The Essentials of Antiretroviral Therapy for Health Care and Program Managers
PATHFINDER INTERNATIONAL

Technical Guidance Series Number 5

The Essentials of Antiretroviral Therapy for
Health Care and Program Managers

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<tr>
<td>NRTIs</td>
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1.0 Introduction

Seventy percent of people needing Antiretroviral Therapy (ART) live in Africa, but until recently, only 10 percent of those in need have been able to access treatment. With the current, unprecedented global mobilization of resources for the fight against HIV and AIDS, people living in resource-limited settings are slowly beginning to access ART. ART reduces the effects of the Human Immunodeficiency Virus (HIV) on the body and often permits many months, if not years, of return to normal, productive life. United Nations organizations, bilateral donors, many foundations, and private voluntary organizations are assisting low- and middle-income countries to rapidly increase access to ART. Although ART can be both expensive and complicated to take, costs are reduced by using generic rather than brand-name drugs. New, fixed-dose combination pills lessen the burden on clients. Once started, ART must be continued for life.

This addition to the Pathfinder International Technical Guidance Series provides basic information and practical guidance on ART and wider care and treatment issues for program implementers and health care managers. Health workers and managers in resource-limited settings are encouraged to follow local Ministry of Health treatment protocols and guidelines, or to apply the World Health Organization global guidelines if there are no specific local guidelines. Citations and direct links are provided where further, more detailed, information may be obtained.

Because many people living with AIDS have tuberculosis, other opportunistic infections, and other AIDS-related conditions, guidance is given on wider aspects of care and treatment. Once antiretroviral and other treatment is commenced, many HIV-infected people will return to normal life, so these guidelines indicate how wider reproductive health care, as well as self-help and support initiatives, should be integrated with ART services. Special mention is given to integration of ART with antenatal care and delivery services for prevention of mother-to-child transmission of HIV. Antenatal services that provide voluntary testing and counseling can be an important entry point for women and their families to ART and wider AIDS care. Meeting the particular needs of infants, children, and adolescents is also discussed.

This guidance paper addresses people’s wider care, support, and treatment needs from the time they are diagnosed as HIV positive, before ART is needed, and after commencing ART; this includes vigorous prevention and treatment of opportunistic infections, nutrition support, and spiritual, psychosocial, and economic support. It discusses the community participation and services essential for mobilizing the wide range of resources that people living with HIV and their families need to optimize their quality of life and increase their use of facility-based services. Community-level support for ART services is critical for improved adherence to treatment and to address stigma and discrimination, which are major barriers to diagnosis and treatment access. The final section discusses end-of-life care for people whose disease does not respond to available drugs. Most end-of-life

care will be in the home, but people living with AIDS will continue to need active medical, psychosocial, and spiritual care. They and their families may be burdened with additional financial needs at this time.

This guidance paper emphasizes that people have needs that are far wider than medical care. Thus, good ART programs must be able to provide for the wider needs of their clients or link/partner with other organizations able to meet the wider needs.

Prevention remains the crucial element in the fight against AIDS. It is vitally important to strengthen prevention efforts in the broader community. The availability of treatment becomes an incentive to be tested as a tangible benefit of counseling and testing, and an encouragement for those testing positive to access services. Prevention messages and services must be continued for people who are diagnosed as HIV positive and integrated into ART services. People living with HIV, especially those who have returned to good health on ART, can be excellent advocates for prevention and living positively, and are a valuable resource to those managing ART services and community-based prevention efforts. People living with HIV can provide spiritual and psychosocial counseling and adherence support for those starting ART in the health facility, and ongoing support in the community through post-test clubs and other associations of people living with HIV.
2.0 Antiretroviral Therapy and the Global Response to HIV

Antiretroviral Therapy (ART) is treatment for AIDS that helps the body's immune system recover from the damage caused by infection with HIV. Although ART cannot cure AIDS, persons on ART will begin to feel better, eat more, and put on weight. Their bodies will recover the ability to fight infections. As persons on ART treatment become well, they can care for their children and return to household activities and productive life, which benefits the household and national economies. They recover their sense of hope for the future and can become powerful advocates for prevention and mitigation of HIV in their families and communities. They may remain well for many years, but must continue to take Antiretrovirals (ARVs) for the rest of their lives. Thus, ART is an important component of the global response to AIDS. Until recently, however, the high cost of ARV drugs and treatment monitoring has limited their availability to poor people and in resource limited settings.

The United Nations and its agencies recognize the importance of equitable access to ART and have set ambitious targets for the numbers of persons receiving ART. The Global Fund for AIDS, Tuberculosis, and Malaria, the US President’s Emergency Plan for AIDS Relief (PEPFAR), and other mechanisms have mobilized unprecedented funding to purchase and make ARV drugs available, rapidly scaling-up access to ART in low- and lower-middle income countries. Some private foundations are working with low- and middle-income countries to facilitate their purchase of ARV drugs at lower cost. Nongovernmental organizations have waged a vibrant, global campaign to pressure drug companies to reduce the cost of ARVs by allowing large-scale production of generic versions of key ARVs for use in resource limited settings. This campaign led to the defeat of law suits launched by US and European drug companies against the South African and Brazilian governments. These governments had increased the availability of ART by using generic drugs manufactured in violation of drug patents held by the big pharmaceutical companies. However, despite these victories, challenges remain. A lawsuit by patent-holding pharmaceutical companies against India is pending and may restrict India's production and export of generic ARVs. However, it is important to recognize that rapid scale-up of access to ART depends on more than just reducing the price of ARVs. Availability of free or affordable monitoring of treatment for those on ART, logistics systems, provider skills, and the will of governments are also necessary for successful scale up.

2.1 The World Health Organization AIDS Medicines and Diagnostics Service

To expand access to quality, effective treatment for AIDS, the World Health Organization (WHO) has established the AIDS Medicines and Diagnostics Service.

\footnote{For definitions of low and lower-middle income countries see: http://web.worldbank.org/WBSITE/EXTERNAL/DATASTATISTICS/0,,contentMDK:20420458-menuPK:64133156-pagePK:64133150-piPK:64133175-theSitePK:239419,00.html (1/12/07)}
(http://www.who.int/hiv/amds/en/), a mechanism for facilitating the increased supply of ARVs and diagnostics in developing countries. The AIDS Medicines and Diagnostics Service helps countries forecast their needs, provides a mechanism for efficient procurement of drugs and diagnostic commodities, and supports effective in-country supply management and local production where applicable. This global service ensures that drug manufacturers know the forecasted needs for their products in advance, thus reducing the chance of bottlenecks in production and ensuring availability of essential AIDS medicines and diagnostics. Approximately 50 countries were using the service at the end of 2005. Services provided include the following:

- Global guidance on simplified treatment regimens, and research evidence on ARVs and on selection of essential HIV diagnostic tests;
- Country-level technical support to promote clinical guidelines and to update the national essential medicines list;
- Global guidance and information on regulatory matters and registration status of ARVs;
- Strengthening countries’ drug regulatory agencies in dealing with ARVs (registration, inspection, importation, local production, and combination products);
- Updated lists of products found to meet WHO standards for quality, safety, and efficacy, including fixed-dose combinations and their suppliers; and
- Operational standards for evaluating supply agencies and quality control laboratories.

2.2 ART Access Increasing, but Slowly

The number of people receiving ART in resource-limited countries more than doubled from 400,000 in December 2003 to approximately one million in June 2005, but access to ART continues to fall way short of the growing need. In Africa, where 70 percent of those who need ART live, only 10 percent are currently receiving it. One of Asia’s most highly populated countries, India, had 42,000 people on ART in 2006, but 5.2 million people living with HIV/AIDS (only 1.2 percent on treatment).

Although many poor countries are now setting national treatment targets and committing their own resources to scaling up, consistent, high-level global political commitment and financial support for services continues to be needed with a sustained sense of urgency.

Building sustainable systems for expanded treatment services is hugely important. UNAIDS has identified bottlenecks to rapid expansion of treatment even where strong commitment exists and treatment programs are in place. The obstacles to scaling up include:

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• Concerns about financial sustainability and reliance on donor assistance;
• The need for more and better-coordinated technical support;
• Lack of simple dosing formulations such as single, fixed-dose combination pills;
• Lack of easy-to-manage, palatable drugs for children;
• Weak procurement and supply chain for medicines and diagnostics; and
• The need to implement standardized, efficient service models for health care delivery, that
  o Build sustainable human resource capacity, and
  o Integrate HIV treatment and prevention with reproductive health, Tuberculosis (TB), and other services—such as obstetrics and midwifery—at the various levels of the health system.\textsuperscript{5}

However, increased health sector spending on ART must not reduce the amount of money available for basic health care such as family planning, safe motherhood, and childhood immunization. Ministries of Health may need to amend local health care regulations and licensing to permit new models for diagnosis and treatment, and to reduce service delivery costs and human resource bottlenecks. Scarce and expensive doctors are best deployed in policy, advisory, and supervisory roles, limiting their clinical care to referral clients with complicated needs. Nurses, clinical officers, medical assistants, and other trained health workers can provide most treatment services. Ministries of Health must also endorse and develop in-service training and simplified treatment protocols that can be used safely and effectively with appropriate guidelines by a broad range of health workers.

In addition, all countries need to increase prevention efforts, including in low-prevalence settings.\textsuperscript{6} Prevention should be included in all health facility and community ART services, as well as integrated into maternal and child health, adult medicine, reproductive health, and TB services. For treatment programs to be effective, and linked to prevention, both facility and community services and systems must function and be linked.

\textsuperscript{6} Ibid.
3.0 Wider Aspects of Care and Treatment

3.1 Integrated ART

Although much of the international debate has been focused on delivery of ART, ART is only one component in a comprehensive package of care for people living with HIV or AIDS that includes:

- A national or regional plan for comprehensive care, including clinical guidelines and treatment protocols;
- Community involvement with enhanced community capacity to respond effectively to HIV (e.g., adherence support, directly observed treatment);
- HIV counseling and testing, for reducing personal risk of infection with HIV or onward transmission of HIV;
- Stigma reduction, including self stigmatization, health worker stigmatization, and community stigma;
- Adequate diagnostics including laboratory services and reagents for monitoring ART, (WHO clinical diagnostic guidelines can be utilized to support monitoring of ART where only minimum laboratory services are available.);
- Care management, referral, and client follow-up for care and treatment beyond the primary health care level;
- ART with reliable supplies of affordable ARVs and local treatment protocols and guidelines for when to commence ART, using which regimens, and to what standards of adherence;
- Management of ART side effects;
- Prevention of Mother-To-Child Transmission (PMTCT) of HIV—including primary prevention of HIV infection, services to reduce unwanted pregnancy in HIV-infected women, use of ARVs, safe delivery services, infant nutritional counseling and support, and, where infrastructure exists, ART for the mother and her partner if indicated;
- PMTCT+, which focuses on ongoing support of mothers, their babies, and partners living with HIV after pregnancy, birth, and postpartum;
- Voluntary family planning;
- Prevention and treatment of sexually transmitted infections and opportunistic infections;
- Nutrition support;
- Social and economic support (including referral to post-test clubs and other associations of people living with HIV, and provision of income generation skills and access to microcredit);
- Psychosocial and spiritual support;
- Home care and care for caregivers;
- Human rights and legal support;
- Management of pain (including use of opioids); and
- End-of-life care.
3.2 Opportunistic Infections

Although ART strengthens the immune system as measured by a rise in CD4 count, people who are infected with HIV, even those receiving ART, are susceptible to Opportunistic Infections (OIs). OIs are a group of infections that usually only affect people with weakened immune systems. ART is still not universally accessible in some countries and/or some HIV-positive people cannot afford the cost of ongoing treatment monitoring, which they have to meet from out-of-pocket expenses, even if ART is free. Thus aggressive diagnosis and treatment of OIs is important to keep them alive and relatively well for as long as possible. In these instances it is important that there is feedback of the issues to the government decision makers, usually through health service information channels as well as lobbying and advocacy. This is an important area for collaboration and linking with organizations that have advocacy skills.

Along with OI prevention and prompt treatment, improved nutrition and psychosocial support—especially self-help groups—contribute to the improved health and wellbeing of those who need ART, whether they are able to access it or not.

3.2.1 Preventing Infection

All persons who are to start ART should be screened for TB and Sexually Transmitted Infections (STIs) and, if infected, treated without delay. In the case of TB infection, there are concerns that starting anti-TB medications and ART close together can lead to the development of Immune Recombination Inflammatory Syndrome (IRIS) (for more information on IRIS, see page 25). Thus, it has been the practice that a diagnosis of TB meant delaying ART until the intensive phase of TB treatment was completed. However, it is now known that delaying HIV therapy by three months in HIV-positive clients with a low CD4 cell count who are diagnosed with TB increases their risk of death by 50 percent. Therefore, if the person is severely immune-compromised, TB treatment and ART can be given simultaneously. Persons who develop IRIS can continue to receive ART. Persons who are co-infected with TB and HIV must also be carefully monitored to rapidly detect and treat any flare up of TB infection, which is very common in HIV-infected persons.

Infections from cuts and grazes become more severe and difficult to treat, as do diarrheal diseases. It is therefore vital to advise clients about personal and domestic hygiene and the importance of clean, boiled drinking water. People who work in farming should take additional care washing their bodies after finishing work, and frequently cleansing cuts and grazes with soap and water. Clients should be advised

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**Box 1: Common and/or Important Opportunistic Infections**

- Recurrent, spreading herpes simplex (cold sores);
- Cuts and grazes that become red, discharge pus, and don’t heal;
- Candidiasis (thrush) in the mouth, throat, esophagus, and vagina;
- Chronic infectious diarrhea or dysentery (Giardia, which does not normally affect adults in developing countries, can cause chronic debilitating diarrhea in HIV-infected adults.);
- TB is commonly a co-infection in persons diagnosed with AIDS. HIV co-infection is also common in persons diagnosed with TB;
- Pneumocystis pneumoniae and other pneumonias;
- Toxoplasmosis;
- Fungal infections such as Cryptococcal meningitis.

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that domestic animals and fowl should be kept out of the house and kitchen.

People on ART should ask other family members to clear messes around the house left by chickens, cats, and kittens, and to clean animal houses and byres. Cleaning fruits and vegetables well and cooking chicken and meat thoroughly before eating is very important, as is frequent hand washing, to avoid microbial infections. OIs must be treated rigorously, and for some severe infections (e.g., TB and malaria), preventive treatment must be given to reduce the risk of infection or reinfection.

**Box 2: Use Of Cotrimoxazole As Prophylaxis**

Cotrimoxazole is a key intervention that should be offered as part of a basic package of infant care to reduce morbidity and mortality.

According to the Joint WHO/UNAIDS/UNICEF Statement On Use Of Cotrimoxazole As Prophylaxis In HIV Exposed And HIV Infected Children, “Cotrimoxazole prophylaxis is...a crucial potentially life-saving intervention that should be given to all HIV exposed children born to HIV-infected mothers, in settings where HIV infection status cannot be reliably confirmed in the first 18 months of life.”

This prophylaxis must be continued until the infant ceases all breastfeeding and is tested and proven to be HIV negative.

**Prophylactic Treatment of Opportunistic Infections**

Persons receiving ART need prophylactic, or preventative treatment, with *cotrimoxazole* (brand name Septrin), a common antibiotic that protects against *Pneumocystis Pneumoniae* (PCP) and malaria infection. PCP and malaria are common causes of death in HIV-infected persons. Cotrimoxazole also protects against toxoplasmosis, another important OI caused by a parasite that passes from birds and mammals to humans. Toxoplasmosis is transmitted through feces of domestic and feral cats, or through the milk of intermediate hosts such as domestic pigs (most commonly), goats, sheep, and occasionally cattle.

In some countries, cotrimoxazole prophylaxis is offered to all people who are HIV positive. In other countries, cotrimoxazole is recommended for HIV-positive adults when their CD4 count falls to 500.

The WHO recommends prophylactic treatment with cotrimoxazole for all HIV-infected children and infants of known HIV-positive mothers from three to four weeks until the infant is no longer breastfeeding and is old enough to be reliably tested for HIV. Prophylactic treatment with cotrimoxazole is also recommended for children with any signs or symptoms suggestive of HIV in areas where there is high HIV prevalence.

Concerns about drug resistance from chronic use of antimicrobials have been discussed in international forums such as the Toronto World AIDS Conference. So while continuing to provide cotrimoxazole as WHO recommends, it is important to stay abreast of changes in national and international protocols.

Studies have demonstrated that using Isoniazid (INH) prophylaxis in HIV-infected individuals is effective in preventing the incidence of TB. However, the use of INH prophylaxis requires ruling out active TB. In the absence of facilities with chest X-rays and skin testing for TB, and because HIV infection can cause false negatives for TB on X-ray and skin testing, many countries have decided not to implement INH prophylaxis in their program. Local Ministry of Health treatment protocols

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and guidelines will indicate if, and how, INH prophylaxis should be used in your situation.

**Prophylaxis** against *cryptococcal meningitis* with an antifungal drug such as fluconazole (brand name Diflucan) is sometimes recommended when CD4 counts fall to 200 or the person commences ART. But fluconazole can cause cryptococcus to develop resistance, so if other antifungal drugs are unavailable, prophylaxis with fluconazole may not be recommended. In this situation fluconazole is reserved for treatment and “secondary prophylaxis” or prophylaxis only for persons who have had cryptococcal meningitis. Fluconazole is also a very expensive drug. Again, it is important to follow local Ministry of Health protocols and guidelines.

### 3.2.2 Treatment of Opportunistic Infections

#### Fungal Infections

Persons who are infected with HIV are susceptible to **fungal infections**. Candidiasis is a common OI in people with HIV. It is caused by candida, a common type of yeast (fungus) that is found in most people’s bodies. A healthy immune system and bacteria normally found in the body keep candida under control, but an immature or weakened immune system may not prevent candida from multiplying and becoming a problem infection. **Candidiasis** usually affects the mouth, throat, or vagina. It can occur months or years before other, more serious OIs. In HIV infection with a CD4 count of around 300 or less, candida can spread and become a severe infection in the esophagus. Candidiasis in the mouth and candida esophagitis make it difficult for persons to eat and they rapidly lose weight. Where possible, candida infections are treated with topical applications of antifungal preparations directly onto the infection. Severe infection and esophagitis may require treatment with fluconazole, or another antifungal drug, taken orally or by injection.

**Cryptococcus** is a common fungus found in soil that can cause meningitis in persons with weakened immune systems. Fluconazole is highly effective against cryptococcal infection. Clinicians and counselors must educate all persons living with HIV about cryptococcal meningitis. Clients must know the symptoms of meningitis (primarily persistent headache) and they must understand the importance of quickly seeking diagnosis and treatment if they develop symptoms. Persons who have had cryptococcal meningitis are likely to get reinfected. Thus, people who have previously been infected should receive fluconazole prophylaxis, if this is recommended in local Ministry of Health treatment protocols.

**Lymphoma and Kaposi’s Sarcoma**

Some cancers are more common in people infected with HIV as their CD4 count falls. These include lymphoma, a group of malignancies of the lymph glands and lymphatic tissue, and Kaposi’s sarcoma. Kaposi’s sarcoma is a malignant tumor found under the skin and in the lining of the mouth and rectum, characterized by brown or purplish spots. It is rare in persons who are not HIV infected and may be thought of as an “opportunistic tumor” in persons with damaged immune systems and low CD4 counts. Malignancies should be treated according to local Ministry of Health guidelines, which often include treatment with vincristine, a commonly-available and relatively low-cost cancer drug.
**Other Common Conditions**

A number of other symptoms and conditions are common among people living with AIDS, including those on ART, and must be addressed as part of a care and treatment package. These common conditions may be side effects of ART or part of AIDS disease, and can often be managed simply, even by community home-based care volunteers, or trained household members. It is important to address these conditions to support the quality of life of people living with HIV and AIDS, and ensure adherence to treatment regimens. Clients on ART are likely to experience some of these common conditions during their first months on ART and it is important to show them how to manage these symptoms and reassure them that side effects will lessen over time. If a client on ART experiences side effects that impede his or her lifestyle for several months, she or he should consult a doctor or qualified provider about changing their drug regimen. The following table shows common conditions and simple management techniques to suggest to clients.

### Table 1. Management Techniques for Common Conditions Experienced by Clients on ART

<table>
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<th>Condition</th>
<th>Management Techniques</th>
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| **Coughing**   | • Keeping active by walking about, turning in bed, or sitting up. This encourages the lungs to drain.  
                    • Other measures which encourage drainage of the lungs include massage or gentle patting on the back of the chest over the lungs. Someone in the home can do this, especially for younger children.  
                    • If pain is felt in the chest or ribs during coughing, a pillow or hand should be held tightly over the area that hurts when coughing. This helps make the cough less painful.  
                    • During the day it may be beneficial to cough and clear the lungs at least four times a day.  
                    • Soothe the throat by drinking tea with sugar or honey. |
| **Diarrhea**   | • Eat small meals more times per day.  
                    • Try not to eat greasy, spicy, and fatty foods.  
                    • Try foods such as bananas, and biscuits.  
                    • Drink a lot of clean water, weak tea, or lemon water.  
                    • Use oral rehydration solution made according to local guidelines, from sachets of oral rehydration salts, or from salt and sugar, or other starches or sweeteners. |
| **Headache**   | • Rest in a quiet, dark room.  
                    • Place a cold cloth over eyes and forehead.  
                    • Try not to drink strong tea or coffee.  
                    • Take paracetamol (acetaminophen).  
                    • Consult a health worker if it lasts more than two days. |
| **Nausea**     | • Take medicine with food, if allowed in the treatment plan.  
                    • Eat smaller meals, more times in the day.  
                    • Try not to eat greasy, spicy, and fatty foods. Try foods like rice, soup, bananas, and biscuits.  
                    • Drink a lot of clean water, weak tea, lemon water, or fresh ginger tea. |
| **Pain**       | • Take paracetamol (acetaminophen).  
                    • Imagine or remember a favorite place or event.  
                    • Learn deep and regular breathing techniques, which may aid in relaxation.  
                    • Learn to deal with pain through distraction and lessening of anxiety.  
                    • Engage in physical activity or receive gentle massage. |
| **Skin rashes**| • Keep skin clean and dry.  
                    • Use mild or weak soaps.  
                    • Drink lots of water.  
                    • Use calamine lotion or get medicines to stop the itching.  
                    • Cover skin when exposed to direct sunlight.  
                    • If blisters or widespread peeling develops, consult an ART provider. |
Cuts and abrasions
- Wear shoes when out of the house and while working in the fields.
- Always wash the arms and legs with soap and water after doing field work.
- Clean wounds with soap and water, and cover them loosely until they heal.

Sore mouth and throat
- Rinse your mouth with clean warm water and salt.
- Avoid sweets.
- Avoid things with caffeine such as coffee, strong tea, and some sodas.
- Eat soft foods rather than hard or crunchy foods.
- Eat bland, not spicy foods.
- Use a straw for liquids and soups. This may help when taking in the food needed while preventing it from touching the sore areas.
- Cold foods, drinks or ice, if available, may help numb the mouth and relieve discomfort.

Tiredness/weakness
- Avoid alcohol and drugs, including smoking cigarettes or chewing tobacco.
- Try moving around more and getting exercise.
- Eat a lot of fruits and vegetables.

3.3 Reproductive Health Needs

3.3.1 Gynecologic Care and STI Prevention and Management
Persons who are receiving ART may have other reproductive health needs. STIs should be diagnosed and promptly treated, as they may increase the risk of transmitting HIV to others and increase the likelihood of reinfection with HIV for themselves. Reinfection with a new strain of HIV may result in a rapid increase in the viral load and worsening of the disease. STIs can also be worse for HIV-infected people and, as with any infection, can hasten progression of their disease. HIV-infected women should be encouraged to have periodic gynecologic exams for STIs (including cervical cancer) as part of ongoing care, since they may be more susceptible and infections are more serious for them. Reinfection with HIV is sometimes called “super infection.” We know that reinfection occurs because sophisticated laboratories are able to identify different strains of HIV, and can demonstrate new infections with different strains on repeat HIV testing.

Once they are feeling better on ART, some women may desire a pregnancy. Others may not want to become pregnant. An important task in caring for a woman on ART is to provide counseling that will allow her informed reproductive choice. Whatever choice she makes should be supported.

3.3.2 Pregnancy
Pregnant women should not use some ARVs, such as efavirenz, as they may damage the fetus. (Note: Please consult your local treatment protocols and guidelines for the recommended ART regimens for pregnant women.) When possible, the woman should be taking the recommended regimen before she becomes pregnant to avoid harm in early pregnancy. Some local treatment protocols and guidelines exclude use of efavirenz for all women of childbearing age (15 years to 49 years). If women of childbearing age have to use efavirenz, they must have access to acceptable, reliable, and affordable contraception. They must also understand the importance of avoiding pregnancy while taking this ARV.

A good relationship between the client and the clinician is important so that the
client is able to share her wishes to become pregnant or terminate a pregnancy in countries where this is legal. If a woman has an unintended pregnancy, care must be taken by clinicians and counselors not to make her feel guilty or disrespected, as she may not come back for her ART. A woman who becomes pregnant while taking efavirenz should cease taking efavirenz if she wants to continue with the pregnancy. Her ART should be changed to an alternative combination of ARVs recommended in local Ministry of Health protocols. It is usually possible to substitute nevirapine for efavirenz during pregnancy.

While pregnant and breast-feeding, the woman and her partner should protect her as much as possible from reinfection with HIV. High levels of virus in the blood can cause further damage to the immune system, and increase the chance that HIV infection is transmitted from the mother to her child. The woman and her partner need information and counseling about the use of condoms—male or female—to protect each other from reinfection and to reduce the risk of mother-to-child transmission of HIV.

### 3.3.3 Contraception

Women who do not wish to become pregnant need contraceptive counseling. The use of barrier methods, condoms most effectively, reduce the risk of further transmission of HIV and reinfection. Couples should know that even if both are infected, it is important to prevent reinfection, which can make them sicker. And if one partner is not infected, he or she should stay that way. Female condoms provide good protection from STIs and HIV but are frequently unavailable or not affordable. Women should be encouraged to use an additional method that provides more effective protection against pregnancy than the condom, or use another form of contraception if their partner is unreliable in the use of condoms.

The most recent evidence on hormonal contraception is that it does not increase transmission of HIV and is safe to use in women on ART. But, ARV drugs (particularly non-nucleoside reverse transcriptase inhibitors and protease inhibitors) have the potential to increase or decrease the effectiveness of the hormones in oral hormonal contraceptives—combined oral contraceptive pills and progestogen-only pills. It is not known whether ARVs change the effectiveness of progestogen-only injectable contraceptives, which provide higher blood hormone levels than either type of oral contraceptive pills. If a woman on ART decides to start or continue hormonal contraceptive use, she should be advised to use condoms consistently.

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to both prevent HIV transmission and to compensate for any reduction in the effectiveness of her hormonal contraceptive.\textsuperscript{10}

The Intrauterine Contraceptive Device (IUCD) is safe for insertion and continued use in women who are clinically well on ART,\textsuperscript{11} as long as they aren’t infected with a STI at the time of insertion (the recommendation for all women). When inserting the IUCD in an HIV-infected woman it is important to use good, aseptic technique and follow local protocols on use of prophylactic antibiotics.\textsuperscript{12}

Surgical contraception (sterilization and vasectomy) should be available to persons on ART if they desire permanent contraception. Surgeons must use universal precautions against HIV infection, which include use of double surgical gloves and thimbles, wearing of surgical face masks and eye protection, safe disposal of surgical waste and sharps, and thorough sterilization of surgical equipment before reuse.

### 3.4 Nutrition and ART

Many people who are diagnosed with AIDS have lost weight through chronic ill health. They may have decreased appetite, be unable to eat much because of candidiasis in the mouth or esophagus, have poor absorption, or have chronic diarrhea. Co-infection with TB is common in HIV infection, and widespread TB infection may also cause weight loss. Weight gain may be rapid for persons commencing ART and after treatment of OIs and TB. Some ARVs must be taken with food and recovery may be assisted by a good diet. Many people recovering from AIDS-related infections have increased appetite, and this can be a problem in poor households that are not food secure.

Where food and nutrition insecurity is a problem, it is helpful to be able to offer food supplements to people on ART. If your clinic does not have food to give poor clients, your clinic or a local nongovernmental organization might be able to obtain food supplements from organizations like the World Food Program or faith-based food-relief groups. Enhancing food and nutrition security in your

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\textsuperscript{12} “IUCDs pose an unacceptable risk if purulent cervicitis or chlamydial infection or gonorrhoea is present. However, it is acceptable to insert an IUCD with other STIs (excluding hepatitis and HIV) or vaginitis present.” World Health Organization, Medical Eligibility for Contraceptive Use, (World Health Organization, Geneva, 2004)
community should be a longer-term goal. If it is beyond your organization’s mandate, consider partnering with a nongovernmental organization or other organization able to support improved agriculture, low-labor-intensity farming, or micro-credit and income generating activities. If well managed, these activities can benefit your clients, orphans and other vulnerable children, and all the poorest members of the community, reducing their vulnerability to HIV/AIDS.

3.5 Psychosocial and Spiritual Needs

Persons receiving ART have social and spiritual needs as well as biomedical needs. Some will benefit from regular, long-term counseling or a support group. Some will want spiritual support from a religious leader of their faith. If these are not available through your clinic, it is important that you establish a local referral network that can offer these vital services. These types of links with community-based groups and initiatives focused on the epidemic can make the difference. People living with HIV/AIDS often form local organizations that advocate for better access to care and treatment and more resources to be spent on addressing HIV/AIDS. Some form or join existing local support groups. These can be very useful for providing psychosocial support. However, not everyone will want to disclose their HIV infection widely and therefore might not want to go to an organization of people who are known to be living with HIV/AIDS. Support groups that can accommodate those who want their status to remain private should also be available.

It is good practice for all persons commencing ART to have a treatment supporter or “buddy”—a close friend or relative who knows that the person is HIV infected and taking ART. People living with AIDS should choose their own buddy. This person should be someone with whom the client is comfortable disclosing that he or she is HIV infected. The buddy provides personal support and encourages the person living with AIDS to take the ARVs as prescribed. This can be particularly important if the person suffers side effects from the ARVs. In some models for ART delivery, the treatment companion receives special advice and counseling to help them in the role. Information about the client and his or her treatment must only be given to the buddy with the clear, advance agreement of the client.

3.6 Pathfinder’s Experience in ART Programming

The following table provides a summary of Pathfinder’s ART support programs.
<table>
<thead>
<tr>
<th>Project</th>
<th>Target population/Regions</th>
<th>Key Interventions</th>
<th>Achievements</th>
<th>Partners</th>
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</table>
| Treatment Acceleration Program in Mozambique, started in 2001 | Increases access to youth-friendly HIV/AIDS care and treatment for youth aged 10-24 in Maputo and Gaza province | • Youth-friendly Voluntary Counseling and Testing (VCT) in 2 clinics  
• STI/HIV/AIDS clinical care and treatment, including ART and follow-up in 2 sites  
• PMTCT+ services for young women at 2 clinics  
• Community Home-Based Care (CHBC) services for families, including youth-headed households through youth CHBC activists and supervisors | • 280 youth on ART receive regular follow-up from peers  
• 20 facilities now involved in youth-friendly AIDS care and treatment  
• VCT introduced into 40 youth-friendly services sites using project training materials and protocols | World Bank; Ministries of Health, Education, and Youth; Provincial Directorate of Health |
| Psychosocial Support and Peer Counseling for HIV-Infected Women and their Families in Botswana, started in 2004 | Trains and supports PMTCT counselors in 11 districts | • Training of counselors who support HIV-positive pregnant women and mothers, spouses, and families by adherence counselors and peer mothers.  
• Referrals of HIV-positive pregnant women for PMTCT and of other mothers and their babies for ART services | • Positive women report being more comfortable receiving PMTCT/ART information from counselors rather than at facilities  
• More women, partners, and babies tested and on ART  
• 8,685 mothers counseled and referred for services along with 2,812 babies between April and December, 2006 | U.S. Centers for Disease Control and Prevention; Ministry of Health; Botswana Christian AIDS Intervention Program; Botswana Network of PLWHA |
| Expansion of PMTCT Services in Kenya, started in 2002 | Supports facilities and families in 18 districts of Nairobi, Eastern, Rift Valley, and Central provinces | • Links pregnant women and newborns requiring prophylactic ARVs with facility- and community-level services  
• Supports availability of PMTCT and ART in remote, underserved areas of Kenya through partnerships with diverse stakeholders | • Achieved 83% uptake of HIV counseling and testing in antenatal care and 74% uptake of prophylactic ARVs  
• Supported facilities to introduce early infant HIV diagnosis, strengthening early referral to care and treatment  
• 12,933 clients referred for PMTCT, and 9,243 clients on ART between July 2006 and February 2007 | U.S. Centers for Disease Control and Prevention; Ministry of Health; Nairobi City Council; nongovernmental organizations/faith-based organizations |
### Table 2 (continued). Illustrative Examples of Pathfinder Treatment and ART and Related Services

<table>
<thead>
<tr>
<th>Project</th>
<th>Target population/Regions</th>
<th>Key Interventions</th>
<th>Achievements</th>
<th>Partners</th>
</tr>
</thead>
</table>
| AIDS, Population, and Health Integrated Assistance (APHIA II) (Nairobi, Central) in Kenya, started in 2006 | Supports women, men, and children for HIV/AIDS care and treatment, including ART, in all districts of the Nairobi and Central provinces | • Trains Community Health Workers (CHWs) in household- and community-level prevention, social support, and nursing care (including support for orphans and vulnerable children, legal protection, CHBC, nutrition, PMTCT, and support groups)  
• Trains health facility staff in data collection, adult and child HIV/AIDS management, logistics, and supervision  
• Supports 2-way referrals for smooth continuum of care between community and facility-level services  
• Although COPHIA ended, hundreds of trained CHWs still refer clients for PMTCT and support clients on ART | • Support 16 public and private facility ART services; trained 35 providers in pediatric HIV management. To train in adult HIV management by mid-2007  
• Supported integration of family planning, reproductive health, and youth-friendly services with HIV/AIDS care and treatment  
• Included referrals for HIV testing and counseling, nutrition, community, and social support, and ART adherence/directly-observed treatment, short course support through CHWs | USAID; Ministry of Health; Nairobi City Council; nongovernmental organizations/faith-based organizations |
| Tutunzane CHBC program in Tanzania, started in 2005                      | Provides CHBC, including community prevention and mobilization, as well as linkages to facility services, in 12 districts within 4 regions of Tanzania | • CHBC supervisor and primary caregiver training on ART  
• Regular coordination with facility-level ART service delivery partners for linkages between community and facility services  
• Training and orientation of facility personnel on CHBC services and referring patients on ART to CHBC for adherence support and follow-up  
• Stakeholder orientation to package of care, including ART and CHBC  
• Organizational capacity building for local community-based organizations on ART support | • Over 4,000 referrals for ART made in 2006  
• Over 100 providers trained in ART support  
• Approximately 20,000 CHBC clients and their households supported  
• 350 stakeholders engaged in community mobilization | U.S. Centers for Disease Control and Prevention; Ministry of Health; National AIDS Control Program; local community-based organizations; Elizabeth Glaser Pediatric AIDS Foundation; Harvard University; Muhimbili Medical Center; Tanzania Red Cross Society; Interchurch Medical Assistance |
4.0 Clinical Care and Follow-Up of Persons Taking ART

4.1 ART Using WHO Clinical Staging Guidelines

Access to treatment in resource-limited settings can be scaled up using the WHO clinical staging system for HIV/AIDS developed in 1990 and revised in 2006. (See Box 4.) This system emphasizes the use of clinical signs and symptoms to guide decision making for the management of HIV/AIDS clients. It was designed for use in resource-limited settings where there is limited access to laboratory services. The WHO clinical staging system has been widely used, particularly in the African Region. It has proved practical and useful in facilities at both the primary health care and referral levels. Non-specialist and non-pediatric health care workers at the primary care level and in peripheral health care facilities are able to diagnose and manage the care of adults and children living with AIDS using the clinical staging system and HIV/AIDS case definitions.

**Box 4: Revised WHO Clinical Staging of HIV/AIDS for Adults and Adolescents**

**Primary HIV infection**
- Asymptomatic (no symptoms)
- Acute retroviral syndrome ("flu-like" illness two to four weeks after being infected with HIV)

**Clinical stage 1**
- Asymptomatic (no symptoms)
- Persistent generalized lymphadenopathy (swollen lymph glands all over the body)

**Clinical stage 2**
- Moderate unexplained weight loss (less than 10% of presumed or measured body weight)
- Recurrent upper respiratory tract infections (sinusitis, bronchitis, ear and throat infections)
- Herpes zoster (shingles)
- Angular cheilitis (sores at the corners of the mouth)
- Recurrent oral ulcerations (sores in the mouth)
- Papular pruritic eruptions (raised, itchy sores)
- Seborrheic dermatitis (red, scaly rash)
- Fungal nail infections of fingers

**Clinical stage 3**

**Conditions where a presumptive diagnosis can be made on the basis of clinical signs or simple investigations**
- Unexplained severe weight loss (more than 10% of presumed or measured body weight)
- Unexplained chronic diarrhea for longer than one month
- Unexplained persistent fever (coming and going or steady for longer than one month)
- Persistent oral candidiasis (thrush infection in the mouth)
- Oral hairy leukoplakia (white patches on the side of the tongue, elsewhere on the tongue or inside the mouth: these patches are similar to thrush patches, but they cannot be scraped off and do not get better with antifungals)
- Pulmonary tuberculosis (TB) diagnosed in last two years
- Severe bacterial infections (e.g., pneumonia, lung abscess, muscle abscesses, bone or joint infection, meningitis, and bacteria in the blood)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis (severe often painful, mouth and gum infections)
Conditions where confirmatory diagnostic testing is necessary
Unexplained anemia (Hgb < 8 g/dl), and or neutropenia (neutrophils <500/mm3) and or thrombocytopenia (wbc <50 000/ mm3) for more than one month

Clinical stage 4

Conditions where a presumptive diagnosis can be made on the basis of clinical signs or simple investigations
• HIV wasting syndrome (unintended, progressive weight loss with weakness, fever, and diarrhea)
• Pneumocystis pneumonia
• Recurrent severe or radiological bacterial pneumonia (signs of pneumonia seen on chest X-rays)
• Chronic herpes simplex infection (cold sores, sores on the genitals or round the anus lasting more than one month)
• Esophageal candidiasis
• Extrapulmonary tuberculosis (TB infection in the glands, bones, abdomen or TB meningitis)
• Kaposi sarcoma (tumors under the skin or the mucosa of the mouth and rectum)
• Central nervous system toxoplasmosis (infection of the brain)
• HIV encephalopathy (damage to the brain that causes significant mental and physical disability, and dementia)

Conditions where confirmatory diagnostic testing is necessary
• Extrapulmonary cryptococcosis including meningitis (cryptococcal meningitis)
• Disseminated non-tuberculous mycobacteria infection (widespread infection with bacteria similar to TB but not TB)
• Progressive multifocal leukoencephalopathy (PML: a rare viral infection of the white matter in the brain)
• Candida of trachea, bronchi, or lungs (candidiasis of the major airways and lungs)
• Chronic cryptosporidiosis (a diarrheal disease with cramping abdominal pains)
• Chronic isosporiasis (a rare diarrheal disease causing malabsorption of food)
• Visceral herpes simplex infection (herpes infection of the liver or pancreas)
• Cytomegalovirus infection (of the retina in the eye or of an organ other than liver, spleen or lymph glands)
• Disseminated mycosis (fungal infection spread throughout the body)
• Recurrent non-typhoidal salmonella septicemia (recurrent blood infection with salmonella food poisoning bacteria)
• Lymphoma (cerebral or B cell non-Hodgkins) (tumors of the lymph glands or lymphatic tissue)
• Invasive cervical carcinoma (spreading cancer of the mouth of the womb)
• Atypical disseminated leishmaniasis (or kala azar, a parasite infection spread by sand flies that causes the spleen to enlarge)
• Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy

http://www.who.int/hiv/pub/guidelines/artadultguidelines.pdf

The WHO clinical staging system is used to decide when to start ART and also gauge whether adherence is sufficient or resistance is developing. Its use reduces the cost of diagnosis and treatment monitoring for the health sector, and for the client in settings where the client must pay for clinical tests.

In resource-limited settings, WHO recommends that HIV-infected adults and adolescents should start ARV therapy when HIV infection has been confirmed and one of the following conditions is present:
• WHO Stage IV HIV disease—Clinical AIDS (per staging criteria)—irrespective of the CD4 cell count,
• WHO Stage III disease, if CD4 cell counts are below 350 per cubic millimeter, or
• WHO Stage I or II HIV disease with CD4 cell counts less than 200 per cubic millimeter.

It is possible to provide ART services and care for people on ART with only standard hematology and blood chemistry tests (liver function tests, renal function tests). This reduces the cost of ART to the health sector and client as CD4 counts and viral load tests require sophisticated equipment and are expensive. An HIV-positive person is started on ART when they have signs diagnostic of AIDS. (See Box 5). Their progress on ART is monitored clinically, with increased weight gain and wellbeing indicative of success. Failure to gain weight and otherwise improve clinically can mean that:
• The person is not taking the ART properly, or
• The HIV infection is resistant to the treatment prescribed.

Also, presence of an OI after a period of weight gain and clinical improvement may be indicative of adherence failure or emergence of HIV resistance.

As money for infrastructure development becomes available, countries are encouraged by the WHO to acquire laboratories that can provide CD4 counts, and routine hematology and biochemistry tests. New technology for CD4 counting is being developed that will reduce the cost and make it more affordable. Clients receiving ART still require skilled clinical care and follow up, even when CD4 counts and viral load estimates are possible. The tests confirm clinical findings but do not replace clinical skills.

4.2 About HIV ARVs

ARVs are powerful drugs that fight viral infections. ARVs can be used to treat people whose HIV infection has progressed to AIDS via clinical staging or a CD4 count less than 200. (Please see Box 5.) Once started, HIV ARV drugs must be taken for life, usually without any break in treatment if they are to be effective. There are three main classes of ARVs currently used in low- and middle-income country settings, which are grouped according to the way they affect HIV.

Nucleoside Reverse Transcriptase Inhibitors (NRTIs), also called nucleoside analogues or “nukes,” slow down the production of the reverse transcriptase enzyme in cells so that HIV cannot duplicate itself. Commonly used NRTIs include abacavir, lamivudine, stavudine, and zidovudine.

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs), non-nucleosides or “non-nukes,” bind to reverse transcriptase in a different way than NRTIs to block
the duplication and spread of the virus. Efavirenz and nevirapine are NNRTIs.

**Protease Inhibitors (PIs)** work at a later stage of new virus production, slowing viral maturation from immature noninfectious virus to mature and infectious. Although NRTIs and NNRTIs only have an effect on newly infected cells, PIs slow down the reproduction of HIV in newly infected cells and those that have been infected for a long time. Saquinavir is a PI. The 2006 WHO ART guidelines recommend that “…PIs be reserved for second-line treatment. This is because there are no second-line treatment options if resistance to PIs occurs in resource poor settings with limited availability of ARVs.”

ARVs reduce the amount of virus in a person's body. This is called the viral load. As the viral load decreases, the damage that HIV does to the person’s immune system decreases and the person's immune system recovers. Recovery of the immune system is indicated by a rise in CD4 cells in the blood, which is measured by the CD4 count. ARVs cannot clear HIV infection completely from the body. HIV frequently mutates as it increases in numbers, and as a result HIV readily becomes resistant to ARV drugs.

Resistant HIV is difficult and costly to treat, and can be transmitted to other people through unprotected sex, contaminated needles and surgical equipment, unsafe blood supply, and from mother-to-child. Therefore, to reduce the development of resistance, three ARVs are used together (including drugs from at least two different categories of ARVs) in a “cocktail” of treatment known as Highly Active Antiretroviral Therapy (HAART). Although there may be local variations, generally first-line ART consists of zidovudine or stavudine, lamivudine, and either nevirapine or efavirenz. Zidovudine is also known as azidothymidine.

ARVs are relatively expensive. The expense can be reduced by use of generic, or unbranded drugs, rather than proprietary, or brand-name drugs. Local manufacturing of generics can also reduce a country’s ARV bill. The US Federal Drug Administration, however, has not licensed all available generic drugs and all ARVs purchased with US government funding must be licensed.

To reduce the burden on clients (cost, number of pills, remembering the schedule, and which pills must be taken with food), simplified treatment can be achieved by combining ARVs into single, fixed-dose combinations. This has only been possible for generic drugs or where one drug company manufactures more than one ARV. An example of a fixed dose combination pill is the combination of lamivudine and zidovudine, which are sold under the brand name Combivir. Some drug companies are cooperating and permitting packaging of their brand-name ARV drugs with brand-name ARV drugs made by another manufacturer. This does not reduce the pill burden, but it makes it easier to remember which drugs to take together.

4.2.1 Treatment Protocols

ART is usually started, following local treatment protocols, when

- A person has symptoms diagnostic of AIDS; or
- A person with a known HIV infection is found to have a low CD4 count or high viral load, if tests for CD4 and viral load are available locally.
Although WHO recommends that ARVs should be made available to all HIV-infected persons if their CD4 count is less than 200 even if they do not have symptoms of AIDS, the U.S. Department of Health and Human Services recommends considering ARVs when the CD4 count falls below 350. The clinician and client must weigh the benefits of this against the risks of side effects before starting ART. (Further details are included in the following sections.) It is very important to follow local Ministry of Health protocols or guidelines for commencing clients on HIV ARV drugs, and for the combinations of ARVs used as first-line treatment.

In developed countries, there are a number of alternative drugs that can be used if resistance develops to first-line treatment. But in developing countries, where few alternative drugs are available, it is important that persons on ART have a secure supply of their drugs and adhere well to their treatment to avoid the emergence of resistant strains of HIV.

WHO recommends that the entire regimen be changed if treatment failure occurs. The second-line regimen has to involve drugs that are active against the client’s virus strain and should ideally include a minimum of three active drugs, one of them from at least one new class of ARVs. This increases the likelihood of treatment success and minimizes the risk of cross resistance—resistance from the first-line treatment transferring as resistance to the second-line treatment. The PI class is thus reserved for second-line treatments, preferably supported by two new NRTIs.

Treatment failure may be diagnosed by a rise in viral load, a fall in CD4 (if these tests are available), or a worsening of the clinical condition including emergence of a new WHO-specified clinical stage four symptom. In general, first line treatment should be maintained for at least a year to ensure maximum ARV benefit before diagnosing treatment failure.

If a change in regimen is needed because of toxicity, an entirely new second-line regimen can be prescribed. Or, if the toxicity is related to an identifiable drug, the latter can be replaced with another drug that does not have the same side effects.

### 4.2.2 Side Effects of ARV Drugs

Since the advent of ART, AIDS is no longer a rapidly fatal condition. Instead, AIDS has become a chronic condition requiring careful care management and multi-faceted support to ensure clients achieve the best health and quality of life while taking ART, to extend their lives. But ARVs are powerful drugs that have side effects and can cause damage to the body. The NRTI class of ARVs can cause
- Disturbance of the body’s chemistry;
- Liver damage;
- Peripheral nerve damage leading to “pins and needles,” pain, and loss of feeling;
- Inflammation of the pancreas (the digestive organ that produces insulin); and
- Anemia.

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The ARV drug abacavir can cause a severe hypersensitivity or allergic reaction resulting in a severe lumpy red rash, swelling of the mouth and eyelids, and widespread skin peeling that requires the drug to be stopped immediately. Abacavir must not be used again in people who have previously experienced hypersensitivity to the drug. Zidovudine may cause flu-like symptoms when first used. It may also cause anemia and muscle weakness.

ARVs in the NNRTI class can cause rashes and liver damage. Efavirenz can cause insomnia (sleeplessness) and vivid dreams, especially in the beginning. Nevirapine can damage the liver and, rarely, cause Stevens Johnson Syndrome—a severe skin reaction that creates big, fluid-filled blisters all over the body.

The PI class of drugs can cause kidney stones, nausea, diarrhea, and disturbance of the body’s chemistry.

Clients who are about to start ART need counseling about the possible side effects of their treatment. Clients who know they might have side effects and how to manage them, and have ongoing support, are more likely to tolerate mild and temporary side effects. Because it is difficult for clients to remember everything they are told about side effects, the following measures should be taken to help clients:

• Clients should be given information sheets that include pictures and text in the local language that summarize the side effects that the client may experience, and how they should manage the side effects.
• A social worker, counselor, or trained community health worker should follow-up with clients, reinforcing advice given by the health provider providing ART. Counseling increases memory and also ensures clients understand the relevance of the advice to their own individual situation.
• See clients for follow up at short intervals of only one or two weeks when the client first commences ART or after changes in the ARVs.
• The treatment supporter or "buddy" should also be taught what the client should do if he or she experiences side effects from the treatment.

People who develop pins and needles, pain, weakness, or slight loss of feeling in their feet should wear loose clothing and footwear. They should walk a little each day, but not long distances or perform any strenuous work until the symptoms have gone away. Clients should inform their ART provider who may change the ART regimen if the symptoms persist for more than two or three weeks, or become worse.

Many clients are presenting with lipodystrophy, or fat collecting in unusual places, which will require another level of counseling since stigma will likely be attached because of altered appearance.

During follow-up sessions, health care providers must examine clients for signs of anemia (pale conjunctivae, nail beds, tongue) and jaundice (yellow eyes, palms, soles of feet), the latter of which is a sign of liver damage. Blood tests for anemia, liver, and kidney function should be undertaken when there are any symptoms, or according to the schedule in the Ministry of Health clinical protocols. But
unnecessary blood tests increase the cost of ART to the health service or client and should be avoided.

4.2.3 Adherence to ART

To be adherent, clients must

- Have access to properly-stored drugs;
- Take all prescribed drugs on time, as often as prescribed, in the proper doses, with no breaks or “drug vacations;” and
- Take with food, if required for a particular drug.

Good adherence is important

- For optimal suppression of HIV reproduction and recovery of the client’s immune system, and
- To reduce the risk of drug-resistant HIV developing. Poor adherence for as little as a week can result in:
  - Rapid increases in viral load,
  - Treatment failure,
  - Recurrence of symptoms of AIDS,
  - Development of resistance to more than one ARV, and
  - Death.

If ARV-resistant HIV strains spread to the wider population, the long-term sustainability of scaled-up ART programs might be harmed. Resistant HIV infections are more difficult and more expensive to treat.

Good adherence to treatment is encouraged by

- Treatment that is affordable;
- A health worker-client relationship with mutual trust and respect;
- Regular supportive counseling;
- Clear two-way communication;
- Certainty that the client understands his or her treatment and the importance of adherence to the treatment by asking the client questions to be sure they can repeat back the instructions;
- Good, clearly-written client information that the client can take to someone who can read if they are unable to read themselves;
- Help and support from a trusted relative or friend acting as a treatment companion or “buddy;”
- Treatment support groups;
- A package of care that empowers clients to make meaningful decisions about their care and treatment; and
- Access to support and resources on the community level, including stigma reduction efforts.

As a client recovers, he or she may no longer feel ill and no longer consider him- or herself a client. The “opportunity cost” of returning for follow up and renewing prescriptions increases. For example, this means that the client might prioritize the use of his or her time and money to travel to a paying job rather than the ART clinic. Health workers and clients need to discuss these issues openly and reach agreement on the follow up treatment plan. Again, involving the treatment buddy in the discussions can be helpful.
Counts of pills remaining in the bottles dispensed at follow-up appointments, or during surprise checks in the client’s home are used by some to monitor compliance with treatment. But pill counts have their limitations. They can easily be manipulated if the client wants to do this. It is far more important that the client wants to adhere to the treatment and can talk candidly with the health worker about difficulties in adherence to ART, such as unpleasant side effects.

If a client is adhering to their treatment, but develops signs of treatment failure, it is likely that the HIV infection has developed resistance to the treatment prescribed. Resistance requires a change in treatment from the first-line treatment to second-line treatment. Treatment and any changes from first-line treatment to second-line treatment should conform to Ministry of Health protocols or guidelines. If these do not exist, consult the WHO treatment guidelines: Scaling Up Antiretroviral Therapy in Resource-Limited Settings: Treatment Guidelines for a Public Health Approach, WHO, Geneva, 2004.14

4.2.4 Complications of ART

Because ARVs are powerful drugs, and because HIV readily mutates into resistant strains, the regimens in Ministry of Health treatment protocols (or the WHO treatment guidelines) must be closely adhered to. For a few drugs, namely efavirenz, lamivudine, and nevirapine, a single mutation in the virus is sufficient to produce resistance.

Some ARVs have actions that strengthen the actions of other ARVs and cause toxicity and some ARVs can negate other ARVs’ actions. These combinations must not be used. Local Ministry of Health treatment protocols must address these issues and must include recommendations for alternative ARVs that can be safely and effectively substituted if a client has a severe reaction or side effects from an ARV. Ministry of Health protocols should also consider the cost of treatment and availability of ARVs to make ART accessible to as many persons as possible. Subsidizing treatment for those who can’t pay should be a Ministry of Health priority.

It is important to identify the causes of any new symptoms or signs developing after starting ART, whenever possible. ART clients should return to the facility for consultation and they and their treatment buddies should be fully aware of what the symptoms mean. If a client complains of symptoms that are side effects of ARVs, these should be explained to the client and appropriate actions implemented, such as:

- Adapting or changing the drug regimen,
- Providing symptomatic treatment, or
- Giving simple reassurance.

It is important that the clinician recognize potentially serious adverse effects like:

- Severe anemia and neutropenia,
- Neuropathy,
- Pancreatitis,
- Hepatitis, and

• Serious hypersensitivity dermatitis with bullae or blisters.

If any of these side effects occur, the clinician should take remedial action. A good relationship with the client, where the clinician listens to the client’s complaints, sympathizes, explains the causes, and encourages clients to accept minor or transient side effects is essential to good care. The social worker, counselor, or trained community health worker has an important role in supporting clients through side effects and other difficulties with adherence to treatment. Before ART is commenced, the social worker should thoroughly counsel clients and their treatment companions on what to expect and what they should do if there are side effects.

**Immune Recombination Inflammatory Syndrome (IRIS)**

When people with AIDS commence ART, they sometimes seem to have a flare up in symptoms of TB or another OI. If this happens within the first few months of commencing treatment, after the person had begun to respond to ART (to feel better, have improved appetite, and increase in weight), and after a fall in viral load or increase in CD4 count (as measured where these tests are available), the person may be experiencing Immune Recombination Inflammatory Syndrome (IRIS). IRIS is more likely to occur in clients who have very low CD4 counts. When the immune system is very damaged, it cannot respond properly to infections and viruses or bacteria can be present in the body without an obvious reaction. For example, chest X-rays may not show evidence of TB infection, or a person who is infected with herpes zoster may not show the symptoms of shingles. As the client’s immune system becomes stronger on ART, the immune system begins to fight infection normally. Symptoms of viral infections or TB may then become evident. **IRIS is not evidence of treatment failure.** IRIS is evidence that ART is working well and the client’s immune system is being restored. Therefore, clients who exhibit symptoms of IRIS must continue with the ART throughout the period of symptoms of IRIS.

**4.2.5 ART for Persons Co-infected with TB**

WHO recommends that people who are co-infected with HIV and TB complete their TB therapy before beginning ARV treatment, **unless** there is a high risk of HIV disease progression and death during the period of TB treatment. There is a high risk of HIV disease progression if the TB is disseminated throughout the body and not focal (that is, it is not just in one part of the body or one spot in the lungs), or the CD4 count is less than 200. We now know that delaying treatment with ART for TB and HIV co-infected clients that are already sick with AIDS increases their mortality by up to 50 percent.\(^\text{15}\) Therefore, AIDS clients who are also infected with TB should receive TB treatment and ART at the same time.

When a person does need TB and HIV treatment concurrently, first-line treatment options include zidovudine and lamivudine, or stavudine and lamivudine, plus either a NNRTI or abacavir. If an NNRTI-based regimen is used, efavirenz is the preferred drug. Efavirenz has less potential than nevirapine to aggravate any liver toxicity caused by TB treatment. Also, efavirenz has less potential for clinically

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\(^{15}\) Lawn S et al., *Early mortality among Patients with HIV-associated TB in Africa: Implications for the Time to Initiate ART.* Fourteenth Conference on Retroviruses and Opportunistic Infections, (Los Angeles, abstract 81, 2007).
significant interactions with the TB drug rifampicin. But if used with rifampicin, efavirenz dosage must be increased to 800 mg per day. PIs, except for ritonavir-boosted saquinavir, are not recommended during TB treatment with rifampicin because of their interactions with rifampicin.16

Because HIV depresses the body’s immune response to infection with TB, skin tests, such as the Mantoux test, may be negative even when infection is present. In many poor communities in Africa people are infected with TB at an early age, but do not develop clinical illness because they receive BCG immunization, which provides protection against disseminated TB. A healthy person’s body responds rapidly to TB, preventing it from spreading. However, the TB bacteria can remain alive but dormant in the body. Dormant infections can spread rapidly through the body if HIV has damaged the immune system. This may occur without TB being present in the sputum. It is therefore important to take a careful clinical history from each person about to commence ART to establish if they have symptoms suggestive of TB, or if they had symptoms in earlier life suggestive of infection with TB. These symptoms might include weight loss and failure to thrive, or chronically enlarged lymph glands. However, even with no history suggestive of TB and no signs or symptoms of current TB infection, some people commenced on ART will begin to improve clinically and then develop symptoms of TB.

While taking ART, if symptoms of TB develop, follow your local clinical guidelines. If possible, continue the ART while giving TB treatment, and thus avoid the potential for development of resistance to the ARVs that were commenced.

4.2.6 ARVs and Prevention of Mother-to-Child Transmission

Clinical trials in resource-limited countries have shown that mother-to-child transmission of HIV can be significantly reduced if the mother, her newborn infant, or both take certain ARV regimens. The simplest and cheapest regimen requires a single dose of nevirapine be given to the mother when she goes into labor, and another dose given to the infant within 72 hours of birth. There are reports of successful use of nevirapine for home births if the mother is diagnosed as HIV positive at an antenatal clinic and is given nevirapine to take home for herself and her newborn infant. Programs that provide nevirapine for PMTCT can be integrated into antenatal and delivery care at relatively little cost. The preventive ARV regimens are a very cost-effective intervention for PMTCT but such use of nevirapine only helps protect the baby and does not treat the mother. In fact, it may compromise the mother’s future treatment by reducing the mother’s response to nevirapine if she receives an ART regimen that includes nevirapine in the future. Adding a second ARV may reduce the possibility of developing resistance to nevirapine. But this increases the complexity and the cost of the intervention. Recently, PMTCT programs have been favoring longer regimens (in the third trimester of pregnancy) using at least two, and often three ARVs (e.g., zidovudine, lamivudine, and nevirapine). Because monotherapy (use of only one ARV) has a much higher chance of causing resistance than does use of multiple ARVs given together, nevirapine is often stopped before the other ARVs that are taken with it for PMTCT. This ensures that nevirapine, which has a long half-life

and clears from the bloodstream slowly, does not persist on its own in the blood.

Pregnant women who have symptoms diagnostic of AIDS or a CD4 count of 200 or less need ART. There is emerging evidence that if pregnant women whose CD4 count is 350 commence ART, there is significantly greater reduction in mother-to-child transmission of HIV in comparison with commencing ART when the pregnant woman’s CD4 count is 200. Therefore, antenatal services that have access to CD4 counts can provide better care for the woman and her infant than those services that must rely on clinical signs of AIDS to commence ART.

PMTCT is best provided by a clinician experienced in ART, sharing clinical care of clients with clinicians who provide antenatal and delivery care. For bureaucratic reasons, referral hospitals often find it difficult to provide midwifery and ART care in one outpatient department, but women generally prefer to attend antenatal care and labor and delivery with the rest of the women, rather than feel stigmatized and “ill.” Hospital managers and clinicians should work together to overcome the barriers to sharing care of pregnant women who are HIV infected. Primary health care services are better able to provide such integrated care in the clinic or through extension services. As ART becomes available in decentralized primary health care services, better care is available for pregnant women who have AIDS.

Women who are infected with HIV before pregnancy and whose CD4 count remains above 500, have very low rates of transmission of HIV to their child. Good nutrition, avoiding infection, and a healthy lifestyle all help extend health. Antenatal care should reinforce these critical measures. New HIV infections in pregnancy and breastfeeding, with high peak viral loads, are associated with increased mother-to-child transmission. Thus, all pregnant and lactating women and their partners in high-HIV-prevalence areas should be counseled about and urged to practice safer sex and use barrier methods, especially condoms, during pregnancy and lactation.

### 4.2.7 Pediatric AIDS Care

It is important that all infants born to HIV-infected women are followed up after birth, even if the mother and infant received preventive ARVs. Because of the risk of acute illness and rapid death, all infants born to HIV-infected mothers should begin taking oral cotrimoxazole between four to six weeks of age. If given to infants under this age, cotrimoxazole can damage the infant's liver and cause severe jaundice.

All infants born to HIV-infected mothers will have antibodies to HIV in their blood at birth. These antibodies have passively transfused across the placenta from the mother’s blood and will persist for up to 18 months. Therefore, the presence of HIV antibody in the blood of an infant is not diagnostic of HIV infection in infants under 18 months of age. Before 18 months of age, diagnosis of HIV infection requires virological testing using Polymerase Chain Reaction (PCR) for the presence of HIV antigen or immune complexes that include antigen in the infant’s blood. By age four to six weeks, PCR approaches 98 percent accuracy for

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diagnosing pediatric infection, but testing cannot exclude infection in infants that are breastfeeding because such infants continue to be exposed to HIV infection.

There is increasing appreciation that most women in the developing world should exclusively breastfeed their babies whether they are infected with HIV or not. Few women and families can meet WHO’s criteria for providing the baby with replacement feeding (accessible, feasible, affordable, sustainable, and safe). If these criteria are not met babies have higher risk of dying from diarrhea and malnutrition than from HIV. Women who have not progressed to AIDS should be able to breastfeed without making their own HIV infection worse.

In settings where PCR testing is not available, HIV infection status cannot be reliably confirmed in the first 18 months of life. Therefore cotrimoxazole prophylaxis must be continued until the infant ceases all breastfeeding, and is tested and proven to be HIV negative after 18 months of age. Infants that are found to be HIV infected must remain on cotrimoxazole long-term to reduce their risk of illness and death. It also decreases the risk of illness and death in other members of their household by removing the infant as a source of infection.\textsuperscript{18}

In high-prevalence areas, cotrimoxazole should be part of the integrated management of childhood illness in the community and clinic. Primary health workers and clinicians in emergency departments must consider HIV infection in infants with unusual infections including:

- Persistent or severe candida infection,
- Severe, frequent, or prolonged pneumonia,
- Meningitis,
- Severe, frequent, or prolonged diarrhea, or
- Failure to thrive.

Because many infants die at home without ever seeing a formal health care worker, it is important to encourage a high level of awareness of pediatric HIV infection and the need for cotrimoxazole prophylaxis during antenatal care. Awareness-raising should extend to the community level among families with young children, traditional health workers, and all cadres of primary health workers including community health workers and other village volunteers.

In countries where ART is available for children who develop AIDS, infants and children live healthily to adolescence and adulthood. But in resource-limited settings, there are

many obstacles to scaling-up pediatric AIDS care. These obstacles include:

- Lack of human capacity—too few health workers, and among them too few with knowledge and skills for treating pediatric AIDS;
- Insufficient advocacy and understanding that ART is effective in children;
- Lack of affordable, simple diagnostic testing technologies;
- Lack of affordable, practicable pediatric ARV formulations (pills and syrups in strengths suitable for children); and
- Limited experience with simplified, standardized treatment guidelines.

Although *presumptive diagnoses* of severe HIV infection can be made in infants less than 18 months of age (see box 6), to date, few children have been started on ART in resource-limited settings. WHO and UNAIDS are now spearheading the provision of ART for infants and children as part of the follow-up to the 3 by 5 Initiative.  

Pediatric formulations are best used for infants and children under five years of age. If these are not available, children should be treated with fractions of adult pills. For accuracy, the pills should be cut in the pharmacy, and not by the caregiver in the home. Pharmacists and clinicians need updated training in pediatric prescribing and dispensing.

ART should be commenced in infants and children according to local clinical guidelines. If local guidelines do not cover pediatric AIDS, the newly-revised WHO draft guidelines should be followed.  

Long-term prognosis in pediatric AIDS is related to the child’s lowest CD4 count ever reached. The total lymphocyte count significantly predicts the risk of mortality in HIV-infected children. Mortality increases with low levels of lymphocytes according to the age of the child. A 20 percent increase in mortality is associated with lymphocyte levels below 4,000 before 11 months of age, below 3,000 between 12 and 35 months, and below 2,500 from three to five years. Thus the total lymphocyte count may be used to guide when to start ART in infants and children when the CD4 count is not available. The threshold CD4 levels for severe immunodeficiency are less than 25 percent for infants 11 months old or younger, less than 20 percent for children aged 12–35 months, or less than 15 percent for children aged three years and above. They are all associated with a 20 percent increase in mortality. For further details, see your Ministry of Health clinical guidelines and protocols, or the WHO guidelines if local guidelines are not available.  

The preferred first-line regimen for infants and children is a NNRTI-based regimen. This consists of two NRTIs, for example zidovudine and lamivudine, plus one NNRTI, nevirapine. Efavirenz cannot be used currently in children less than three years of age because of a lack of appropriate dosing information, although this is

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20 Ibid.

21 Ibid.
under study.

As in the treatment of adolescents and adults with ART, adherence to treatment, development of resistance, and toxicity are all issues when treating infants and children. (More information may be obtained from WHO.) Skilled counseling and support must be offered to the parent or guardian and to the older children undergoing ART, to ensure that they understand the importance of adherence. The child may need increased calories in his or her diet to help fight infection and to fully recover from failure to thrive and ill health. Breastfeeding remains an important source of calories for many babies in the second year of life in resource-limited settings. There are no known problems from extended breastfeeding in infants who are already infected with HIV.

4.2.8 Considerations for ART in Adolescents

Although adolescents are treated according to adult treatment protocols, they have special needs resulting from their stage in social and emotional development. In traditional societies, adolescence is a time for preparation for marriage and having children. Adolescence is often a time for experimentation and risk taking, which includes sexual risk taking. Special effort must be made to ensure that adolescents understand their own feelings and frustrations, and know how to protect themselves against STIs and unwanted pregnancy.

Counseling, peer education, and support groups are particularly important for HIV-infected adolescents. HIV-infected adolescents have the additional burden of needing to prevent the forward infection of others with HIV. Such adolescents will need additional psychosocial support. Abstinence and delayed sexual debut are important aspects of sex education. But adolescents who are sexually active or who are going to become sexually active need to have knowledge about their sexuality, condoms, and partner negotiation skills, and youth-friendly services available and accessible to them to prevent unwitting onward transmission of HIV. Sexually-active adolescents also need information and services to protect themselves against other STIs and unwanted pregnancy.

Additional care and support must be given to adherence counseling and monitoring, since HIV-infected adolescents often believe in their own immortality and fail to take ART even though they had good adherence as younger children. Guidance on choosing treatment buddies who will not reinforce developmental behaviors that are dangerous for the adolescent can be given, but the choice belongs to the person on treatment. Although in many countries adolescents cannot give consent to treatment, clinicians and social workers need to foster self-responsibility and ownership of treatment plans by adolescents, to ensure adherence to treatment and prepare them for continued ART in adult life.22

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22 The guidance on integrated management and treatment of adolescent and adult AIDS goes by weight for change from pediatric to adult doses. Follow local treatment protocols or WHO Guidance that will clarify at what weight children become adolescents for ART purposes.
5.0 Community Support for Treatment

To complement facility treatment services, resources in the community are needed to make sure care is continuous, those on treatment aren’t lost to care, and people on treatment can be supported by and integrated into the community to live long and well.

Community resources for people living with HIV include community home-based care programs, spiritual, and other support from faith-based organizations, jobs and economic resources, food relief and programs that enhance food security, and legal assistance and support for making wills and succession planning for the future care of children. These are all necessary adjuncts to clinical treatment services. Care management at the community level is an effective tool for living positively with AIDS as a chronic disease. People living with HIV can be an important part of prevention efforts for the broader community by increasing understanding, encouraging testing, and putting a human face on AIDS. These activities can also help build their own self-esteem and stature in the community and decrease stigma.

5.1 Community Home-Based Care, Including Support for Treatment

The role that community-based organizations, community health workers, and faith-based organizations can play in support of HIV-infected people on treatment is very broad. We encourage readers of this guidance to access, as a companion piece, Pathfinder’s recently-published training guide and handbook, Community-Home Based Care for People and Communities Affected by HIV and AIDS: A Comprehensive Training Course for Community Health Workers for a comprehensive view of HIV prevention, care, and support at the community level. Unit 18, Antiretroviral Therapy (ART), provides practical guidance for support of those needing and on treatment. (http://www.pathfind.org/Publications_Training_and_Capacity_Building_CHBC)

Provision of care for people who are HIV positive is very different from traditional health facility treatment. In the past in low-income countries, people came to hospitals and health facilities for acute care for sudden illness or trauma. There was little attention to continuity of care and maintenance of individual client records. The clinic register tabulated clients’ personal details, presenting complaints, diagnosis, and treatment. Few clients returned for follow-up treatment. However, people who are diagnosed as HIV positive need lifelong care, support, and treatment. Medical records must be kept confidentially, and be available, referred to, and updated as required by the health worker. Information from clients’ records should be included in referral letters for health care in other facilities and hospitals. Health information systems must track people who are diagnosed as HIV positive over time to ensure that they are screened for TB, that OIs are diagnosed and treated without delay, that people receive ART at the appropriate time, and that they are referred for STI diagnosis and treatment, family planning, and other reproductive
Case managers are part of the shared confidentiality that health workers have with HIV-positive clients. It is important to note that, clients must give permission for case managers to be involved in their care.

### 5.1.2 The Need for Care Management

When people first receive the diagnosis that they are HIV positive they may react with anger or denial. They may not hear advice on keeping well, avoiding infections, and seeking prompt treatment for symptoms of STIs, TB, and other infections. Many people are fearful of disclosing that they are HIV positive to their spouse, others at home, or close friends. Because AIDS is frequently stigmatized and persons who are thought to be HIV positive may be discriminated against at home, in the community, and in the workplace, a person who is newly diagnosed as HIV positive may be reluctant to return to the health facility for follow up, and may not be willing to join a support group. But health facility staff must follow up with HIV-positive clients to ensure they receive optimum care and they know when they should next seek care and treatment at the health facility.

Care management undertaken by health facility staff or by lay people who have received training and are supervised by health care workers is an effective way of conducting HIV-infected clients’ continuous care. Some models for care and treatment—for example in Rwanda—use community volunteer care managers. Other models—for example Ethiopia—use a new cadre of non-clinical health facility employees.

#### The Care Manager’s Role

The role of the care manager is to know what services and resources are available for care, support, and treatment of people who are HIV positive, to refer them for services when necessary, and help the HIV-positive person access available resources. For hospital and health facility services and resources, managers of HIV services should work with staff to develop appropriate designs for clinical care and client flow plans. The care manager training and the care managers’ supervisors must ensure that the care manager understands the clinical care and client flow plans. For community services and resources, the care manager must work with community health workers and others in the community who can help map the available local resources. The map of community services should include psychospiritual support, legal advice, and economic opportunities offered by faith-based organizations and nongovernmental organizations. It should also include resources, such as retired nurses living in the community, religious leaders with a particular interest in pastoral care, and associations of people living with HIV. It will need to be periodically updated as the local situation changes.

Although the counselor or social worker may need to follow up with HIV-positive clients until they are willing to be referred to support groups in the community, the counselor or social worker should introduce HIV-positive clients to the care manager, in confidence, as soon as a positive diagnosis is made. The care manager
should outline a care plan for each HIV-positive client with the referrals that will be needed over time outlined and the resources and services available locally noted.

**The Care Plan**

From the time of diagnosis as HIV positive before ART is needed, and continuing after commencing ART, the objective of the plan for wider care, support, and treatment is to maximize HIV-positive clients’ quality of life. It is a comprehensive care plan that includes vigorous prevention and treatment of OIs, and nutrition, spiritual, psychosocial, and economic support.

As people living with HIV accept their diagnosis, the care manager helps each client eventually disclose their HIV status to their sexual partner. Care managers ensure their clients are screened for TB and STIs and receive cotrimoxazole, impregnated bed nets, and preventative treatment for malaria (and TB and cryptococcal infection if required by local protocols). Care managers refer their clients to community health workers and advise clients on living positively and protecting their health and the health of sexual partners.

Over time, the care manager takes responsibility for ensuring their clients’ families receive guidance on succession planning for their children, drawing up wills, identifying who will care for the children in the future, and who will receive property and land. They may also help develop memory books or boxes for the children. The care manager works with the community health worker or home care volunteer ensuring ART support, managing treatment side effects, and treating common symptoms. If a person living with AIDS fails to seek clinical care—either in cases of acute need, or missing routine appointments—the care manager follows up with the client or seeks the assistance of the community health worker for community follow up.

**5.2 Addressing Stigma and Promoting Prevention**

People living with HIV can be powerful advocates for effective response to the epidemic in the community. Once a person is comfortable disclosing that they are HIV infected—for example, once they are receiving psychosocial support from an association of people living with HIV or once they begin to feel well on treatment—the person living with HIV can be an important resource in the community for effective prevention campaigns, for providing psychosocial support to the newly diagnosed, and educating families and communities on how they can support people to take ART. Not all persons who are diagnosed as HIV positive are able to become a resource in their community, but many do and contribute to reducing the stigma associated with HIV by their openness. The care manager or the community health worker should encourage HIV-infected persons who are able, to volunteer with local faith-based and community-based organizations, join local health office prevention campaigns, or just raise awareness of prevention, living positively, and availability of ART among their own friends and neighbors. People living with HIV should be accorded great respect by the local health office as experts who know better than any health worker the local drivers of risk behaviors, and the barriers to prevention and accessing care, support, and treatment in their local environment.
5.3 End-of-Life Care

Although the objective of ART is many years of normal, productive life, people on ART can fail to respond to treatment, alternatives may run out for them, and they may become seriously ill and die at any time. Therefore, it is important that persons receiving ART and their families also receive counseling and support for planning for the future.

Discussions about death are uncomfortable for most people, and are taboo in some cultures. Some people believe that talking about death hastens it in some way. But open discussion about death—ideally beginning soon after diagnosis—can help clients feel that their concerns are heard and can help empower them to make provisions for their children and property. Parents may need guidance on appointing guardians for their children and writing wills that determine inheritance of their property. In situations where traditional mechanisms can result in “property grabbing” by the husband’s relatives—leaving wives without property, a home, and even their children—establishing a modern, legally recognized will is crucial to the future of the bereaved widow and orphans. Counseling and legal support for clients should include educating the spouse and other relatives on legal protection and enforcing provisions in the client’s will. Clients may want to plan for their own funeral costs and future school fees for their children. They may decide to sell property and land. These decisions should be well considered and not rushed.

Persons with AIDS whose disease is not responsive to available drugs, because of resistance to ARVs or lack of appropriate drugs for malignancies or infection, still need active care. The goal of end-of-life care is to achieve the best quality of life for clients and their families when treatment is not available or no longer working. End-of-life care seeks to keep persons physically, mentally, and spiritually comfortable and ensure dignity in dying.

In resource-limited countries, the health infrastructure is unable to provide in-hospital care for all who are terminally ill. Often the only option for people dying from AIDS is care at home, and most people prefer to die peacefully at home. Pressing medical needs include control of pain and often relief of diarrhea. Health workers must address their own anxieties about prescribing adequate pain relief for the terminally ill, as addiction to painkillers is not an important consideration for the dying. There are estimates that in resource-limited settings between one-quarter and one-half of all people dying from AIDS needlessly suffer severe pain. Medication and provisions to manage diarrhea in the home may incur expenses requiring financial assistance at this time.

Other needs are emotional, psychosocial, and spiritual. Even those who have not been active in their church or mosque may appreciate the spiritual peace that a minister of their religion can bring as they face death. Quarrels in the family and community may need to be resolved. Family and neighbors may need to visit to “say goodbye,” though this may be unspoken. Family members may need additional counseling as they care for a terminally-ill relative and this need may increase after their bereavement, especially if the family members are themselves HIV infected or living with AIDS. Much of this end-of-life support
can be provided by community organizations, community health workers, and other support services.

Health service managers need to be aware of the continuing need for reliable and affordable medication, social work, and counseling support for clients who are terminally ill. Health budgets and annual plans must ensure that adequate funding and other resources are available for these crucial aspects of care.
Annex 1

Antiretroviral agents included in the WHO ARV guidelines approved for inclusion in WHO’s Essential Drug List as of March 2005

<table>
<thead>
<tr>
<th>Nucleoside reverse transcriptase inhibitors (NRTIs)</th>
<th>Non-nucleoside reverse transcriptase inhibitors (NNRTIs)</th>
<th>Protease inhibitors (PIs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>zidovudine (ZDV or AZT)</td>
<td>nevirapine (NVP)</td>
<td>saquinavir (SQV)</td>
</tr>
<tr>
<td>didanosine (ddI)</td>
<td>efavirenz (EFV or EFZ)</td>
<td>ritonavir</td>
</tr>
<tr>
<td>stavudine (d4T)</td>
<td></td>
<td>indinavir (IDV)</td>
</tr>
<tr>
<td>lamivudine (3TC)</td>
<td></td>
<td>nelfinavir (NFV)</td>
</tr>
<tr>
<td>abacavir (ABC)</td>
<td></td>
<td>lopinavir + ritonavir (LPV/r)</td>
</tr>
</tbody>
</table>

### Annex 2

Recommended first-line antiretroviral regimens in adults and adolescents with documented HIV infection

<table>
<thead>
<tr>
<th>Regimen&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Pregnancy considerations</th>
<th>Major toxicities</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZDV/3TC/EFZ or ZDV/3TC/NVP</td>
<td>Substitute NVP for EFZ in pregnant women or women for whom effective contraception cannot be assured</td>
<td>ZDV-related anemia; EFZ-associated CNS symptoms; possible teratogenicity of EFZ; NVP-associated hepatotoxicity and severe rash NRTI-related metabolic side-effects</td>
</tr>
<tr>
<td>ZDV/3TC/ABC&lt;sup&gt;a&lt;/sup&gt;</td>
<td>ABC safety data limited</td>
<td>ZDV-related anemia; ABC hypersensitivity; NRTI-related metabolic side-effects</td>
</tr>
<tr>
<td>ZDV/3TC/RTV-PI&lt;sup&gt;b&lt;/sup&gt; or ZDV/3TC/NFV</td>
<td>LPV/r safety data limited NFV: most supportive safety data</td>
<td>ZDV-related anemia; NFV-associated diarrhea IDV-related kidney stones PI- and NRTI-related metabolic side-effects</td>
</tr>
</tbody>
</table>

<sup>a</sup> ZDV/3TC is listed as the initial recommendation for dual NRTI component based on efficacy, toxicity, clinical experience, and availability of fixed-dose formulation. Other dual NRTI components can be substituted, including d4T/3TC, d4T/ddI and ZDV/ddI, depending on country-specific preferences (see text). ZDV and d4T should never be used together because of proven antagonism. Fixed dose formulations are preferred whenever possible as they promote enhanced drug adherence.

<sup>b</sup> RTV-PI includes IDV/r, LPV/r or SQV/r.

The major pharmaceutical manufacturers currently produce three fixed-dose combinations of ARVs included in these guidelines: ZDV/3TC, ZDV/3TC/ABC and LPV/r. Fixed-dose formulations have also been produced by generic manufacturers (d4T/3TC/NVP and ZDV/3TC/NVP), which may facilitate simplified regimens, decrease cost, and promote adherence if they can be legally used and their quality and bioequivalence have been demonstrated.

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Annex 3

WHO-recommended second-line regimens in adults and adolescents, 2006

<table>
<thead>
<tr>
<th>First line regimens</th>
<th>Second line regimens for treatment failure</th>
<th>Alternative second line regimens for treatment failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZDV/3TC/EFZ or ZDV/3TC/NVP</td>
<td>d4T/ddI/RTV-PI&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>RTV-PI&lt;sup&gt;a&lt;/sup&gt;/ABC/ddI&lt;sup&gt;c,d&lt;/sup&gt; or d4T/ddI&lt;sup&gt;b,c&lt;/sup&gt;/NFV</td>
</tr>
<tr>
<td>ZDV/3TC/ABC</td>
<td>d4T/ddI&lt;sup&gt;b,c&lt;/sup&gt;/EFZ or d4T/ddI/NVP</td>
<td>d4T/ddI&lt;sup&gt;b,c&lt;/sup&gt;/RTV-PI&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>ZDV/3TC/RTV-PI or ZDV/3TC/NFV</td>
<td>d4T/ddI&lt;sup&gt;b,c&lt;/sup&gt;/EFZ or d4T/ddI/NVP</td>
<td>ABC/ddI&lt;sup&gt;c,d&lt;/sup&gt;/EFZ or ABC/ddI/NVP</td>
</tr>
</tbody>
</table>

<sup>a</sup> RTV-enhanced PI = IDV/r, LPV/r, SQV/r. An RTV-enhanced PI regimen is preferred because of the potency of these regimens. NFV can be considered as an alternative for the PI component of second-line therapy if RTV-enhanced PI is not available or if there is a clinical contraindication to its use.

<sup>b</sup> Nucleoside cross resistance may compromise the potency of d4T/ddI at the time of switching for treatment failure as it is assumed that virological failure will have been prolonged at that point and several nucleoside analogue mutations are likely to be present. However, choices are limited in the setting of treatment failure. See also, footnote c.

<sup>c</sup> Tenofovir is a once-daily nucleotide nucleotide reverse transcriptase inhibitor (NtRTI) with activity against some nucleoside-resistant strains. If available, TDF can either be added to d4T/ddI or ABC/ddI or substituted for either d4T or ABC in these combinations. Its currently restricted availability in resource-limited settings is recognized

<sup>d</sup> High-level ZDV/3TC co-resistance confers diminished susceptibility to ABC. If d4T/3TC is used as the first-line dual nucleoside backbone, AZT/ddI can be used as the second-line nucleoside component and vice versa.

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