Viewpoint

Community-based approaches to HIV treatment in resource-poor settings

Paul Farmer, Fernet Léandre, Joia S Mukherjee, Marie Sidonise Claude, Patrice Nevil, Mary C Smith-Fawzi, Serena P Koenig, Arachu Castro, Mercedes C Becerra, Jeffrey Sachs, Amir Attaran, Jim Yong Kim

Last year, HIV surpassed other pathogens to become the world's leading infectious cause of adult death. More than 90% of deaths occur in poor countries, yet new antiretroviral therapies have only led to a drop in AIDS deaths in industrialised countries. The main objections to the use of these agents in less-developed countries have been their high cost and the lack of health infrastructure necessary to use them. We have shown that it is possible to carry out an HIV treatment programme in a poor community in rural Haiti, the poorest country in the western hemisphere. Relying on an already existing tuberculosis-control infrastructure, we have been able to provide directly observed therapy with highly-active antiretroviral therapy (HAART) to about 60 patients with advanced HIV disease. Inclusion criteria and clinical follow-up were based on basic laboratory data available in most rural clinics. Serious side-effects have been rare and readily managed by community-health workers and clinic staff. We discuss objections to the widespread use of HAART, and suggest that directly-observed therapy of chronic infectious disease with multidrug regimens can be highly effective in settings of great privation as long as there is sustained commitment to uninterrupted care that is free to the patient.

Why AIDS prevention alone is insufficient

The dimensions of the global HIV crisis are such that predictions termed alarmist a decade ago are now revealed as sober projections.[1] In 2000, HIV overtook tuberculosis as the world's leading infectious cause of adult deaths. HIV has, in fact, overtaken the 1918 influenza epidemic as the most devastating communicable cause of adult death since the bubonic plague of the 14th century.[2] The social impact of HIV has been particularly severe in Africa, where an estimated 14 million children have been orphaned by AIDS; if trends hold, 40 million African children will be orphaned by the close of this decade.[3,4] Because poverty and social inequalities are leading co-factors in HIV transmission, the virus promises to wreak similar havoc in India and other parts of Asia.[5] At the same time, AIDS mortality has dropped precipitously in affluent countries, in large part because of access to highly-active antiretroviral therapy (HAART).[6,7,8] This ever-widening outcome gap is evident globally.

The response of the affluent countries and their institutions—from aid agencies, non-governmental organisations, and the pharmaceutical industry—has been insufficient. (The death toll and increasing HIV incidence are the most eloquent rebuke to contrary assessments.) The quasitotality of AIDS assistance to the heavily-burdened countries has consisted of the promotion of education and condom distribution to prevent HIV transmission. It has taken two decades to acknowledge the central irony of AIDS prevention: "Towards the end of the second decade of the AIDS pandemic, we still have no good evidence that primary prevention works."[9] Many of those at greatest risk already know that HIV is a sexually transmitted pathogen and that condoms could prevent transmission. Their risk stems less from ignorance and more from the precarious situations in which hundreds of millions live; gender inequality adds a special burden, and is the main reason that, globally, HIV incidence is now higher among women than among men.[10,11]

Clearly, the prevention strategies currently in use will not inflect HIV incidence among the poorest populations, even though these prevention strategies have proven effective in settings from San Francisco to Thailand and merit greater support. Other complementary strategies, including vaccines protective against clades prevalent in Africa, are needed if the most vulnerable are to be protected.

The acknowledgment that there is the need for better prevention is important, and it is also time to turn our attention to the more than 30 million individuals already living with HIV.[12] They need more than palliative care. The programmes extolled as "community-based care" or "home care" are inadequate whenever these terms are euphemisms to describe what amounts to hospice, and not very good hospice at that: no real analgesia, no antifungals, too few antibacterials, and no parenteral lines for rehydration.

There is an unmentioned elephant in the conference rooms of many scientific meetings: the prospect of providing HAART to those living with both poverty and HIV. Even though this describes 90% of the potential beneficiaries of recent therapeutic developments, use of HAART in poor countries is rarely the primary topic of discussion in scientific congresses. Access to treatment is, however, the primary topic of discussion in communities beset by HIV, just as it is the primary topic of discussion among AIDS activists. Some groups in sub-Saharan Africa already express hostility to humanitarian organisations and funders who express interest only in education and condom promotion. We report our experience of treating HIV disease in a poor community in rural Haiti and examine the main objections to making HAART available in resource-poor settings.

Lancet 2001; **358:** 404–09

Partners in Health and Department of Social Medicine, Harvard Medical School, Boston, MA 02115, USA (P Farmer MD, J S Mukherjee MD, M C Smith-Fawzi ScD, S P Koenig MD, A Castro PhD, M C Becerra ScD, J Y Kim MD); **Centre Thomas J White, Zanmi Lasante, Cange, Haiti** (F Léandre MD, M S Claude RN, P Nevil BSc); **and Center for International Development, Harvard University, Boston, MA, USA** (J Sachs PhD, A Attaran JD)

Correspondence to: Dr Paul Farmer
(e-mail: paul_farmer@hms.harvard.edu)

One community's experience: the HIV Equity Initiative

Haiti is by all conventional criteria the poorest country in the western hemisphere and one of the poorest in the world:[13] per capita gross national product (GNP) is around US$400; unemployment exceeds 70%; and fewer than one in 50 Haitians have regular employment.[14] Not coincidentally, Haiti is also the hemisphere's most HIV-burdened country.[15] In 1999, UNAIDS reported national HIV seroprevalence as 5% among women attending antenatal clinics—and rates were twice as high in urban slums.[11] The latest estimates of life expectancy at birth are 47·5 years for men and 49·2 years for women, with HIV considered the chief contributor to premature adult death.[16]

Initially an urban epidemic, HIV prevalence is lower in rural Haiti, where we have worked for more than 15 years. Most of the local inhabitants in the lower Central Plateau are peasant farmers working small plots of infertile land. Many are sharecroppers. Local health indicators are worse than national estimates.

Our clinical facility, founded in 1985 in the middle of a settlement of individuals displaced by a hydroelectric dam, documented its first case of HIV disease in 1986. Following international convention, prevention efforts were tightly linked to education and condom promotion.[17] These efforts have been hampered by political violence and resulting migration, and by gender inequality and poverty, which conspire to make the male condom an imperfect prevention measure. Thus, HIV transmission continued in spite of aggressive prevention campaigns.[18]

Our modest therapeutic efforts have been aggressive when compared with other clinics in poor, rural regions of the less-developed world. Shortly after the publication of the ACTG-076 trial,[19] we began offering zidovudine to pregnant women to block mother-to-child transmission. More than 90% of women offered HIV testing accepted it after zidovudine was made available free of charge; dramatic declines in vertical HIV transmission ensued. In 1997, we began offering post-exposure prophylaxis with a three-drug regimen (usually zidovudine, 3TC, and a protease inhibitor) to victims of rape or professional injury.[20] Beginning in late 1998, a small number of patients with long-standing HIV disease who no longer responded to syndromic treatment of opportunistic infections were offered directly observed HAART.

Inclusion criteria for HAART have not been codified rigidly, but follow a certain logic in the absence of CD4 lymphocyte counts and viral-load testing. Patients assessed for HAART are those with chronic enteropathies or other forms of HIV-associated wasting; patients with presumed neurological complications of HIV (encephalopathy, distal-sensory, or other polyneuropathies); those with repeated opportunistic infections unresponsive to antibacterials and antifungals; and patients with severe leukopaenia, anaemia, or thrombocytopaenia (panel 1). Assessments are done by two physicians, one with infectious-disease training.

Patients diagnosed with active tuberculosis are not offered HAART because most respond to antituberculous therapy and are subsequently symptom-free for long periods of time, often years. It is significant, then, that most patients diagnosed with HIV infection present with active tuberculosis, as figure 1 shows.[21]

Panel 1: Guidelines for inclusion in DOT-HAART project, Clinique Bon Saveur

- Absence of active tuberculosis
- Recurrent opportunistic infections difficult to manage with antibacterials or antifungals
- Chronic enteropathy with wasting
- Otherwise unexplained and significant weight loss
- Severe neurologic complications attributable to HIV
- Severe leukopaenia, anaemia, or thrombocytopaenia

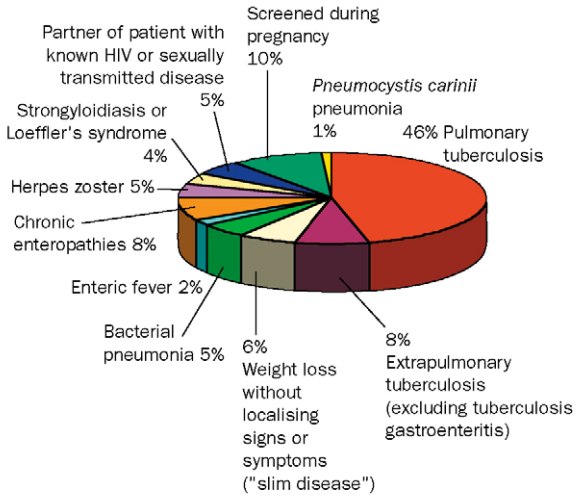


Figure 1: **Presenting diagnoses in 200 patients with HIV disease, Clinique Bon Sauveur, 1993–95**
From reference 21.

In our clinic, directly observed therapy with HAART (DOT-HAART) is modelled on successful tuberculosis-control efforts. That is, each HIV patient has an *accompagnateur* (often a community-health worker) who observes ingestion of pills; responds to patient and family concerns; and offers moral support (figure 2). Social support—including assistance with children's school fees—is included in services offered. Monthly meetings, in which patients discuss their illness and other concerns, are notable for high attendance (figure 3).

Response to HAART in an initial cohort of 60 patients has been dramatic (panels 2–4). Side-effects have been rare and readily managed (only six patients have required a change in regimen). As elsewhere, patients receiving HAART are far less likely to require admission to hospital than are patients with untreated HIV disease.[22] In the event that ambulatory care is not feasible for the initiation of HAART or for the treatment of an acute illness, patients with HIV are admitted to the general ward, which is in a facility separate from the tuberculosis ward.

Expanding the HIV Equity Initiative

We believe that if DOT-HAART can be implemented in the devastated Central Plateau of Haiti it can be implemented anywhere. Our experience further suggests that HIV therapy can reinvigorate flagging prevention efforts. Although AIDS remains a stigmatised disease in Haiti, we believe that access to effective therapy has lessened AIDS related-stigma. The demand for HIV testing, and the opportunity for counselling, has risen since HAART was made available.

During the next 3 years, we hope to expand the HIV Equity Initiative to better meet the needs of the population of Central Haiti. Another nurse, an archivist, and a second social worker would represent the first full-time employees of the initiative. A part-time HIV prevention and care clinician will also work with the team based in Haiti.

Even though we initially enrolled only about 60 patients in the DOT-HAART programme, we achieved nearly full coverage in parts of the catchment area: using the enrolment criteria noted in panel 1, we have been able to treat most patients with signs and symptoms suggestive of

Figure 2: **Accompagnateur training, Thomonde, Haiti**

advanced HIV disease. If the catchment area served consists of 250 000 individuals, the seroprevalence of HIV is about 5% among sexually active adults, and sexually active adults aged 15–40 years comprise 30% of the population, some 3750 HIV-positive individuals would live within the catchment area. If 10% of these patients meet enrolment criteria, then about 375 patients would need HAART. With additional staff, the treatment of 375 patients is well within the capacity of many district hospitals in less-developed countries. With national and international support, a larger number of patients could be enrolled in life-saving therapy.

How might patients be equitably and effectively enrolled in a DOT-HAART project? They must of course want to be treated, but we have yet to meet one who does not. Until tests of viral load, CD4 count, or other surrogate markers are available, simple clinical criteria can identify those most likely to benefit from HAART. The most important—weight loss or decreased body-mass index—has been shown to predict survival and disease progression in HIV infection.[23,24] Other criteria include the presence of a wasting enteropathy; severe neurological complications of HIV; severe leukopaenia, anaemia, or thrombocytopaenia; or recurrent opportunistic infections unresponsive to antibacterial or antifungal therapy.[25–27] In collaboration with colleagues at the Association François-Xavier Bagnoud, we are developing more formal inclusion criteria, but these need not be based on tests and measures unavailable in rural clinics in poor countries.

Figure 3: **Medical and human-resources infastructure necessary to implement DOT-HAART**
Top: Thomas J White Center, Cange, Haiti.Bottom: monthly patient meetings notable for high attendance.

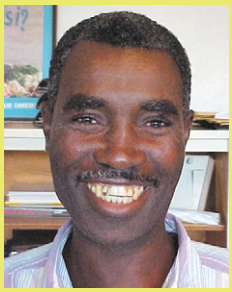
Panel 2: **Enna, 26-years-old**

Enna has already had six children. Born to an impoverished family in Savanette, she was sent to Port-au-Prince as a *restavèk*—a child servant—at 10 years of age: "I used to mop the floor and cook. I also used to babysit." Enna was not paid but "they gave me food to eat." At age 14, she was raped: "A man who was a friend of the family where I was staying raped me. He waited until no one was home, then he jumped on me. I was just a child; I did not know what was happening. This happened four times, and then I was pregnant. The family [in Port-au-Prince] sent me away." Enna returned to Savanette, where she almost died in childbirth. She later sold produce in regional markets and in Port-au-Prince. At 18 years of age, while sleeping in a communal market depot, Enna was raped by three men. "I didn't see them, so what could I tell the police? Besides, I was afraid of the police." Enna regards "my entire life as a disaster. I had three children for two different men, but neither of them would help me [financially]." In 1997, sapped by recurrent fevers and chronic diarrhoea, she was diagnosed with tuberculosis and HIV co-infection. Treated for tuberculosis, she gained weight but later developed oropharyngeal candidiasis and mental slowing. She lost weight and had intermittent diarrhoea. Enna received zidovudine during her sixth pregnancy, but the newborn baby died of severe jaundice. When her weight dropped to 108 lb, she was started on a regimen of zidovudine, 3TC, and efavirenz. She gained 9 lb in the first 6 months of therapy and now has no symptoms.

Many have expressed concern that HAART is too complicated for settings without specialists to guide therapy. It is true that rifamycins decrease blood concentrations of protease inhibitors; as noted, however, most patients who present with tuberculosis do not need concurrent anti-retroviral therapy. Furthermore, HAART in resource-poor settings need not rely on protease inhibitors. Given adequate financing, we plan to base our initial regimen on a combination of two reverse-transcriptase inhibitors and a non-nucleoside reverse-transcriptase inhibitor. Another promising possibility, already available in the USA, is the triple-nucleoside-analogue pill—zidovudine and 3TC together with abacavir, the most potent drug in its class. Such a fixed-dose combination would make DOT-HAART significantly simpler than tuberculosis treatment and would preserve protease inhibitors and non-nucleosides for cases of suspected or documented treatment failure.

Some have expressed alarm regarding the spread of drug-resistant virus if HAART is used where health infrastructure is weak. Just as it is possible to exaggerate the complexity of these regimens, so too is it possible to

Panel 3: **St Ker, 41-years-old**



St Ker, is from the village of Savanette. After completing 4 years of primary school, his parents could no longer pay tuition. "I went to Port-au-Prince to learn how to become a welder. I worked in factories." He lost his first job when the company he worked for was sold. He has since been intermittently employed. St Ker fathered two children, but his marriage foundered: "We used to argue about money. Then I became sick and she left me." He later struck up a relationship with another woman, who bore him another child, but by then, the summer of 1998, he was too sick to work. He had chronic diarrhoea and weight loss. "I wandered from clinic to clinic [in Port-au-Prince], but no one could tell me what was wrong. So I came back here." St Ker was diagnosed with HIV in June 1999, when he presented to our clinic with cachexia, chronic enteropathy, anaemia, and mucocutaneous candidiasis. He was treated with broad-spectrum antibacterials and loperamide, but continued to lose weight. He suffered cognitive decline and by May 2000, was too weak to stand. When his weight dropped to 90 lb, St Ker was started on a regimen of zidovudine, 3TC, and efavirenz. "I feel that these drugs have been miraculous. My diarrhoea stopped and I started to gain weight." His candidiasis and odynophagia disappeared by December 2000, when St Ker weighed 140 lb. He is ready to resume his work as a welder.

Panel 4: **Adeline, 34 years old**

Adeline, 34 years old, was born in the village of Kay Epin. Of Adeline's eight siblings, five are living. Her parents are peasant farmers, although her father supplements his income by helping to run a local school. Adeline grew up in the village, leaving rarely except to accompany her mother to market. When she was 18, she left for Port-au-Prince to continue her primary education. Adeline didn't remain in school for long—her grades were poor; the cost of tuition, high—and she ended up in a part-time vocational school, where she learned to sew and embroider. She lived with a sister in Cité Soleil, a slum on the northern edge of the city. Finding enough to eat was a constant struggle. Not long after her arrival, Adeline married Joel, a young man from the Central Plateau. Joel fell ill shortly after their son was born, and Joel died only a year later. Adeline does not know what killed him, but now assumes it was HIV. When Adeline's son was about 2 years old, she met Ronald, the father of her second child. He's still around, she notes, "but I'm no longer with him. He doesn't help me at all with feeding these children. I never see him."
During her early twenties, Adeline had an episode of pneumonia, which led her back to our clinic. She was also diagnosed with herpes zoster, which led to her diagnosis of HIV infection. For almost 10 years, Adeline's therapy was limited to treatment of opportunistic infections. By early 1999, Adeline's chronic enteropathy no longer responded to antimotility agents. By October, she weighed 79 pounds and could no longer get out of bed. In November 1999, Adeline began therapy with zidovudine, 3TC, and indinavir. Her diarrhoea disappeared within 2 weeks; she gained 26 pounds in the first 5 weeks of treatment.

confound the main causes of acquired resistance. Most are to be found in settings such as the USA, where HIV patients face concurrent problems such as housing instability, lack of medical insurance, drug addiction, and lack of access to addiction-treatment programmes. Furthermore, there is in resource-poor settings no history of the widespread use of monotherapy with nucleoside reverse-transcriptase inhibitors. The use of monotherapy, once the rule in HIV therapy in the USA and Europe, is a leading contributor to the widespread existence of drug-resistant strains there. If tuberculosis offers an instructive example, drug resistance is far less likely to emerge where DOT is used from the outset and where drugs are made available to those who need them most.

Funding for expansion of this pilot project was sought from a number of international agencies charged with responding to AIDS; all declined to support this effort on the grounds that the drug costs were too high to meet so-called sustainability criteria. Pharmaceutical companies were approached for contributions or concessional prices but referred us back to the same international agencies that had already termed the project unsustainable.

Objections to HAART in resource-poor settings

The two primary objections to use of HAART in poor communities have been the high costs of the medications and the lack of infrastructure necessary to deliver them effectively. The debate regarding pricing of antiretrovirals has been reviewed elsewhere.[28,29] As noted, there is little science to drug pricing. Several firms, including one based in India, have developed very low-cost formulations of zidovudine, 3TC, D4T, ddI, and nevirapine. The monthly retail cost of three drugs is already as low as US$83, as compared with US$768 per month from manufacturers in the USA.[30]

The second chief objection has been that poor countries lack the infrastructure necessary to deliver HAART. Much is made of the complexity of HIV management, which would defeat, according to conventional wisdom, the overburdened and undertrained health personnel in the countries most affected by HIV. In poor countries, HIV therapy is the privilege of local elites (who have, almost invariably, far lower rates of infection than the poor majority) and of a small number who live in capital cities and have access to specialty clinics partnered with first-world research universities.

There is merit to observations regarding weak implementation capacity, since health infrastructures are manifestly deplorable in most HIV-endemic areas. But there is reason to believe that minor modifications could improve local capacity to care for those sick with advanced HIV disease. One is the fact that we have piloted a DOT-HAART project in one of the poorest parts of the poorest country in the western hemisphere. Another is that other chronic infections have been well managed in equally poor settings.

Tuberculosis offers important lessons. Although tuberculosis remains a ranking cause of premature death, some extremely poor countries with high burdens of tuberculosis have low tuberculosis mortality rates. These countries have often been those adopting the DOTS strategy (directly observed therapy, short-course).[31] Since prompt diagnosis and effective therapy mean less transmission, treatment is prevention.

Tuberculosis treatment is easily as complex as HIV therapy, since both consist of a multidrug regimen (most initiate tuberculosis therapy with four drugs). Although fixed-dose combinations can reduce pill burden, the

number of pills is not the primary determinant of outcome. The chief innovations have been directly-observed therapy; treatment that is without interruption and free of charge to the patient; and good case holding. Adjuvant social services further boost adherence and thus outcomes, which can be excellent in settings of enormous privation.[32,33] These innovations require political will at high government levels.

Some argue that the way in which tuberculosis is treated is not relevant to HIV care, since tuberculosis treatment lasts only 6–8 months whereas HIV therapy must be ongoing. For sceptics, the effective treatment of multidrug-resistant tuberculosis (MDR-TB) in impoverished regions may offer a more compelling example. MDR-TB treatment is more than three times as long as short-course therapy. The same arguments now heard in policy discussions of AIDS—high drug prices and complexity of management render antiretroviral therapy impracticable for use in resource-poor settings—were advanced to dissuade those seeking to treat MDR-TB in poor countries. Working in rural Haiti and in a slum in Lima, Peru, our group pioneered a community-based strategy to treat MDR-TB. Using strict DOT and the same standards of care as in tertiary medical centres in the USA or Europe, we achieved results better than those reported in industrialised countries.[34] Patients tolerated drug regimens more complex and far more toxic than HAART, with low rates of abandonment. We called this approach "DOTS-Plus," because it incorporates the managerial strengths of the DOTS strategy but relies on drug-susceptibility testing to determine treatment regimens appropriate for each patient.[35,36] This strategy is now being replicated in the former Soviet Union, where MDR-TB constitutes a growing problem.

Furthermore, the WHO, humanitarian groups such as Médecins Sans Frontières, and partners in the pharmaceutical industry developed a coordinated strategy of pooled procurement and distribution of second-line antituberculosis drugs. Concessional prices were offered to agencies able to demonstrate to a Green Light Committee their capacity to use these drugs prudently and to work under the aegis of a national tuberculosis programme.[37] This mechanism offers a concrete example of how coalitions can promote the prudent use of antibiotics while at the same time lowering drug prices by as much as 90%.

Tuberculosis offers examples of what needs to be done once the international community acknowledges that HIV is an international public-health emergency. Tuberculosis control, considered a public good, is by convention financed publicly. Patients do not pay for their own treatment, since those unable to pay remain sick and often infectious, perpetuating the epidemic; patients unable to pay regularly acquire resistance to first-line drugs and, subsequently, transmit drug-resistant strains of *Mycobacterium tuberculosis*. With tuberculosis, good treatment is prevention of both transmission and drug resistance.

Again, HIV offers important parallels. Although few would have predicted otherwise, we now have proof that high viral load is a strong predictor of HIV transmission.[38] HAART drops viral load to undetectable levels in most patients, and should be considered central to the AIDS-prevention arsenal.

Finally, tuberculosis offers a cautionary note. Reviewing published work reveals confident claims that rifampin would prove too expensive for use in less-developed countries; rifampin is now central to DOTS, advanced by the WHO and the World Bank as one of the most cost-effective interventions available.[39] The spread of MDR-TB across national boundaries makes different standards of care—treatment for the affluent, no treatment for the poor—unacceptable on epidemiological grounds. For some, double standards of care have long been objectionable on moral grounds.[40]

Rethinking costs and benefits

We believe that much of the policy debate regarding the role of HAART in responding to AIDS has been misguided. The belief that treatment may be reserved for those in wealthy countries whereas prevention is the lot of the poor might be less repugnant if we had highly effective preventive measures. We do not. We have argued that we need better preventives, including vaccines, and also a campaign to make HAART available to those who need it most. Where HIV is the leading cause of adult death, a basic minimum package that does not include antiretrovirals is not worthy of the name. We have instituted a very different basic minimum package in one of the poorest parts of the world (panel 5), and believe that policy makers should take note. DOT-HAART is a safe way to provide a minimum package that includes HAART.

We also argue that it is wise to avoid confident claims regarding "appropriate technology". Brazil has introduced sophisticated assays of viral load costing a small fraction of test costs in the USA; it has manufactured many antiretrovirals locally. Cipla, the Indian pharmaceutical company, has introduced a substantial formulary of antiretrovirals at a small fraction of the cost in Europe and North America. These developments lead us to a consideration of the economics of intervening to slow the spread of HIV and to diminish the death toll.

In settings of affluence, it seems as if no expense is too great in order to prolong life, even when patients are elderly and have irreversible conditions. In sub-Saharan Africa and Haiti, where HIV is the reason for plummeting life expectancies and for increasing numbers of orphans, we discern fairly overt obstructionism to the use of HAART. Leaving aside all moral arguments, any economic logic that justifies as acceptable the orphaning of children is unlikely to be sound, since the cost to society, though difficult to tabulate, is far higher than the cost of prolonging parents' lives so that they can raise their own children. Furthermore, HAART causes a dramatic drop not only in mortality, but also in the number of opportunistic infections and consequent number of admissions to hospital.[22] HAART has already been declared cost-effective in Europe, North America, and even Brazil, where HIV has become, for many, a chronic infection.[41,42]

Health economists suggest that a life-saving intervention that costs between two to three times the gross national product (GNP) per year-of-life saved represents a reasonable expenditure.[43] Even by this crude calculus, it

Panel 5: **Basic minimum package for HIV in endemic settings**

- Post-exposure prophylaxis for rape and professional accidents
- Aggressive AIDS prevention programmes, including barrier methods
- Maternal-child transmission package (including milk supplements)
- Social assistance to HIV-affected families, including orphans
- Diagnosis and treatment of opportunistic infections and sexually transmitted diseases
- HAART with DOT

should be clear that in South Africa or Botswana, for example, a three-drug HAART regimen at generic prices would prove a sound investment by any criteria as long as drugs are used correctly. Even in Haiti, where GNP is about US$400 per annum, a regimen that costs US$800 per year—again, well within our grasp even now—will be a wise expenditure even before considering favourable impact on transmission.

We conclude by acknowledging that our DOT-HAART project is a humble enough example. A small, effective pilot project might not warrant mention in the international medical literature if widespread paralysis had not led to a near-universal absence of DOT-HAART projects in regions such as rural Haiti, with minimum health infrastructure but high rates of both HIV and poverty. We know from experience that repeated claims of unfeasibility are simply not true. Multiple research projects carried out in sub-Saharan Africa have shown that more-developed world diagnostic tests can be used to follow viral load and to reveal the genotype of drug-resistant strains of HIV. It is time that more-developed world therapeutics follow.

We thank Thomas J White, the Association François-Xavier Bagnoud, FOKAL/Open Society Institute, Cambridge Cares about AIDS, OASIS, the Dunn family, and the Infectious Disease division of the Brigham and Women's Hospital. Photographs and case histories are used with patient's permission.

References

1 Mann JM, Tarantola DJM, Netter T. AIDS in the world. Cambridge: Harvard University Press, 1992.
2 Garrett L. Of epidemic proportions/ UN report: AIDS deaths to surpass plague, Spanish flu. *Newsday*. Nov 29, 2000 (A08 News).
3 International Federation of Red Cross and Red Crescent Societies. World Disaster Report 2000. Geneva: International Federation of Red Cross and Red Crescent Societies, 2000.
4 Joint United Nations Programme on HIV/AIDS. AIDS epidemic update: December 2000. Geneva: Joint United Nations Programme on HIV/AIDS, 2000.
5 Farmer PE, Walton DA, Furin JJ. The changing face of AIDS: implications for policy and practice. In: Mayer KH, Pizer HF, eds. The emergence of AIDS: the impact on immunology, microbiology, and public health. Washington, DC: American Public Health Association, 2000: 139–61.
6 Mocroft A, Vella S, Benfield TL, et al. Changing patterns of mortality across Europe in patients with human immunodeficiency virus infection. *Lancet* 1998; **352:** 1725–30.
7 Moore RD, Chaisson RE. Natural history of HIV infection in the era of combination antiretroviral therapy. *AIDS* 1999; **13:** 1933–42.
8 Palella FJ, Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. *N Engl J Med* 1998; **338:** 853–60.
9 Mayaud P, Hawkes S, Mabey D. Advances in control of sexually transmitted diseases in developing countries. *Lancet* 1998; **351** (suppl 3): S29–32.
10 Farmer PE, Connors M, Simmons J, eds. Women, poverty, and AIDS: sex, drugs, and structural violence. Monroe, Maine: Common Courage Press, 1996.
11 Joint United Nations Programme on HIV/AIDS. Report on the global HIV/AIDS epidemic, June 2000. Geneva: Joint United Nations Programme on HIV/AIDS, 2000.
12 Farmer PE. Prevention without treatment is not sustainable. *National AIDS Bulletin (Australia)* 2000; **13:** 6–9.
13 United Nations Development Programme. Human Development Report 2000. New York: Oxford University Press for UNDP, 2000.
14 World Bank. Poverty reduction and human development in the Caribbean: a cross-country study. Washington, DC: World Bank Discussion Paper, 1997 (WDP 366).
15 Deschamps MM, Pape JW, Williams-Russo P, Madhavan S, Ho J, Johnson W. A prospective study of HIV-seropositive asymptomatic women of childbearing age in a developing country. *J Acquir Immune Defic Syndr* 1993; **6:** 446–51.
16 Central Intelligence Agency. The world factbook 2000. http:www.odci.gov/cia/ publications/factbook/geos/ha.html, accessed April, 2001.
17 Farmer PE. Ethnography, social analysis, and the prevention of sexually transmitted HIV infection. In: Inhorn M, Brown P, eds. The Anthropology of Infectious Disease. Amsterdam: Gordon and Breach, 1997: 413–38.
18 Farmer PE, Walton DA. Condoms, coups, and the ideology of prevention: facing failure in rural Haiti. In: Keenan J, ed. Catholic ethicists in HIV/AIDS prevention. Maryknoll, NY: Orbis Books, 2000: 108–19.
19 Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. *N Engl J Med* 1994; **331:** 1173–80.
20 Centers for Disease Control and Prevention. Update: provisional Public Health Service recommendations for chemoprophylaxis after occupational exposure to HIV. *MMWR Morb Mortal Wkly Rep* 1996; **45:** 468–72.
21 Farmer PE. Letter from Haiti. *AIDS Clinical Care* 1997; **9:** 83–85.
22 Gebo KA, Chaisson RE, Folkemer JG, Bartlett JG, Moore RD. Costs of HIV medical care in the era of highly active antiretroviral therapy. *AIDS* 1999; **13:** 963–69.
23 Wheeler D, Gilbert C, Launer C, et al. Weight loss as a predictor of survival and disease progression in HIV infection. *J Acquir Immune Defic Syndr* 1998; **18:** 80–85.
24 Graham NMH, Munoz A, Bacellar H, Kingsley LA, Visscher BR, Phair J. Clinical factors associated with weight loss related to infection with human immunodeficiency virus in the multicenter AIDS cohort study. *Am J Epidemiol* 1993; **137:** 439–46.
25 Blatt SP, McCarthy WF, Bucko-Krasnicka B, et al. Multivariate models for predicting progression to AIDS and survival in human immunodeficiency virus-infected persons. *J Infect Dis* 1995; **171:** 837–44.
26 Fuchs D, Zangerle R, Artner-Dworzak E, et al. Association between immune activation, changes of iron metabolism and anaemia in patients with HIV infection. *Eur J Haematol* 1993; **50:** 90–94.
27 Chan ISF, Neaton LD, Saravolatz LD, Crane LR, Osterberger J. Frequencies of opportunistic diseases prior to death among HIV-infected persons. Community Program for Clinical Research on AIDS. *AIDS* 1995; **9:** 1145–52.
28 The Panos Institute. Beyond our means? The cost of treating HIV/AIDS in the developing world. London: Panos, 2000.
29 Pécoul B, Chirac P, Trouiller P, Pinel J. Access to essential drugs in poor countries: a lost battle? *JAMA* 1999; **281:** 361–67.
30 McNeil DG Jr. Selling cheap 'generic' drugs, India's copycats irk industry. *New York Times*. Dec 1, 2000: 1(A).
31 Raviglione MC, Dye C, Schmidt S, Kochi A. Assessment of worldwide tuberculosis control. *Lancet* 1997; **350:** 624–29.
32 Sumartojo E. When tuberculosis treatment fails: A social behavioral account of patient adherence. *Am Rev Respir Dis* 1993; **147:** 1311–20.
33 Farmer PE, Robin S, Ramilus SL, Kim JY. Tuberculosis, poverty, and 'compliance': lessons from rural Haiti. *Sem Respir Infect* 1991; **6:** 254–60.
34 Farmer PE, Furin JJ, Shin SS. The clinical management of multidrug-resistant tuberculosis. *J Resp Dis* 2000; **21:** 53–56.
35 Farmer PE, Kim JY. Community-based approaches to the control of multidrug-resistant tuberculosis: introducing 'DOTS-Plus'. *BMJ* 1998; **317:** 671–74.
36 Farmer PE, Kim JY, Mitnick C, Timperi R. Responding to outbreaks of multidrug-resistant tuberculosis: introducing 'DOTS-Plus'. In: Reichman LB, Hershfield ES, eds. Tuberculosis: a comprehensive international approach, 2nd edn. New York: Marcel Dekker, 2000: 447–69.
37 Gupta R, Brenner JG, Henry CL, et al. Procurement of second-line anti-tuberculosis drugs for DOTS-Plus pilot projects. WHO Working Group on DOTS-Plus for MDR-TB. Proceedings of a meeting, Cambridge, MA July 5-6, 1999. Geneva: World Health Organization; 2000 (WHO/CDS/TB/2000.276).
38 Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. *N Engl J Med* 2000; **342:** 921–29.
39 Anonymous. Rifampicin or ethambutol in the routine treatment of tuberculosis. *BMJ* 1973; **4:** 568.
40 Farmer PE, Bayona J, Becerra M, et al. The dilemma of MDRTB in the global era. *Int J Tuberc Lung Dis* 1998; **2:** 869–76.
41 Gellman B. An unusual calculus of life and death; as millions perished in pandemic, firms debated access to drugs; players in the debate over drug availability and pricing. *The Washington Post*, Dec 16, 2000; Section A:1.
42 Freedberg KA, Losina E, Weinstein MC, et al. The cost effectiveness of combination antiretroviral therapy for HIV disease. *N Engl J Med* 2000; **344:** 824–31.
43 Garber AM. Advances in cost-effectiveness analysis of health interventions. In: Culyer AJ, Newhouse JP, eds. Handbook of Health Economics, Volume 1. Amsterdam: Elsevier Science, 2000: 182–221.