Abstract In 2000, acquired immunodeficiency syndrome (AIDS) overtook tuberculosis (TB) as the world’s leading infectious cause of adult deaths. In affluent countries, however, AIDS mortality has dropped sharply, largely because of the use of highly active antiretroviral therapy (HAART). Antiretroviral agents are not yet considered essential medications by international public health experts and are not widely used in the poor countries where human immunodeficiency virus (HIV) takes its greatest toll. Arguments against the use of HAART have mainly been based on the high cost of medications and the lack of the infrastructure necessary for using them wisely. We re-examine these arguments in the setting of rising AIDS mortality in developing countries and falling drug prices, and describe a small community-based treatment programme based on lessons gained in TB control. With the collaboration of Haitian community health workers experienced in the delivery of home-based and directly observed treatment for TB, an AIDS-prevention project was expanded to deliver HAART to a subset of HIV patients deemed most likely to benefit. The inclusion criteria and preliminary results are presented. We conclude that directly observed therapy (DOT) with HAART, “DOT-HAART”, can be delivered effectively in poor settings if there is an uninterrupted supply of high-quality drugs.

Keywords HIV infections/drug therapy; Acquired immunodeficiency syndrome/drug therapy; Tuberculosis, Multidrug-resistant/drug therapy; Highly active antiretroviral therapy/economics; Drug costs; Community health services; Poverty; Haiti (source: MeSH).

Mots clés HIV, Infection/ chimiothérapie; SIDA/chimiothérapie; Tuberculose résistante à la polychimiothérapie/ chimiothérapie; Thérapie antirétrovirale hautement active/économie; Coût médicamente; Service public santé; Pauvreté; Haiti (source: INSERM).

Palabras clave Infecciones por VIH/quimioterapia; Síndrome de inmunodeficiencia adquirida/quimioterapia; Tuberculosis resistente a multidrogas/quimioterapia; Terapia antirretroviral altamente activa/economia; Costos en drogas; Servicios de salud comunitaria; Pobreza; Haití (fuente: BIREME).

Introduction A comprehensive and equitable strategy is needed to stem the worsening burden of human immunode-

Round Table

Community-based treatment of advanced HIV disease: introducing DOT-HAART (directly observed therapy with highly active antiretroviral therapy)

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Ref. No. 01-1424

Voir page 1150 le résumé en français. En la página 1150 figura un resumen en español.
violence (18, 19) and gender inequality (20, 21). Similar factors account for a lack of access to medical care, resulting in untreated sexually transmitted diseases (22), unchecked mother-to-child HIV transmission (23), and lack of treatment of AIDS-related illnesses. Preventive activities, based largely on education and the promotion of the male condom, do not confront these social factors.

The potential efficacy of preventive programmes has been widely discussed by advocates (24, 25), yet prevention has not proved very effective in the regions where HIV is taking its greatest toll (26, 27). Indeed, it was recently acknowledged that such programmes have never been subjected to rigorous clinical trials (28). More than 36 million people are infected with HIV; for them, primary prevention has clearly failed. In contrast, the advent of highly active antiretroviral therapy (HAART) has reduced AIDS mortality significantly in North America and Europe. The use of antiretrovirals in the USA has decreased AIDS-related morbidity and mortality by up to 90% and has significantly affected the trajectory of the epidemic (29). Yet in sub-Saharan Africa and the poorest parts of Latin America the resources made available by public health systems or donor agencies have been dedicated solely to HIV prevention (30).

In the arena of public health, the supposed conflict between prevention and treatment has dominated recent discussion about AIDS. It has been argued that, in a setting of limited resources, either prevention or treatment must be prioritized (31). Policy debates about AIDS are also marked by disputes about resource allocation: between development, the vaccination of children, or the treatment of TB on the one hand and the treatment of AIDS on the other. Perhaps the two most significant objections to treating HIV disease with HAART are the high cost of antiretroviral medications and the lack of an infrastructure capable of delivering the therapy in poor countries. As financial barriers have fallen (Fig. 1), the response to a potential increase in access has added more objections to the treatment of AIDS with HAART, including those of unfeasibility and patients’ non-compliance (32). The spectre of acquired drug resistance is also frequently raised, although this has not yet been reported in the developing world. The concern has also been raised that the use of antiretrovirals might hamper preventive efforts if people lost their fear of becoming infected (33).

Certain of these objections to treatment may be cast in doubt by our experience in rural Haiti, where there are both high rates of HIV infection and a poor health infrastructure. More significantly, in terms of experience to date, are lessons learned in treating another chronic infectious disease, tuberculosis. Indeed, the epidemiology of the two diseases is increasingly enmeshed as HIV spreads rapidly in the regions where TB is endemic (33), such as Haiti. In Haiti, the only Latin American country in which life expectancy has declined over the past decade (34), HIV is probably the leading infectious cause of mortality among young adults. Surveys in poor urban regions of Haiti demonstrate a national HIV prevalence of 5%; a figure of up to 13% has been reported for women presenting to prenatal clinics (35).

**Lessons from TB control**

The history of TB control offers many lessons to those committed to responding more effectively to the HIV epidemic (36). Like HIV, TB requires multidrug therapy over an extended period. Consequently, treatment adherence and drug resistance are critical programme issues. Direct observation of therapy (DOT) has assisted in increasing TB cure rates and lowering drug resistance in a wide range of settings. The lessons are particularly significant in rural Haiti, where TB remains endemic and a major cause of morbidity and mortality. During the previous decade, more than half the patients we diagnosed with HIV presented with pulmonary or extrapulmonary TB (Fig. 2). Many HIV-positive patients therefore became known to us as TB patients and were offered daily DOT by community health workers, called accompagnateurs (Fig. 3), because they “accompany” patients on a daily basis. The accompagnateurs ensure that DOT-HAART is effectively monitored once it is initiated.

**The HIV Equity Initiative**

Between 1998 and 2000 we launched the “HIV Equity Initiative” in order to deliver antiretroviral therapy to some of the western hemisphere’s poorest AIDS patients (40). Over the past decade, Partners in Health and local collaborators in Haiti have attempted to establish a comprehensive AIDS programme to serve a small region of central Haiti. It includes access to free voluntary testing and counselling, the provision of AZT (zidovudine) for the prevention of mother-to-child transmission, and aggressive diagnosis and treatment of opportunistic infections, including TB. The chief AIDS prevention activities have consisted of community education and the development of culturally appropriate preventive tools. Despite these efforts, HIV transmission has
continued in rural Haiti. Furthermore, HIV acquired in urban areas, where its prevalence has always been higher, was diagnosed in rural areas when sick young adults returned to die in the villages where they had been born. Local preventive efforts have no impact on transmission events occurring far away (41).

Over the past few years a team based at the Clinique Bon Sauveur in central Haiti has developed a set of algorithms that could identify, initially without the help of CD4+ T-cell counts or viral load testing, those patients most likely to need life-sustaining treatment with HAART (Box 1). These guidelines include a series of enrolment criteria reflecting local epidemiology. In countries where TB is endemic, such as Haiti, the disease usually results from an infection acquired in childhood (42). As such, HIV-associated TB is often a reactivation disease, rather than being attributable to progressive primary infection, and occurs early in the course of HIV infection.

Our patients with HIV-associated TB respond well to antituberculous therapy alone. Their HIV disease often remains asymptomatic without HAART for years after the completion of TB treatment. Of 246 patients diagnosed with TB in 1994, 38 were diagnosed with HIV coinfection. Of these, 36 responded to directly observed treatment, short-course (DOTS) chemotherapy for TB. Six years later, follow-up was possible for 29 of these patients: 27 were still alive, two had died. Of the 27 patients with a known diagnosis of HIV for six years or more, two initiated DOT-HAART in 1999, one in 2000, and two in 2001. The other 22 are outpatients and remain stable without antiretroviral therapy.

In contrast, patients who present to the Clinique Bon Sauveur with wasting disease, chronic enteropathies, neurological complications of HIV disease, severe anaemia, or severe leukopenia are believed more likely to have significant immunodeficiency and a more urgent need to start HAART. Of over 1350 HIV-positive patients diagnosed and followed at the clinic it was estimated that between 120 and 150 would benefit from the immediate introduction of antiretroviral therapy. Most of these patients are now receiving DOT-HAART.

Consequences of the DOT-HAART project
The introduction of DOT-HAART had both intended and unforeseen consequences (Box 2). The clinical response to therapy was favourable in 59 of the first 60 patients (over 40 more were enrolled in 2001). We estimate that 48 of these patients were able to resume working and caring for their children. The weights of all but two patients increased by more than 2 kg within the first 3 months of therapy. In a subset of 21 DOT-HAART patients whose viral loads were tested, 18 (86%) had no detectable virus in peripheral blood. This suggests that therapy was quite effective. Most studies based in the USA demonstrate viral suppression in only about 50% of patients after one year of treatment (43).

Emotional problems have been reported among health care workers in areas where AIDS is endemic but therapy is unavailable (44). The provision of life-saving care through the HIV Equity Initiative has had a favourable impact on staff morale. It is our belief that the stigma associated with AIDS has diminished as a result of 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. A related consequence of introducing DOT-HAART is an increased use of the clinic’s free HIV testing and counselling services. HIV testing has been available since 1988 but during the past two years its utilization has increased by more than 300%. Thus the provision of AIDS treatment has strengthened AIDS prevention.

The success of this small demonstration project as one of the few attempts to provide DOT-HAART in a resource-limited setting led us to propose a “basic minimum package” for AIDS prevention and care (Box 3). Because this far exceeds what exists in Haiti, Africa, and Asia, concerns have been raised about replicability in other low-income settings. Indeed, our own attempts to obtain funding were often met with resistance on the grounds that the project would be unsustainable in a country as poor as Haiti. The chief barrier has been the high costs of antiretroviral agents.

Drug costs
We estimate that 75–80% of project expenditures have been for medications. Although price estimates vary widely, in the established market economies most regimens cost more than US$ 10 000 per year per person (45). Nevertheless, HAART has been judged cost-effective not only in the USA, largely because of a reduction in hospitalizations, but also in Brazil (46, 47). At such prices, however, the implementation of HAART in a poor country, even with the DOT-HAART approach to assure compliance, is considered in international medical and public health circles as neither sustainable nor cost-effective.

High drug costs in the face of the devastation caused by AIDS have induced vigorous debate on the use of generic as opposed to brand-name drugs. The introduction of generic drugs has coincided with a steep fall in the price of antiretrovirals (Table 1 and Fig. 4). The question arises as to whether public health emergencies should be confronted by novel strategies attempting to deal with the underlying inequities of the global economy. The market itself will not suffice in responding to the health problems of the poor. The treatment of onchocerciasis with ivermectin is a commonly cited example of an alternative or complementary strategy, as this drug is made available free of charge by a major pharmaceutical company. However, onchocerciasis is treated with a single drug. Examples of effective responses to complex infectious diseases requiring long-term treatment with multidrug regimens are scarce, but TB offers instructive examples. Precisely the same market logic was once applied to rifampicin, now the mainstay of short-course chemotherapy in resource-poor settings. In 1973 the suggestion was made that rifampicin was unlikely to prove useful in developing countries because of its cost (49). Similarly, until recently, multidrug-resistant TB was considered untreatable in resource-poor settings because drug costs alone could exceed US$ 10 000 per patient per year. As with the treatment of HIV disease, most of the cost of multidrug-resistant TB treatment was attributable to drug costs.

However, local demand does not disappear merely because international policies decree that treatment is unsustainable. Demand follows the epidemiology of disease and its wake of human suffering. When multidrug-resistant TB was recognized as a growing problem, treatment advocates sought examples of centrally coordinated drug procurement that might reduce prices and allow the proper use of medications. One such example is WHO’s International Coordinating Group for meningococcal vaccine, which was formed to streamline the distribution of vaccine to poor countries in Africa’s “meningococcal belt”. This helped to move low-cost vaccine purchased by WHO to epidemics when local health authorities demonstrated the capacity to use the vaccine correctly.

**Box 1. Guidelines for inclusion of patients in the DOT-HAART project, Clinique Bon Sauveur, Haiti**
- Absence of active TB
- Recurrent opportunistic infections that are difficult to manage with antibacterials or antifungals
- Chronic enteropathy with wasting
- Otherwise unexplained significant weight loss
- Severe neurological complications attributable to HIV disease
- Severe leukopenia, anaemia, or thrombocytopenia

Source: ref. 40.

**Box 2. The DOT-HAART project, Clinique Bon Sauveur, Haiti:**
- is effective, according to clinical and virological criteria
- reduces mortality
- responds to widespread demands for equity
- lessens AIDS-related stigma
- improves medical staff morale
- boosts interest in HIV testing and counselling and thus contributes to prevention.

**Box 3. Basic minimum package for AIDS prevention and care in HIV-endemic settings**
- Post-exposure prophylaxis for rape and occupational accidents
- Aggressive AIDS prevention programmes (including the use of barrier methods)
- Mother-to-child transmission package (including the use of milk supplements)
- Social assistance to HIV-affected families, including orphans
- Diagnosis and treatment of opportunistic infections and sexually transmitted diseases
- DOT-HAART

Source: ref. 40.
A coalition of nongovernmental organizations, WHO, and national governments formed the “Green Light Committee” for access to drugs for multidrug-resistant TB. Using a model based on the pooled procurement of vaccines for meningitis control, pooled purchasing and capacity assessment were adopted to make second-line antituberculous drugs available to countries and programmes needing them. Through negotiations with the research-based and generic pharmaceutical industries, the cost of drugs for multidrug-resistant TB was reduced by up to 98%. Furthermore, the Green Light Committee has established a system that both evaluates and provides technical assistance to projects seeking access to drugs for multidrug-resistant TB. Access is improved at the same time as rational use is promoted (50). It should be noted that this process was delayed until a commitment was made by both the scientific and public health communities to provide free treatment for patients with multidrug-resistant TB.

Conclusions

The rapid spread of HIV demands a comprehensive global AIDS strategy that includes prevention, testing, and counselling, the treatment of opportunistic infections, and the use of HAART. Social assistance to families and communities affected by HIV is also critical. For most of the hardest hit communities, AIDS is the latest in a long line of health threats. The greatest of these are poverty and inequality, both of which are co-factors for and consequences of HIV transmission. If HIV reveals a lack of basic primary care services for the poor, an aggressive response to this comparatively new disease may help to solve a host of old problems. High drug costs and the need for sustained monitoring have led many observers to conclude that aggressive treatment of chronic disease is neither feasible nor sustainable in those communities where the demand for treatment is greatest. The result is a growing “outcome gap” between rich and poor even as diseases become treatable by means of new medical technologies among people who have access to them (51).

Successful DOTS programmes for TB are a reminder that chronic infectious diseases can be treated effectively in the poorest of settings, even though treatment regimens contain several antibiotics. The demand for HAART can be expected to grow as the burden of HIV disease grows. The rapid fall in drug prices can be expected to lead to the introduction of drugs into settings with poor health infrastructures. Incorrect or inconsistent use of these drugs will result in the emergence of HIV strains that are resistant to them. However, the use of some of the strategies outlined above — namely DOT-HAART, a centralized Green Light Committee for the procurement and distribution of drugs, and technical assistance as appropriate — might make it possible to enhance both access to antiretroviral agents and the rational use of the drugs within a given health infrastructure. Moreover, experience in central Haiti demonstrates that it is possible to incorporate work on AIDS treatment into established prevention efforts, and indeed to fortify prevention efforts where they are most needed.

If the response to HIV matched the gravity and dimensions of the problem it causes, resources could be expected to flow to both afflicted communities and the scientific establishment so that better diagnostics, therapeutics, and vaccines could be developed. Until this happens, a basic minimum package is required which focuses on both prevention and the treatment of people already living with HIV disease. The DOT-HAART project described above is so small that it

Table 1. Differences in costs of drugs used to treat AIDS and opportunistic infections

<table>
<thead>
<tr>
<th>Drug</th>
<th>Form</th>
<th>Wholesale price in USA (US$)</th>
<th>Best price(a) (US$)</th>
<th>Price differential(b) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Didanosine (ddI)</td>
<td>100 mg capsule</td>
<td>1.80</td>
<td>0.50</td>
<td>360</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>200 mg capsule</td>
<td>4.40</td>
<td>2.30</td>
<td>190</td>
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<tr>
<td>Lamivudine (3TC)</td>
<td>150 mg capsule</td>
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<tr>
<td>Nevirapine</td>
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<td>230</td>
</tr>
<tr>
<td>Stavudine (d4T)</td>
<td>40 mg capsule</td>
<td>4.90</td>
<td>0.30</td>
<td>1630</td>
</tr>
<tr>
<td>Zidovudine (AZT)</td>
<td>100 mg capsule</td>
<td>1.70</td>
<td>0.20</td>
<td>850</td>
</tr>
<tr>
<td>AZT + 3TC</td>
<td>300 mg + 150 mg capsule</td>
<td>9.80</td>
<td>0.70</td>
<td>1400</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>250 mg tablet</td>
<td>3.40</td>
<td>0.05</td>
<td>6800</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>200 mg capsule</td>
<td>12.20</td>
<td>0.30</td>
<td>4060</td>
</tr>
</tbody>
</table>

Source: ref. 48.

\(a\) Best price refers to the lowest price among 7 selected countries.

\(b\) The percentage by which the price in the USA is greater than the best price.

Fig. 4. Costs of antiretrovirals in 2001: proprietary, concessional, and generic prices for three regimens of triple therapy


**Proprietary**

**Concessional**

**Generic**

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would not merit attention in the public health literature if we could point to larger and better studies that respond aggressively to the growing challenge of HIV. Because we cannot, we hope that our experience might be instructive in other settings where HIV and poverty are the top-ranking threats to health.

Acknowledgements
The treatment of patients in Zanmi Lasante’s HIV Equity Initiative is made possible by the accompagnateurs who deliver therapy and through the generosity of Partners in Health supporters. We thank especially Thomas J. White, the Open Society Institute, the Brigham and Women’s Hospital, Bruce Walker and the Partners AIDS Research Center, and the Charlotte Taylor Foundation.

Conflicts of interest: none declared.

Résumé
Traitement communautaire des stades avancés de l’infection à VIH: introduction du DOT-HAART (traitement antirétroviral hautement actif sous surveillance directe)
En 2000, le syndrome d’immunodéficience acquise (SIDA) l’a emporté sur la tuberculose en tant que principale cause infectieuse de décès chez l’adulte à l’échelle mondiale. Dans les pays riches, la mortalité par SIDA a toutefois fortement baissé grâce aux thérapies antirétrovirales hautement actives (HAART). Les antirétroviraux ne sont pas encore considérés comme médicaments essentiels par les experts internationaux de santé publique et sont peu utilisés dans les pays pauvres, où le virus de l’immunodéficience humaine (VIH) fait le plus de victimes. Les arguments contre l’utilisation de ces médicaments reposent essentiellement sur leur coût élevé et sur l’absence des infrastructures nécessaires à une utilisation judicieuse. Nous réexaminons ici ces arguments dans le contexte de l’augmentation de la mortalité par SIDA dans les pays en développement et de la baisse considérable des prix des médicaments, et décrivons un programme à petite échelle de traitement communautaire utilisant les acquis de la lutte contre la tuberculose. Avec la collaboration d’agents de santé communautaires haïtiens expérimentés dans la délivrance du traitement à domicile sous surveillance directe pour la lutte contre la tuberculose, un projet de prévention du SIDA a été étendu à la délivrance de HAART à un sous-groupe de patients infectés par le VIH et jugés les plus susceptibles d’en tirer profit. Les critères d’inclusion dans l’étude et les résultats préliminaires sont présentés ici. Nous concluons que le traitement sous surveillance directe (DOT) par des antirétroviraux hautement actifs (HAART), le « DOT-HAART », peut être délivré efficacement en milieu pauvre sous réserve d’un approvisionnement continu en médicaments de bonne qualité.

Resumen
Tratamiento comunitario de la infección avanzada por el VIH: introducción del tratamiento DOT-HAART (tratamiento bajo observación directa con antirretroviricos de gran potencia)
En 2000, el síndrome de inmunodeficiencia adquirida (SIDA) superó a la tuberculosis como principal causa infectiosa de defunciones de adultos a nivel mundial. En los países prósperos, sin embargo, la mortalidad por SIDA ha caído pronunciadamente, en gran parte gracias a la terapia con antirretroviricos de gran potencia (HAART). Los antirretroviricos todavía no son conside-rados medicamentos esenciales por los expertos internacionales en salud pública, y tampoco han empezado a ser ampliamente utilizados en los países pobres donde el virus de la inmunodeficiencia humana (VIH) se cobra más vidas. Como argumentos contra el uso de los HAART se han esgrimido fundamentalmente el elevado costo de esos medicamentos y la falta de la infraestructura necesaria para usarlos correctamente. En este artículo reanalizamos esos argumentos a la luz del aumento de la mortalidad por SIDA registrado en los países en desarrollo y de la caída de los precios de los medicamentos, y describimos un pequeño programa de tratamiento comunitario basado en las lecciones extraídas de la lucha contra la tuberculosis. Con la colaboración de agentes de salud comunitarios de Haití experimentados en la administración domiciliaria de tratamiento antituberculoso bajo observación directa, se procedió a ampliar un proyecto de prevención del SIDA para que incluyese la administración de HAART a un subgrupo de pacientes infectados por el VIH que se consideró que podrían ser los más beneficiados. Se presentan los criterios de inclusión y los resultados preliminares. Nuestra conclusión es que, si se garantiza el suministro ininterrumpido de medicamentos de alta calidad, la terapia bajo observación directa (DOT) con HAART, «DOT-HAART», se puede aplicar eficazmente en entornos pobres.
References


Antiretroviral therapy is only part of it
Anthony Mbewu

There is as yet no cure for AIDS, but therapeutic strategies must play a part in any comprehensive approach to the epidemic — even in resource-poor countries. Farmer et al. (1) provide a starting point, but many more clinical trials are needed to investigate the efficacy of antiretrovirals (ARVs) in prolonging life and improving the quality of life lived with AIDS in developing countries (2).

This is because AIDS treatment in developing countries involves more than simply using western therapies in tropical settings (3); ARVs neither eradicate the virus from the body nor cure the disease. Also, potentially more effective new treatments are being developed in countries of the South or in collaboration with the North, including immunomodulatory agents isolated from traditional medicines, holistic approaches to AIDS care, and fusion inhibitors. Lastly, intersectural approaches are vital to improve access to drugs, such as the recent successful court action of the South African government against the pharmaceutical industry.

Lack of monitoring facilities forced Farmer et al. to adopt treatment algorithms that may actually be the most appropriate — i.e. treatment late rather than early in the course of the disease, as recently recommended by the expert committee convened by the US National Institutes of Health. This could cut costs by reducing the numbers for whom treatment is indicated. Nevertheless initial diagnosis should include a CD4 count, as accurate diagnosis and appropriate selection of patients for treatment is crucial. Treatment of newly infected patients requires more research.

Piggybacking highly active antiretroviral therapy (HAART) on the standard directly observed treatment short course for tuberculosis (DOTS) seems logical because both conditions require a multidrug regimen; direct observation may be necessary for the effective use of HAART, for which default from treatment can be as high as 60%; and pulmonary TB is the commonest severe AIDS-related condition in African countries. However, this approach loses credibility when one considers that DOTS is curative whereas HAART is not; compliance is much higher for DOTS than for HAART; DOTS is a six-month regimen, whereas HAART is lifelong; mortality during DOTS is low whereas annual mortality of patients on HAART can be 5–10%; and even with the drastic reductions in price of ARVs, to US$ 350 per annum, they remain unaffordable for most developing countries. Even in an “upper middle” income country such as South Africa, per capita health care expenditure in the public sector is only US$ 88 per annum.

Further pilot studies of ARV therapy in the public sector in developing countries (such as the ‘Protest initiative’ of WHO) are needed and, as Farmer et al. show, must be comprehensive, incorporating counselling, fixed dose combinations, structured treatment interruption protocols, prevention strategies, behavioural research, multivitamins, nutrition, treatment for opportunistic infections, therapy for sexually transmitted diseases, sexual health education, psychological support, poverty alleviation, social welfare support, and provision of clean water and sanitation as well as housing.


HAART — the need for strategically focused investments
Richard Feachem

Farmer and his colleagues stress the importance of both prevention and treatment of HIV, in the light of an unparalleled global catastrophe (1). I fully agree. Their paper also describes some of the good progress made in Haiti through the work of their team. I am impressed by this work. The paper calls for antiretroviral drugs to be made available at a greatly reduced cost (as indeed is occurring). Again, I am in full agreement.

My dilemma is that the world is still a long way from being able to make antiretroviral drugs, even if they were free, effectively available to the majority of the people who are infected with HIV. I wish that the world was different. I wish that poor countries were not so poor. I wish that the health systems of poor countries were not so dysfunctional. I wish that rich countries were far more generous in their support for health sector activities in poor countries. Regrettably, none of this is the case in the real world in which we live. Farmer and his colleagues do not give us a clear idea of how to overcome these major constraints.

Let me caricature the debate on highly active antiretroviral therapy (HAART). On one side is the opinion: “HAART is too difficult, too expensive, and insufficient investment and insufficient research.” The other side is the opinion: “It’s too cheap, it’s too simple, it’s too easy to adopt treatment algorithms that may actually be the most appropriate — i.e. treatment late rather than early in the course of the disease, as recently recommended by the expert committee convened by the US National Institutes of Health. This could cut costs by reducing the numbers for whom treatment is indicated. Nevertheless initial diagnosis should include a CD4 count, as accurate diagnosis and appropriate selection of patients for treatment is crucial. Treatment of newly infected patients requires more research.

Piggybacking highly active antiretroviral therapy (HAART) on the standard directly observed treatment short course for tuberculosis (DOTS) seems logical because both conditions require a multidrug regimen; direct observation may be necessary for the effective use of HAART, for which default from treatment can be as high as 60%; and pulmonary TB is the commonest severe AIDS-related condition in African countries. However, this approach loses credibility when one considers that DOTS is curative whereas HAART is not; compliance is much higher for DOTS than for HAART; DOTS is a six-month regimen, whereas HAART is lifelong; mortality during DOTS is low whereas annual mortality of patients on HAART can be 5–10%; and even with the drastic reductions in price of ARVs, to US$ 350 per annum, they remain unaffordable for most developing countries. Even in an “upper middle” income country such as South Africa, per capita health care expenditure in the public sector is only US$ 88 per annum.

Further pilot studies of ARV therapy in the public sector in developing countries (such as the ‘Protest initiative’ of WHO) are needed and, as Farmer et al. show, must be comprehensive, incorporating counselling, fixed dose combinations, structured treatment interruption protocols, prevention strategies, behavioural research, multivitamins, nutrition, treatment for opportunistic infections, therapy for sexually transmitted diseases, sexual health education, psychological support, poverty alleviation, social welfare support, and provision of clean water and sanitation as well as housing.


HAART — the need for strategically focused investments
Richard Feachem

Farmer and his colleagues stress the importance of both prevention and treatment of HIV, in the light of an unparalleled global catastrophe (1). I fully agree. Their paper also describes some of the good progress made in Haiti through the work of their team. I am impressed by this work. The paper calls for antiretroviral drugs to be made available at a greatly reduced cost (as indeed is occurring). Again, I am in full agreement.

My dilemma is that the world is still a long way from being able to make antiretroviral drugs, even if they were free, effectively available to the majority of the people who are infected with HIV. I wish that the world was different. I wish that poor countries were not so poor. I wish that the health systems of poor countries were not so dysfunctional. I wish that rich countries were far more generous in their support for health sector activities in poor countries. Regrettably, none of this is the case in the real world in which we live. Farmer and his colleagues do not give us a clear idea of how to overcome these major constraints.

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too prone to divert resources from other priority health investments, fuel drug resistance, and undermine progress in behavioural change. We should not launch this on a large scale." On the other side is the position: “HAART is a human right. Therapy that is available to gay men in San Francisco and Sydney should also be available to all infected people everywhere. We have no choice and no alternative. We must act on a huge scale and we must do so immediately.”

The first position, it seems to me, is clearly wrong, from both a public health and an ethical perspective. The second position may be right in a moral sense, but it is not practical. To advocate the impossible is to put at risk the achievement of more limited objectives.

The key to the achievement of more limited objectives is geographical focus. The experience of health development work is full of examples in which international agencies, with the best intentions, have tried to do too many things in too many places and have, as a result, achieved little. Being spread too thin is as undesirable in health investment as in any other form of human endeavour. What is needed is selected areas (these could be districts, or small countries, or towns and their rural hinterlands) in which the appropriate drugs and delivery systems are put in place on a serious scale and with adequate levels of investment. This investment should include the funding of the necessary research and evaluation efforts, so that epidemiological and clinical data can be collected and the programmes can be modified and improved over time.

These sites would achieve three things. First, they would bring HAART to tens of thousands of infected people in an effective way. Second, they would be islands of good practice where new drugs and new delivery techniques are continually being applied and evaluated and a major learning experience is going on. Third, they would provide powerful demonstration sites where the cost, impact and feasibility of using HAART in resource-poor settings could be clearly seen.

This is not to argue that HAART should be unavailable in other places in other ways. But it is to argue that an international effort focused on establishing and sustaining a number of islands of learning and good practice is likely to make a greater contribution to the reduction of suffering and unnecessary death than spreading limited resources thinly across the low-income countries.

The approach that I recommend is very difficult for international agencies to adopt, for obvious political reasons. It is, however, an approach that the major foundations can take. The investment by the Bill and Melinda Gates Foundation in HIV/AIDS therapy in Botswana is a case in point. Let us make sure that the best is not seen as the enemy of the good and that we do not, by calling for unachievable objectives, undermine the prospects of making good progress and bringing substantial rewards in the longer term.

AIDS care is learnt by doing it
Ariel Pablos-Mendez1

There is consensus that prevention is the most important strategy to halt the AIDS pandemic (1), and introducing an HIV vaccine is our ultimate tool for doing this. However, the inconsistent success of prevention programmes, and the absence of effective vaccines now and in any near future, provide ample grounds for looking more seriously at care for AIDS patients in resource-poor countries. We have reached a point of no return, moving from the if and the when of effective care to the how.

Reasons for taking up the challenge of care now include the following. First, the sheer magnitude of the global AIDS crisis. Silently infected before, millions of people living with HIV/AIDS are now falling sick and dying. Second, there is moral outrage over this tragedy when therapy exists for those who can afford it. Public opinion now demands a shift from unmitigated suffering to hope. Third, indifference to such suffering reduces the credibility of prevention efforts. Treatment is thus an essential component of the AIDS control continuum. Fourth, a 97% reduction in antiretroviral (ARV) prices (2) and hospital cost savings in Brazil have made previous arguments over affordability obsolete, and given rise to confidence that AIDS care in poor countries is not only feasible but inevitable. Fifth, mounting pressure — politically and even legally — on multinational pharmaceutical companies, local governments, and the international community is opening the door to new resources.

Universal access to highly active antiretroviral therapy (HAART) for millions of people is not feasible today, but doing nothing is unacceptable. One parallel with tuberculosis (TB) is that a much simpler and curative regimen reaches only 25% of patients despite a decade-long campaign (3). AIDS care is daunting by comparison. Talking of billions of dollars is easy compared with the demands of setting priorities (e.g. what regimen, where to start) and raising and allocating vast resources. But if the risks are high, so too are the opportunities.

Moving forward, there are at least two steps we need to take before going full speed ahead: demonstration projects, and targeted research. Small pilot projects by dedicated physicians, such as the Partners in Health work in Haiti (4), bring hope and suggest the feasibility of AIDS care in poor countries. Newer models designed to target a specific subset of

the population (e.g. HIV-infected pregnant women) are another way to advance public health without overburdening fragile health care systems. Their experience will show the way forward to the scale-up of AIDS care in the coming years.

Farmer et al. draw on the lessons and infrastructure of the directly observed treatment short course for TB (DOTS) to plan for AIDS care (4). TB programmes, however, cannot be taken for granted, nor did they evolve overnight (5–7). The DOTS strategy, for example, calls for passive case finding, targeting smear-positive cases, and supervised outpatient treatment. These controversial parameters were set through clinical epidemiology and operational research, enlightened leadership and management, and unrelenting advocacy and training. We are not there yet in AIDS care, though we are not short of ideas to test.

Until recently, AIDS care research in Africa and its rationale had been neglected (8). Most non-experts had assumed that we knew how to treat AIDS from what had been done in the OECD countries (9). In fact, we are today with AIDS treatment where we were in 1970 with anti-tuberculosis treatment: there were many drugs developed a decade earlier, which were life-saving in the hands of experts. It took over two decades of sound research to develop a standardized TB programme (DOTS) that could be implemented in developing countries (later it was adopted in OECD countries too (10)). Africa cannot afford to wait two decades to tackle AIDS. Yet, the required research has been scant, owing to reservations about the feasibility of HAART, clinical overconfidence and ethical paralysis.

Scientific research must be marshalled to “fast track” the scaling-up of AIDS care beyond pilot projects. Research can bridge the gap between increasingly cheaper ARVs and the limited infrastructure to deliver them in Africa. Research need not hold back care. We should learn by doing. Better action can be informed by research, just as research priorities should be driven by the imperatives of action. Competing needs in the fight against AIDS and poverty demand that we go into comprehensive care armed with the right weapons. The seeds are sown.


HAART in Haiti — evidence needed
Charles Gilks,1 Carla AbouZahr,2 & Tomris Türmen3

Farmer et al. present a remarkable achievement: the establishment of a care service for people with HIV/AIDS in a community of poor displaced people living in a remote rural area of Haiti (1). The conditions under which this has been accomplished are particularly difficult, yet the service has included the provision of antiretroviral therapy (ART) to 60–100 people. This has been possible, they argue, by learning from the history of tuberculosis control and using a model they have called DOT-HAART (directly observed therapy with highly active antiretroviral therapy), implemented through a team of community-health workers called “accompagnateurs” to supervise therapy.

If the claims of the authors are substantiated, such a model would have enormous potential for replication in other resource-poor settings. If, on the other hand, the authors’ claims are exaggerated, the potential for doing more harm than good would be great (and the authors dismissal of the “spectre of

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Ref. No. 01-1611
acquired drug resistance” is alarming). In the end, the scientific soundness of the evidence must be the decisive factor. It is unfortunate, therefore, that the paper reads more like a statement of positive self-evaluation than a careful presentation and analysis of the facts. The paper is instructive not so much for what it presents as for what it does not reveal. It makes no serious attempt to consider what really are the lessons for Haiti, and other countries, if they want to scale up efforts to provide care to those infected with HIV/AIDS.

The authors’ main contention is that the concerns voiced about treating HIV-positive people with HAART — namely high cost of drugs, lack of health system capacity to deliver them effectively, possibility of non-compliance, and risk of drug resistance — are ill-founded. If we are to be convinced that this is so, we need better evidence than that provided in this paper. Let us look briefly at some important issues the authors did not mention.

First, logistics: what clinical input and staff time was required to set up and then run this intervention? Apart from the “accompagnateurs”, how many physician hours were involved? In the real world, any broadly accessible initiative will have to be clinical-officer or nurse-practitioner led — there just are not enough physicians to go around. With rapidly falling prices, capacity, not cost, will be the big issue. The human resources and capacities needed to implement the model intervention need to be very carefully listed for a real evaluation of their programme to be made.

Second, entry criteria: ad hoc criteria are used to start individuals on treatment. What are “recurrent opportunistic infections difficult to manage with antibacterials or antifungals”? What is “otherwise unexplained and significant weight loss” compared to “chronic enteropathy with wasting”? The severe neurological complications include peripheral neuropathy which may be more present in the earlier stages of disease than other problems. The reliance on haematological indices including low platelet counts and “severe leukopenia” (not defined) suggests access to automated haematology analysers, which are not available outside research projects or capital cities. Also, why have patients with active TB been excluded?

Third, unforeseen benefits: what is the evidence that the intervention has improved staff morale? What observations have been made for the group to form an “impression” that AIDS-related stigma has been reduced? And how do they relate the increase in voluntary counselling and testing to this intervention rather than other changes (there is no control group and many things have changed over the three years)? We would all want these benefits to be forthcoming, but public health physicians need evidence rather than impressions.

Fourth, costs: how much did it cost to deliver the drugs? Reference is made to 75–80% of the costs being for medication — but this is for drugs purchased in which market and at what price? Eighty per cent of current US prices for triple drug (perhaps US$ 8000–10 000) is a lot more than 80% of the current best (cheapest) prices quoted by Médecins Sans Frontières and other nongovernmental organizations — around US$ 350 per patient per year. This incomplete presentation of the facts the group may well have at hand suggests that the costs are high, which would then put the intervention in a very different light. Of course any research initiative will have additional costs which will be shed if other nongovernmental organizations start to deliver the model. But if very costly, how can this intervention ever be scaled up and replicated, and sustained?

By any evaluation criteria — whether cost-effectiveness, sustainability, feasibility, or absence of unintended negative consequences — this success story must be classified as non-proven. Yes, we know with exceptional circumstances, motivation, resources and generous research funding positive outcomes can be achieved, but replication is something else entirely. Yes, it is true that with huge inputs the miracle of ART will produce stunning successes. And certainly, acting when others have failed to do so is noble. However, for lack of appropriate design and scientific evaluation, important lessons that might have been applied in other settings simply cannot be drawn from this study.