoking and alcohol intake.

Nutritional advice for persons with common HIV-related illnesses, such as, mouth sores, chronic diarrhoea, fever, chronic cough, and wasting, is the same as described above. However more attention needs to be paid to preserving functional independence. The following principles should be followed when managing persons with AIDS:

- Preserve body mass by the early institution of nutritional supplementation
- During periods of nausea and vomiting patients should eat small meals and snacks frequently and throughout the day
- Dehydration should be prevented by taking adequate amounts of fluids
- Increase the dietary content of fibre and reduce the dietary content of fat to reduce constipation and abdominal discomfort caused by gas and bloating
- Patients should be encouraged to eat favourite foods
- Avoid tobacco and alcohol
- Treat all infections promptly
- Give supplements of vitamins A, B and C
- Review the drug history and make sure that drug intolerance is not leading to nutritional problems

4.17. Psychological support

It is important that only patients with AIDS and HIV infection are given psychological support but their family members, relatives, friends and carers should also receive this support. HIV infection remains an incurable condition but with appropriate care can be managed as a chronic illness. Patients with HIV infection need not only medical care but psychological care spiritual support as well.

Infected persons who learn that they have HIV infection may go through different emotions, such as, shock, denial, anger, acceptance, bargaining, and depression. During these stages the patient or family members may need different forms of psychological support.

HIV infected persons should always be counseled before the HIV test is performed. In this pre-test counselling the patients should be prepared for undergoing testing and should be informed of how a positive test result may affect them. It is important to also discuss issues relating to shared confidentiality. When the result of the test is known patients should be counselled so that they may be able to cope and live with the result. Patients found to be HIV negative should be counselled on safe sexual behaviour and to live a lifestyle that will allow them to remain negative.

HIV positive individuals should be counselled to cope with knowing that they are HIV infected and how they may still enjoy a full and fruitful life despite the infection. However soon after learning of the result the patient will require further psychological support as they go through the different emotional stages. It is important that the patient has an open channel for access to psychological support whenever he/she needs it. As the patient goes through the different stages of grief with eventual acceptance he/she will need to talk to the counsellor so that he/she can discuss the infection and ask questions which may not be obvious at first. Counselling is a long-term process and should be carried out on a continuing basis in numerous sessions. Some patients who have accepted and living with the infection for some months or years may suddenly go into crises when he/she develops symptoms related (or un-related) to HIV infection and special counselling sessions are needed for these episodes.

4.18. Palliative care

(See also Protocol on Palliative Care)

Palliative care is an integral part of active total care for AIDS patients as there is no cure. Many aspects of palliative care, such as, pain management, symptom control and psychological support, are applicable early in the course of the illness. The palliative care needs of persons with AIDS vary from person to person and from illness to illness.

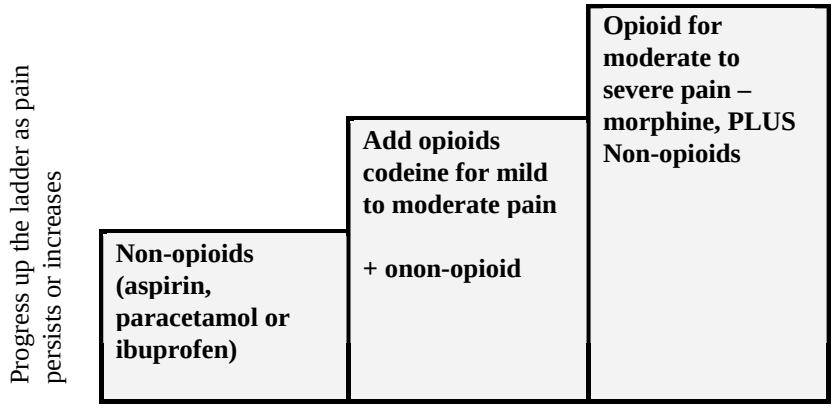
4.18.1. Symptom management

Pain

Determine the site of the pain and grade the severity of the pain. Pain control in adults should be achieved as follows:

- Initially use non-opioids such as aspirin 600mg every 4 hours, increasing to 1000mg every 6 hours, or paracetamol 500mg every 4 to 6 hours, or ibuprofen 400mg every 6 hours
- The next level of treatment for pain control is with a mild opioid such as codeine given in a dose of 30mg every 4 hours (possible to increase up to 60mg every 4-8 hours- maximum dose 180-240mg daily due to constipation)) If this still does not control pain then a strong opioid such as morphine may be used initially in a dose of 2.5- 5mg every 4 hours. The dose should be increased (there is not ceiling dose) to levels that control pain. Chronic pain should be treated by mouth and on a regular basis. It is advisable to start with mild analgesia and progress in a step-wise to more potent analgesics and opioids if necessary. The pain control "ladder" is shown in Figure 1.

Figure 1: Achieving pain control in persons with chronic pain



Breathlessness

Patients with AIDS often develop severe breathlessness terminally. This may be the result of a severe unresponding lung infection or cancer such as Kaposi's sarcoma or lymphoma affecting the lungs and pleura. Relief of dyspnoea may be achieved by treating the pneumonia if present and in some cases, e.g., *Pneumocystis* pneumonia, by the addition of steroids to the antibiotic regimen. In patients with pulmonary Kaposi's sarcoma pleural effusion commonly occur. In this situation the breathlessness may be relieved by aspirating pleural fluid and by administering steroids. All patients with breathlessness should be given oxygen administered by mask or nasal prongs. In persons with breathlessness give morphine to relieve anxiety, pain and discomfort. Nebulised bronchodilators will also provide relief if there is an element of bronchospasm. In addition to the medication, the patient should sit in the best position; use extra pillows or some back support; windows should be open to allow fresh air in; fan can help; should be given frequent water to drink to loosens sputum.

Vomiting

Vomiting may lead to poor fluid intake and hence dehydration and therefore it is necessary to correct dehydration. Encourage the patient to take small amounts of fluids frequently. Vomiting may be relieved by administering prochlorperazine 5mg PO TID or metoclopromide 10mg PO TID.

Mouth care

Good mouth care should always be practiced. This includes brushing the teeth with a soft toothbrush two times a day and gargling after food. In persons with mouth sores oral care helps. If the sores are painful patients will not be

able to eat or swallow and should be given soft foods and liquid diets. If a specific cause for the ulcers is found these should be treated as described.

Itching

The cause should be always assessed and specific treatment provided. For pruritus bath oils or other emollients such as emulsifying ointment may be useful. If a rash is present then antifungal creams will help if the rash is due to a fungal infection or topical steroids will relieve inflamed areas of the skin if a bacterial or viral infection is not present. Orally administered antihistamines, such as, diphenhydramine or hydroxyzine 25mg PO given at night may reduce the pruritus and allow a relatively more comfortable sleep. If multiple skin infections are present, 0.05% chlorhexidne rinse after bathing isi very useful.

Skin care

Prevent the development of bedsores by changing the position of the patient every 4 hours and arrange for the patient to lie on an extra soft material. Avoid pressure on any one part of the body for prolonged periods of time. Protect areas that have become inflamed because of pressure by avoiding any pressure at all on the area and by applying soothing lotions. Change soiled bed sheets immediately. Massage pressure points such as the heels, elbows, ankles, back and hips frequently. Cover all open sores with a gauze bandage after applying an antiseptic cream.

4.19. Terminal care

All persons with terminal illnesses need end of life care. Towards the end of life it is essential that the patient and the family have social, emotional and spiritual support. In palliation in terminal illness one attempts to allow the patient to die with dignity and relieve him/her of distressing symptoms. Palliation also offers support to help the patient live as actively as possible until death and enables the family to cope with their loved-one's illness and with their own bereavement. The carer needs to listen with empathy and should encourage communication within the family. Issues such as family and child support, schooling and welfare should be discussed. The patient should be told that he/she is loved and will be missed by family members. Spiritual support and discussion with the pastor may relieve feelings of guilt. The carer should be available and should visit regularly.

Symptom control in terminally ill patients is an essential component of palliation. Guidance given in 18.1 on symptom management should be followed.

V. Palliative care

1. Policy

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

- provides relief from pain and other distressing symptoms;
- affirms life and regards dying as a normal process;
- intends neither to hasten or postpone death;
- integrates the psychological and spiritual aspects of patient care;
- offers a support system to help patients live as actively as possible until death;
- offers a support system to help the family cope during the patients illness and in their own bereavement;
- uses a team approach to address the needs of patients and their families, including bereavement counselling, if indicated;
- will enhance quality of life, and may also positively influence the course of illness;
- is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications.

Why it is Important

Palliative care is an essential component of a comprehensive package of care for people living with HIV/AIDS because of the variety of symptoms they can experience - such as pain, diarrhoea, cough, shortness of breath, nausea, weakness, fatigue, fever, and confusion. Palliative care is an important means of relieving symptoms that result in undue suffering and frequent visits to the hospital or clinic. Lack of palliative care results in untreated symptoms that hamper an individual's ability to continue his or her activities of daily life. At the community level, lack of palliative care places an unnecessary burden on hospital or clinic resources.

2. Principles

- Palliative care is a core component of comprehensive HIV/AIDS care
- Symptomatic treatment and terminal care are part of palliative care
- Palliative care can be provided through home care projects , hospitals and palliative wards
- A patient may access palliative care, when (symptom management during acute and chronic care)
  - the patient is refusing curative treatment and/or requests palliative care
  - appropriate treatment is not available or affordable
  - no medical progress or cure anticipated – based on the findings of physical examination and appropriate diagnostics
  - the patient's condition deteriorates under proper treatment
- Regional AIDS centres will be coordinating the referral to palliative care and other services, at the request of specialists and organizations in delivering palliative care services.
- Partners, such as non-governmental organizations (NGOs), will be encouraged to deliver palliative care, thereby adhering to the national standards.
- Access to palliative care will not be artificially restricted due to political or social constrains. All patients

in need of palliative care and want treatment will receive it without exception.
- Palliative care will be provided according to needs of the patient and WHO standards of care
- Treatment for other illnesses and conditions will not be withheld at any stage of the disease (e.g. treatment for tuberculosis (TB), ART, substitution treatment for IDUs)
- Drug substitution therapy should be offered to all IDUs, if appropriate

3. Initial evaluation

Table 1: Initial evaluation of Person living with HIV/AIDS in need of palliative care

ASSESSMENT	
History: General health status	+
Current symptoms	+
Co-morbidities, pain and current medication	+
Determine cause, type and grade of pain	+
Mental health	+
Past medical history (*incl. major illnesses (e.g. TB), hospitalizations and surgeries, the length of time since the diagnosis of HIV-infection*	+
Physical examination	+
Gynecologic exam	If necessary
Laboratory assessment	
• Hemoglobin	+
• White blood cell count and differential	+
• Urinalysis	+
• Liver function tests (ALT, AST, bilirubin)	+
• Creatinine	+
• HIV test	if not performed
• CD4 count	if not known
Chest x-ray	At indication
Pregnancy test	At indication
Other tests	At indication

The assessment should result in a staging of the HIV infection, identification of co-morbidities and conditions, and a classification and grading of the pain.

4. Treatment

4.1. Pain management

General principles:
- If possible, give by mouth or alternatively rectal – avoid intramuscular
- Give pain-killers at fixed time intervals
- Link the scheme to the sleep rhythm
- Next dose must be given before effect of previous dose wears off
- Start with a small dose and increase gradually, until the patient is comfortable
- For breakthrough pain, give an extra dose (50-100% of the 4-hourly dose) in addition to the regular scheme
- While aspirin can be effective in the control of mild to moderate pain, care should be taken due to the increased prevalence of bleeding tendencies in HIV infected people. Decreased liver function may also make use of paracetamol and aspirin contraindicated.

Table 2. Pain management

TREATMENT	USUAL STARTING DOSE ADULTS	CONSIDERATIONS
A. Medical treatment*		
STEP 1		
Mild pain		
Non opioid	**Aspirin (acetylsalicylic acid)** 325 mg, 2 tablets, every 4 hours or 1000 mg every 6 hours	Stop if indigestion or black stools Do not give to children under 12 years Avoid in stage lll or lV HIV
	Paracetamol 500 mg (2 tablets) every 4-6 hours	Do not exceed 8 tablets in 24 hours
	Ibuprofen 400 mg every 6 hours	
STEP 2		
Mild to moderate pain		
Non opioid	**Aspirin (acetylsalicylic acid)** 325 mg, 2 tablets, every 4 hours or 1000 mg every 6 hours	Stop if indigestion or black stools Do not give to children under 12 years Avoid in stage lll or lV HIV
	Metamizol 500 – 1000 mg /dose < 6000 mg / day	Ind.: tumor, colic, chronic pains
	Paracetamol 500 mg (2 tablets) every 4-6 hours	Do not exceed 8 tablets in 24 hours
Opioid **	**Codeine** 30 mg every 4 hours (range: 30-60 mg every 4 to 8 hours) *If codeine is not available consider alternation aspirin and paracetamol.*	Maximum daily dose for pain 180-240 mg due to constipation – otherwise shift to morphine Constipation: give laxative with it unless diarrhea
STEP 3		
Moderate to severe pain		
Non opioid	**Aspirin (acetylsalicylic acid)** 325 mg, 2 tablets every 4 hours or 1000 mg every 6 hours	Stop if indigestion or black stools Do not give to children under 12 years Avoid in stage lll or lV HIV
	Paracetamol 500 mg every 4-6 hours	Do not exceed 8 tablets in 24 hours
	Tramadol ret., 2 –3 x 100 – 200 mg < 600 mg / day	
Opioid **	**Oral morphine** 2.5-5 mg every 4 hours Drop into mouth, or give rectally by syringe Dose can be increased by 1.5 or doubled after 24 hours if pain persists. There is no CEILING DOSE	If oral Morphine is not available, injectable one will be the choice: 5 mg/5 ml or 50 mg/5 ml. According to need and respiration (no ceiling; consider holding if respirations < 8/minute) Give laxative with it.
B. Special pain problems		
Burning pains, abnormal sensation pains, shooting pains, pins and needles	**Amitriptyline** 25 mg at night or 12.5 mg twice daily	Wait 2 weeks for response then increase gradually to 50 mg at night or 25mg twice daily
Muscle spasms	**Diazepam,**	

TREATMENT	USUAL STARTING DOSE ADULTS	CONSIDERATIONS
	5mg 2-3 times daily	
When terminal care with no referral and: • Swelling around tumour • Severe oesophageal candidiasis with ulceration and swallow problems • Nerve compression • Persistent severe headache due to increased intracranial pressure	**Dexamethasone** 2-6 mg per day **or prednisolone** 15-40 mg for 7 days or as provided by trained health worker	Helpful in terminal care, helps to improve appetite and make patient feel happier Reduce dose to lowest possible Withdraw if no benefit in3 weeks Dexamethasone is about 7 times stronger than prednisone. If you need to use prednisone (or prednisolone) rather than dexamethasone, multiply the dexamethasone dose by seven.
Herpes zoster	**Amitriptyline** Low dose: 12.5 - 25 mg at night or 12.5 mg twice daily Early eruption: **valcyclovir (acyclovir?)** 1 gr, every 8 hours, 5-7 days or: **Gabapentin** < 2400 mg / day, increasing dosages acute: **Tramadol**	post-zoster acute
Gastrointestinal pain from colic	**Hyoscine (Buscopan)** 10mg twice daily **Butylscopolamin** 3 – 5 x 10 – 20 mg **Codeine** 30mg every 4 hours	
C. Non-medical treatment		
Support and counseling	Psychological, spiritual and/or emotional support and counselling To accompany pain medication	Pain can be more hard to bear in case of guilt, fear of dying, loneliness, anxiety, depression Explain what is happening or may happen to relieve fear and anxiety
	Relaxation techniques, e.g. physical methods, e.g. massage and breathing techniques; and cognitive methods, e.g. music	Unless the patient is psychotic or severely depressed

* give only one drug from the non-opioid and the opioid at a time; aspirin every 4 hours can be given with paracetamol every 4 hours, ensuring overlap so one is given every 2 hours.

****** if pain is controlled, reduce morphine rapidly or stop if used for only a short time; reduce gradually if used for weeks

Table 3. Management of side-effects of Morphine or other Opioids

IF THE PATIENT HAS A SIDE-EFFECT	THEN MANAGE AS FOLLOWS:
Constipation	• Increase fluids and bulk • Give stool softener (lactulose, 10 ml TID) - docusate is milder at time of prescribing plus stimulant (uvesorb or belasorb) • Prevent by prophylaxis (unless chronic diarrhoea)
Nausea and/or vomiting	• Anti-emetic. Usually resolves in several days. May need round-the-clock dosing.
Respiratory depresion (rare if oral morphine is titrated against pain)	• Stimulate, remind to breathe • If severe, consider withholding next opiood dose then halve dose • If severe pain in terminal care, consider accepting some respiratory depression
Confusion or drowsiness (if due to opioid)	• Usually occurs at start of treatment or dose increase. • Usually resolves within few days. • Can occur at end of life with renal failure. • Halve dose or increase time interval.
Itching/twitching (myoclonus – if severe or present during waking hours)	• If on high dose,consider reducing dose or alternatingdoses or two opioids. • Re-evaluate – pain may not be morphine responsive
Somnolence	• Extended sleep can be from exhaustion due to pain. • If persists more than 2 days after starting, reduce the dose by half.
How to reduce morphine when cause of pain is controlled (common in HIV/AIDS complications)	• **If used only for a short time: stop or rapidly reduce.** • **If used for weeks: reduce gradually.**

4.2. Management weight loss

Table 4. Management weight loss

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
General weight loss	• Encourage the sick person to eat, but do not force as the body may not be able to accept it and he/she may vomit. • Offer smaller meals frequently of what the person likes	• Avoid cooking close to the sick person • Let the sick person choose the foods he/she wants to eat from what is available • Accept that intake will reduce as patient gets sciker • Seek help from trained health worker in case of rapid weight loss, or if the sick person consistently refuses to eat any food or is not able to swallow.
If end-of- life care	Prednisone 5 – 15 mg daily	To stimulate appetite.
If nausea and vomiting with antiemetics	Provide anti-emetics (see table 5)	Offer smaller meals frequently of what the person likes; don't force
If thrush or mouth ulcer	Treat thrush or mouth ulcer (see table 6)	
If diarrhoea	Treat diarrhoea (see table 8)	

4.3. Management nausea and vomiting

Table 5. Management nausea and vomiting

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
Nausea and vomiting • (If known abdominal tumour with obstruction)	**Metoclopromide** 10 mg every 4-8 hours (only for a day at a time) **or haloperidol** 1-2 mg once daily **Chlorpromaizine** 25-50mg every 6-12 hours **Cyclizine** Up to 5 mg. If not available, Clemastine 1mg BID or Cetirizine 10mg QD	• Seek foods which the patient likes and which cause less nausea • Offer smaller meals and drink frequently and slowly • **Seek help from trained health worker for vomiting more than one day, or dry tongue, or passing little urine or abdominal pain**

4.4. Management mouth ulcers or pain on swallowing

Table 6. Management mouth ulcers or pain on swallowing

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
General		• Use soft toothbrush to gently scrub teeth, tongue, palate and gums to remove debris • Rinse mouth with dilute salt water (a finger pinch of salt in a glass of water) after eating and at bedtime (usually 3-4 times daily)
If candida	**Myconazole buccal tablets** 1 tablet daily – 7 days If severe and/or no response, refer. **Fluconazole** initial loading dose: 200 mg (1 day); maintenance: 100 mg daily; 10-14 days or until symptoms resolve	• Topical anaesthetics can provide some relief • Mix 2 tablets of aspirin in water and rinse the mouth up to four times a day • Pain relief may be required (see table 2) • Remove food rests with gauze/cloth soaked in salt water • Diet: o Soft diets may decrease discomfort o Textured foods and fluids may be swallowed more easily o Avoid very hot, cold or spicy foods
If aphtous ulcers	**Prednisone** Crush and apply a few grains **Dexamethasone** solution as mouthwash **Kenalog cream** applied to sores	
If Herpes Simplex	**Metronidazole** acyclovir, 400 mg, PO	
If smelly mouth due to oral cancer or other lesions:	**Metronidazole mouthwash: c**rush 2 tablets in water and rinse mouth	

4.5. Management dry mouth

Table 7. Management dry mouth

CONDITION	TREATMENT	CONSIDERATIONS FOR HOME CARE
Dry mouth	Review medications – can be side effect	• Frequent sips of drinks • Moisten mouth regularly with water • Let the sick person suck on fruits such as orange
If serious problem with lack of saliva	Refer to dentist	

4.6. Management of diarrhoea

Table 8. Management diarrhoea

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
General	• Increase fluid intake, to prevent dehydration • Use ORS if large volume of diarrhea • Suggest a supportive diet	• Encourage plenty of fluids to replace lost water • Increase frequency of small amounts of food intake Special care for rectal area: • After the person has passed stool, clean with toilet paper or soft tissue paper • Wash the anal area 3 times a day with soap and water • If the sick person feels pain when passing the stool, apply Vaseline around the anal area • Seek help of a trained health worker for any of the following: o Vomiting with fever o Blood in stools o Diarrhea for more than 5 days o Increasing weakness patient o Broken skin around the rectal area
Give constipating drugs, unless blood in stool or fever or child less than 5 or elderly	**Loperamide** 4 mg start than 2 mg after each stool OR codeine or morphine (if approved by MOH) Unless blood in the stool or fever or child less than 5 years **Codeine** 10 mg 3 times daily (up to 60 mg every 4 hours) Oral morphine 2.5-5mg every 4 hours (if severe)	
If local tenderness:	Suggest local anesthetic ointment or petroleum jelly	
If incontinent:	Use petroleum jelly to protect perianal skin	

4.7. Management constipation

Table 9. Management constipation for more than 2 days

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
If impaction	Perform rectal exam and remove manually	• Offer drinks often • Encourage any fruits (including dried fruits), vegetables, porridge, soft foods • Take a tablespoon of vegetable oil before breakfast • Gently put petroleum jelly or piece of soap into the rectum if the patient cannot do it • Use protective gloves
If otherwise constipation	• Give laxative: First time: bulk enhancing agent • bisocodyl 5-15 mg at night • senna start 2 tablets (7.5mg) twice daily (up to two tablets every 4 hours) Second time: give uvesorb • Dose varies by individual Remember: Always give laxative with morphine or codeine	

4.8. Management of fever

Table 10. Management of fever.

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
General – assess and treat cause	• Paracetamol or acetylsalicylic acid every 4 hrs (no more than 8 tablets paracetamol in 24 hrs). • Make sure that patient stays hydrated	• Encourage that patient frequently drinks water, diluted tea, fruit juices.

4.9. Management of hiccups

Table 11. Management of hiccups

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
General: If oral thrush:	Treat accordingly	***First try maneuvers to control:*** Stimulate the throat: • Quickly eat 2 heaped teaspoons sugar OR • drink cold water OR • eat crushed ice OR • rub with a clean cloth inside the top of the mouth (towards the back where it is soft) OR Interrupt the normal breathing: • hold breath or breathe into paper bag – stop when you feel uncomfortable • pull knees to chest and lean forward (compress the chest)
If advcanced cancer with distended stomach	Simethicone	
If no response or recurrent	• Metoclopromide (10 mg tablet, 1-2 tablets 3-4 times daily) OR • Haloperidol (2 mg tablet: ¼ to 1 tablet 1-3 times daily)	
If brain tumor	Try anti-epileptic medication	

4.10. Management of anxity and agitation

Table 12. Management of anxiety and agitation

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
If new problem, consider cognitive impairment what is the cause?	• If severe anxiety, consider use of antianxiety medications. • Counsel on managing anxiety according to specific situation • Teach relaxation techniques • Listen carefully and provide emotional support • Make sure that patient has good care and psychosocial support	***Help with worries:*** • Take time to listen to the sick person • Discuss the problem in confidence • Providing soft music or massaging may help the sick person to relax • Pray together if requested
If mild:	• Low dose diazepam (2.5-5mg at night or twice daily) for short time – rarely required if given enough care (avoid – can cause depression) • If bipolar disorder suspected, refer for evaluation and treatment	
If severe anxiety/agitation/delerium	Haloperidol 5-10 mg	

4.11. Management of sleeping problems

Table 13. Management of sleeping problems

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
Consider: uncontrolled pain, anxiety, depression, drug withdrawal (alcohol, diazepam, phenobarbitol)	• Diazepam (avoid long-term use, as it can cause depression) OR • Diphenhydramine • Lorazepam, 0,5 – 1 mg, < 4 mg / day	• Listen to the sick person's fears that may be keeping them wake, answer their fears • Reduce noise where possible • Do not give the sick person strong tea or coffee late in the evening • Treat pain if present

4.12. Prevention contractures and stiffness

Table 14. Prevention of contractures and stiffness

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
• Check range of motion • If spasms or severe spastic	**Diazepam** **Baclofen** <3 x 10 – 25 mg or: **Tetracepam** 50 mg / day, < 200 mg / day	• Do not confine – encourage mobilization • Do simple range of motion exercises if patient is immobile: - Exercise limbs and joints at least twice daily - Protect the joint by holding the limb above and below it and support it as much as you can - Bend, straighten, and move joints as far as they normally go. Be gentle and move slowly without causing pain - Stretch joints by holding as before but with firm steady pressure - Bring the arms above the head and lift the legs to 90 degrees – let the patient do it as far as they can and help the rest of the way • Massage

4.13. Care for patient with dementia.

Table 15. Care for patient with dementia

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
If symptoms are new problem ***Patients with the mental problems (dementia) will show the following signs:*** • Forgetful • Lacks concentration • Trouble speaking or thinking • Frequently changing mood • Non-acceptable behaviour such as going naked and using bad language	Assess for confusion, difficulty speaking or loss of oreintation (assess for malaria, hypoglycemia or other systemic illness or alcohol or drug/ medication toxicity or withdrawal; consider HIV related illness.) Treat according to findings; Low dose sedation if agitated and and not alcohol or drug intoxicated.	***Patients with the mental problems (dementia) will show the following signs:*** • Forgetful • Lacks concentration • Trouble speaking or thinking • Frequently changing mood • Non-acceptable behaviour such as going naked and using bad language ***What to do?*** • As far as possible, keep in a familiar environment • Keep things in the same place -easy to reach and see • Keep familiar time pattern to the days activities • Remove dangerous objects • Speak in simple sentences, one person at a time • Keep other noises down (such as TV, radio) • Make sure somebody is present to look after the sick person
If paranoia or getting up at night purposefully	• Haloperidol 5-10 mg • Lorazepam	

4.14. Management of depression

Table 16. Management of depression

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
Consider depression if abnormally sad, insomnia, loss of interest Symptoms of depression: Sad, depressed Loss of interest, pleasure Loss of enegy *if any of the above present ask for:* • *Disturbed sleep* • *Appetite changes* • *Poor concentration* • *Decreased liido* • *Slow movements* • *Loss of self-confidence, esteem* • *Thoughts of suicide or death* • *Guilty feelings* *If 5 or more symptoms and duration more than 2 weeks, diagnosis of major depression* If less than 5 symptoms or more than 2 months of bereavement with functional impairment diagnosis is minor depression/complicated bereavment	Assess and classify Assess and classify: suicide risk, major depression, minor depression/complicated bereavement, difficult life events/loss If bipolar disorder suspected refer for lithium treatment; otherwise start amitryptiline Amytriptyline is indicated	Provide support Do no leave alone if suicide risk Provide counseling and support: *Major depression:* • Educate patient and family about medication • Refer for counseling if available • Ensure follow-up *Minor depression/complicated bereavement:* • Counsel • Assist in finding solutions if sleep disturbed • Follow-up
If suicidal thoughts	Assess if person has a plan and the means to carry out. If yes, consider high risk and refer for hopitalisation	• Do not leave alone if suicide risk • Remove harmful objects • Mobilize family/friends

4.15. Management of vaginal discharge from cervical cancer

Table 17. Management of vaginal discharge from cervical cancer

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
If vaginalanl discharge from cervical cancer	Use metronidazole tablets as pessary	Daily hygiene

4.16. Management of itching

Table 18. Management of itching

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
Assess for scabies prurigo eczema Ringworm Dry, itchy skin Psoriasis	General care • Local steroid creams may be useful if inflammation is present in absence of infection (bacterial, fungal or viral) • Antihistamines (diphenhydramine 25 mg. at bedtime) may be useful for severe itching • If recurrent skin infections, 0.05% chlorhexidine rinse after bathing • If itching from obstructive jaundice, try prednisone or haloperidol • For eczema, gently wash and dry skin. Use topical steroids for short-term (not on face) • For ringworm, use Whitfield's ointment (or other antifungal cream). If extensive use fluconazole • Consider treatment for scabies even if no typical lesions • For psoriasis use coal tar ointment 5% in 2% salicylic acid; expose to sunlight 30 to 60 minutes per day • Chlorpheniramine (4mg x 2) maybe useful for severe itching	Try to offer relief through any of the following: • Apply Vaseline on the itching part of the body • Put one spoon of vegetable oil in 5 litres of water when washing the sick person • After a bath, apply on body one teaspoon in a litre diluted Dettol (chlorhexidine) • Use warm water for bathing • Seek help from a trained heath worker for painful blisters or extensive skin infection

4.17. Management of bedsores

Table 19. Management of bedsores

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
• Check for signs of infection • Check for other problems	***All patients need skin care to avoid pressure problems*** • Check for signs of infection, making sure it isi not another problem • If red, tender, warm, pus or crusts present, assess for fever, if systemically unwell, or if infection extends to muscle: if yes, refer to hospital, start IV/IM antibiotics (or oral cloxacillin)See Acute Care • If size of lesion is greater than 4 cm, or red streaks, or tender nodes or more than 6 abcesses: start Flucloxacillin, drain pus if fluctuant, elevate limb, follow-up next day • If only red, tender and warm: clean sores with antiseptic, drain pus if fluctuant, follow-up in 2 days	***The following can help to soothe the pain of bedsores and quicken their healing*** • For small sores clean gently with salty water and allow to dry • For bedsores that are not deep leave the wound open to the air • If painful, give painkillers such as paracetamol or aspirin regularly • For deep or large sores, every day clean gently with pure honey, cover with clean light dressing to encourage healing • Seek help from a trained health worker for any discoloured skin or bedsores getting worse ***Prevent bedsores in all bedridden patients:*** • Help the bedridden patient to sit out in a chair from time to time if possible • Lift he sick person up the bed – do not drag as it breaks the skin • Change the sick person's position on the bed often, if possible every 1-2 hrs – use pillow or cushions to keep the position • Keep the beddings clean and dry • Put extra soft material, such as a soft cotton towel, under the sick person • Provide privacy during bathing • Dry the skin after bath gently with a soft towel • Oil the skin with cream, body oil, lanolin or vegetable oil • Use plastic sheets under the bed sheets to keep the bed dry when one cannot control urine or faeces • Massage the back and hips, elbows, ankles, with Vaseline • If there is leakage of urine or stolls, protect the skin with Vaseline applied around private parts, back, hips, ankles and elbows • Support the sick person over the container when passing urine or stool, so as to avoid injury and wetting the bed.
• For smelly tumours or ulcers	• Sprinkle crushed metronidozole – enough to cover the area	

4.18. Management of incontinence of urine or soiling

Table 20. Management of incontinence of urine or soiling

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
If boy/man: use urine bottle If girl/woman: consider catheterization	Keep stooles firm with loperamide	• Regular changing or diapers • Keep skin clean and dry; apply protective ointments as needed

4.19. Management of cough or difficult breathing

Table 21. Management of cough or difficult breathing

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
This includes patients dying from COPD, lung cancer, HIV/AIDS lung infection or any terminal pulmonary problem Relieve dyspnoe: • If bronchospasm is contributing:	Asthma prototocols • Give bronchodilators by metered-dose inhaler with spacer/mask or, if available, by nebulizer. • Continue until patient is not able to use them or has very shallow or laboured breathing • Prednisolone orally – waith 2 weeks to assess response	For simple cough: • Local soothing remedies, such as honey, lemon or steam – plain or with Eucalyptus leaves • If patient has a new productive cough for more than 2 weeks, it may be tuberculosis. Arrange with health worker to send 3 sputums for examination for TB. ***In addition to the treatment gfiven by health worker:*** • Help the sick person into the best position that eases breathing – usually sitting up is the best. Leaning slightly forward resting arms on a table may help. • Use extra pillows or some back support • Open windows to allow in fresh air • Fan with a newspaper or clean cloth • Give patient water frequently (it loosens sputum) ***Safe handling and disposal of sputum:*** • Handle sputum with care to avoid spreading infection • Use a tin for spitting and cover • Empty container in the toilet and wash with a detergent such as JIK or OMO or clean the tin with boiled water.
• If heart failure or excess fluid: Relieve excessive sputum:	• Oral morphine/tramadol –small dose, when recommended by a doctor- For patient not on oral morphine for pain, give 2.5mg, for patient on oral increase the dose progressively by 25% • Furosemide 40 mg	
• If cough with thick sputum	• Nebulized saline	
• If excess, thin sputum	• Hyocine may help (as an anticholinergic)) 10 mg every 8 hours	
• If more than 30 ml/day	• Try forced expiratory techniques (‚huffing') with postural drainage • Avoid tracheal suction which is very distressing to the patient	
Relieve bothersome cough: • If new, productive cough more than 2 weeks, send 3 sputums for AFB	• Give codeine or, if no response, oral morphine (2.5-5 mg) (tramadol)	
• if positive to prevent TB transmission	• Treat (see TB Care module) • Patients on treatment for TB should continue treatment to prevent spread to others.	
Educate on most efficient use of remaining long function.	• How to plan activities	

5. General Management of a patient with HIV/AIDS

Table 22. Management of a patient with HIV/AIDS

CONDITION	TREATMENT AND DOSE ADULTS	CONSIDERATIONS FOR HOME CARE
Precautions against infection:		• Health workers and family can safely care for AIDS patient – emphasize extremely low risk to health workers and household contacts • HIV present in blood and body fluids – wear gloves when contacting these fluids • Keep wounds covered (both caregivers and the person with HIV/AIDS) • No risk from casual household contact (no gloves needed) • Can clean up blood, faeces, urine with ordinary household bleach • Can clean cutlery, linen, bath etc with ordinary washing products • Keep clothing and sheets stained with blood, diarrhea or other body fluids separate from other household laundry. Use a piece of plastic or paper, or gloves to handle soiled items. • Don't share toothbrushes, razors, needles, or other sharp instruments that pierce the skin • Wash your hands with soap and water after changing soiled bedsheets and clothing and after any contact with body fluids.
Persistent diarrhoea: ***Illness unpredictable:*** • Course of illness can change • Complex family issues • Medical treatment for chronic diarrhoea	***Treatment of infection often improves the patient's condition*** • Acute Care module • see table 8	***Suggest a supportive diet***: • Carrot soup contains pectin; it soothes the bowels and stimulates the appetite, and helps to replace vitamins and minerals • Rice and potatoes may help reduce diarrhea • Eat bananas and tomatoes for potassium • Eat 5-6 meals rather than 3 large ones • Add nutmeg, as it slows food • Avoid coffee, strong tea, alcohol • Avoid raw foods, cold foods, high-fibre foods, food containing too much fat • Test benefit of avoiding milkd and cheese (yoghurt is better tolerated) • Consult the patient as to what suits him/her the best
Complex family issues		• Fear in family of also being infected if status is not known • Economic problems are common • Anger, blame and regret around source of infection in family • Role reversals (older parents caring for young adults, young children caring for parents, grandparents caring for orphans) • Stigma can be a serious problem

Table 23. Instructions for the family or community care provider at home

Teach the family or community care provider on the management of symptoms.	• Explain the management of a few symptoms or a few skills at a time. • Choose those that are most important for the care of the patient now. • Demonstrate skills such as the correct method for range or motion or how todraw up the exact dose of a liquid medicine such as morphine into the syringe. • Check skills and knowledge,by asking them to demonstrate the skill or asking a good checking question. • Ask them to return if they have questions, or are confused or concerned about how to give care. • Make sure they know when and who to call for help. Let them know how you can provide back-up to their home care.
Teach family or community care provider how to give pain medications.	• Explain frequency and importance of giving regularly – do not wait for the pain. • The next dose should be given before theprevious dose wears off. • Write out the instructions clearly.
Advise the family or community care provider on additional methods for pain.	• Emotional support • Physical methods: touch (stroking, massage,rocking,vibration); ice or heat;deep breathing. • Cognitive methods: distraction, music,imagery. • Prayer (respect patient's practice)
Teach family to give oral morphine. • Give oral morphine • How to give small amounts with a syringe: • How to deal with side effects that may occur:	Oral morphine is a strong painkiller, which is only available from specially trained health workers. If the sick person has been prescribed oral morphine: • At the dose prescribed • Every 4 hrs very regularly (by the clock or by sun/moon estimates) – do not wait for the pain • Give a double dose at bedtime • If the pain is getting worse,or if pain occurs before the next dose is due, givean extra dose and inform the health worker – the regulardose may need tobe increased • Prevent constipation in all patients except those with diarrhoea – give local remedies or a laxative such as senna • Pour a smallamount into a cup • Draw up the exact dose intoa syringe using mlmarks • Drop the liquid from the syringe into the mouth (no needle on the syringe) • **Nausea:** this usually goes away after a few days of morphine and does not usually come again • **Constipation:** see page on constipation • **Dry mouth:** give sipsof water • **Drowsiness:** this usually goes away after a few days of morphine. If it persists or gets worse,half the dose and inform the healhth worker. • **Sweating or muscle jerks:** tell the health worker

6. Special advice for terminal care

6.1. Preparing for death

- Encourage communication in family
- Discuss worrying issues such as custody of children, family support, future school fees, old quarrels, funeral costs
- Tell the patient they will be loved and remembered
- Talk about death if the person wishes to
- Make sure patient gets help with feelings of guiltor regret
- Connect with spiritual counsellor or pastoral care as patient wishes

6.2. Presence

- Be present with compassion
- Visit regularly, hold hand, listen, converse

6.3. Caring

- Provide comfort measures
- ·Moisten lips, mouth, eyes
- Keep patient clean and dry; skin care
- Treat fever and pain (around the clock if necessary)
- Control other symptoms with medical treatment as needed
- Provide liquids, small amount of food as needed
- Provide physical contact

7. Referral

- The regional AIDS centre will be the coordinating institution to refer the patient to palliative care providers – according to what is required
- Other disciplines and partners will contact the (regional) AIDS centre to initiate the referral process
- NGOs will be active partners of the (regional) AIDS centres in the referral services and the actual provision of palliative care
- Referral should be a 2-way mechanism to re-evaluate the conditions and refer to curative care, if needed
- In case the patient is on ART and any other treatment, such as substitution therapy, continued monitoring needs to be ensured (see ART protocol)

8. Monitoring and Evaluation

Monitoring and evaluation will be undertaken to:

a. Ensure follow up
b. Ensure proper planning and budgeting

Reporting will at minimum include:

- No of patients in need of and receiving palliative care
- Presenting signs and symptoms
- Referrals
- Health care need
- Resource needs

VI. Prevention of HIV infection in infants and young children (PMTCT)

1. Key policy issues

- Protocol is created within the framework of the strategy for the elimination of HIV infection in infants in the European Region, indicated by a) less than one HIV infection in infants per 100'000 live births, and b) less than 2% of infants born to HIV infected women acquiring HIV infection by the end of 2010, by which time the United Nations General Assembly Special Session (UNGASS) on HIV/AIDS committed to reduce the proportion of infants infected with HIV by 50 per cent,
- Political commitment of a country's government is crucial for implementation of the strategy for the elimination of HIV infection in infants at country level
- Efforts are required to reduce stigma and discrimination of HIV infected women in health care settings and the community
- Protection of the rights of HIV infected women and children born to them should be ensured
- All medical records, whether or not they involve HIV-related information, should be treated in accordance with appropriate standards of confidentiality. Only health-care professionals with a direct role in the management of patients or clients should have access to such records, and only on a "need-to-know" basis
- PMTCT is part of continuum of care for HIV infected women and their children and should be linked with other relevant governmental and non-governmental services (AIDS centres, paediatric out-patient district clinics, Harm Reduction services, psycho-social support, and child protection services etc.)

1.1. Minimum standard:

- HIV testing in women's consultations should be voluntary and although the process of obtaining informed consent may vary, all those offered the test should receive sufficient information and should be helped to gain an adequate understanding of what is involved
- HIV infected pregnant women should have informed choice between giving birth and termination of pregnancy based on information on risk of MTCT and available interventions to reduce it
- HIV infected pregnant women should not be forced to undergo termination of their pregnancy
- ARV prophylaxis of MTCT should be available for all HIV infected pregnant women before, during and after delivery, regardless of their stage of HIV/AIDS, and to their newborns as well, according to a schedule which seeks to ensure maximum efficacy and remains feasible. Early diagnosis of HIV infection in newborns by using PCR should be available.

1.2. Hard-to-reach women (injecting drug users, sex workers)

- Women's consultation centres should initiate, play leading role in close collaboration with out-reach services of NGOs so to attract pregnant women who practice risky behaviour, to early antenatal services
- Women - sex workers and injecting drug users should not be discriminated against and should have equal rights with other women in accessing and obtaining PMTCT services

2. Initial assessment of pregnant women in women's consultation centres

- HIV testing and counselling should be routinely offered. Pre-test counselling or in-depth information provision should be provided to all women. Even if result is negative, the woman should be provided the test result with prevention information and services for prevention (e.g. condom provision). If the result is positive, confirmation of initial test and result provision with post-test counselling should be provided according to HIV Testing and Counselling protocol
- Blood samples from pregnant women for HIV antibodies' test should be send to relevant laboratory (refer to HIV Testing and Counselling protocol)
- Firstly identified HIV infected women in women's consultation centres should be examined in collaboration with specialist on HIV treatment and care from AIDS centres. Prophylaxis/treatment options should be based on clinical and immunological assessment
- Counselling on risk of MTCT, informed choice of continuation or termination of pregnancy, disclosure, safer sex (refer to Testing and Counselling protocol)
- Counselling and initiation of ARV prophylaxis after information on risks and benefits

3. Course of action in women's consultation centres and maternities

Administration of ARV regimens should be considered in close collaboration with AIDS centre

3.1. Clinical scenarios for ARV regimens for PMTCT

CLINICAL SCENARIOS	GESTATION AT PRESEN-TATION	ARV REGIMENS FOR WOMAN DURING PREGNANCY AND IN LABOUR	POSTPARTUM MOTHER AND INFANT	COMMENTS	RECOMMENDATIONS FOR DELIVERY
a) Woman does not need treatment for own health (asymptomatic)	<28 weeks	1) ZDV+3TC+SQV/r[2] if available, started from 28 weeks	**Mother:** Stop all three drugs after delivery **Infant:** • oral ZDV syrup 4 mg/kg body weight every 12 hours for 1 week[3] OR • single dose NVP 2mg/kg body weight after birth OR • both	• Doses of ARV drugs used in pregnancy are the same as for non-pregnant adults. • Adherence to the regimen could be more problematic because of pregnancy associated complications (nausea etc)	Elective caesarean section at 38 weeks of pregnancy[4]
		2) ZDV from 28 weeks • throughout pregnancy and labour (oral ZDV 300mg twice daily) plus single-dose 200mg NVP at onset of labour	**Mother:** Stop ZDV after delivery **Infant:** • oral ZDV syrup 4 mg/kg body weight every 12 hours for 1 week[3] OR • single dose NVP 2mg/kg body weight after birth OR • both	This regimen could be used if triple combination is unavailable, not feasible, not tolerated or rejected by women	
		Alternatives (NVP-sparing regimens)[5]			
		ZDV alone from 28 weeks, continue same dose in labour	**Mother:** Stop ZDV after delivery **Infant:** oral ZDV syrup 4 mg/kg body weight every 12 hours for 1 week[3]		

[2] If SQV/r is not available and women not co-infected with TB – NFV could be considered as an option
[3] If mother received < 4 weeks of antenatal ARV prophylaxis then need to consider longer infant prophylaxis up to 4 weeks
[4] If viral load test available and less then 1000 copies per ml, vaginal delivery could be considered
[5] Concerns about development of resistance after single-dose NVP in labour, which could limit choices ARV for women when she will need it

		ZDV 300 mg PLUS 3TC 150 mg oral twice daily from 36 weeks	**Mother:** Stop ZDV+3TC after delivery **Infant:** oral ZDV syrup 4 mg/kg body weight PLUS 3TC syrup 2 mg/kg every 12 hours for 1 week[3]	This regimen could be considered for women presented after 34-35 weeks gestation and without access to PI	
b) Pregnant woman needs treatment for own health (triple ARV not available)	Any time	Same recommendations as in clinical scenario A	**Mother:** Start ARV treatment of women as soon as drugs become available **Infant:** As for all babies, according to MTCT prevention regimen	• MTCT prophylaxis received, if any, does not effect choice of 1st – line ARV regimen	Elective caesarean section at 38 weeks of pregnancy[3]
c) Pregnant woman needs treatment for own health	Any time	ZDV[6]+3TC+NVP[7]	**Mother:** Continue the same regimen **Infant:** • oral ZDV syrup 4 mg/kg body weight every 12 hours for 1 week[3] • single dose NVP 2mg/kg body weight OR • both	• Choice of ARV regimen as for non-pregnant adults with first line regimen recommended • Delay start of treatment until after the 1st trimester of pregnancy, unless severely ill • Proceed as for non-pregnant adults except EFV (avoid in 1st and 2nd trimester). • Start NVP[8] with the half dose for the first 2 weeks.	Elective caesarean section at 38 weeks of pregnancy[3]
d) Woman started ARV therapy before pregnancy for own health	Any time	• Continue current ARV regimen. Do not suspend drugs during first trimester. If women received EFV substitute to NVP or PI if in 1st or 2nd trimester. • If women on the 2nd line regimen: benefits outweigh potential risks. Keep on current regimen during pregnancy and labour.	**Mother:** • Continue same maternal ARV therapy after delivery **Infant:** • oral ZDV syrup 4 mg/kg body weight every 12 hours for 1 week OR • single dose NVP 2mg/kg body weight after birth OR • both	• Substitute EFV with NVP or PI, if presents in 1st or 2nd trimester • Don't use combination d4T/ddI[9]. Substitute one of components in combination with ZDV or other NRTI.	Elective caesarean section at 38 weeks of pregnancy[3]

[6] ZDV could be substituted for d4T in anemic women, or those who are intolerant for ZDV

[7] If CD4 cell count > 250, the risk of NVP-associated hepatotoxicity increased 12 times. Close monitoring leaver function test during first 18 weeks of NVP treatment is recommended.

[8] Stop NVP in case of NVP-associated toxicity, switch to PI OR continue ZDV alone

[9] Use of combination d4T/ddI during pregnancy associated with increased risk of fatal lactic acidosis

e) Woman presents in labour with known HIV positive status or positive rapid HIV test	During delivery	**NVP prophylaxis** • During labour single 200 mg oral dose NVP at onset of labour[9]	**Mother:** • Evaluation of the health status **Infant:** • oral ZDV syrup 4 mg/kg body weight every 12 hours for 4 weeks and single dose NVP 2mg/kg body weight at 72 hours[10]	If women presents in labour with unknown HIV status, rapid HIV testing with postpartum counselling should be an option	• Spontaneous vaginal delivery • Avoidance of invasive obstetrical procedures such as fetal scalp monitoring and episiotomy
f) TB and pregnant and require ARV treatment		Refer to TB/HIV guidelines			Elective caesarean section at 38 weeks of pregnancy[3]

[10] If mother misses NVP dose, or takes NVP < 2h before delivery, then two NVP doses for infant: 1st dose immediately after delivery, 2nd dose at the age of 72 hours

3.2. Case management of HIV infected pregnant women who are active IDUs, in maternity homes

- Assessment of drug use status
- Substitution treatment (methadone or other opioids) provided by obstetrician in consultation with IDU specialist during all period of staying in a maternity
- Treatment of withdrawal syndrome in newborn, provided by neonatologist.

4. Referrals needed

4.1. Women's consultations

- HIV infected women should be referred to support groups of PLWHA
- HIV infected women who inject drugs should be referred to Harm Reduction services.

4.2. Maternity

- Women should be referred to district outpatient clinic for continuum of care and to AIDS clinic for follow up regarding HIV/AIDS
- Referral to women's consultation centres for post-partum family planning
- Newborns should be referred to paediatric out-patient clinics and/or AIDS centre for continuum of care
- Detailed report on ARV regimens received by mother and her newborn in maternity should be sent to AIDS centre and district paediatric outpatient clinic for follow up.

5. Follow-up schedule for newborns in maternity

5.1. Immunization

- All HIV-exposed children should be immunized with BCG in maternity on the same schedule as HIV non-exposed infants

5.2. Infant feeding

- All mothers should receive counselling on risks of transmission through breastfeeding and recommendations to provide appropriate replacement feeding
- When using replacement feeding, it should be stressed not to breastfeed at all
- Health workers should check that mothers understand how to safely prepare and give the formula
- Mothers should be counselled for a follow-up visit to paediatric outpatient clinics within two weeks after birth to check and ensure that there are no feeding problems

6. Follow-up schedule for HIV-exposed and HIV-infected infants

Basic care for HIV exposed infants and children should be provided in paediatric outpatient clinics and AIDS centres.

Regular follow-up is essential for children born to HIV-infected women, since they are at increased risk of morbidity and mortality, regardless of infant HIV infection status.

6.1. Follow-up visits are recommended at…

- Birth;
- Age 1 to 2 weeks;
- Age 6, 10 and 14 weeks;
- After age 14 weeks, monthly through age 12 months; and
- After age 12 months, every 3 months through 24 months

6.2. During follow-up visit

- Assess for common illnesses and manage appropriately
- Assess if non-specific symptoms or conditions that could be related to HIV infection are present
- Test for HIV infection, when appropriate
- Conduct health promotion and prevent illness:

- Monitor growth and development;
- Check immunisation status, and immunize if needed;
- Provide prophylaxis to prevent PCP, if appropriate;
- Screen for TB
- Look for and treat anaemia;
- Counsel the caregiver(s) on infant feeding/nutrition and other care needs as appropriate

6.3. HIV diagnostic testing

- HIV DNA PCR test should be performed first time within 48 hours after birth (don't test the umbilical cord blood because of possible risk of contamination with maternal blood) and if negative do a second test at age of 3 months for final diagnosis of HIV. A positive test indicates probable HIV infection, but should be repeated on a second specimen to confirm the result and obtain a definitive diagnosis of HIV infection.
- If PCR is not available recommended HIV antibody test at the age 15-18 months: if positive result child is infected and if negative – non-infected. For breastfeeding infant test if the test is negative at 18 month, it should be repeated 6 months after complete weaning (or earlier if symptoms suspicious for HIV infection are present)

HIV diagnostic testing for infant should be accompanied with counselling for caregivers, explaining the possible test results, need for additional test to definitively determine infection status of the child.

6.4. PCP prophylaxis

- PCP prophylaxis is recommended for all infants born to HIV infected mothers for at least 6 months or preferably until HIV infection can be ruled out. It should be started at age of 4-6 weeks. The recommended regimen is as follows: oral TMP/SMX 150/750 mg/m^2/day (divide BD) dose three days/week (Mon, Tues, Wed, i.e., consecutive days). At 2 and 4 months evaluate for adherence and tolerance. If adherence is not assured recommend daily administration of the same dose.
- Prophylaxis should be continued for children found to be HIV-infected until age 12 months.
- For HIV-infected children over 12 months, prophylaxis should be started and continued indefinitely if the child has symptoms of HIV disease, CD4+ percentage <15% (when available), or has had prior episode of PCP

6.5. Immunization

- All HIV-exposed children should be fully immunized according to their age
- Children of known status or with suspected infection should be given all appropriate vaccines according to the national schedule, including BCG
- HIV-infected children should be given as early as possible after the recommended age of vaccination
- Only 3 contraindications to immunization:
  1. children with symptomatic HIV infection or AIDS should not receive BCG (but should receive all other immunizations)
  2. children who have had shock or convulsions within 3 days of receiving DPT, should not receive subsequent DPT, and should have DT vaccine substituted for DPT
  3. children with recurrent convulsions or who have active central nervous system disease should not receive DPT and have DT substituted

7. Monitoring and Evaluation

See Part 2 "Monitoring prevention mother-to-child HIV transmission".

VII. Antiretroviral treatment of children with HIV/AIDS

1. Policy statement

Since 1996 we are observing a dramatic improvement of health of children with HIV infection in the countries of North America and Western Europe. It became possible due to specific interventions which include wide implementation of clinical and laboratory monitoring tools, introduction of highly active antiretroviral therapy (HAART) and increased capacity to diagnose and manage HIV infection in children. Mother to child transmission of HIV virus is the main source of HIV infection in children of the eastern Europe. An increasing number of reported paediatric AIDS cases in the countries demands pressing actions to improve survival and quality of life in children.

The policy for ART in paediatric cases should be based on following statements:

- ARV treatment should be available and be part of comprehensive package of paediatric HIV care
- It should be consistent with protocols for prevention of mother to child HIV transmission and follow up for infant born to HIV infected mother.
- Pediatricians should provide routine care, with referral to an HIV specialist for monitoring of HIV status and ART.
- ART should be initiated and followed according to protocols on using ARV in paediatric patients.
- Assurance of an adequate and uninterrupted supply of quality ARV drugs

Initiation and sustain of HAART in paediatric patients should be based on detailed recommendations from the WHO guidelines on scaling up of use ARV therapy in resource poor settings with adaptation to country's peculiarities. This objective could be achieved through Regional and/or National technical working-groups that define and regularly update technical recommendations and clinical protocols regarding antiretroviral regimens, monitoring procedures and management of HIV infection in children.

Because the care of HIV-infected children receiving ART is complex, these children's caregivers should have ready access to health care providers to discuss medical problems. A coordinated family-centered comprehensive care team of physicians, nurses, psychologist, and social workers facilitates the treatment of these patients and the work of the caregiver. That would help to reduce stigma and discrimination, be more accessible and provide a more holistic approach to the children health in a safe, confidential and comfortable environment.

2. ART goal

The goal of combination antiretroviral therapy in paediatrics is to preserve and recover the immune system, which prevents the clinical disease progression. This goal could be achieved by maximum suppression of HIV replication in the child's body.

3. Child assessment and counselling caregiver before starting ART

Regular follow-up is essential to monitor growth, morbidity and mortality. Follow-up visits with the health care provider for HIV-positive children during the first 2 years of life are recommended for the same intervals as for an HIV-exposed children of unknown HIV status. The proposed follow-up schedule will help to identify children who meet the criteria for

starting ART and improve therapy outcomes:

- Birth
- Age 1 to 2 weeks
- Age 6, 10 and 14 weeks
- After age 14 weeks, monthly through age 12 months
- After age 12 months, every 3 month through 24 months
- After age 24 months, every 6 months unless HIV symptoms developed and required more frequent visits.

Before starting ART every child should be carefully assessed and his/her health status should be discussed within the comprehensive care team. Team members include paediatrician, HIV specialist, trained nurse, psychologist and social worker. Collaboration with community volunteers including people leaving with HIV/AIDS should be proposed to the extend possible, and their support should be offered to families with HIV infected children.

3.1. Identification of the individual

Provided by nurse.
It includes information about date of birth, sex, address, education, information about caregivers.

3.2. Anthropometrical measurements

Provided by nurse.

- Measure the ***weight***, write it down and plot it on a growth chart (weight for age). Weight is a milestone for the treatment follow up. Therefore correct measurements are very important.
- Measure the ***height/length***, write it down and plot it on a growth chart (weight for height). Up to 2 years old the length is measured when the child is lying down. If the child is older than 2, the height is measured in upright position.
- Measure the ***head circumference*** for children younger than 2 years old.

Some remarks:
- For short-term follow-up: use weight for height.
- For long term follow the weight for age
- Height for age is used for a very long-term follow up.
- Indicate the date of record on the growth chart.
- Correct measurements are very important: take off shoes etc.

3.3. Nutrition assessment

Provided by nurse, physician with possible involvement of social worker.

Start with assessment of dietary intake and feeding history. Actual food intake from a 24-hour patient diet recall (a recall determines what the patient normally eats and/or ate in the last 24 hours) or a 3-day food intake record (which is a written record the patient or caretaker keeps) is valuable for an assessment of nutrient intake and the adequacy of intake. It is important to interview the patient/caretaker to find out the types of foods/formulas/fluids/breast milk consumed and estimated amounts. The length of time it takes the patient to eat, their appetite, any chewing, sucking or swallowing problems, nausea, vomiting /diarrhea, abdominal pain, any feeding refusal, food intolerance, allergies and fatigue are also important information. Identify caregiver who feeds the child and provides the food for the child.

If malnutrition is present identify the cause of it. Discuss possible health problems or social causes of child malnutrition. Start treatment or refer to the hospital sever malnourished child. After discharge from hospital follow up the case in outpatient department.

3.4. Social status assessment

Performed by nurse and/or social worker and/or community volunteer.

A caregiver should be identified and the home visit should be performed to assess the general living conditions. The house should be checked for general hygiene and access to safe water, the availability of fridge and identification the secure place for drug storage. Identify the family relationship and caregiver ability to be adherent to treatment protocol. All data should be recorded and attach to the case record before the decision to start treatment was made. If the problems were identified possible solutions should be proposed.

3.5. Psychological status assessment

Performed by psychologist or by physician

Both caregiver and child should be assessed to identify the need of special interventions and support in taken the decision on started ART. The group workshops should be the first step with followed group or individual sessions for support and encouraging both caregivers and children. Peer support from parents who already started their children on ART should be widely implemented as the affordable and an effective tool to achieve sustain results of treatment and improving the family's quality of life.

3.6. Counselling of a caregiver

Provided by nurse and physician.

Parents and/or other caregivers of HIV infected children prior to start ART should be counseled about:

- Infant feeding and nutrition for HIV-infected children, including optimal use of local foods, appropriate nutrition supplements, and nutritional management of HIV-related conditions that affect appetite and ability to eat. Infant feeding counseling should be provided..
- Prevention of infections, including administration of PCP prophylaxis, TB prophylaxis when required, and the importance of routine immunizations.
- When to seek care for illness of child, including the need for rapid evaluation and treatment for common illnesses in HIV-infected children.
- The importance of adherence to ARV therapy

3.7. Clinical exam

Provided by physician. Include assessment of signs and symptoms for HIV disease progression. Collect information about current and past HIV related illnesses and exposure to infectious diseases. Identification of co-existing medical conditions that may influence choice of therapy (such as TB) as well as current symptoms and physical signs. After examination the clinical stage of HIV disease should be identified and written in the case record specifying the date of diagnosis.

3.8. Lab tests to be done before starting on ARV

- Documentation about HIV diagnostic testing by PCR for children < 18 months, or ELISA/WB for children > 18 months old;
- Complete blood count (including haemoglobin, haematocrit, total lymphocyte count, trombocytes);
- Liver enzymes (ALT, AST);
- CD4 (absolute count and percentage for children < 6 years old) if available;
- Additional tests: bilirubine, creatinine, urinalysis, glucose.

3.9. History of previous child antiretroviral drugs exposure, including drugs used for prevention of mother to child transmission

If the mother has received ARV drugs during pregnancy, either for reducing risk of MTCT or for her own disease, there is a possibility that she may transmit resistant virus to her infant. This is particularly a problem when NVP or 3TC have been used as part of intrapartum prophylaxis regimen, as the resistance to these drugs can be induced rapidly by a single point mutation.

4. Criteria for starting ART

RECOMMENDATIONS FOR INITIATING ANTIRETROVIRAL THERAPY IN CHILDREN			
CD4 TESTING	**AGE**	**HIV DIAGNOSTIC TESTING**	**TREATMENT RECOMMENDATION**
If CD4 testing is available	<18 months	Positive HIV virologic test[1]	• WHO Pediatric Stage III (AIDS), irrespective of CD4 cell percentage[2] • WHO Pediatric Stage I disease (asymptomatic) or Stage II disease with CD4 percentage <20%[3]
		HIV virologic testing not available but infant HIV seropositive or born to known HIV-infected mother (Note: HIV antibody test must be repeated at age 18 months to obtain definitive diagnosis of HIV infection)	WHO Pediatric Stage III disease (AIDS) with CD4 cell percentage <20%
	>18 months	HIV antibody seropositive	• WHO Pediatric Stage III disease (AIDS) irrespective of CD4 cell percentage[2] • WHO Pediatric Stage I disease (asymptomatic) or Stage II disease with CD4 percentage <15%[3]
If CD4 testing is not available	<18 months	Positive HIV virologic test	WHO Pediatric Stage III[2]
		HIV virologic testing not available but infant HIV seropositive or born to known HIV-infected mother	Treatment not recommended[4]
	>18 months	HIV antibody seropositive	WHO Pediatric Stage III[2]

[1]HIV DNA PCR or HIV RNA or immune complex dissociated p24 antigen assays.

[2]Initiation of ARV can also be considered for children who have advanced WHO Pediatric Stage II disease including such as severe recurrent or persistent oral candidiasis outside the neonatal period, weight loss, fevers, or recurrent severe bacterial infections, irrespective of CD4 count.

[3]The rate of decline in CD4 percentage (if measurement available) should be factored into the decision-making.

[4]Many of the clinical symptoms in the WHO Pediatric Stage II and III disease classification are not specific for HIV infection and significantly overlap those seen in children without HIV infection in resource-limited settings; thus, in the absence virologic testing and CD4 cell assay availability, HIV-exposed infants <18 months of age should generally not be considered for ART regardless of symptoms.

- Acute infections should be treated before starting ART
- CD4 cell measurements, when available should be performed after resolution of any acute infection.

5. Drug regimen and dosage

5.1. First line regimen

The choice of first-line ARV regimens for children follows the same principles as in adults, with additional considerations about pharmacokinetic data and formulations available for children and infants (Annex 1)

Group distribution based on exposure to other drugs and co-existing medical conditions	ARV therapy regimen*
Not exposed to other drugs with potential for negative drug-drug interactions and resistance	AZT** (Zidovudine) + 3TC (Lamivudine) + NVP (Nevirapine) or EFV (Efaverenz) ***
Those who were exposed to NVP (Nevirapine) during PMTCT	AZT (Zidovudine) + 3TC (Lamivudine) + LPV/r or NFV (Nelfinavir)
TB/HIV co-infection****	AZT* (Zidovudine) + 3TC (Lamivudine + ABC (Abacavir) or EFV (Efaverenz) **
* Availability of appropriate formulations of ARV drugs (liquid forms for children <6 years old) that children can take in appropriate doses is an important issue. ** Don't start with AZT containing regimen if the child is anaemic *** For children older then 3 years **** ARV therapy should be defer until at least 2 months of intensive phase of antituberculous therapy has been completed, and, if deemed safe, until completion of all anti-TB therapy. This is to avoid interactions with rifampicin and all possible decreased adherence to ARV therapy and anti-TB medications. Early initiation of ARV treatment should be considered if an HIV infected child with TB has significant HIV symptoms and /or severe immunodeficiency.	

Anaemia in children

		Anaemia
Infant	6 months – 6 years	Hb < 7 g/dl
Child	7 – 12 years	Hb < 8 g/dl
Teen	> 12 years	Hb < 9 g/dl (Hct < 30%)

General statement

The ARV drug regimen may need to be changed for either treatment failure or toxicity. Switching ART regimen to another one should be done by the same responsible physician who initiated the ART with the first regimen. The patient and family should be reassessed for likelihood of adherence when a change is considered. If treatment failure is the case of switching for the new regimen, all 3 drugs should be changed simultaneously.

5.2. Second line regimen

PREVIOUS TREATMENT	**RECOMMENDED TREATMENT REGIMEN**
AZT (Zidovudine) + 3TC (Lamivudine) + NVP (Nevirapine) or EFV (Efaverenz)	ABC (Abacavir) + ddI (Didanosine) + LPV/r* or NFV
AZT (Zidovudine) + 3TC (Lamivudine) + NFV (Nelfinavir) or LPV/r	ABC (Abacavir) + ddI (Didanosine)+ NVP (Nevirapine) or EFV (Efaverenz)
*For children who can swallow capsules and for whom the current capsule formulations allow appropriate weight or body surface area calculated dosing, additional options include SQV/r, IDV/r ZDV/d4T should never be used together due to proven antagonism.	

6. Follow-up for children receiving ART

6.1. Follow-up visits

	TIME OF VISIT	WEIGHT/HEIGHT MEASUREMENT	EXAMINATION	LAB TESTS
1st follow up	2 weeks after ART start	+	+	Complete blood count, liver enzymes; urinalysis
2nd follow up	1 month after the 1st visit	+	+	Complete blood count, liver enzymes; urinalysis
Other[11]	Every 3 month unless need more frequent	+	+	Complete blood count; liver enzymes; CD4+ should be checked every 3-4 month unless needs more frequent

6.2. Monitoring clinical markers of effectiveness: height, weight, and morbidity

Healthy children grow normally (both in weight and height). Children with HIV and immune suppression stop growing. If children with HIV and immune suppression start ART, there is normally a rapid increase in growth.

- The ratio weight / height is a very sensitive indicator of treatment effectiveness and should be assessed using growth charts (may be the most important tools if CD4 cell assays are unavailable). If a child taking ART falls away from normal centiles on the weight / height chart we know there is a problem. Several conditions could be considered:
  - Development of OI. (This will show rapid curve decline on the weight / height chart)
  - Poor adherence to ART (This will show more slowly decline of the curve on the weight / height chart)
- Developmental milestones assessment;
- Neurological symptoms including signs of encephalopathy;
- Types and frequency of infections.

6.3. Monitoring laboratory markers

CD4+ cell count (if available); complete blood count; liver enzymes (ALT, AST) and additional tests based on ARV therapy regimen and drugs side effects.

6.4. Adapting the dose to the weight of the child

Every 3 months the HAART-drug doses of the child should be adapted according to the weight. Otherwise there is a risk of under dosage and development of resistance. Doses are calculated either on a milligram per kilogram or milligram per square meter body surface area basis, and standardization so that non-expert personnel can safely dispense correct doses to children is important.

6.5. Monitoring adherence

Provided by nurse, social worker, and physician.

Adherence could be counted by the formula:

N pills given – (minus) N pills received / (divided by) N pills patient should have taken in this period. Ideally it should be 100%. Good adherence means that the child takes >95% of the prescribed doses correctly.

To achieve good adherence several rules should be followed:

- First of all: **Identify a caretaker** for each child. Caregiver should be able to give everyday at the same time the drugs to the child, take the child to the hospital, pick up every month new batch of ARV medications from clinic.
- Discuss issues of drugs palatability. This is of particular importance in young children as refusal of or spitting out medications can lead to major difficulties with adherence and appropriate dosing.
- Develop adherence checklist for caregiver; identify the potential constraints for adherence. Discuss together with caregiver possible solutions.
- Consider all issues which could have an impact in adherence: e.g. sleep pattern, food habits, school schedule,
- Education on mechanisms how ARV drugs work in the body should be done for the child and the caregivers. It is necessary to let them understand the importance of compliance to the regimen in order to achieve a maximum drug benefit and to prevent the occurrence of drug resistance.
- If the diagnosis is disclosed to older children (usually after age of 7-8 years old), the adherence can improve. The

[11] If nevirapine containing regimen, closely monitor liver function every 4 weeks during first 18 months of treatment initiation

age, maturity, and social circumstance of these children must be taken into consideration, and disclosure should be done in a language and at a level that these children understand.

- Find out what the own believes of the caretaker (and the child) are.
- Give clear information about HIV, nutrition and medication to the caretaker and to the child.
- Use of **technical tools** to enhance adherence:
  - Medicines Week Planner
  - Developed a fairy tales, games about HIV, nutrition and HAART
  - Medicines boxes or houses
  - Alarm clock
- Try to establish a **'children's self support group'**. On scheduled basis children come 1 day to the hospital and play (educational) games together. Children learn they are not the only one with HIV, their caregivers talk with each other etc.

6.6. Monitoring and management of side effects

- In case drug adverse effects occur, they should be well explained to the caregivers and to the child. General measures include: providing symptomatic treatment, adapting drug regimen or giving simple reassurance in cases of known transient side-effect (Annex 2).
- All ARV drugs can cause nausea, vomiting or diarrhea early in therapy, but these effects are often transient.
- For most drugs, if side effects are still invalidating after 4-6 weeks of treatment, the best option is to change the drug - or the combination itself when the causing drug is difficult to identify (e.g. nausea caused by most drugs). When some severe side effects occur (e.g. hypersensitivity with ABC, pancreatitis) the causing drug should be rapidly stopped.
- Combinations of drugs presenting the same type of adverse effects should be avoided
- In case of development of severe life threatened side effects (Annex 3) patient should be immediately referred to the hospital with intensive care unit. Hospital staff should be able to provide appropriate syndromic care for children with ART adverse effects. If decision made to stop ART all drugs should be discontinued simultaneously.

7. Criteria to switch to second line ART regimen

7.1. Changing the regimen because of side effects

If a side effect occurs, change the responsible drug to another one. Never decrease the dose. Continue giving the other drugs. In case of liver toxicity due to NVP, stop all ARV until the ALT is normal or nearly normal. Then commence a different regimen (with EFV).

SIDE EFFECT	REGIMEN CHANGES
AZT anaemia	Change to d4T
NVP rash	Change to EFV

7.2. Changing the regimen due to therapeutic failure

Clinical signs of failure:

- Lack of growth response to treatment or falling off of growth with cross down two percentile curves in the weight in children who show an initial growth response to therapy;
- Loss of developmental milestones or development of encephalopathy;
- Recurrence of infections during the follow-up period (for example recurrent oral candidiasis refractory to treatment), or developed a new episode of opportunistic infection, or progress from Stage 2 to Stage 3.

Immunologic failure:

In areas where CD4 cells are available, immunologic failure could be confirmed by persistently declining CD4 cells, as measured on at least two separate occasions. Blood should be drawn the same time of the day. Measure not only absolute CD4 cell count but also percentage, because for children CD4 cell count (and to lesser extend CD4 percentage) normally decline with age in children until they reach adult levels at about age 8 years.

- CD4 percentage returns to (or below) pre-therapy baseline
- CD4 percentage falls >30% below peak value observed after 6 months or more of ART - for example, if the peak value was 40%, a drop to 30% or less indicates failure.

8. Criteria to discontinue therapy

8.1. Clinical

Severe life threatening side effects: drug hypersensitivity reaction, severe rash; Stevens-Johnson, toxic hepatitis, pancreatitis, lactic acidosis, severe peripheral neuropathy.

8.2. Social

Patient (caregiver) did not appear on any of the follow-up visits (missed more then 3 visits).

Patronage nurse informs about non-adherence of the caregiver (mother) and there are no alternative sustainable caregivers (i.e. grandparents).

References:

1. Antiretroviral treatment in MSF projects, Germaine Hanquet, Médecins Sans Frontières, 2001
2. Clinical care for HIV-positive children in Phra Chom Klao Hospital Pethburi, Thailand. MSF-B, *Mieke Ponnet, Koen Frederix and David Wilson,* 2002
3. Penta Guidelines for the use of Antiretroviral Therapy in Paediatric HIV Infection – 2001, Sharland M, Castelli G, Ramos JT, Blanche S. Gibb DM.
4. WHO Guidelines “SCALING UP ANTIRETROVIRAL THERAPY IN RESOURCE LIMITED SETTINGS: GUIDELINES FOR A PUBLIC HEALTH APPROACH”, 2003
5. Bartlett JG . The Johns Hopkins Hospital 2000-2001 Guide to Medical Care Of Patients With HIV Infection. Philadelphia: Lippincott, Williams & Wilkins, 2000.
6. Braunwald E, Fauci AS, Isselbacher KJ, et al. Harrison's Principles of Internal Medicine. New York: McGraw Hill, 2000.

APPENDIX VII-A.
Summary of drug dosages and toxicity

NAME OF DRUG	*DAILY DOSE (FREQUENCY)*	MAJOR TOXICITY'S	OTHER COMMENTS
NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS			
Zidovudine (ZDV, AZT)	• Oral 360 mg/m^2/day (divide BD) • Neonatal dose 2mg/kg q hourly • IV 120 mg/m^2 6 hourly or 20 mg/m^2/hour	Neutropenia; anaemia; nausea; headaches; myopathy (rare)	• Large volume of syrup not well tolerated in older children. • Needs storage in glass jars and is light sensitive • Can give with food • Double dose for HIV encephalopathy • Do not use with d4T (antagonistic antiretroviral effect)
Didanosine (ddI)	• 240 mg/m^2 / day (daily or BD) • Adolescents (<60 kg 250 mg OD; > 60 kg 200 mg BD or 400 mg OD) • Enteric Coated 125/250/400 mg capsules OD for older children	Pancreatitis rare (dose related); peripheral neuropathy rare (dose related); diarrhoea and abdominal pain.	• Constituted suspension stable for 30 days in fridge. • Ideally taken 1 hour before food or two hours after, but may be less important in children. • Suspension must be shaken well before taken
Stavudine (d4T)	• 2mg/kg/day (up to 30 kg) (divide BD) • Adolescents (<60 kg 30 mg BD; > 60 kg 40 mg BD)	Headache, GI upset, rash, Peripheral neuropathy and pancreatitis (rare)	• Large volume of suspension; capsules opened up well tolerated. • Keep solution refrigerated. Stable for 30 days. Can give with food.
Lamivudine (3TC)	• 8mg/kg/day (divide BD) • In neonates < 30 days 4mg/kg/day given 12 hourly • >60kg 150mg (BD)	Headache, abdominal pain, pancreatitis, peripheral neuropathy, and neutropenia, abnormal liver function tests - all rare	• Well tolerated • Can give with food • Store solution at room temperature (use within one month of opening)
Abacavir (ABC)	• 16mg/kg/day (divide BD)	1-3% may develop hypersensitivity reaction, fever, malaise, mucositis +/- rashes, usually in first 6 weeks STOP DRUG - DO NOT RECHALLENGE.	• Can be given with food. • Syrup well tolerated or crush tablets. • MUST WARN PARENTS ABOUT HYPERSENSITIVITY REACTION.
NON NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS			
Nevirapine (NVP)	3-400 mg/m^2/day (divide BD). Start at 150-200 mg/m^2/day once daily for 2 weeks then escalate to 3-400 mg/m^2/day if no rash.	Rash 10-20% can treat through, Stevens-Johnson very rare, but STOP drug. Monitor liver enzymes. Induces cytochrome P450. Note possible drugs interactions. Decreases concentrations of most PI	• Store suspension at room temperature • Can be given with food • Must warn parents about rash. Do not dose escalate if rush occurs
Efavirenz (EFV)	• Limited PK in <3 years. • 15mg/ kg or • 10-15 kg - 200 mg; 15-20 kg - 250 mg;	Rash (mild). CNS toxicity's, somnolence, abnormal dreams, "Spacey kids". Drug interactions.	• Syrup available. • Capsules may be opened and added to food but have very peppery taste; however can mix with sweet foods or jam to disguise taste.

	20-25 kg - 300 mg; 25-33 kg - 350 mg; 33-40 kg - 400 mg; > 40 kg - 600mg OD • Syrup increase dose.		• Can give with food but avoid high fat meals, which increase absorption by 50%. • Best given at bedtime, especially, first 2 weeks, to reduce central nervous system side effects
PROTEASE INHIBITORS			
Indinavir (IDV)	• Do not use in neonates. • 500mg/m2 /dose given 8 hourly. • Adult 800 mg every 8 hours.	Nausea; hyperbilirubinaemia (10%) Renal stones/nephritis (4%); haemolytic anaemia, liver dysfunction rare. Abnormal lipids	• Do not take with meals. Formula for syrups available. • Advise fluid intake but not Coke.
Ritonavir (RTV)	• 800mg/m2/day (divide BD) • Start with 250mg/m2 /dose 12 hourly & increase over 5 days. • Infants 900 mg/m2/day. (Syrup 80 mg/ml)	GI intolerance ++, headache; increase liver enzymes; increase bleeding in haemophiliacs, abnormal lipids.	• Take with food but liquid tastes bitter. • Can help to take with peanut butter and follow with chocolate sauce or cheese. Note drugs interactions.
Saquinavir (SQV), if body weight > 25kg	• 150 mg/kg/day (divide TDS)	Rash; headache; GI upset; diabetes Abnormal lipids	• Give with food. • Sun photosensitivity.
Nelfinavir (NFV)	• 110-120mg/kg/day (divide BD) • Adolescents need > than adult doses • Crush tablets; Powder available • Infants 150 mg/kg/day	Mild /moderate diarrhoea Vomiting; rash; Abnormal lipids. Drug interactions.	• Powder is sweet, faintly bitter, but gritty and hard to dissolve; must be reconstituted immediately prior to administration in water, milk, formula, pudding, etc – do not use acidic food or juice (increases bitter taste). • Because of difficulties with use of powder, use of crush tablets preferred (even for infants) if appropriate dose can be given. • Powder and tablets could be stored at room temperature. • Take with fatty food.
Lopinavir/ritonavir, (LPV/r)	• 450/112.5 – 600/150 mg/m2/day (divide BD). • Higher dose used with NNRTI. (syrup 80/20 mg/ml)	Rash (2%), GI intolerance, abnormal lipids.	• Liquid formulation – low volume bitter taste. Capsules large. • Preferable oral solution and capsules should be refrigerated; however could be stored at room temperature up to 25^0C for 2 months. • Should be taken with food.
Amprenavir (APV)	• 40mg/kg/day (divide BD) capsules • Increase dose for syrup	GI upset. Abnormal lipids	• Large volume of syrup – bitter taste. • Capsules either large size (200 mg) or need to take many small (50 mg).

APPENDIX VII-B. Management of common side effects during ARV treatment

DRUG	SIDE EFFECTS	COMMENT	WHAT TO DO
AZT	**GI symptoms:** Nausea, vomiting, diarrhoea	Minor degrees are quite common, but almost always improve during the first month of treatment.	Explain this side effect well to the child and caretaker
	CNS symptoms: Headache, muscle pains, fatigue, insomnia	90% of patients can tolerate these side effects	If it is impossible to tolerate, switch to d4T
	Finger-nails become dark	Does not affect the skin	Try to ignore it
3TC	Well tolerated		
d4T	Well tolerated		
EFV	**CNS symptoms:** Dizziness, insomnia, abnormal dreams, personality change	These side effects are **NOT common** in children.	Give the drug at bed time
NVP	**Liver toxicity**	Follow up SGPT on 2 weeks, 1 month and every 3 months	If ALT elevated >200 IU, stop all ARV, wait until SGPT falls and then start with a new regimen with EFV
	Rash	Mild: macules, papules or dry desquamation	Continue NVP, but do not escalate dose until rash resolves. Explain this side effect well to the child and caretaker
		Sever: vesicles, ulceration, moist desquamation or mucous membrane involvement	Stop NVP and switch to EFV
NFV	**Diarrhoea**	Usually watery stools 1-3 times a day	Keep the child well hydrated

APPENDIX VII-C.
Clinical signs, symptoms, monitoring and management of symptoms of serious adverse effects of antiretroviral drugs that require drug discontinuation

ADVERSE EFFECT	POSSIBLE OFFENDING DRUG(S)	CLINICAL SIGNS/SYMPTOMS	MANAGEMENT
Acute hepatitis	NVP; EFV less common; more uncommon with AZT, ddI, d4T (<1%); and protease inhibitors (PI), most frequently with RTV	Jaundice, liver enlargement, gastrointestinal symptoms, fatigue, anorexia; NVP associated hepatitis may have hypersensitivity component (drug rash, systemic symptoms, eosinophilia)	• If possible, monitor ALT, AST, bilirubine • All ARV should be stopped until symptoms resolve • NVP should be permanently discontinued
Acute pancreatitis	ddI, d4T; 3TC (infrequent)	Nausea, vomiting, and abdominal pain	• If possible, monitor serum pancreatic amylase, lipase • All ARV should be stopped until symptoms resolve • Restart ART with change to different NRTI, preferably one without pancreatic toxicity (e.g., AZT, ABC).
Lactic acidosis	All nucleoside analogue reverse transcriptase inhibitors (NRTI)	Initial symptoms are variable: a clinical prodromal syndrome may include generalized fatigue and weakness, gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal pain, hepatomegaly, anorexia, and/or sudden unexplained weight loss), respiratory symptoms (tachypnea and dispnea) or neurologic symptoms (including motor weakness).	• Discontinue all ARV; symptoms may continue or worsen after discontinuation of ART. • Supportive therapy. • Regimens that can be considered for restarting ART include a PI combined with an NNRTI and possibly ABC.
Hypersensitivity reaction	Abacavir (ABC) and Nevirapine (NVP)	ABC: Constellation of acute onset of symptoms including fever, fatigue, myalgia, nausea/vomiting, diarrhea, abdominal pain, pharingitis, cough, dyspnoea, (with or without rash). While these symptoms overlap those of common infectious illness, the combination of acute onset of both respiratory and gastrointestinal symptoms after starting ABC is more typical of a hypersensitivity reaction. NVP: Systemic symptoms of fever, myalgia, arthralgia, hepatitis, eosinophilia with or without rush.	• Discontinue all ARVs until symptoms resolve. • The reaction progressively worsens with drug administration and can be fatal. • Administer supportive therapy. • Do not rechallenge with ABC (or NVP), as anaphylactic reactions and death have been reported. • Once symptoms resolve, restart ARVs with change to different NRTI if ABC/associated or to PI- or NRTI-based regimen if NVP-associated.

Sever rash/Stevens/Johnson syndrome	Non nucleoside reverse transcriptase inhibitors (NNRTIs): NVP, EFV	Rash usually occurs during first 2-4 weeks of treatment. The rash is usually erythematous, maculopapular, confluent, most prominent on the body and arms, may be pruritic and can occur with or without fever. Life-threatening Stevens-Johnson syndrome or toxic epidermal necrolysis has been reported on 0.3% of infected individuals receiving NVP	• Discontinue all ARVs until symptoms resolve. • Permanently discontinue NVP for rash with systemic symptoms, such as fever, sever rash with mucosal lesions or urticaria, or SJS/TEN. • Once resolves, switch ART regimen to different ARV class (e.g., 3 NRTI or 2 NRTI and PI).
Sever peripheral neuropathy	ddI, d4T, 3TC	Pain, tingling, numbness of hands or feet; distal sensory loss, mild muscle weakness, and areflexia can occur.	• Stop suspect NRTI and switch to different NRTI that does not have neurotoxicity (e.g., ZDV, ABC). • Symptoms usually resolve in 2-3 weeks.

APPENDIX VII-D.
Interim Proposal for a WHO Staging System for HIV Infection and Disease in Children

Clinical Stage I:

1. Asymptomatic
2. Generalised lymphadenopathy

Clinical Stage II:

3. Unexplained chronic diarrhoea
4. Severe persistent or recurrent candidiasis outside the neonatal period
5. Weight loss or failure to thrive
6. Persistent fever
7. Recurrent severe bacterial infections

Clinical Stage III:

8. **AIDS defining opportunistic infections**
   - Candidiasis, esophageal or pulmonary (bronchi, trachea, lungs)
   - Coccidioidomycosis, disseminated (at site other than or in addition to lungs or cervical or hilar lymph nodes)
   - Cryptococcosis, extrapulmonary
   - Cryptosporidiosis or isosporiasis with diarrhea persisting > 1 month
   - Cytomegalovirus disease with onset of symptoms at age > 1 month (at a site other than liver, spleen, or lymph nodes)
   - Herpes simplex virus infection causing a mucocutaneous ulcer that persists for > 1 month; or bronchitis, pneumonitis, or esophagitis for any duration affecting a child > 1 month of age
   - Histoplasmosis, disseminated (at a site other than or in addition to lungs or cervical or hilar lymph nodes)
   - *Mycobacterium tuberculosis*, disseminated or extrapulmonary
   - *Mycobacterium*, other species or unidentified species, disseminated (at a site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)
   - *Mycobacterium avium* complex or Mycobacterium kansasii, disseminated (at site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)
   - Pneumocystis carinii pneumonia
   - Toxoplasmosis of the brain with onset at > 1 month of age

10. **Severe failure to thrive** in the absence of a concurrent illness other than HIV infection that could explain the following findings:

a) persistent weight loss > 10% of baseline OR
b) downward crossing of at least two of the following percentile lines on the weight-for-age chart (e.g., 95th, 75th, 50th, 25th, 5th) in a child ≥ 1 year of age OR
c) < 5th percentile on weight-for-height chart on two consecutive measurements, ≥ 30 days apart PLUS a) chronic diarrhea (i.e., at least two loose stools per day for ≥ 30 days) OR b) documented fever (for ≥ 30 days, intermittent or constant)

11. **Progressive encepahlopathy** (at least one of the following progressive findings present for at least 2 months in the absence of a concurrent illness other than HIV infection that could explain the findings):

a) failure to attain or loss of developmental milestones or loss of intellectual ability, verified by standard developmental scale or neuropsychological tests;
b) impaired brain growth or acquired microcephaly demonstrated by head circumference measurements or brain atrophy demonstrated by computerized tomography or magnetic resonance imaging (serial imaging is required for children < 2 years of age);
c) acquired symmetric motor deficit manifested by two or more of the following: paresis, pathologic reflexes, ataxia, or gait disturbance

12. **Malignancy**
   - Kaposi's sarcoma
   - Lymphoma, primary, in brain
   - Lymphoma, small, noncleaved cell (Burkitt's), or immunoblastic or large cell lymphoma of B-cell or unknown immunologic phenotype

13. **Recurrent septicaemia**

VIII. POST EXPOSURE PROPHYLAXIS

1. Policy statement

Post Exposure Prophylaxis (PEP) is short-term antiretroviral treatment to reduce the likelihood of HIV infection after potential exposure, either occupationally or through sexual intercourse or isolated high risk exposure. Within the health sector, PEP should be provided as part of a comprehensive universal precautions package that reduces staff exposure to infectious hazards at work.

The risk of exposure from needlesticks and other means exists in many settings where protective supplies are limited and the rates of HIV infection in the patient population are high. The availability of PEP may reduce the occurrence of occupationally acquired HIV infection in health care workers. It is believed that the availability of PEP for health workers will serve to increase staff motivation to work with people infected with HIV, and may help to retain staff concerned about the risk of exposure to HIV in the workplace.

PEP should also be provided to persons who acquired needle sticks in other than occupational settings (assault victims, e.g.). It also applies to IDUs accidentally exposed.PEP should also be provided after sexual exposure to the victims of sexual assaults.

2. Universal precautions

In the health care settings PEP should be a part of the broader approach to the prevention of occupational exposures to bloodborne pathogens. It is accepted that such strategy is based on the principles of universal precautions.

Universal precautions are infection control guidelines measures that reduce the risk of transmission of bloodborne pathogens through exposure to blood or body fluids among patients and health care workers.

Because it is not possible to identify all peoples who may be infected with bloodborne pathogens guidance to protect health care workers against HIV and hepatitis viruses has been issued based on the concept that all patients should be assumed to be infectious for bloodborne diseases.

Instead of relying on being able to identify "high risk" patients, the application of universal precautions requires that all blood and body fluids should be regarded as potentially infectious and appropriate protective action taken.

Health care workers (HCW): persons (e.g., employees, students, contractors, attending clinicians, public-safety workers, or volunteers) whose activities involve contact with patients or with blood or other body fluids from patients in a health-care, laboratory, or public-safety setting. The potential exists for blood and body fluid exposure to other workers, and the same principles of exposure management could be applied to other settings .

An exposure involves a percutaneous injury (e.g., a needle stick or cut with a sharp object); contact of mucous membrane or nonintact skin; or contact of intact skin with blood, tissue, or other body fluids when the duration of contact is prolonged (several minutes or more) or involves an extensive area.

Blood and other potentially infectious materials.

In the workplace, universal precautions should be followed when workers are exposed to blood and certain other body fluids, including:

- semen
- vaginal secretions
- any fluids contaminated with visible blood
- **HIV-containing cultures**
  or culture media all of which have been implicated in HIV transmission, and:

- synovial fluid
- cerebrospinal fluid
- pleural fluid
- peritoneal fluid
- pericardial fluid
- amniotic fluid

for which the risk of transmitting HIV has not yet been determined.

Universal precautions do not apply to:

- feces
- nasal secretions
- sputum
- sweat
- tears
- urine
- vomitus
- saliva (except in the dental setting, where saliva is likely to be contaminated with blood)

Universal precautions should be applied also to **any unfixed tissue or organ (other than intact skin) from a human (living or dead)** and **blood or tissues from experimental animals that have been infected with bloodborne pathogens, and to** all body fluids when it is difficult to identify the specific body fluid.

All medical institutions and all HCW should follow this rule.

2.1. Guidelines

Avoid the exposure routes that can transmit bloodborne infections, including:

- Accidental injuries with a contaminated needle or other sharp instruments.
- Exposure to infected blood or other body fluids via your mouth, eyes, nose, or open lesions on your skin, such as cuts, scrapes, dermatitis, or acne.
- Touching a contaminated environmental surface and then transferring the pathogen to a skin lesion or to the mucous membranes of the eyes, nose, or mouth.

Institute the following controls and protective equipment**:**

- Engineering controls that isolate or remove bloodborne pathogen hazards from the workplace (e.g., puncture-resistant, leak-proof sharps disposal containers that are placed near the point of use and replaced before becoming overfilled, self-sheathing needles and needleless IV access systems),
- Work practice controls that reduce the likelihood of exposure by altering the manner in which a task is performed (e.g., prohibiting needle recapping by the two-hand technique or bending, breaking or otherwise handling used needles),
- Personal protective equipment such as specialized clothing or equipment worn for protection against a hazard (e.g., gloves, liquid-resistant gowns, and face and eye protection).

2.1.1. Engineering Controls and Work Practices

Engineering controls (such as sharps disposal containers) isolate or remove bloodborne pathogens from the workplace. They are considered the first line of defense against occupational exposure to bloodborne pathogens.

Work practice controls, on the other hand, reduce the likelihood of exposure by altering the way in which a task is performed.

It is up to the employer to provide engineering controls and to inform the employee about appropriate work practice controls, but it is up to the employee to use them correctly.

To prevent transmission of bloodborne pathogens, an employee should take the following precautions:

- Avoid splashing, spraying, splattering, and generation of droplets of blood or other potentially infectious materials.
- Wash his/her hands immediately or as soon as feasible after he/she removes gloves or other personal protective equipment (PPE) or attire (PPA).
- Wash his/her hands and any other exposed skin with soap and water or flush mucous membranes with water immediately or as soon as feasible following contact of such body areas with blood or other potentially infectious materials.
- Wash his/her hands with soap and running water. If running water isn't available, use an appropriate antiseptic hand cleanser and clean towels or antiseptic towelettes, followed by regular handwashing as soon as feasible.
- Use a mechanical device that protects the hand or a safe one-handed technique if needle recapping or removal is determined to be absolutely necessary.
- Immediately or as soon as possible after use, discard contaminated reusable sharps in puncture-resistant, labeled or color-coded, and leakproof (side and bottom) containers until properly reprocessed.

- Position sharps disposal containers so that they are easily accessible and maintained upright throughout use.
- Replace sharps disposal containers regularly and don't allow them to overfill.
- Before moving a container of contaminated sharps, close it completely; place it in a secondary container if leakage is possible.
- Place potentially infectious specimens in properly labeled containers that will prevent leakage. Use a secondary container if the primary container becomes contaminated or punctured.
- Before servicing or shipping, decontaminate any equipment that is contaminated with blood or other potentially infectious materials. If decontamination is impossible, attach a label that states which portions of the equipment remain contaminated.
- Place all regulated waste in closable, leakproof containers.
- Handle contaminated laundry as little as possible, bag it in labeled bags or containers, and transport wet laundry in leakproof bags or containers.

In addition, he/she must:

- Not eat, drink, smoke, apply cosmetics or lip balm, or handle contact lenses in work areas where occupational exposure to bloodborne pathogens is likely.
- Not keep food and drink in refrigerators or other locations where blood or other potentially infectious materials are present.
- Never mouth-pipette/suction blood or other potentially infectious materials.
- Never use his/her hands to pick up broken glassware that may be contaminated.
- Not bend, recap, break, or remove contaminated needles and other contaminated sharps unless here is no feasible alternative or the action is required by a specific medical procedure.
- Never use his/her hand to reach into or to open, empty, or manually clean reusable sharps containers.

2.1.2. Personal Protective Equipment (PPE)

If the potential for occupational exposure remains after a HCW uses engineering and work practice controls, the employer must also provide PPE. This equipment must be provided in a readily accessible location and at no cost to you.

- Gloves (including special gloves if a HCW is allergic to conventional medical gloves)
  It is critical that a HCW wears gloves whenever he/she anticipates hand contact with blood and other potentially infectious materials or surfaces. Don't reuse single-use gloves or reusable gloves that show signs of deterioration. Do not use petroleum-based lubricants because they can eat through latex rubber gloves.
- Gowns/Laboratory Coats
  Wear outer garments in occupational exposure situations. Wear surgical caps or hoods and/or shoe covers or boots for protection only if you anticipate gross contamination of the head or feet.
- Face Shields/Masks/Eye Protection
  Wear chin-length face shields or masks combined with eye protection devices with side shields whenever splashes, spray, spatter, or droplets of blood or other potentially infectious materials may be generated. Regular eye glasses do not provide sufficient protection against bloodborne contaminants.

Personal protective equipment must not permit blood or other potentially infectious materials to pass through to or reach your work clothes, street clothes, undergarments, skin, eyes, mouth, or other mucous membranes under normal conditions of use and for the duration of time which the protective equipment will be used.

If a protective garment is penetrated by blood or other potentially infectious materials, should be removed it as soon as possible. Wash the affected area with soap and water. Remove all PPE prior to leaving the work area and place them in the designated receptacle. The employer is responsible for cleaning, laundering, repair, replacement, and disposal of used personal protective equipment.

2.2. Recommendation for the health care administration - ensuring adherence to universal precautions

2.2.1. Staff understanding of universal precautions

Health care workers should be educated about occupational risks and should understand the need to use universal precautions with all patients, at all times, regardless of diagnosis. Regular in-service training should be provided for all medical and non-medical personnel in health care settings. In addition, pre-service training for all health care workers should address universal precautions.

2.2.2. Reduce unnecessary procedures

Reduce the supply of unnecessary procedures: Health care workers need to be trained to avoid unnecessary blood transfusions (e.g., using volume replacement solutions), injections (e.g., prescribing oral equivalents), suturing (e.g.

episiotomies) and other invasive procedures. Standard treatment guidelines should include the use of oral medications whenever possible. Injectable medications should be removed from the national Essential Drug List where there is an appropriate oral alternative.
Reduce the demand for unnecessary procedures: Create consumer demand for new, disposable, single-use injection equipment as well as increased demand for oral medications.

2.2.3. Make adequate supplies available

Adequate supplies should be made available to comply with basic infection control standards, even in resource constrained settings. Provision of single use, disposable injection equipment matching deliveries of injectable substances, disinfectants and "sharps" containers should be the norm in all health care settings. Attention should also be paid to protective equipment and water supplies. (While running water may not be universally available, access to sufficient water supplies should be ensured.)

2.2.4. Adopt locally appropriate policies and guidelines

Use of sterilizable injection equipment should be discouraged, as evidence shows that the adequacy of the sterilization is difficult to ensure. National health care waste management plans should be developed. The proper use of supplies, staff education and supervision needs should be outlined clearly in institutional policies and guidelines. Regular supervision in health care settings can help to deter or reduce risk of occupational hazards in the workplace. If injury or contamination result in exposure to HIV infected material, post exposure counseling, treatment, follow-up and care should be provided.

3. Procedures for PEP

PEP should be provided in every medical institution where the risk of exposure exists.

It is necessary that a set of antiretrovirals and trained physicians are available.

Regional AIDS Centers serve as a referral centers to the medical institutions, and also provide post-sexual and non-occupational PEP.

3.1. Post Exposure Prophylaxis

3.1.1. Risks for Occupational Transmission

Following percutaneous exposure to HIV-infected blood, the average risk of transmission has been shown to be approximately 0.3% (95% confidence interval [CI], 0.2% to 0.5%). The risk following mucosal exposure is approximately 0.09% (95% CI, 0.006% to 0.5%).The risks of transmission following exposure of intact skin or exposure to body fluids other than HIV-infected blood have not been quantified. These risks may be higher if any of the factors associated with increased transmission are present.

Regular supervision in health care settings can help to deter or reduce risk of occupational hazards in the workplace. If injury or contamination result in exposure to HIV infected material, post exposure counseling, treatment, follow-up and care should be provided. Post exposure prophylaxis (PEP) with antiretroviral treatment may reduce the risk of becoming infected.

3.1.2. Exposures For Which PEP is Indicated

- Break in the skin by a sharp object (including both hollow-bore and cutting needles or broken glass-ware) that is contaminated with blood, visibly bloody fluid, or other potentially infectious material, or that has been in the source patient's blood vessel.
- Bite from an HIV-infected patient with visible bleeding in the mouth that causes bleeding in the HCW.
- Splash of blood, visibly bloody fluid, or other potentially infectious material to a mucosal surface (mouth, nose, or eyes).
- A non-intact skin (e.g., dermatitis, chapped skin, abrasion, or open wound) exposure to blood, visibly bloody fluid, or other potentially infectious material.

3.1.3. Managing Occupational Exposure to HIV

- First aid should be given immediately after the injury: wounds and skin sites exposed to blood or body fluids should be washed with soap and water, and mucous membranes flushed with water.
- The exposure should be evaluated for potential to transmit HIV infection (based on body substance and severity of exposure).
- PEP for HIV should be provided when exposure to a source person with HIV has occurred (or the likelihood that the source person is infected with HIV).
- The exposure source should be evaluated for HIV infection. Testing of source persons should only occur after obtaining informed consent, and should include appropriate counseling and care referral. Confidentiality must be maintained. The standard rapid HIV antibody tests should be used and the results of tests should be obtained as

quickly as possible.

- Clinical evaluation and baseline HIV testing of the exposed health care worker should proceed only after informed consent.
- Exposure risk reduction education should occur with counselors reviewing the sequence of events that preceded the exposure in a sensitive and non-judgmental way.
- An exposure report should be made.

3.1.4. Providing PEP ARV Treatment

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

- If the source patient is HIV negative no further post-exposure prophylaxis is necessary for the exposed health worker.
- If the exposed health worker is HIV positive no further post-exposure prophylaxis is necessary for the health worker, but the health worker should be referred for further counseling and management on a long-term basis for his/her HIV infection.
- If the health worker is HIV negative and the source patient is HIV positive then continue antiretrovirals for a period of four weeks and monitor the health worker for possible side effects of treatment; repeat the health worker's HIV tests at 1, 3 and 6 months after the initial test, if the health worker should seroconvert during this time then provide appropriate care and counseling and refer for expert opinion and long term treatment. If the health worker's HIV status remains negative provide appropriate counseling for him/her to remain negative.
- If it is not possible to determine the HIV status of the source patient then assume that the source is positive and proceed according to guidelines in the previous bullet.
- Advise on the need to use condoms for 6 months after the injury.
- Determine the health worker's hepatitis B virus immune status and if non-immune, institute hepatitis B virus passive and active specific prophylaxis, if appropriate.

3.2. Post-sexual exposure prophylaxis

The risk of sexual exposure was estimated as 0.1% to 3% for receptive anal intercourse, 0.1% to 0.2% for receptive vaginal intercourse, and 0.03% to 0.09% following insertive vaginal intercourse. Recent studies suggest that it can be even lower, especially when the HIV viral load is low.

There is not enough evidence to recommend prophylaxis against infection following casual sexual exposure. However in the event that there has been sexual abuse or rape then it is recommended that the victim be managed in the same manner as outlined in the section on post-occupational exposure prophylaxis described above. It is important to try and determine the HIV status of the perpetrator. If this is not possible then it may be assumed that the perpetrator is HIV positive and the victim is provided with the treatment as listed in the following paragraph.

In the event of rape it is important to arrange for counseling and support to be provided to the victim. The victim needs to be provided with information regarding STIs, pregnancy and legal matters.

- If the source is HIV negative or the victim is HIV positive then drug administration should be discontinued and the victim should be referred for further counseling and management on a long-term basis for his/her HIV infection.
- If the victim is HIV negative and the source is HIV positive or the source's HIV status is not determined then continue this regimen for 4 weeks.

3.3. Non-occupational HIV exposure (isolated high risk exposure) prophylaxis

There are certain situation in which an isolated high exposure can happen. They include (but are not limited to) accidental or criminal sticks with needles contaminated with blood. All the measures provided to HCW are also appropriate to this situation.

3.4. IMPLEMENTING PEP

3.4.1. Recommendations:

PEP should be initiated as soon as possible, ideally within 2 hours and no later than 72 hours post-exposure. The prescribing provider should ensure that the patient has access to the full course of ARV medications.

HAART is always recommended as the regimen of choice for at-risk exposures. The therapeutic regimen will be decided on the basis of drugs taken previously by the source patient and known or possible cross resistance to different drugs. It may also be determined by the availability of the various ARVs in that particular setting. In that case consultation with an HIV specialist or an occupational health clinician experienced in providing PEP is advised.

3.4.2. Indications for postexposure prophylaxis

A. Occupational HIV exposure
B. Non-occupational HIV exposure
- Isolated high risk exposure within last 72 hours
- Exposure to HIV positive or high risk sexual partner

3.4.3 Protocol: Medications

A. Start within hours of exposure (under 72 hours)
B. Triple therapy for 4 weeks
1. First two medications: AZT and 3TC
   a) Zidovudine (AZT) 300 mg PO bid and
   b) Lamivudine (3TC) 150 mg PO bid
2. Third medication (choose one PI)
   a) Nelfinavir 750 mg PO tid or
   b) Nelfinavir 1250 mg PO bid or
   c) Lopinavir/ritonavir 3 capsules PO bid, or
   h) Saquinavir/ritonavir – 1000/100 mg PO bid or

3. Alternatively:
   a)Instead of AZT: Stavudine (d4T) 40 mg orally twice daily if body weight is more than 60 kg, or 30 mg orally twice daily if body weight is less than 60 kg
   b) Instead of 3TC: Didanosine (ddI) 400 mg PO daily if body weight is more than 60 kg, or 250 mg PO daily if body weight is less than 60 kg.

C. Obtain baseline labs to monitor for adverse reaction
1. Pregnancy Test
2. Complete Blood Count with differential and platelets
3. Liver Function Tests
   - Aspartate Aminotransferase
   - Alanine Aminotransferase
   - Alkaline Phosphatase
   - Total Bilirubin

Notes: When the source is known to be HIV infected, past and current ARV therapy experience, viral load data, and genotypic or phenotypic resistance data (if available) may indicate the use specific PEP regimen. Consult an HIV specialist.

† NNRTIs should be considered only when 1) the HCW cannot tolerate either nelfinavir, or lopinavir/ritonavir, or indinavir, or 2) when the HCW has been exposed to a patient with known drug-resistant HIV that is sensitive to the NNRTIs. Recent reports of nevirapine-induced hepatotoxicity in PEP recipients have led to the recommendation that nevirapine be considered an alternative only when NRTIs or PIs are not an option. Consultation with an HIV specialist is strongly recommended. If the individual decides to take nevirapine after a review of the risks and benefits, he/she would need to be monitored closely for side effects. Specifically, serum liver enzymes should be checked at baseline, weeks 2 and 4, or at any time the patient complains of significant constitutional complaints, such as fever, rash, anorexia, or abdominal pain. Use of efavirenz should only be considered in men and women not capable of bearing children because it has been associated with teratogenicity in animal studies and in humans anecdotally. The initial central nervous system toxicity that is often seen with efavirenz use may affect one's ability to work.

References

1. Post Exposure Prophylaxis, © Copyright 2003 World Health Organization
2. GUIDELINES FOR CLINICAL MANAGEMENT OF HIV INFECTION AND HIV-RELATED ILLNESSES, World Health Organization Africa Regional Office, March 2003.
3. HIV Prophylaxis Following Occupational Exposure - HIV Clinical Guidelines For The Primary Care Practitioner – NYSDOH-AI, March 2003,
4. Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxi, *MMWR*. 2001;50, RR-11
5. Expert Advisory Group on AIDS. Guidelines on Post-exposure Prophylaxis for Health Care Workers Occupationally Exposed to HIV. London: UK Health Departments; 2000.
6. Epidemiología y prevención del sida, Miguel A. Martínez-González, Álvaro Alonso Gutiérrez, Félix Alegre Garrido "Epidemiología y prevención de enfermedades infecciosas. Vacunas". Pamplona: Newbook, 2002.

7. *Istituto Nazionale per le Malattie Infettive Lazzaro Spallanzani Istituto di Ricovero e Cura a Carattere Scientifico*, Proposta di raccomandazioni per la chemioprofilassi con antiretrovirali dopo esposizione occupazionale ad HIV, ed indicazioni di utilizzo nei casi di esposizione non occupazionale Roma 19 marzo 2002. Documento predisposto nell'ambito delle attività del Registro Italiano delle profilassi post-esposizione ad HIV. Ministero della Sanità: Progetto AIDS – ISS

APPENDIX VIII-A.
Consent Form
Post-exposure HIV Prophylaxis

1. I understand that the medications: …… are for post-exposure prophylaxis (PEP) against HIV infection based on the recommendations of the …… and should be taken as directed.
2. I understand that current knowledge about PEP is limited, and the treatment is not 100% effective.
3. I understand that these medications may cause side effects such as headache, fatigue, nausea/vomiting and/or diarrhea.
4. I understand that …….will supply me with 28 days of medications and that it is my responsibility to see my own physician as soon as possible for further evaluation and treatment follow-up.

_____

Name

_____

Signature Date

APPENDIX VIII-B.
Monitoring The HCW Following Occupational Exposure

RECOMMENDATIONS

The exposed HCW should be advised to:

(1) use sexual abstinence or condoms to prevent potential secondary transmission,

(2) avoid pregnancy,

(3) refrain from donating blood, blood products, semen, or organs, and

(4) discontinue breastfeeding during the follow-up duration.

Because of the complexity and potential adverse effects of the treatment regimens, longitudinal care of the exposed HCW should be provided either directly by or in consultation with an HIV specialist or an experienced occupational health clinician who is familiar with the most current PEP guidelines.

Sequential confidential HIV testing should be obtained at baseline, 1, 3, and 6 months post-exposure even if PEP is declined .If the test result is positive, a Western blot assay must be performed to confirm the diagnosis of HIV infection. Any acute febrile illness following HIV exposure accompanied by one or more of the following signs or symptoms—rash, lymphadenopathy, myalgias, sore throat—suggests the possibility of acute HIV seroconversion and requires urgent evaluation. If this constellation of complaints is encountered, consultation with an HIV specialist should be sought for optimal diagnostic testing and treatment options.

The HCW should be evaluated weekly over the first month to assess PEP adherence, adverse effects of the ARV therapy, interval physical complaints, and emotional status. When psychological adverse events develop referral for psychiatric/psychological consultation is recommended.

Adverse events related to the institution of PEP ARV medication are to be treated according to existing guidelines (e.g Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents *February 4, 2002,* DHHS&Henry J. Kaiser Family Foundation or HIV Prophylaxis Following Occupational Exposure - HIV Clinical Guidelines For The Primary Care Practitioner – NYSDOH-AI, March 2003, http://www.hivguidelines.org).

APPENDIX VIII-C.
Primary side effects associated with antiretroviral agents used for PEP

ANTIRETROVIRAL CLASS/AGENT	PRIMARY SIDE EFFECTS AND TOXICITIES
Nucleoside reverse transcriptase inhibitors (NRTIs):	
Zidovudine (ZDV; AZT)	anemia, neutropenia, nausea, headache, insomnia, muscle pain, and weakness
Lamivudine (3TC)	abdominal pain, nausea, diarrhea, rash, and pancreatitis
Stavudine (d4T)	peripheral neuropathy, headache, diarrhea, nausea, insomnia, anorexia, pancreatitis, increased liver function tests (LFTs), anemia, and neutropenia
Didanosine (ddI)	pancreatitis, lactic acidosis, neuropathy, diarrhea, abdominal pain, and nausea
Protease inhibitors (PIs)	
Nelfinavir (NFV)	diarrhea, nausea, abdominal pain, weakness, and rash
Lopinavir/Ritonavir	diarrhea, fatigue, headache, nausea, and increased cholesterol and triglycerides
Saquinavir-SGC	GI intolerance, headache, hepatotoxicity, lipodystrophy

APPENDIX VIII-D.
INFORMED CONSENT FORM

INFORMED CONSENT TO PERFORM AN HIV TEST AND AUTHORIZATION FOR RELEASE OF HIV-RELATED INFORMATION FOR PURPOSES OF PROVIDING POST-EXPOSURE CARE TO A HEALTH CARE WORKER EXPOSED TO A PATIENT'S BLOOD OR BODY FLUIDS

An employee has been exposed to your blood or a body fluid in a manner which may pose a risk for transmission of a blood-borne infection. Many individuals may not know whether they have a bloodborne infection because people can carry these viruses without having any symptoms. We therefore are asking for your consent to test for the presence of human immunodeficiency virus (HIV). You will also be tested for hepatitis B virus (HBV) and hepatitis C virus (HCV). According to_____ HIV testing is voluntary and requires your consent in writing (consent can be withdrawn for the test at any time.) There are a number of tests that can be done to show if you are infected with HIV. Your provider or counselor can provide specific information on these tests. These tests involve collecting and testing blood, urine, or oral fluid. The most common test for HIV is the HIV antibody test. In this circumstance, the test result will be used to help determine whether the exposed health care worker is now at risk for HIV and needs treatment for that exposure. Additional testing also will tell whether you are carrying HBV or HCV.

Meaning of HIV Test Results

- A negative result on the HIV antibody test most likely means that you are not infected with HIV, but may not show recent infection. If you think you have been exposed to HIV, you should discuss this with the person requesting your consent for HIV testing and you should take the test again three months after the last possible exposure.
- A positive result on the test means that you are infected with HIV and can infect others.
- Sometimes the HIV antibody test result is not clearly positive or negative. Your provider or counselor will explain this result, and may ask that you give your consent for further testing.

You also are being asked to authorize the release of confidential HIV-related information related to this request to the health professional, named below, who is treating the exposed health care worker. This is necessary to provide appropriate care and to counsel the worker about his or her risk of becoming infected and possibly infecting others. According to_____, except for certain people, confidential HIV-related information can only be given to persons you allow to have it by signing a release. These individuals are prohibited by law from subsequently disclosing these test results in a way that could result in your identity. A list of people who can be given confidential HIV-related information without a release form appears on the reverse side of this form.

_____ _____

Name of exposed employee's health care provider to whom HIV test result will be disclosed

_____ _____

(Optional) Name of exposed health care worker to whom HIV test result will be disclosed

Prior to executing this consent, you must be counseled about the implications of HIV testing and your confidentiality protections under the law.

I understand the purpose for which I am being asked to submit a specimen for HIV testing. My questions about the HIV test were answered. I agree to be tested for HIV and I authorize release of this information to the exposed health care worker and his/her health care providers. This release is effective for one year after the date listed below.

_____ _____

Print name of the person to be tested Date

_____

Signature of the person to be tested or of the person consenting if different from the person to be tested

I provided pretest counseling in accordance with _____. I answered the above individual's questions about the test and offered him/her an unsigned copy of this form.

Signature_____Title_____

Facility/Provider Name_____

* Although confidential testing with identifiers is necessary for occupational exposure. According to_____you be informed that HIV testing can be performed anonymously. For a list of anonymous sites, call_____.

APPENDIX VIII-E.
Case registration occupational exposure report

- date and time of exposure;
- details of the procedure being performed, including where and how the exposure occurred; if related to a sharp device, the type and brand of device and how and when in the course of handling the device the exposure occurred;
- details of the exposure, including the type and amount of fluid or material and the severity of the exposure (e.g., for a percutaneous exposure, depth of injury and whether fluid was injected; for a skin or mucous membrane exposure, the estimated volume of material and the condition of the skin [e.g., chapped, abraded, intact]);
- details about the exposure source (e.g., whether the source material contained HBV, HCV, or HIV; if the source is HIV-infected, the stage of disease, history of antiretroviral therapy, viral load, and antiretroviral resistance information, if known);
- details about the exposed person (e.g., hepatitis B vaccination and vaccine-response status); and
- details about counseling, postexposure management, and follow-up.

APPENDIX VIII-F.
Occupational exposure report (proposal)

Name (Last, First, M):		Address (workplace):		Address (home):
Birth date:	Sex:	Position:	Years in practice	Telephone No.
Date/time of exposure:	Location exposure occurred:		Activity at time of exposure:	
Nature of injury (e.g., needle stick, cut, splash):				
Details of the procedure being performed, including where and how the exposure occurred:				
Details of the exposure, including the type and amount of fluid or material and the severity of the exposure				

Details about the exposure source: The source material contained: HBV: HCV: HIV: Is the source HIV-infected: Stage of disease: Viral load: History of antiretroviral therapy: Antiretroviral resistance: Pre-test counseling provided:	Details about the exposed person: Infected with: HBV: HCV: HIV: Concomitant diseases: Hepatitis B vaccination: Vaccine-response status: Pre-test counseling provided:
Results of the tests: HBV HCV HIV Post-test counseling provided: Referral:	Results of the tests: HBV HCV HIV Post-test counseling provided: Referral:
	PEP prophylaxis commenced: Informed consent obtained: Drugs:

Postexposure management:	CBC With Differential	Serum Liver Enzymes	Sign.
visit 1st week			
visit 2nd week			
visit 3rd week			
visit 4th week			

HIV Antibody test results: 1 month 3 month 6 month	
Signature/Stamp	Date:

APPENDIX VIII-G.
Non-Occupational exposure report (proposal)

<table>
<tr><td colspan="2">Name (Last, First, M):</td><td colspan="2">Address (workplace):</td><td>Address (home):</td></tr>
<tr><td>Birth date:</td><td>Sex:</td><td></td><td></td><td>Telephone No.</td></tr>
<tr><td>Date/time of exposure:</td><td colspan="2">Location exposure occurred:</td><td colspan="2">Activity at time of exposure:</td></tr>
<tr><td colspan="5">Nature of injury (e.g., needle stick, cut, splash):</td></tr>
<tr><td colspan="5">Details of the procedure being performed, including where and how the exposure occurred:</td></tr>
<tr><td colspan="5">Details of the exposure, including the type and amount of fluid or material and the severity of the exposure</td></tr>
<tr><td colspan="2">Details about the exposure source:
The source material contained: HBV:
HCV:
HIV:
Is the source HIV-infected:
Stage of disease:
Viral load:
History of antiretroviral therapy:
Antiretroviral resistance:
Pre-test counseling provided:</td><td colspan="3">Details about the exposed person:
Infected with: HBV:
HCV:
HIV:
Concomitant diseases:
Hepatitis B vaccination:
Vaccine-response status:
Pre-test counseling provided:</td></tr>
<tr><td colspan="2">Results of the tests:
HBV
HCV
HIV
Post-test counseling provided:
Referral:</td><td colspan="3">Results of the tests:
HBV
HCV
HIV
Post-test counseling provided:
Referral:</td></tr>
<tr><td colspan="2"></td><td colspan="3">PEP prophylaxis commenced:
Informed consent obtained:
Drugs:</td></tr>
<tr><td>Postexposure management:</td><td colspan="2">CBC With Differential</td><td>Serum Liver Enzymes</td><td>Sign.</td></tr>
<tr><td>visit 1st week</td><td colspan="2"></td><td></td><td></td></tr>
<tr><td>visit 2nd week</td><td colspan="2"></td><td></td><td></td></tr>
<tr><td>visit 3rd week</td><td colspan="2"></td><td></td><td></td></tr>
<tr><td>visit 4th week</td><td colspan="2"></td><td></td><td></td></tr>
<tr><td colspan="2">HIV Antibody test results:
1 month
3 month
6 month</td><td colspan="3"></td></tr>
<tr><td colspan="4">Signature/Stamp</td><td>Date:</td></tr>
</table>

Part 2. Monitoring HIV/AIDS Treatment and Care

MONITORING TESTING and COUNSELLING

Background

A simple reporting format is proposed for three health facility levels: primary, secondary, and tertiary. Within each of these levels, program monitoring information is requested from two different types of providers:

1) NGOs and other, non-pubic (private), organizations

2) Government facilities.

The purpose of these reporting forms is to provide a simple mechanism by which each of the above audiences can report on their testing and counseling activities. Two forms are provided, one is specifically for primary health care facilities, the second for secondary and tertiary facilities. The forms are designed so that one can determine whether the facilities are government or non-governmental, and whether they are primary or secondary.

Data collection:

The idea is that the reporting formats will be sent to each set of audiences separately. For NGOs, this can be done by selecting a random sample of Organizations if there are many in a country or by selecting all if the number is more limited. For public facilities, a systematic reporting mechanism needs to be put in place to assure that the information requested can be collected and does not over burden programs. This reporting system needs to build into and draw upon the monitoring of HIV/AIDS programmes that is now being developed or in place.

Below is an outline of **the information that will be sought from governmen and non-governmental facilities**:

Primary level

- Total number of people counseled on HIV testing during last month (30 days)
- Testing availability
- Total number of people referred for HIV testing during last month (30 days)
- Total number of people tested on-site, if applicable, during last month (30 days)
- Total number of people found to be HIV positive during last month (30 days)
- Total number of people that received their results
- Total number of HIV positive people referred to support group(s) in the community during last month (30 days)

Secondary and tertiary levels

- Total number of people counseled on HIV testing during last month (30 days)
- Total number of people tested on-site during last month (30 days)
- Total number of people found to be HIV positive during last month (30 days)
- Total number of people that received their results
- Total number of HIV positive people referred to support group(s) in the community during last month (30 days)

The following forms are to be use by non-governmental and other private organizations and well as government facilities that provide testing and counseling services to the population.

There are ***2 forms***, each corresponding to different levels of the health care system. Each form is made up of ***2 parts***. The first part collects basic service provider information, the second looks specifically at the testing and counseling service.

For use by ***primary health care level facilities*** (government and non-government) providing HIV testing and counseling services.	
Part 1: Facility information	
Check the box that applies to the facility type:	❑ Government ❑ Non-government
Check the box(es) that describe the facility's target population:	❑ General population ❑ Specific population(s) ❑ Specify which one(s): _____
Check the box corresponding to the type of services provided at facility:	❑ HIV/AIDS specific prevention and/or care services only ❑ HIV/AIDS prevention and/or care as well as other services (i.e. family planning, vaccination, etc.)

Part 2: HIV counseling and testing services	
1. Total number of individuals *counseled* on HIV testing during last month (30 days): 2. Of these, how many were women? 3. How many were men?	1. Total number of individuals: _____ 2. Number of women: _____ 3. Number of men: _____
Does this facility refer for HIV testing *or* is testing available on-site? (Check the box that applies)	❑ Referrals to testing are made ❑ Testing is available on-site
If referrals are made for HIV testing, of the total number of persons counseled (number 1) during the last month (30 days), how many were *referred* to other sites for testing?	Total number of persons referred for testing at other sites: _____
If testing is provided on-site, of the total number of people counseled (number 1) during the last month (30 days), how many were *tested* at your facility?	Total number of people tested for HIV at facility: _____
If testing is provided on-site, of the total number of people tested during the last month (30 days), *how many were HIV positive*?	Total number of HIV positive individuals: _____
If testing is provided on-site, of the total number of people tested during the last month (30 days), how many *received* their results?	Total number of people that received their results: _____
If testing id provided on-site, of the total number of people that received their results and were found to be HIV positive, how many were *referred* to support group(s) in the community?	Total number of people referred to support group(s) in the community: _____

For use by ***secondary and tertiary health care level facilities*** (government and non-government) providing HIV testing and counseling services.	
Part 1: Facility information	
Check the box that applies to the facility type:	❑ Government ❑ Non-government
Check the box that applies to the level of health care facility:	❑ Secondary ❑ Tertiary
Check the box(es) that describe the facility's target population:	❑ General population ❑ Specific population(s) Specify which one(s): _____
Check the box corresponding to the type of services provided at facility:	❑ HIV/AIDS specific prevention and/or care services only ❑ HIV/AIDS prevention and/or care as well as other services (i.e. family planning, vaccination, etc.)

Part 2: HIV counseling and testing services	
1. Total number of individuals *counseled* on HIV testing during last month (30 days): 2. Of these, how many were women? 3. How many were men?	1. Total number of individuals: _____ 2. Number of women: _____ 3. Number of men: _____
Of the total number of people counseled (number 1) during the last month (30 days), how many were *tested* at your facility?	Total number of people tested for HIV at facility: _____
Of the total number of people tested, *how many were HIV positive*?	Total number of HIV positive individuals: _____
Of the total number of people tested during the last month (30 days), how many *received* their results?	Total number of people that received their results: _____
Of the total number of people that received their results and were found to be positive, how many were *referred* to support group(s) in the community?	Total number of people referred to support group(s) in the community: _____

MONITORING ANTIRETROVIRAL THERAPY

Background

A simple reporting format is proposed for three health facility levels: primary, secondary, and tertiary. Within each of these levels, program monitoring information is requested from two different types of providers:

1) NGOs and other, non-pubic (private), organizations, and

2) Government (public) facilities.

The purpose of these reporting forms is to provide a simple mechanism by which each of the above audiences can report on their ART activities. Three forms are provided, one is specifically for primary health care facilities, a second for secondary, and a third for tertiary facilities. The forms are designed so that one can determine whether the facilities are government or non-governmental.

Data collection:

The idea is that the reporting formats will be sent to each set of audiences separately. For NGOs, this can be done by selecting a random sample of Organizations if there are many in a country or by selecting all if the number is more limited. For public facilities, a systematic reporting mechanism needs to be put in place to assure that the information requested can be collected and does not over burden programs. This reporting system needs to build into and draw upon the monitoring of HIV/AIDS programmes that is now being developed or in place.

Below is an outline of **the information that will be sought from non-governmental and government facilities**:

Primary level

- Number of clients seen during last month (30 days)
- Number of referrals made to assess need to initiate ART in last month (30 days)
- Number of clients on ART
- Monitoring of adherence, toxicity, treatment failure, and resistance
- Referral to secondary level facilities if toxicity is detected
- Provision of ART drugs
- Stock out of ART drugs

Secondary level

- Number of clients seen during last month (30 days)
- Number of assessments made to determine need to initiate ART in last month (30 days), including method(s) used
- Number of clients that initiated ART in last month (30 days)
- Number of clients on ART
- Provision of adherence counseling
- Monitoring of adherence, toxicity, treatment failure, and resistance
- Refer to primary health care facility for follow-up
- Initiation of second line ART if indicated

Tertiary level

- Number of clients seen during last month (30 days)
- Number of assessments made to determine need to initiate ART in last month (30 days), including method(s) used
- Number of clients that initiated ART in last month (30 days)
- Number of clients on ART
- Provision of adherence counseling
- Monitoring of adherence, toxicity, treatment failure, and resistance
- Refer to primary health care facility for follow-up
- Initiation of second line ART if indicated
- Description of “hard case” management

The following forms are to be use by non-governmental and other private organizations and well as government facilities that provide ART services to the population.

There are ***3 forms***, each corresponding to different levels of the health care system. Each form is made up of ***2 parts***. The first part collects basic service provider information, the second looks specifically at the ART service.

For use by ***primary health care level facilities*** (government and non-government) providing ART.	
Part 1: Facility information	
Check the box that applies to the facility type:	❑ Government ❑ Non-government
Check the box(es) that describe the facility's target population:	❑ General population ❑ Specific population(s) Specify which one(s): _____
Check the box corresponding to the type of services provided at facility:	❑ HIV/AIDS specific prevention and/or care services only ❑ HIV/AIDS prevention and/or care as well as other services (i.e. vaccinations, family planning, etc.)

Part 2: ART	
1. Total number of HIV positive individuals seen during the last month (30 days): 2. Of these, how many were women? 3. How many were men?	1. Total number of individuals: _____ 2. Number of women: _____ 3. Number of men: _____
Of the total number of HIV positive individuals seen during the last month (30 days), how many were referred for to another facility in order to *evaluate their need to initiate ART*?	Total number of individuals referred to evaluate need to initiate ART: _____
Of the total number of HIV positive individuals seen during last month (30 days), how many are currently on ART?	Total number currently on ART: _____
Of the total number of HIV positive individuals seen who are *already on ART* during the last month (30 days), are they monitored in your facility? (Check one box)	❑ Yes ❑ No
If HIV positive individuals who are *already on ART* are monitored in your facility, what are they monitored for? (Check all boxes that apply)	❑ Adherence ❑ Toxicity ❑ Treatment failure ❑ Resistance ❑ Other (specify):
Of the total number of HIV positive individuals seen who are *already on ART* during the last month (30 days), how many were referred to a secondary level facility because they *showed signs of toxicity*?	Total number referred because of toxicity: _____
Does your facility provide HIV positive individuals who need ART with the required ART drugs? (Check one box)	❑ Yes ❑ No
If your facility provides individuals who need ART with the required drugs, how many individuals do you currently supply drugs for?	Total number of HIV positive individuals that are supplied with ART drugs: _____
If your facility provides individuals who need ART with the required drugs, how many times in the last 6 months was there a stock-out of the required ART drugs?	Number of times during last 6 months that ART drugs were not available: _____

For use by ***secondary health care level facilities*** (government and non-government) providing ART.	
Part 1: Facility information	
Check the box that applies to the facility type:	❑ Government ❑ Non-government
Check the box(es) that describe the facility's target population:	❑ General population ❑ Specific population(s) Specify which one(s): _____
Check the box corresponding to the type of services provided at facility:	❑ HIV/AIDS specific prevention and/or care services only ❑ HIV/AIDS prevention and/or care as well as other services (i.e. in patient care, surgery, consultations, etc.)

Part 2: ART	
1. Total number of HIV positive individuals seen during the last month (30 days): 2. Of these, how many were women? 3. How many were men?	1. Total number of individuals: _____ 2. Number of women: _____ 3. Number of men: _____
Of the total number of HIV positive individuals seen during the last month (30 days), how many were assessed to determine *their need to initiate ART*?	Total number of individuals assessed: _____
How are these assessments made? (Check all boxes that apply)	❑ Clinical assessment ❑ CD4 counts ❑ Viral load ❑ Other (specify):
Of the total number of individuals assessed during the last month (30 days), *how many initiated ART*?	Total number of individuals that initiated ART during last month (30 days): _____
Of the total number of HIV positive individuals seen during the last month (30 days), how many are currently on ART?	Total number currently on ART: _____
Is adherence counseling provided to individuals on ART in your facility? (Check one box)	❑ Yes ❑ No
Of the total number of HIV positive individuals seen who are *already on ART*, are they monitored in your facility? (Check one box)	❑ Yes ❑ No
If HIV positive individuals who are *already on ART* are monitored in your facility, what are they monitored for? (Check all boxes that apply)	❑ Adherence ❑ Toxicity ❑ Treatment failure ❑ Resistance ❑ Other (specify):
If HIV positive individuals who are *already on ART* are *not* monitored in your facility, are they referred to primary level facilities for follow-up and monitoring? (Check one box)	❑ Yes ❑ No
If monitoring indicates treatment failure, is second-line ART initiated at your facility? (Check one box)	❑ Yes ❑ No

For use by ***tertiary health care level facilities*** (government and non-government) providing ART.	
Part 1: Facility information	
Check the box that applies to the facility type:	❑ Government ❑ Non-government
Check the box(es) that describe the facility's target population:	❑ General population ❑ Specific population(s) Specify which one(s): _____
Check the box corresponding to the type of services provided at facility:	❑ HIV/AIDS specific prevention and/or care services only ❑ HIV/AIDS prevention and/or care as well as other services (i.e. in patient care, surgery, consultations, etc.)

Part 2: ART	
1. Total number of HIV positive individuals seen during the last month (30 days): 2. Of these, how many were women? 3. How many were men?	1. Total number of individuals: _____ 2. Number of women: _____ 3. Number of men: _____
Of the total number of HIV positive individuals seen during the last month (30 days), how many were assessed to determine *their need to initiate ART*?	Total number of individuals assessed: _____
How are these assessments made? (Check all boxes that apply)	❑ Clinical assessment ❑ CD4 counts ❑ Viral load ❑ Other (specify):
Of the total number of individuals assessed during the last month (30 days), *how many initiated ART*?	Total number of individuals that initiated ART during last month (30 days): _____
Of the total number of HIV positive individuals seen, how many are currently on ART?	Total number currently on ART: _____
Is adherence counseling provided to individuals on ART in your facility? (Check one box)	❑ Yes ❑ No
Of the total number of HIV positive individuals seen who are *already on ART*, are they monitored in your facility? (Check one box)	❑ Yes ❑ No
If HIV positive individuals who are *already on ART* are monitored in your facility, what are they monitored for? (Check all boxes that apply)	❑ Adherence ❑ Toxicity ❑ Treatment failure ❑ Resistance ❑ Other (specify):
If HIV positive individuals who are *already on ART* are *not* monitored in your facility, are they referred to primary level facilities for follow-up and monitoring? (Check one box)	❑ Yes ❑ No
If monitoring indicates treatment failure, is second-line ART initiated at your facility? (Check one box)	❑ Yes ❑ No
How are "hard cases" dealt with in your facility? Description of case management for "hard cases": _____ _____	

MONITORING OPPORTUNISTIC INFECTIONS

Background

A simple reporting format is proposed for three health facility levels: primary, secondary, and tertiary. Within each of these levels, program monitoring information is requested from two different types of providers:

1) NGOs and other, non-pubic (private), organizations, and

2) Government (public) facilities.

The purpose of these reporting forms is to provide a simple mechanism by which each of the above audiences can report on their treatment activities for common opportunistic infections (OIs) and cancers. Two forms are provided, one is specifically for primary health care facilities, a second for secondary and tertiary facilities. The forms are designed so that one can determine whether the facilities are government or non-government as well as what level of health care is provided.

Data collection:

The idea is that the reporting formats will be sent to each set of audiences separately. For NGOs, this can be done by selecting a random sample of Organizations if there are many in a country or by selecting all if the number is more limited. For government facilities, a systematic reporting mechanism needs to be put in place to assure that the information requested can be collected and does not over burden programs. This reporting system needs to build into and draw upon the monitoring of HIV/AIDS programmes that is now being developed or in place.

Below is an outline of **the information that will be sought from non-government and government facilities:**

Primary level:

- Total number of HIV positive individuals seen during last month (30 days)
- Total number of HIV positive individuals diagnosed with an OI or HIV-related cancer during last month (30 days)
- Methods of diagnosis
- Total number of individuals diagnosed that needed hospitalization or specialized care
- Total number of individuals diagnosed that were referred to secondary, tertiary, or specialized clinic
- Total number of individuals provided with secondary prophylaxis
- Total number of individuals followed up by facility

Secondary and tertiary:

- Total number of HIV positive individuals seen during last month (30 days)
- Total number of HIV positive individuals diagnosed with an OI or HIV-related cancer during last month (30 days)
- Methods of diagnosis
- Total number of individuals diagnosed that needed hospitalization or specialized care
- Total number of individuals treated on an out-patient basis
- Total number of individuals treated on an in-patient basis
- Total number of individuals referred to specialized clinics
- Total number of individuals provided with secondary prophylaxis
- Total number of individuals referred for follow up by primary health care facility
- Total number of individuals followed up by facility, if applicable

The following forms are to be use by non-governmental and other private organizations and well as government facilities that provide ART services to the population.

There are ***2 forms***, each corresponding to different levels of the health care system. Each form is made up of ***2 parts***. The first part collects basic service provider information, the second looks specifically at the treatment of opportunistic infections and cancers.

For use by ***primary health care level facilities*** (government and non-government) providing treatment for opportunistic infections and HIV-related cancers.	
Part 1: Facility information	
Check the box that applies to the facility type:	❑ Government ❑ Non-government
Check the box(es) that describe the facility's target population:	❑ General population ❑ Specific population(s) Specify which one(s):
Check the box corresponding to the type of services provided at facility:	❑ HIV/AIDS specific prevention and/or care services only ❑ HIV/AIDS prevention and/or care as well as other services (i.e. vaccinations, family planning, etc.)

Part 2: Treatment for opportunistic infections and HIV-related cancers	
1. Total number of HIV positive individuals seen during the last month (30 days): 2. Of these, how many were women? 3. How many were men?	1. Total number of individuals: _____ 2. Number of women: _____ 3. Number of men: _____
Of the total number of HIV positive individuals seen during the last month (30 days), *how many were diagnosed with an opportunistic infection (OI) or an HIV-related cancer*?	Total number of individuals diagnosed: _____
How are diagnosis of OIs and HIV-related cancers made in your facility? (Check all boxes that apply)	❑ Clinical signs ❑ Biochemical diagnosis ❑ Routine blood analysis ❑ X-rays ❑ Other (specify): _____
Of the total number of HIV positive individuals seen during the last month (30 days), *how many were in need of hospitalization or other specialized care?*	Total number in need of hospitalization or specialized care: _____
Of the total number of HIV positive individuals seen during the last month (30 days) that were in need of hospitalization or specialized care, *how many were referred to secondary, tertiary, or specialized clinics*?	Total number of people referred:
Of the total number of HIV positive individuals seen during the last month (30 days), how many are provided *with secondary prophylaxis by your facility*?	Number of people provided with secondary OI prophylaxis: _____
Of the total number of HIV positive individuals seen during the last month (30 days) that are receiving treatment or prophylaxis for OIs, *how many are followed up by your facility*?	Number of people followed up: _____

For use by ***secondary and tertiary health care level facilities*** (government and non-government) providing treatment for opportunistic infections and HIV-related cancers.	
Part 1: Facility information	
Check the box that applies to the facility type:	❑ Government ❑ Non-government
What level of care is provided by your facility? (Check one box)	❑ Secondary ❑ Tertiary
Check the box(es) that describe the facility's target population:	❑ General population ❑ Specific population(s) Specify which one(s): _____
Check the box corresponding to the type of services provided at facility:	❑ HIV/AIDS specific prevention and/or care services only ❑ HIV/AIDS prevention and/or care as well as other services (i.e. in-patient services, surgery, etc.)

Part 2: Treatment for opportunistic infections and HIV-related cancers	
1. Total number of HIV positive individuals seen during the last month (30 days): 2. Of these, how many were women? 3. How many were men?	1.Total number of individuals: _____ 2. Number of women: _____ 3. Number of men: _____
Of the total number of HIV positive individuals seen during the last month (30 days), *how many were diagnosed with an opportunistic infection (OI) or an HIV-related cancer*?	Total number of individuals diagnosed: _____
How are diagnosis of OIs and HIV-related cancers made in your facility? (Check all boxes that apply)	❑ Clinical signs ❑ Biochemical diagnosis ❑ Routine blood analysis ❑ X-rays ❑ IFA ❑ Ultrasound ❑ Biopsy ❑ PCR ❑ MRI ❑ CT ❑ Other (specify): _____
Of the total number of HIV positive individuals seen during the last month (30 days), *how many were in need of hospitalization or other specialized care?*	Total number in need of hospitalization or specialized care: _____
Of the total number of HIV positive individuals seen during the last month (30 days) that were in need of hospitalization or specialized care, *how many were treated on an out-patient basis*?	Total number of people treated as out-patients: _____
Of the total number of HIV positive individuals seen during the last month (30 days) that were in need of hospitalization or specialized care, *how many were treated on an in-patient basis*?	Total number of people treated as in-patients: _____

Of the total number of HIV positive individuals seen during the last month (30 days) that were in need of hospitalization or specialized care, *how many were referred to a specialized clinic*?	Total number of people referred to specialized clinics: _____
Of the total number of HIV positive individuals seen during the last month (30 days), how many are provided *with secondary prophylaxis by your facility*?	Number of people provided with secondary OI prophylaxis: _____
If follow-up is *not* provided by your facility, of the total number of HIV positive individuals seen during the last month (30 days) that are receiving treatment or prophylaxis for OIs, *how many were referred for follow up to another facility*?	Number of people referred for follow up: _____
If follow-up is provided by your facility, of the total number of HIV positive individuals seen during the last month (30 days) that are receiving treatment or prophylaxis for OIs, *how many were followed up by your facility*?	Number of people followed up: _____

MONITORING PREVENTION MOTHER-TO-CHILD HIV TRANSMISSION

Background

A simple reporting format is proposed for three health facility levels: primary, secondary, and tertiary. Within each of these levels, program monitoring information is requested from two different types of providers:

1) NGOs and other, non-pubic (private), organizations, and
2) Government (public) facilities.

The purpose of these reporting forms is to provide a simple mechanism by which each of the above audiences can report on their PMTCT activities. Three forms are provided, one is specifically for primary health care facilities, a second for secondary, and a third for tertiary facilities. The forms are designed so that one can determine whether the facilities are government or non-government.

Data collection:

The idea is that the reporting formats will be sent to each set of audiences separately. For NGOs, this can be done by selecting a random sample of Organizations if there are many in a country or by selecting all if the number is more limited. For public facilities, a systematic reporting mechanism needs to be put in place to assure that the information requested can be collected and does not over burden programs. This reporting system needs to build into and draw upon the monitoring of HIV/AIDS programmes that is now being developed or in place.

Below is an outline of the **information that will be sought from non-government and government facilities:**

Primary level:

- Number of women counseled on HIV testing in last month (30 days)
- Number of women counseled on vertical transmission in last month (30 days)
- HIV testing availability
- Number of women referred for HIV testing in last month (30 days)
- Number of women tested on-site in last month (30 days), if applicable
- Number of women that received their results
- Number of women found to be HIV positive
- Number of women referred support group(s) in the community
- Follow-up for HIV+ women before and after delivery

Secondary level:

- Number of women counseled on HIV testing in last month (30 days)
- Number of women counseled on vertical transmission in last month (30 days)
- Number of women tested on-site in last month (30 days)
- Number of women that received their results

- Number of women found to be HIV positive
- Number of women referred support group(s) in the community
- Number of women clinically assessed to evaluate need to initiate HAART (including process of assessment) in last month (30 days)
- Number of women initiated on HAART in last month (30 days)
- Number of women initiated on AZT to prevent vertical transmission in last month (30 days)
- Number of HIV positive women that received adherence counseling
- Number of HIV positive women that were referred for follow-up at primary care level
- Number of births to HIV positive women in last month
- Number of newborns provided with ARVs to prevent HIV infection

Tertiary level:

- Number of women counseled on HIV testing in last month (30 days)
- Number of women counseled on vertical transmission in last month (30 days)
- Number of women tested on-site in last month (30 days)
- Number of women that received their results
- Number of women found to be HIV positive
- Number of women referred support group(s) in the community
- Number of women clinically assessed to evaluate need to initiate HAART (including process of assessment) in last month (30 days)
- Number of women initiated on HAART in last month (30 days)
- Number of women initiated on AZT to prevent vertical transmission in last month (30 days)
- Number of HIV positive women that received adherence counseling
- Number of HIV positive women that were referred for follow-up at primary or secondary level care facilities
- Number of births to HIV positive women in last month
- Number of Cesarean sections in last month (30 days)
- Number of newborns assessed using PCR an CD4 counts
- Number of newborns provided with ARVs to prevent HIV infection
-

The following forms are to be use by non-governmental and other private organizations and well as government facilities that provide PMTCT services to the population.
There are ***3 forms***, each corresponding to different levels of the health care system. Each form is made up of ***2 parts***. The first part collects basic service provider information, the second looks specifically at the PMTCT services.

For use by ***primary health care level facilities*** (government and non-government) PMTCT services.	
Part 1: Facility information	
Check the box that applies to the facility type:	❑ Government ❑ Non-government
Check the box(es) that describe the facility's target population:	❑ General population ❑ Specific population(s) Specify which one(s): _____
Check the box corresponding to the type of services provided at facility:	❑ HIV/AIDS specific prevention and/or care services only ❑ HIV/AIDS prevention and/or care as well as other services (i.e. vaccinations, family planning, etc.)

Part 2: PMTCT services	
Total number of women counseled on HIV testing during last month (30 days):	Total number of women counseled: _____
Total number of women counseled on the risks of vertical transmission (dual protection, breastfeeding, and safe delivery practices):	Total number of women counseled on risks of vertical transmission: _____
Does this facility refer for HIV testing or is testing available on-site? (Check the box that applies)	Referrals to testing are made Testing is available on-site
If referrals are made for HIV testing, of the total number of persons counseled during the last month (30 days), how many were referred to other sites for testing?	Total number of persons referred for testing at other sites: _____
If testing is provided on-site, of the total number of women counseled during the last month (30 days), how many were tested at your facility?	Total number of people tested for HIV at facility: _____
Of the total number of women tested during the last month (30 days), how many received their results?	Total number of people that received their results:
Of those women that were tested, how many were found to be HIV positive?	Total number found to be HIV positive: _____
If testing id provided on-site, of the total number of women that received their results and were found to be positive, how many were referred to support group(s) in the community?	Total number of women referred to support group(s) in the community: _____
Are HIV positive women followed up during pregnancy and after delivery by your facility? (Check one box)	❑ Yes ❑ No

For use by ***secondary health care level facilities*** (government and non-government) providing PMTCT services.	
Part 1: Facility information	
Check the box that applies to the facility type:	❑ Government ❑ Non-government
Check the box(es) that describe the facility's target population:	❑ General population ❑ Specific population(s) Specify which one(s): _____
Check the box corresponding to the type of services provided at facility:	❑ HIV/AIDS specific prevention and/or care services only ❑ HIV/AIDS prevention and/or care as well as other services (i.e. in-patient care, family planning, etc.)

Part 2: PMTCT services	
Total number of women *counseled* on HIV testing during last month (30 days):	Total number of women counseled: _____
Total number of women counseled on the risks of vertical transmission (dual protection, breastfeeding, and safe delivery practices):	Total number of women counseled on risks of vertical transmission: _____
Total number of women counseled during the last month (30 days), how many were *tested* at your facility:	Total number of people tested for HIV at facility: _____
Total number of women tested during the last month (30 days) who *received* their results:	Total number of people that received their results: _____
Of those women that were tested, how many were *found to be HIV positive*?	Total number found to be HIV positive:
Of the total number of women that received their results and were found to be positive, how many were *referred* to support group(s) in the community?	Total number of people referred to support group(s) in the community: _____
Of the total number of HIV positive women seen during the last month (30 days), how many were assessed to determine *their need to initiate HAART*?	Total number of individuals assessed: _____
How are these assessments made? (Check all boxes that apply)	❑ Clinical assessment ❑ CD4 counts ❑ Viral load ❑ Other (specify): _____
Of these women, *how many were initiated on HAART*?	Total number of women initiated on HAART: _____
Of the total number of women assessed during the last month (30 days), *how many were initiated on AZT* to prevent vertical transmission?	Total number of women initiated on AZT: _____
Of the total number of women who were initiated on AZT, how many received adherence counseling?	Total number of women counseled on adherence: _____
Of the total number of women who were initiated on AZT or were found to be HIV positive, how many were referred for follow-up at primary care facilities?	Total number of women referred for follow-up at primary health care facilities: _____
How many HIV positive women gave birth in your facility during the last month (30 days)?	Number of women giving birth, last month: _____
Of the newborns born to these HIV positive women, how many were provided with ARVs to prevent HIV infection?	Number of newborns provided with ARVS: _____

For use by ***tertiary health care level facilities*** (government and non-government) providing PMTCT services.	
Part 1: Facility information	
Check the box that applies to the facility type:	❑ Government ❑ Non-government
Check the box(es) that describe the facility's target population:	❑ General population ❑ Specific population(s) Specify which one(s): _____
Check the box corresponding to the type of services provided at facility:	❑ HIV/AIDS specific prevention and/or care services only ❑ HIV/AIDS prevention and/or care as well as other services (i.e. in-patient care, family planning, etc.)

Part 2: PMTCT services	
Total number of women *counseled* on HIV testing during last month (30 days):	Total number of women counseled: _____
Total number of women counseled on the risks of vertical transmission (including dual protection, breastfeeding, and safe delivery practices):	Total number of women counseled on risks of vertical transmission: _____
Total number of women counseled during the last month (30 days), how many were *tested* at your facility:	Total number of people tested for HIV at facility: _____
Total number of women tested during the last month (30 days) who *received* their results:	Total number of people that received their results: _____
Of those women that were tested, how many were *found to be HIV positive*?	Total number found to be HIV positive: _____
Of the total number of women that received their results and were found to be positive, how many were *referred* to support group(s) in the community?	Total number of people referred to support group(s) in the community: _____
Of the total number of HIV positive women seen during the last month (30 days), how many were assessed to determine *their need to initiate HAART*?	Total number of individuals assessed: _____
How are these assessments made? (Check all boxes that apply)	❑ Clinical assessment ❑ CD4 counts ❑ Viral load ❑ Other (specify):
Of these women, *how many were initiated on HAART*?	Total number of women initiated on HAART: _____
Of the total number of women assessed during the last month (30 days), *how many were initiated on AZT* to prevent vertical transmission?	Total number of women initiated on AZT: _____
Of the total number of women who were initiated on AZT, how many received adherence counseling?	Total number of women counseled on adherence: _____
Of the total number of women who were initiated on AZT or were found to be HIV positive, how many were referred for follow-up at primary or secondary level care facilities?	Total number of women referred for follow-up at primary or secondary level health care facilities: _____
How many HIV positive women gave birth in your facility during the last month (30 days)?	Number of women giving birth, last month: _____
Of these women, how many had a Cesarean section?	Number of Cesarean sections: _____
Of the newborns born to these HIV positive women, how many were assessed using PCR and CD4 counts?	Number of newborns assessed: _____
Of the newborns born to these HIV positive women, how many were provided with ARVs to prevent infection?	Number of newborns provided with ARVS: _____

MONITORING POST EXPOSURE PROPHYLAXIS

Background

A simple reporting format is proposed for two health facility levels: primary and secondary. Within each of these levels, program monitoring information is requested from two different types of providers:

1) NGOs and other, non-pubic (private), organizations, and

2) Government (public) facilities.

The purpose of these reporting forms is to provide a simple mechanism by which each of the above audiences can report on their PEP activities. Two forms are provided, one is specifically for primary health care facilities, the second for secondary facilities. The forms are designed so that one can determine whether the facilities are government or non-government.

Data collection:

The idea is that the reporting formats will be sent to each set of audiences separately. For NGOs, this can be done by selecting a random sample of Organizations if there are many in a country or by selecting all if the number is more limited. For public facilities, a systematic reporting mechanism needs to be put in place to assure that the information requested can be collected and does not over burden programs. This reporting system needs to build into and draw upon the monitoring of HIV/AIDS programmes that is now being developed or in place.

Below is an outline of **the information that will be sought from government and non-government facilities**:

Primary level:

- Total number of individuals attending for PEP during last month (30 days)
- Total number of individuals receiving a risk evaluation to determine needs in ARV during last month (30 days)
- Total number of individuals receiving counseling on HIV testing during last month (30 days)
- Total number of individuals receiving an HIV rapid test prior to PEP during last month (30 days)
- Total number of individuals found to be HIV positive prior to receiving PEP during last month (30 days)
- Total number of individuals provided with PEP during last month (30 days)
- Total number of individuals followed up by facility during last month (30 days)

Secondary level:

- Total number of individuals attending for PEP during last month (30 days)
- Total number of individuals receiving a risk evaluation to determine needs in ARV during last month (30 days)
- Total number of individuals receiving counseling on HIV testing during last month (30 days)
- Total number of individuals receiving an HIV rapid test prior to PEP during last month (30 days)
- Total number of individuals found to be HIV positive prior to receiving PEP during last month (30 days)
- Total number of individuals provided with PEP during last month (30 days)
- Total number of individuals referred for follow-up to a primary health care facility during last month (30 days)

The following forms are to be use by non-governmental and other private organizations and well as government facilities that provide PEP to the population.

There are ***2 forms***, each corresponding to different levels of the health care system. Each form is made up of ***2 parts***. The first part collects basic service provider information, the second looks specifically at the PEP service.

For use by ***primary health care level facilities*** (government and non-government) providing PEP services.	
Part 1: Facility information	
Check the box that applies to the facility type:	❑ Government ❑ Non-government
Check the box(es) that describe the facility's target population:	❑ General population ❑ Specific population(s) Specify which one(s): _____
Check the box corresponding to the type of services provided at facility:	❑ HIV/AIDS specific prevention and/or care services only ❑ HIV/AIDS prevention and/or care as well as other services (i.e. family planning, vaccination, etc.)

Part 2: Post-exposure prophylaxis service	
1. In the last month (30 days) how many people have attended your facility in need of post-exposure prophylaxis (PEP)? 2. Of these, how many were women? 3. How many were men?	1. Total number of individuals: _____ 2. Number of women: _____ 3. Number of men: _____
Of the total number of people that attended your facility in need of PEP during the last month (30 days), how many *received a risk evaluation* to determine their need for ARVs?	Total number that were evaluated for risk: _____
Of the total number of people that attended your facility in need of PEP during the last month (30 days), how many *received counseling on HIV testing*?	Total number of persons counseled: _____
Of the total number of people that attended your facility in need of PEP during the last month (30 days), how many *were tested for HIV* prior to receiving PEP using rapid test kits?	Total number of people tested for HIV: _____
Of the total number of people that attended your facility in need of PEP that were tested during the last month (30 days), *how many were already HIV positive*?	Total number of HIV positive individuals: _____
Of the total number of people that attended your facility in need of PEP that were tested during the last month (30 days), *how many received immediate assistance with ARVs?*	Total number of people that received ARVs for PEP purposes: _____
Of the total number of people that attended your facility in need of PEP that were tested during the last month (30 days), how many were followed up by your facility?	Total number of people followed-up: _____

For use by ***secondary health care level facilities*** (government and non-government) providing PEP services.	
Part 1: Facility information	
Check the box that applies to the facility type:	❑ Government ❑ Non-government
Check the box(es) that describe the facility's target population:	❑ General population ❑ Specific population(s) Specify which one(s): _____
Check the box corresponding to the type of services provided at facility:	❑ HIV/AIDS specific prevention and/or care services only ❑ HIV/AIDS prevention and/or care as well as other services (i.e. in-patient care, etc.)

Part 2: Post-exposure prophylaxis service	
1. In the last month (30 days) how many people have attended your facility in need of post-exposure prophylaxis (PEP)? 2. Of these, how many were women? 3. How many were men?	1. Total number of individuals: _____ 2. Number of women: _____ 3. Number of men: _____
Of the total number of people that attended your facility in need of PEP during the last month (30 days), how many *received a risk evaluation* to determine their need for ARVs?	Total number that were evaluated for risk: _____
Of the total number of people that attended your facility in need of PEP during the last month (30 days), how many *received counseling on HIV testing*?	Total number of persons counseled: _____
Of the total number of people that attended your facility in need of PEP during the last month (30 days), how many *were tested for HIV* prior to receiving PEP using rapid test kits?	Total number of people tested for HIV: _____
Of the total number of people that attended your facility in need of PEP that were tested during the last month (30 days), *how many were already HIV positive*?	Total number of HIV positive individuals: _____
Of the total number of people that attended your facility in need of PEP that were tested during the last month (30 days), *how many received immediate assistance with ARVs?*	Total number of people that received ARVs for PEP purposes: _____
Of the total number of people that attended your facility in need of PEP that were tested during the last month (30 days), how many were referred to primary health care facilities for follow-up?	Total number of people referred-up: _____

The WHO Regional Office for Europe

The World Health Organization (WHO) is a specialized agency of the United Nations created in 1948 with the primary responsibility for international health matters and public health. The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health conditions of the countries it serves.

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