

PERSPECTIVES AND PRACTICE IN ANTIRETROVIRAL TREATMENT

**A PUBLIC HEALTH APPROACH
TO ANTIRETROVIRAL
TREATMENT:
OVERCOMING CONSTRAINTS**



World Health Organization

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Introduction

Triple-drug combination antiretroviral (ARV) therapy has remarkable effects on the lives of people living with HIV/AIDS. When it is provided on a large scale, AIDS wards in hospitals are emptied, people living with HIV/AIDS return to their families and jobs and AIDS-related morbidity and mortality fall dramatically¹⁻⁶.

However, since ARV therapy was introduced in 1996, these benefits have been reserved almost exclusively for industrialized countries, which bear only 5% of the global burden of HIV/AIDS. Of the 38 million people now living with HIV/AIDS in developing countries, between 5 and 6 million in the advanced stages of disease urgently need ARV treatment. Only about 300 000 currently have access to it. In sub-Saharan Africa, more than 4 million people need treatment, but only 50 000 have access, slightly less than 2% of those in need⁷. This disparity is unacceptable given that effective treatment is available.

A growing, global movement of people living with HIV/AIDS and their advocates, civil society organizations, health professionals, philanthropic foundations, international agencies, governments and private corporations is now working to reverse this injustice. The efforts of this movement have helped to shape a global consensus that allowing millions of deaths from a treatable disease is intolerable and that prevention strategies alone are insufficient to contain the HIV/AIDS epidemic. Treatment and care are therefore the crucial, missing link in the global response because, by alleviating suffering, reducing stigma and mitigating the economic and social impact of disease, they can reinforce the fight against HIV/AIDS.

Positive developments in the last few years mean that, for the first time, ARV therapy is now within the reach of developing countries. Drug prices have fallen as a result of the Accelerating Access Initiative⁸ and increased generic competition in the pharmaceutical sector. New funding is available to support treatment and care from the Global Fund to Fight AIDS, Tuberculosis and Malaria and the World Bank Multi-Country HIV/AIDS Programme for the Africa Region. Resources for access to care are likely to grow significantly in the future, for example through support from the United States, which has passed legislation authorizing such support⁹. In 2002, WHO released new guidelines on scaling up access to ARV treatment in resource-limited settings¹⁰ and included 12 antiretroviral drugs in the WHO Model List of Essential Medicines¹¹. To ensure access to quality drugs for the treatment of HIV-infected people, WHO initiated a programme to prequalify HIV/AIDS medicines¹².

In preparation for the United Nations General Assembly Special Session (UNGASS) on AIDS in 2001, global resource needs for the HIV/AIDS epidemic were estimated to be US\$ 9.2 billion per year¹³. Included in this estimate was the need to expand access to antiretroviral therapy from about 800 000 people at the end of 2002 to about 3 million people by the end of 2005. UNAIDS estimates that annual global spending on HIV/AIDS reached almost US\$ 3 billion in 2002, compared with US\$ 300 million just 3 years before¹⁴. Raising more resources is vital to achieve the scale of response needed to alter the course of the epidemic.

However, deploying resources for treatment and care wisely in the future requires developing as much experience and capacity as possible now. A growing number of developing countries – including Botswana, Brazil, Senegal, Thailand and Uganda – already have significant national ARV programmes. Others are using the prevention of mother-to-child transmission as an entry point to care for women and their children. These are the pioneers. Other countries still need to match their need for ARV treatment with sufficiently ambitious goals and plans and to mobilize all the stakeholders who must play their part. The target of 3 million people on ARV therapy by 2005 can only be realized through simultaneous action on multiple fronts.

Many obstacles must be overcome to reach this target. Political commitment is crucial. Health care workers must be trained and communities educated and mobilized. Sustainable financing, procurement and regulatory mechanisms must be established. All contacts with the public health system – such as for antenatal care, sexually transmitted infections and tuberculosis services – must be used, and private-sector initiatives need to be developed. The results of monitoring, evaluation and operational research must be used to improve programme delivery.

Treatment with antiretroviral therapy has yielded remarkable results in affluent countries and some middle-income countries such as Brazil. Lessons can be learned from these examples, but this publication reviews the experiences of ARV programmes already underway in countries with very severe HIV epidemics but severely constrained resources – as in most of Africa and part of the Caribbean. The publication aims to show how some of the key policy issues for scaling up HIV/AIDS treatment have been dealt with and to identify common elements that should be considered by everyone seeking to provide HIV/AIDS care on a significant scale.

The challenges of expanding access

Concerns persist about the feasibility of providing ARV treatment to large numbers of people in resource-limited settings. The objections usually raised are the high cost of drugs, the complexity of regimens, the scarcity of trained health care providers, insufficient infrastructure to monitor people receiving therapy, the challenges of adhering to therapy and the threat of drug resistance.

These challenges are formidable but not insurmountable. WHO believes that health systems in developing countries can provide high-quality ARV therapy to many more people than currently receive it by significantly simplifying the choice of treatment regimens and the complexity of clinical monitoring¹⁰. Standardizing treatment means that health systems with few resources can maintain a globally acceptable quality of care and deal with human resource constraints, promote adherence to treatment and avoid resistance. Most importantly, the number of people receiving ARV treatment will increase, and the quality of that treatment will be improved. However, some of the important challenges of making ARV therapy available also lie in the way decisions are made and programmes managed. This determines to what extent stigma can be dealt with and openness about HIV can be fostered and how prevention efforts are supported. For these reasons, WHO proposes a public health approach to ARV treatment that focuses on treating many more people, mainly poor people, and on promoting a dramatic increase in efforts to prevent HIV transmission.

A public health approach to ARV therapy

The public health approach to HIV/AIDS treatment proposed here builds on the experience of ARV programmes now underway in developing countries, including those by Médecins Sans Frontières (MSF) in South Africa¹⁵ and Malawi¹⁶, the Lilongwe Central Hospital in Malawi¹⁷, Partners in Health in Haiti^{18,19} and the experience of scaling up access to treatment in Uganda^{20,21}. These programmes share a number of common features that are crucial elements in a public health approach to ARV therapy.

- ▶ Decisions on treatment selection and management of treatment and care for each person are made by using **standardized treatment protocols and simplified clinical monitoring**.
- ▶ They make **optimal use of available human resources** by delegating aspects of the care of and follow-up of people living with HIV/AIDS, including supervision by physicians, nurses, other health care workers and community members.
- ▶ They **involve community members and people living with HIV/AIDS** in programme design and management, and in supporting care of people living with HIV/AIDS, in particular adherence to treatment.
- ▶ **Strategies to minimize costs**, such as introducing generic drugs or alternative laboratory technologies, are used to make ARV therapy more affordable to the populations they serve.

Making decisions simpler

Uganda provides a very good example of how ARV treatment can be simplified in practice. Since October 2000, when price reductions helped to make increased use of highly active

ARV therapy (HAART)²² feasible, two regimens, zidovudine + lamivudine + efavirenz and stavudine + lamivudine + nevirapine, have been prescribed as first-line regimens. Projects in other countries, including Haiti^{18,19}, Kenya (personal communication, David Stanton, United States Agency for International Development) and Cameroon, have adopted similar approaches (Table 1).

The availability of the drugs and their cost were the overriding considerations for choosing these regimens. Pill count, side effect profile and the availability of at least part of the regimen as a fixed-dose combination were also factors.

Many treatment programmes in developing countries have also drastically simplified their approaches to identifying the people who need therapy and to monitoring therapy. The rationale for these approaches is that «until tests of viral load, CD4 count, or other surrogate markers are available, simple clinical criteria can identify those most likely to benefit from highly active antiretroviral therapy»^{18,19}. Likewise, except for demonstration projects, the monitoring of treatment has often relied mainly on clinical assessment, as in Haiti, Uganda and Lighthouse Malawi. In these examples, laboratory tests have been used only when there were problems, such as side effects or suspected treatment failure.

Building on the experience of these programmes, the WHO guidelines on the use of ARV drugs in resource-limited settings¹⁰ promote a public health approach to HIV/AIDS treatment by recommending standardized first- and second-line ARV regimens. This greatly simplifies decision-making for everyone procuring, prescribing, dispensing or taking ARV drugs. The guidelines also provide clear guidance on when to start and change ARV therapy based on clinical condition and, when possible, laboratory testing. For follow-up, clinical monitoring options ranging from «absolute minimum» to «optional» laboratory tests are recommended, based on the resources available¹⁰.

Table 1. First-line regimens adopted by treatment programmes serving populations with high HIV prevalence

Regimen	Programme *
stavudine + lamivudine + nevirapine	Uganda, Burkina Faso, Partners in Health Haiti, Lighthouse Malawi, Kenya
zidovudine + lamivudine + efavirenz	Uganda, Burkina Faso, Partners in Health Haiti, Lighthouse Malawi, Kenya

* This refers to the national programme unless the name of the country is preceded by the name of an organization.

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The aim of these simplified approaches is to strike a balance between what may be desirable and what is currently feasible in resource-limited settings. The ARV regimens recommended by WHO are the same as those now used in industrialized countries. Good clinical results using simplified monitoring techniques show that an immediate lack of laboratory infrastructure should not stop the expansion of treatment access.

Making optimal use of human resources

The shortage of trained health care providers is severe in many high-prevalence countries, not only in HIV/AIDS but across the health sector. According to the International Labour Organization, for example, Kenya has one trained physician for every 7000 people and Cote d'Ivoire one physician for every 10 000 people. HIV/AIDS itself is taking its toll on health care workers in many countries.

A sustained effort is needed to improve clinical training and to provide incentives for health care workers to overcome this human resources shortfall in the future. But millions of people living with HIV/AIDS need access to ARV therapy today. A public health approach to HIV/AIDS treatment should therefore include strategies to reduce dependence on highly trained physicians. To do this, routine aspects of managing treatment and care should be delegated to other health care workers, and tasks suitable for community and family members should be assigned to them.

The national ARV programme in Uganda has adopted this approach for the expansion phase to be supported by the Global Fund. Under its public health and primary care model, physicians will play the lead role in assessing people living with HIV/AIDS, initiating or switching therapy, managing serious conditions and supervising staff. However, clinical officers, nurses and counsellors, including those based in primary care settings, will routinely follow up ARV therapy – including counselling and the initial diagnosis and treatment of common opportunistic infections such as thrush, herpesvirus infections and certain skin conditions. In taking this decision, Uganda built on the experience of its own community AIDS service organizations, such as the AIDS Support Organization (TASO). MSF in Khayelitsha in South Africa¹⁵ and in Chiradzulu in Malawi¹⁶, as well as Partners in Health in Haiti^{18,19}, have adopted similar approaches, aided by standardized ARV regimens and simplified monitoring procedures.

Most programmes in developing countries have relied on in-service training for the introduction of ARV therapy, which in many cases has also covered topics such as HIV testing and

counselling, opportunistic disease management, tuberculosis diagnosis and treatment and palliative care. This has led to improvements in services for people with other health problems and to trainees acquiring skills in HIV prevention. However, the current content of curricula is variable. For example, current HIV/AIDS training programmes range from 1 week in duration in Uganda for all physicians, nurses, laboratory technicians, pharmacists and counsellors based in hospitals and health centres to a suggested minimum of 3 months for clinical officers in Kenya²³. Further, there is still limited published experience with training community and family care providers to support ARV therapy, suggesting that efforts to mobilize their involvement are still in their infancy. A working group convened by WHO under the umbrella of the International HIV Treatment Access Coalition has identified several programmes that are beginning to target these groups⁴.

Community partnership and capacity-building

Evidence is growing that involving communities, peers and family members is critical for large-scale roll-out and increased coverage of programmes. For example, lessons from tuberculosis and river blindness programmes show that systematically engaging these groups can improve treatment outcomes and generate more effective local responses^{25,26}.

Involving the communities that are most concerned has also been a decisive factor in many of the most successful responses to HIV/AIDS. It is a notion that is widely accepted in HIV prevention²⁷ but is equally true for HIV treatment. Partnerships with affected communities, including people living with HIV/AIDS themselves, critically determine how people living with HIV/AIDS understand ARV treatment, their health-seeking behaviour and the acceptability of treatment. The inclusion of those living with HIV/AIDS, their families and communities, will help to overcome the key obstacles to an effective response, including denial, stigma and discrimination.

The extent to which different stakeholders have been involved in ARV programmes has varied greatly. Many programmes – such as those linked to research projects or the medical community – have not incorporated the community at all, at least in their initial phases, and have only recently realized that such input is needed²⁸. Others, such as those of Uganda²⁷ and Cote d'Ivoire³⁰, have explicitly involved community members in programme design through participation in the advisory boards of the UNAIDS HIV Drug Access Initiative²⁰. The advisory board model means that dif-

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difficult decisions, such as where ARV drugs are to be introduced first and who will be eligible for government subsidies, can be shared among all stakeholders. It has also led to the development of communication materials targeting communities affected by HIV. On the other extreme of the spectrum, mutual support programmes established and managed by organizations of people living with HIV/AIDS took the lead and introduced ARV treatment with the help of motivated health service providers³¹.

Long-term adherence to ARV regimens is essential to getting optimal results from treatment and to minimizing the emergence of viral resistance. Initial attempts to involve community members in psychosocial support for people living with HIV/AIDS and in adherence counselling were not very successful. This was because insufficient resources were available to support their work, and access to the treatment used in the programme was not guaranteed²⁹. Later programmes have been more successful using different approaches. The Partners in Health ARV programme in Haiti, for example, uses a method known as directly observed highly active anti-retroviral therapy (DOT-HAART), in which community health care workers known as *accompagnateurs* visit people receiving ARV therapy at home on a daily basis. Although these are often in remote areas, the workers deliver ARV drugs, observe the person take at least one of two daily doses, provide support and respond to family concerns. Adherence levels have been high and clinical results good³².

However, an assessment among people with HIV/AIDS in Trinidad and Tobago found that, although most were willing to take a lifelong ARV regimen, they did not want a health care worker visiting them at home to give medication³³. Another drawback is that directly observed treatment approaches draw heavily on human resources. This is being recognized by several national tuberculosis programmes which – straining under the dual burden of tuberculosis and HIV – are expanding directly observed treatment approaches to involve church group volunteers, people who previously received treatment and women's organizations, among others, in the role of «treatment supporters»²³.

ARV treatment programmes are also beginning to appreciate the potential of family members and peers for treatment support in two areas. Initially this was to ensure that the person living with HIV/AIDS continues the therapy, but they are increasingly involved in generating awareness and direct responses to HIV/AIDS in the community. The AIDS Healthcare Foundation, working in South Africa and Uganda, stresses three factors that enhance ARV adherence: on-site support by nongovernmental organizations; ongoing

education by peers who are also in ARV therapy; and involvement of family members before and during treatment (personal communication, Dickson Opol, Executive Director, Uganda Business Coalition for HIV/AIDS, May 2003). The Botswana ARV programme is successfully employing a buddy system in which each person receiving therapy is encouraged to form a special bond with someone who makes sure that they take their medication³⁴. In MSF's programmes in Khayelitsha and Chiradzulu, adherence support involves trained counsellors, adherence plans and a treatment assistant, usually someone living in the household of the person living with HIV/AIDS who can assist with adherence issues^{15,16}. In addition, support groups on ARV therapy organized for people living with HIV/AIDS enable discussion of barriers to adherence, adverse events, disclosure and other psychosocial issues and serve as fora for health promotion and education.

As ARV programmes are established in high-prevalence settings, everyone needing therapy may not be able to get it immediately. Community input into the processes used to determine who gets therapy is therefore crucial to ensure that these difficult decisions are made in an ethical and equitable manner. Programmes in Senegal²⁷, Malawi¹⁷ and South Africa¹⁵ have already demonstrated the benefits of involving community members in this selection process. MSF has found selection committees and home visits to be valuable in building support and a sense of community ownership of the programme and in assessing family acceptance and disclosure.

Partnerships of this kind involve challenges for the health sector and communities alike. They require a degree of interaction and sharing of responsibility to which health care workers are often not accustomed. Health care providers have few incentives to work in partnership, they seldom have the benefits of doing so explained to them and they often have little time to become involved. Communities, too, may lack the necessary structures, be unfamiliar with medical terms or have reason to be apprehensive about engaging in debate and dialogue with health professionals³⁵. However, if expanded access to ARV drugs is to succeed, programmes must be explicit about the mechanisms and methods that will be used to overcome these obstacles. They should include community education and capacity-building as a key component of budgets and planning for HIV/AIDS treatment and care. Although these investments in time and resources may initially be substantial, they are essential for the long-term success and sustainability of ARV programmes.

Supporting prevention and generating benefits for society

Monitoring and evaluating the broader impact of HIV/AIDS treatment is vitally important to the success and future expansion of ARV programmes. Beyond the well documented benefits of ARV therapy for people living with HIV/AIDS, even in the least developed countries³⁶⁻⁴⁰, evidence is gradually emerging of the favourable effect of ARV treatment on households and society at large, especially when programmes strongly involve their communities.

According to a report from a community consultation on ARV treatment in Zambia⁴¹, efforts to involve families have been constrained by the sense of shame that a person who has contracted HIV is perceived to bring on a family as well as the family's fear of being burdened by orphaned children. Such concerns can lead to people with HIV/AIDS being shunned or abandoned. The report⁴¹ notes that: «Respondents who were already receiving ARV treatment shared how their family support is revitalized when ARV treatment is effective. Family members become more hopeful and less anxious about increasing economic burdens and the workload of caring for the sick and for orphans. The introduction of scaled-up ARV-treatment programmes should therefore help to restore strained family structures, reversing the break down of family life in high-prevalence, low-income settings.»

Beyond homes and families, ARV therapy has resulted in significant community mobilization against AIDS and increased the uptake of interventions to prevent HIV transmission such as HIV testing and counselling and condom use. For example, a health survey conducted after MSF's ARV project in Khayelitsha started found that Khayelitsha has the highest level of condom use, desire to join an AIDS club and willingness to be HIV tested among nine sites reviewed in South Africa¹⁵. Voluntary counselling and testing uptake has also increased in the district, rising from less than 1000 HIV tests in 1998 to more than 12 000 in 2002. The number of HIV support groups grew from 4 to 22 over the same period. People living with HIV/AIDS have also formed their own group – known as Ulwazi («knowledge») – to raise awareness and prevention in high schools, workplaces and churches¹⁵. Other treatment programmes in developing countries, such as the Partners in Health programme in Haiti^{18,19} and MSF in Chiradzulu¹⁶, have reported similar findings but not quantified them.

Taken together, these positive benefits demonstrate the huge potential for ARV therapy to mitigate the grave social and security effects of the HIV/AIDS epidemic. Its widespread

introduction in high-prevalence, low-income settings will not only reverse the breakdown of family life but will also affect the workforce. Both are important to preserve household food security and the ability to educate and care for future generations.

Ensuring the long-term affordability of treatment

There are too few resources to sustain the fight against HIV/AIDS and a very real obligation to use available resources as efficiently as possible. This not only requires that interventions result in tangible benefits but also that strategies be adopted that are affordable, especially when competing alternatives of similar efficacy but with differing costs are available.

For most treatment programmes in developing countries, cost is an important factor in ensuring a secure drug supply. This is shown by the preference for regimens that contain non-nucleosides versus the more expensive abacavir or protease inhibitors. Further, most treatment programmes referred to here use generic drugs in their treatment regimens when generic drugs are less expensive than the drugs of the originator companies. Apart from the advantages of regular supply for adherence, cost has also been a factor in the rapid acceptance of fixed-dose combinations, which today offer the cheapest⁴², most convenient treatment.

As the prices of antiretroviral drugs have fallen, the diagnostic tests to monitor their use have become an increasingly large component of the cost of HIV/AIDS care. Although many programmes have minimized the number of tests performed, others are seeking to reduce the cost of reagents and testing equipment. Reducing the cost means negotiating lower prices from suppliers⁸, replacing proprietary reagents with cheaper generic alternatives^{15,20} and advocacy to promote the introduction of new technologies, including once-daily ARV therapy dosing^{43,44} and simpler, cheaper assays for laboratory monitoring (personal communication, Papa Salif Sow, Fann Hospital, Dakar, Senegal)^{45,46}.

WHO, UNAIDS and the Global Fund to Fight AIDS, Tuberculosis and Malaria, which endorse these cost-minimization strategies, have urged decision-makers in ARV programmes to examine all options available to them, including use of the safeguards embodied in the Agreement on Trade-Related Aspects of Intellectual Property Rights⁴⁷⁻⁴⁹.

Conclusion

As the HIV/AIDS epidemic expands, the global response must include access to ARV therapy for people living with HIV/AIDS.

The ability to provide effective treatment for HIV infection presents us with unprecedented opportunities. It will save lives and prevention efforts will be more effective. Community structures will be safeguarded, a generation of children who would otherwise be orphaned will be protected, fragile economies will benefit from a healthy and productive workforce and development and global security will be supported.

ARV programmes now underway in developing countries have successfully capitalized on existing resources and infrastructure through the use of standardized treatment regimens, simplified monitoring procedures and making use of available human resources, including communities and family members. The involvement of affected communities in treatment programmes has catalysed HIV prevention, and several programmes have demonstrated increased awareness, less stigma, more use of testing and counselling services and increased condom use. Treatment is beginning to mobilize groups of people living with HIV/AIDS as both agents for prevention and sources of support for their community and peers.

Many challenges remain, but this is not the time for doubt or hesitation, as the potential consequences of inaction are too serious, including an epidemic of multiresistant HIV infection generated by poorly structured treatment approaches, a continued ineffective response to the HIV epidemic and a growing threat to global security. As the programmes discussed here demonstrate, technical challenges can be overcome by taking advantage of the existing opportunities and resources. What is needed now is a continued political commitment for action. Only by «building the ship at the same time that it is being sailed» will countries create the competence they need to use future resources wisely, foster the partnerships that are so crucial to the success of ARV programmes and thus maximize their response to the HIV/AIDS pandemic.

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