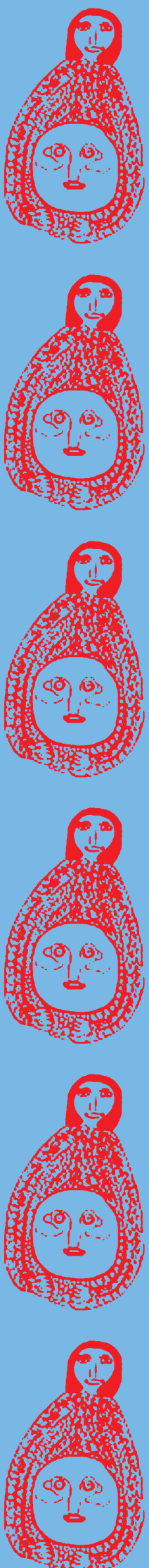

PERSPECTIVES AND PRACTICE IN ANTIRETROVIRAL TREATMENT

Access to antiretroviral treatment and care : the experience of the HIV Equity Initiative, Cange, Haiti

CASE STUDY

World Health Organization

Partners In Health

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About This Series

With 42 million people now living with HIV/AIDS, expanding access to antiretroviral treatment for those who urgently need it is one of the most pressing challenges in international health. Providing treatment is essential to alleviate suffering and to mitigate the devastating impact of the epidemic. It also presents unprecedented opportunities for a more effective response by involving people living with HIV/AIDS, their families and communities in care and will strengthen HIV prevention by increasing awareness, creating a demand for testing and counselling and reducing stigma and discrimination.

The challenges are great. Sustainable financing is essential. Drug procurement and regulatory mechanisms must be established. Health care workers must be trained, infrastructure improved, communities educated, and diverse stakeholders mobilized to play their part. This series, *Perspectives and Practice in Antiretroviral Treatment,* provides examples of how such challenges are being overcome in the growing number of developing countries in which antiretroviral treatment programmes are underway. The case studies and analyses in this series show how governments, civil society organizations, private corporations, and others are successfully providing antiretroviral treatment and care to people with HIV/AIDS, even in the most resource-constrained settings. In documenting these pioneering programmes, WHO hopes that their experiences will both inform and inspire everyone who is working to make access to treatment a reality.

In most industrialized countries, the introduction of antiretroviral (ARV) therapy has led to a sharp decrease in AIDS-related mortality. However, the majority of people infected with HIV lack access to such treatments. Haiti is the poorest country in the Western Hemisphere and the one most affected by AIDS. Until recently, contracting HIV has been a sentence of death for poor Haitians. The experience of the HIV Equity Initiative – an integrated HIV prevention and care project in rural Haiti – suggests that, despite widespread concerns, live-saving ARV therapy can indeed be brought to the poorest and most vulnerable communities.

Background

In 1998, Partners In Health, a not-for-profit charity affiliated with Harvard Medical School, and its Haitian sister organization Zanmi Lasante (Creole for Partners In Health) launched the HIV Equity Initiative to deliver ARV therapy to some of the poorest people living with HIV/AIDS in the Western Hemisphere.

The HIV Equity Initiative is based on many years of experience in rural Haiti. Over 15 years ago, Partners In Health and Zanmi Lasante began AIDS prevention efforts in the lower Central Plateau, where most people are peasant farmers and health indicators are far below the national estimates. The clinical facility, Clinique Bon Sauveur, is situated in Cange, a squatter settlement of 3000 people displaced by a hydroelectric dam, in a province that has no electricity and only a few roads that allow passage.

For many years, political instability and an economic crisis have further contributed to increasing poverty and deteriorating health and social care infrastructures. Not surprisingly, Haiti faces the world's worst AIDS epidemic outside Africa, with an estimated 6% of adults being infected annually and more than 300 000 currently living with HIV/AIDS. In 2001, the epidemic claimed about 30 000 lives, and HIV is now the leading cause of death among young adults. About 200 000 children have already lost one or both parents to the disease. Among women attending antenatal care clinics, HIV seroprevalence was 5% nationwide in 1999 and twice as high in urban slums.

The Clinique Bon Sauveur documented the first case of HIV-related disease in Haiti's Central Plateau in 1986. Voluntary HIV counselling and testing has been offered free of charge since 1988, and condom promotion and the provision of culturally-appropriate HIV education and prevention programmes were linked closely to access to HIV testing.

The introduction of zidovudine in 1995 at the prenatal clinic decreased the rate of mother-to-child HIV transmission and considerably enhanced the uptake of voluntary counselling and testing (VCT) among pregnant women. The acceptance of prenatal HIV testing rose from 30% to 90% once AZT was made available, demonstrating that the provision of ARV drugs enhanced the utilization of prevention services. When voluntary HIV counselling and testing became part of routine prenatal care for pregnant women in Cange, over 97% of those offered the complete care package for preventing the vertical transmission of HIV accepted. This experience in Cange also demonstrated the feasibility of procuring, storing, and using ARV agents in a resource-limited setting.

The effect of these comprehensive prevention programmes was limited, however, by political unrest, pervasive work-related migration, and increasing rural poverty, and the magnitude of the suffering caused by HIV grew in Haiti's Central Plateau. An increasing number of young people returned to the area with HIV infection acquired far from their home villages. In the early 1990s, over 25% of admissions to the Clinique Bon Sauveur were related to HIV. By 1995, about 40% of adults admitted were infected with HIV. As the efficacy of combination ARV therapy was not yet known, the focus of HIV care was the treatment of opportunistic infections. In Haiti, as in other parts of the developing world, half the people living with HIV/AIDS had tuberculosis co-infection. Death in such people can be postponed substantially by treating tuberculosis when HIV is not advanced. Thus, treatment of tuberculosis with the WHO strategy of directly observed therapy, short course (DOTS) became a critical component of HIV care, and the detection and treatment of every case of active tuberculosis was the first important programmatic link in developing the HIV care strategy in Haiti.

As HIV infection surpassed tuberculosis and malaria as the leading cause of death among young adults in Haiti, Partners In Health had no choice but to move from preventing HIV infection to actively treating it. Starting in 1998, highly active ARV therapy (HAART) was offered to people living with HIV/AIDS who no longer responded to aggressive clinical treatment of opportunistic infections.

Objectives

With the launch of the HIV Equity Initiative, Partners In Health sought:

- to replicate the methods of its successful community-based tuberculosis treatment and control programme, based on DOTS;
- to train community health workers (*accompagnateurs)* in the administration and daily follow-up of ARV therapy; and
- to prove that, in poor countries, HAART can be delivered by harnessing the capacity of the rich human infrastructure that exists, and that the barriers to treatment in such settings are not so much a lack of infrastructure or education but rather the lack of will.

Clients served

The Clinique Bon Sauveur includes paediatric, infectious disease, general medicine and women's health clinics, adult and paediatric inpatient wards, two operating rooms, a pharmacy, and a village school. Because of Haiti's economic and health crisis, the number of ambulatory visits at the clinic has risen from 30 000 to 200 000 in just two years. The patients selected for enrollment in the HIV Equity Initiative came from about 60 villages. Some of these villages are more than five hours away by foot, but each is served by *accompagnateurs.* In 2002, the Clinique Bon Sauveur followed more than 4000 HIV-positive people, and over 400 people living with HIV/AIDS have started directly observed therapy with HAART (DOT-HAART) based on laboratory and clinical criteria.

Selection of people for therapy

From 1998 to 2002, candidates for therapy were selected based exclusively on clinical status. A set of guidelines that allows identification of patients for inclusion in the DOT-HAART project was developed by the team at the Clinique Bon Sauveur (Box 1). (As a reflection of the local epidemic situation, these guidelines suggest deferring ARV therapy for people diagnosed with pulmonary tuberculosis, which is the case for more than half of all Haitians living with HIV/AIDS. For most patients with active pulmonary tuberculosis, effective anti-tuberculosis therapy alone results in symptom-free periods that can last for years.) Two physicians, one with training in infectious diseases, assess the patients, while most of the care is delivered by *accompagnateurs*.

Initiating ARV therapy according to these criteria does not require any laboratory testing. In accordance with the 2002 WHO recommendations for scaling up access to ARV therapy in resource-limited settings, people who are HIV positive and have clinical AIDS are eligible for treatment, regardless of CD4 count.

However, based on a review of the first 300 patients followed at the Clinique Bon Sauveur at the time HAART was introduced, a subset of patients who appeared well in fact died within two years of diagnosis with HIV, most likely as a result of subclinical immune suppression leading to aggressive opportunistic infections. In late 2002, the Clinique Bon Sauveur, with help from the Division of AIDS of Harvard Medical School, acquired a flow cytometer and can now measure CD4 counts on site. While the sickest patients are still triaged directly into ARV therapy, HIV-positive patients without clear AIDS-defining illnesses are now screened to determine whether they meet immune criteria for initiating HAART (CD4 count <350 cells/mm^3).

Box 1. Criteria for inclusion of patients in DOT-HAART

- Absence of active tuberculosis
- Recurrent opportunistic infections that are difficult to manage with antibacterial or antifungal agents
- Chronic enteropathy with wasting
- Otherwise unexplained significant weight loss
- Severe nervous system complications attributable to HIV disease
- Severe leukopoenia, anaemia, or thrombocytopoenia

Source: Farmer et al. [1]

Laboratory and clinical monitoring

The HIV Equity Initiative uses a modest laboratory infrastructure to initiate and follow therapy. HIV serology, a haematocrit test, and a white blood cell count are prerequisites for starting treatment with ARV drugs. Liver function tests are performed in the case of gastrointestinal side-effects, and a complete blood count is ordered if symptoms of anaemia or thrombocytopoenia develop. The patient's weight, which has been shown to predict survival and disease progression, is one of the most important indicators in a simplified monitoring approach and is closely followed during the course of treatment. CD4 counts are not used to monitor the response to therapy unless the patient begins to lose weight or develops new opportunistic infections.

Clinical monitoring of treatment is performed at one week, one month, three months, and every three months thereafter. It should be noted, however, that patients treated through the HIV Equity Initiative were monitored daily by *accompagnateurs*.

ARV regimens used

Once admitted to the programme, patients were treated with a three-drug standard regimen. At the end of 2002, the Haitian government adopted new ARV therapy guidelines based on the WHO guidelines published that same year. The Haitian government further decided to procure drugs that have been approved by the WHO prequalification project. People being treated at HIV Equity Initiative clinics therefore receive the drug combinations shown in Table 1.

Adherence support strategies

DOT-HAART is modeled after the clinic's experience with its tuberculosis programme. DOT administered by community health workers has achieved outstanding tuberculosis cure rates. To ensure comparable adherence to ARV therapy, each person eligible for the programme is followed by an *accompagnateur*. During the daily visits, the *accompagnateur* observes the person in therapy taking one dose of HAART and may leave the second treatment dose at that time. In many cases – although this is not part of the protocol – the *accompagnateur* visits people in therapy more than once a day to watch them take the second dose as well or to provide emotional and other types of social support. In addition, *accompagnateurs* are trained to assess for common side-effects of the medications and signs of HIV-related illness.

New patients, in addition to the clinical and laboratory assessments, also undergo detailed social assessment to identify and address other barriers to good health and adherence to HAART. Patients' interviews with social workers are followed by an inspection of living quarters and an analysis of their financial situation and social support network. Based on the results of all three assessments, a management plan is elaborated. All medical consultations, drugs, social services, and social support are provided free of charge, as is the case with tuberculosis care.

The interaction between the community and the patient has been the cornerstone of the HIV Equity Initiative: meetings of community outreach workers with people new to therapy, nutritional and family support (school, housing, and financial), and monthly patient meetings that facilitate information exchange have been extremely popular and underpin the success of the programme.

Table 1. ARV drug combinations dispensed at HIV Equity Initiative clinics in Haiti

Regimen	Drug combination
Primary first-line regimen	Stavudine/lamivudine/nevirapine
Primary first line regimen for pregnant women	Zidovudine/lamivudine/nevirapine
Primary first-line regimen for people coinfected with HIV and TB	Stavudine/lamivudine/efavirenz
Second-line regimen	Zidovudine/didanosine/protease inhibitor or stavudine/didanosine/ protease inhibitor; indinavir, nelfinvir, or lopinavir boosted by ritonavir as options for protease inhibitors

Benefits resulting from the programme

The active community support offered to DOT-HAART patients was key to the dramatic clinical responses visible to everyone, including neighbours, *accompagnateurs,* physicians, and nurses. Patients for whom therapy resulted in return to health became known as HIV-treatment successes in their communities and proved to be valuable human resources for HIV prevention activities. In addition, Partners In Health believes that «the stigma associated with AIDS has diminished as a result of the dramatic responses to therapy. Decreased stigma is reflected in an increased willingness of patients to discuss their diagnosis openly, an increased demand for HIV testing, and a reduced number of patients' complaints regarding abusive behaviour of family members or neighbours». [2] For example, within the first two years of the programme's existence, utilization of the clinic's free HIV counselling and testing services increased by more than 300 %. Moreover, in contrast to reported emotional problems among health care workers in areas without available AIDS treatment, staff morale in the HIV Equity Initiative was significantly boosted by the availibility of the life-saving therapies.

According to Farmer, «small victories that are thought to be big miracles by patients are more rewarding than one could ever deserve.» [3]

Results

An interim assessment[2] of the programme prior to 2001 suggested that DOT-HAART was very effective (Box 2) :

- The clinical response to therapy was beneficial in 59 of the first 60 people receiving therapy (not including the more than 40 people who started therapy in 2001).
- In a subset of patients in whom viral load testing was performed, 86% had no detectable virus in peripheral blood.
- A weight increase of more than 2 kg within the first three months of therapy was observed in 58 patients.
- An estimated 48 patients resumed working and caring for their children.

Box 2. Successful treatment with ARV drugs shows results within weeks

Adeline contracted HIV far from home, in Port-au-Prince, when she was only 18 years old. She attended the Clinique Bon Sauveur a few years later when she had an episode of pneumonia. The additional diagnosis of herpes zoster and HIV infection resulted in treatment of opportunistic infections for almost 10 years. By 1999, her chronic diarrhoea no longer responded to the treatment, and her weight had dropped to 36 kg (Fig. 1). Within the first five weeks of treatment with zidovudine, lamivudine, and indinavir, she gained 12 kg (Fig. 2).

Fig. 1. Adeline before ARV therapy

Fig. 2. Adeline after ARV therapy was initated

Source : Farmer et al. [1]

A more recent review[4] in 2003 of key clinical and laboratory parameters compared outcomes among a group of 100 patients who received DOT–HAART based on the clinical criteria of advanced disease (generally bed-bound with significant weight loss) and two other groups, each with 100 HIV-positive patients in whom ARV drugs were deferred because they 1) were deemed less sick (generally ambulatory without significant weight loss) or 2) because they lived too far from the clinic to arrange for an *accompagnateur*. Even though the patients in the first group were far sicker than those in the two groups in which HAART was deferred, the first group showed superior improvement in terms of fewer hospitalizations, opportunistic infections, tuberculosis, and mortality (Table 2). In addition to the outcomes listed above, the assessment confirmed the reduction of stigma and increased staff morale as favourable results of the programme.

Table 2. Comparison of outcomes among three different intervention groups

OUTCOME	GROUP A	GROUPS B, and C
n	**100**	**200 (100 each in Groups B and C)**
Mortality at end of study period	**0**	**43 (14 and 29 in Groups B and C, respectively)**
Tuberculosis incidence	**2**	**21 out of 100 (data available only for Group B)**
Number of opportunistic infections from start of interventions	**0.24**	**3.3**
Average weight change	**10.3 kg increase**	**6.0 kg decrease**
Number of days in hospital from start of intervention to end of study period or death	**0**	**23.4**
Activities of daily living score for people surviving one year after the intervention	At beginning of study period: **2** At end of study period: **3.8**	At beginning of study period: **2.7** At end of study period: **2.3**

Group A: the first people receiving DOT-HAART from a community health worker for more than 1 month (n = 100).

Group B: people diagnosed with HIV infection at the same time and from the same catchment area as those in Group A, receiving regular care (such as prophylaxis for opportunistic infections) but no DOT-HAART (n = 100).

Group C: people diagnosed with HIV infection during the same time period but living outside the area served by community health workers (n = 100), who thus received only clinic-based care.

Source: adapted from Farmer et al.[4]

The drop-out rate from the programme was remarkably low – less than 2% since 1999. Side-effects of the treatment have been rare, and only a few patients required a change in drug regimen.

Prevention versus care: a false dichotomy

The HIV Equity Initiative was designed as an integrated prevention and care programme. The treatment component, from the prevention of opportunistic infections to ARV therapy, was grafted onto an existing DOTS programme and was linked to clinic- and community-based prevention efforts from the outset. Nevertheless, one unexpected benefit of improving the quality of care was the positive effects on the quality and efficacy of prevention projects.[5] Seven effects are noted here.

First and most significant was the sharply increased uptake of voluntary counselling and testing services. Free VCT was made available at the Clinique Bon Sauveur beginning in 1988, but the demand for such services was limited. Staff clinicians initiated almost all testing, and an estimated 60% of those offered these services before 1995 declined the offer. This meant that 60–75% of all serological tests were positive. After 1995, when zidovudine was introduced to prevent mother-to-child transmission, requests for voluntary counselling and testing and a high rate of acceptance were registered largely in the prenatal clinic. By 1999, however, VCT was considered part of routine prenatal care, but an increase in VCT in the general ambulatory clinic was temporally associated with the introduction of DOT-HAART.

In the first year of the HIV Equity Initiative, demand for VCT increased by more than 300%, and demand soon surpassed the capacity to offer these services. By 2000, most HIV serological tests were negative; in 2002, only 11% of more than 4500 tests indicated seropositivity. Clinic- and community-based staff agree that improved care has driven increased demand for VCT.

Second, the introduction of ARV agents has changed the nature of clinic exchanges considerably. Before the establishment of the HIV Equity Initiative, most HIV clinic visits were devoted to managing chronic diarrhoea, thrush, weight loss, and fatigue. People receiving ARV therapy do not often have such problems, however, and physicians and nurses can now spend more time reinforcing safe-sex messages (i.e. secondary prevention).

Third, the decreased viral loads associated with ARV therapy render people living with HIV/AIDS less infectious when they do have unprotected sex.

Other means by which improved care may reinforce prevention activities are less well documented but no less important. A fourth benefit encountered in rural Haiti is the decreased stigma associated with AIDS. Prior to the advent of ARV agents, a diagnosis of HIV infection was regarded locally as a death sentence. There are now so many stories of dramatic improvement on ARV agents that most villagers in the Zanmi Lasante catchment area know someone who has responded to therapy. Decreased stigma improves the quality of life of people living with HIV/AIDS and their families and also leads to increased general willingness to be tested and to discuss HIV prevention more openly.

Fifth, the lack of ARV agents before 1998 meant that physicians, nurses, and community health workers had to stand by helplessly as people wasted away from AIDS. ARV agents have permitted health care workers to offer people living with HIV/AIDS hope of survival, thereby improving morale among the staff.

Sixth, people receiving ARV therapy are less likely to require hospitalization, and decreased expenditure for hospital care means that more resources may be devoted to prevention activities. A similar experience has been well-documented in Brazil.

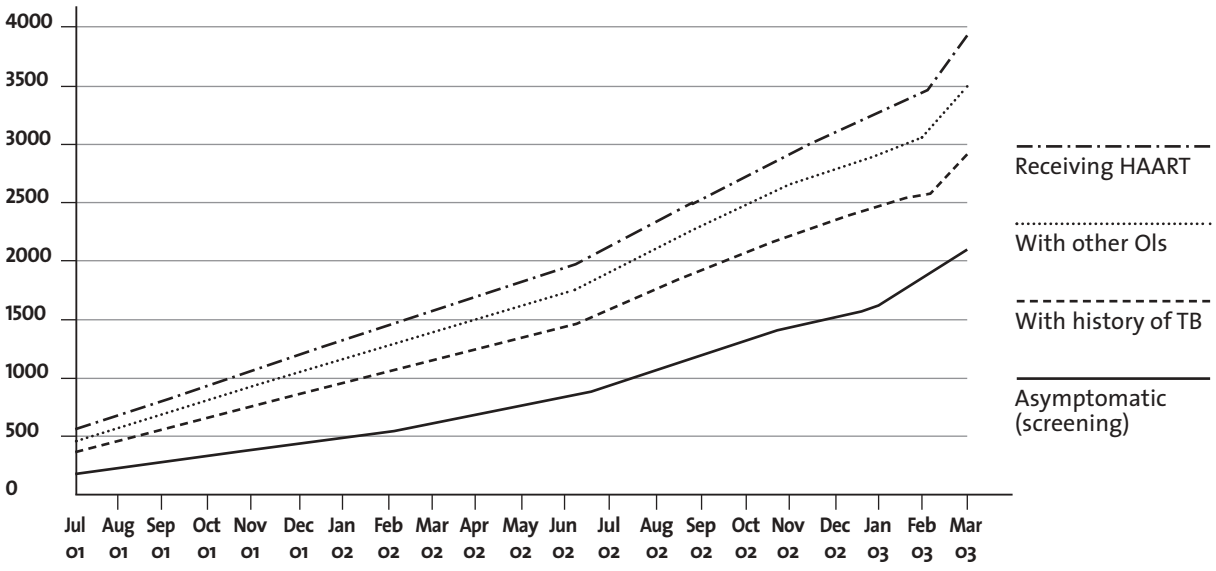
Seventh, the incidence of tuberculosis has declined sharply among people receiving ARV therapy.

Scaling up

Partners In Health believes that the HIV Equity Initiative has already proven the efficacy of community-based care vis-à-vis ARV therapy. In contrast to claims that expansion will divert resources from other health priorities, the increased attention to AIDS has in fact resulted in new emphasis on primary health care and drug procurement.

At the end of 2002, the Global Fund to Fight AIDS, Tuberculosis, and Malaria granted Haiti US$ 67 million for programmes to battle the HIV/AIDS epidemic. With some of the funds awarded to Partners In Health, comprehensive HIV/TB programmes have been launched at four new sites: Lascahobas, Belladère, Boucan Carré, and Thomonde.

Fig. 3 Progression of HIV+ Patient Enrollment, Partners In Health, Rural Haiti



The expanded services and the addition of a number of newly-trained community health workers resulted in a ten-fold increase in ambulatory visits in less than six months at each of these facilities. With a growing demand for HIV testing, the case load is expected to double in the next year. Up to 5000 patients will be treated by the end of 2007.

Box 3. Excerpt from the Cange Declaration

«We, the patients of Partners In Health, are fortunate to receive medication and health care even if we do not have the money. Many of our problems have been resolved with the medications. Given how bad off we used to be, we have greatly benefited. But while we feel fortunate to receive the medications, we feel sad for others who don't receive the same treatment we do.»

Source: Cange Declaration[6]

Also notable is the dramatic fall in drug prices with the introduction of generics into the market. Partners In Health is a founder of the Green Light Committee, a WHO group that coordinates the efforts of projects seeking to treat mutltiple-drug-resistant tuberculosis (MDR-TB) in the context of tuberculosis control. By proving demand, placing MDR-TB drugs on the essential medicines list, and using pooled procurement and multiple sources, the Green Light Committee was able to reduce the price of antituberculosis medications by 90%.[7] A similar success was achieved for ARV drugs: concessional pricing agreements with pharmaceutical companies, purchase of drugs from WHO-prequalified manufacturers, and collaboration with the International Dispensary Association, a wholesale distributor of essential drugs based in the Netherlands, have drastically driven down prices in Haiti from US$ 10 000 per patient per year in 1999 to below US$ 300 per patient per year in 2003. Thus, drugs as a proportion of programme costs declined from about 80% to below 15%.

Plans for district-wide expansion and scale-up within the next five years have necessitated the development of improved information management systems. In response, Partners In Health has developed and implemented a system with three components: a Web-based medical records system, an application that allows off-line data entry, and a drug inventory system.

The introduction of advanced diagnostic methods, such as flow cytometry, has also improved local capacity to identify patients who need ARV therapy.

Feasibility of replication

With the sole help of a start-up fund of US$ 100 000 from a small Haiti-based foundation, the HIV Equity Initiative was piloted in one of the poorest areas of the world, where health infrastructure has been seriously compromised by years of conflict and extreme poverty. Partners In Health believes that, through reinforcing the existing public health infrastructure, many district hospitals in developing countries would have the capacity to provide HAART to patients with advanced HIV disease. Hence, the central concept of the HIV Equity Initiative, in applying the lessons learned from a tuberculosis control programme to an AIDS treatment programme, has not only been expanded to additional sites in Haiti but is now also being further exported to health facilities in Peru (Lima), the Russian Federation (Siberia), and the United States (Massachusetts).

The example of the HIV Equity Initiative offers hope that the voices of people living with HIV/AIDS – as expressed in the Cange Declaration (Box 3) – may be heard. With more national and international support and an environment responsive to the increasing demand for effective AIDS treatment among people in resource-limited countries, there should be no barriers to access to life-saving HAART for those who need it most.

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