Fighting against AIDS: the Brazilian experience

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Introduction

Brazil was among the countries to be the earliest and the most intensely affected by the AIDS epidemic. After the first AIDS case was reported in 1982 \cite{1} new cases sky-rocketed to more than 10 000 in the beginning of 1990 \cite{2}. In that year, the World Bank estimated that Brazil would experience 1 200 000 HIV infections by the year 2000, explicitly expressing the fear that the epidemic would then be totally out of control. However, a recent estimate by the Brazilian Ministry of Health (MoH) has reduced that number to under 600 000, and all AIDS-related figures are much more encouraging than anticipated a decade ago. The objective of this article is to review the actions taken that have prevented the above expectations.

General aspects

Table 1 summarizes the Brazilian response to the AIDS epidemic. The fight against the disease set the stage for a new kind of interaction between state and society. Whether addressing the rights of those living with HIV/AIDS, or fighting against prejudice, discrimination and social isolation (often rooted in personal views towards sexual behaviour) social movements and organizations drastically changed the relationship between the public and private sectors to make them both more collaborative and more participative. Importantly, the Brazilian experience with HIV/AIDS has contributed substantially to stronger democratic institutions, to a greater recognition of all Brazilians as citizens, and to an open debate on the ethics of national healthcare. In this regard, Brazil was one of the first countries in the world to establish in 1988 ethical guidelines for the management of HIV/AIDS, and these guidelines were the standard for all physicians in the nation \cite{3}.

At the onset of the epidemic, however, most government agencies were both in denial of the severity of the problem and reluctant to respond to the needs of the new epidemic. Civil pressure and the growing number of cases ultimately mandated more effective federal intervention. In May 1985, the MoH established the guidelines for the creation of the National AIDS Control Program (NACP) of Brazil. At that time, governmental activities focused on epidemiological surveillance, medical assistance, and the release of non-discriminating and prevention messages to pa-

\begin{table}[h]
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\caption{Characteristics of the Brazilian response to the AIDS epidemic.}
\begin{tabular}{|l|}
\hline
• Early governmental response \\
• Strong civil society participation at all decision levels \\
• Multisectorial mobilization \\
• Balanced prevention and treatment approach \\
• Human rights perspective in all strategies and actions \\
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tients and the general public. Funding was scarce, though. As of 1986, the NACP was consolidated with the inclusion of sexually transmitted infections as the centre of action. The AIDS/sexually transmitted diseases (STD) approach grew increasingly more pragmatic and technical, and counted on increasing international cooperation. In 1987, the National AIDS Control Committee of Brazil, made up of scientific community representatives as well as organized civil society members, was created to act as the focus for a social and political approach towards the epidemic, with the intent of involving Brazilian society as a whole, and to somehow get Brazil ‘up to speed’ after the period of denial of AIDS treatment in the early 1980s.

After some delays in the early 1990s, the NACP was reorganized in 1992: links with civil society and with other areas in government were formed, and key agreements were established with other countries and international institutions for technical cooperation with Brazil. Fig. 1 shows the organization of the National AIDS Program in the MoH, its location in the Secretariat of Health Policies, and its structure as of July 2002.

In 1992, a loan agreement with the World Bank was signed to support prevention and control activities. The agreement, called AIDS Project I, was effective between 1992 and 1998, with funding reaching US$250 million, of which US$160 million comprised the loan and US$90 million was derived from domestic contributions. AIDS Project II followed, effective from 1998 to 2002, with funds reaching US$300 million.

As of 1992, after a specific and financially more attractive payment system was implemented for the hospitalization of AIDS patients, the MoH established procedures for the accreditation of public hospitals, and expanded the hospital network for the care of HIV-infected patients. With the creation of the Alternative Assistance Program, professionals were trained in HIV care and funds were transferred to state and municipal governments to assist patient care at different need levels. As a result, outpatient assistance services, day-hospital services, and home care services were established. Multidisciplinary teams that served the needs of both patients and their families typically provided these services. It should be pointed out that the expansion of outpatient units and day-hospital services proved cost-effective when compared with pre-existing inpatient services for individuals with HIV/AIDS.

With time, this framework expanded and improved.

Fig. 1. Position of the National AIDS Program in the Ministry of Health of Brazil and its structure, July 2002. MSM, Men who have sex with men; NGO, non-governmental organizations; STD, sexually transmitted diseases.
By March 2002, the NACP already comprised 375 accredited hospitals, 79 hospitals with day clinics, 53 home care service agencies and 381 specialized outpatient services, covering practically the whole of Brazil [4].

**Prevention**

Key targets were identified for the prevention of infection: the promotion of HIV testing; promotion and education on condom use; the provision of disposable syringes; increasing the availability and provision of incentives for pre-natal testing, and the prevention of other STD. Priority messages were:

‘Consistent condom use is the safest way to prevent HIV/AIDS and other sexually transmitted diseases’.

‘Syringes and needles must not be shared’.

‘Every pregnant woman must be informed that she must be tested for HIV. If HIV-positive she is entitled to treatment as recommended to prevent HIV transmission to the baby before, during, and after delivery’.

‘Every citizen must be entitled to free access to antiretroviral therapy (ART). Effective compliance with treatment is key for prevention and control, with direct, positive impact on the life of HIV/AIDS patients’.

These messages were spread through a number of informational/educational campaigns. During the ‘Carnival’ periods between 1994 and early 2000, 35 campaigns were broadcast on radio stations, at movie theatres, on TV, on billboards, and through magazine print-ads. Many addressed the entire population; some focused on specific targets: injection drug users, people already infected, truck drivers, women of childbearing age. Carnival and World AIDS Prevention Day were targeted for focused preventative campaigns. In 2002, the first campaign was launched focusing on homosexual men, because cases reported in that population, especially among young homosexual men, are now increasing after a long period of decreasing incidence. The campaign will focus not only on the use of condoms for sexual intercourse, but will also aim at making health and education professionals more open and more aware, so that they can play key roles both in the prevention of STD and AIDS and in the fight against prejudice based upon sexual orientation.

**Condom use**

A 1986 study showed that only 4% of the Brazilian population used condoms during their first sexual encounter. In 1999, that rate had increased to 48% [5]. This increase was caused both by greater population awareness, and also by the more affordable price of condoms, and greater availability of free condoms. Fig. 2 shows the increase in men’s condom sales in parallel with the approximately 50% decrease in the cost per condom between 1996 and 2000 [6,7]. In addition, the MoH increased its acquisition of condoms fourfold between 1999 and 2000, reaching 200 million units acquired in the year of 2000 [8].

**Needle exchange**

Another important intervention was the implementation of syringe and needle exchange. Between 1994 and 1998 only 12 projects were implemented; this number increased to 40 by the end of 2000, with a total exchange of 1,500,000 syringes in the period 1999–2000.

The initial results, analysed in two major cities covered by the programme, were encouraging, with a reduction in the incidence of HIV prevalence in intravenous drug users from 63 to 42% in one city in 7 years, and from 50 to 7% in 4 years in the other. These findings stimulated the MoH to increase the number of cities with this type of intervention in the future.

**Blood testing**

In the early days of the epidemic, HIV infection through blood and blood products was common in Brazil [9,10] (Fig. 3). In 1986, São Paulo, the state most affected by the epidemic, made HIV screening tests compulsory at all blood banks. By 1988, screening tests were compulsory nationwide. Initially, first generation enzyme-linked immunosorbent assay tests were used. Currently, two third-generation enzyme-linked immunosorbent assay tests are used, and blood components with a single positive test are discarded. Con-
Confirmation for the purpose of donor notification and counselling is provided by Western blot.

These policies had a demonstrable impact on HIV transmission by blood and blood components. As a result of the long incubation period, the number of new AIDS cases in this subcategory remained high for a decade; by 2000, the cases acquired by transfusion were rare [9,10] (Fig. 3), and now we believe that this form of transmission is practically non-existent. Even so, in an attempt to reduce even further the risk of possible transmission in the window period, there are plans to implement nucleic acid testing at blood banks in the near future.

**Heterosexual transmission: HIV-infected women**

In Brazil, as in other parts of the world, the steady increase in HIV/AIDS incidence through heterosexual exposure has had an enormous impact on women: the male:female ratio, which in 1985 was 28:1 reached 4:1 in 1992, and in the most recent 5 years has been 2:1. Among individuals aged 15–19 years the male:female ratio is now 1:1 [11].

Because of both biological and cultural vulnerability, women, who originally accounted for fewer than 5% of all AIDS cases reported in Brazil, now account for 30% of current cases, with more than 90% of all women’s cases diagnosed in the past 10 years [12]. During this time, the incidence among women, which in 1992 was 0.03 cases per 100 000, now stands at 5.41 cases per 100 000, reflecting an annual rate increase of 0.53 cases per 100 000 women a year [13].

**Mother-to-child transmission**

Among over 40 000 women with AIDS, 80% are of childbearing age, most are concentrated in the 25–39 year age group [14]. As nearly all paediatric cases reported in the past 10 years result from mother-to-child transmission, AIDS reports for children have been increasing, paralleling women’s cases until 1997. In the year 2000, it was estimated that the number of individuals in the 0–14 year range living with HIV/AIDS was approximately 13 000 [15]. By 1997, with the implementation of zidovudine-based prophylaxis to prevent perinatal HIV transmission, as per AIDS Clinical Trials Group Protocol 076 findings, perinatal HIV transmission rates in Brazil have diminished. Mother-to-child transmission case incidence, which in 1997 reached 3.6% of cases for all categories, shows the same trend (Fig. 4) [10], even if data from 2000 have not been closed yet, and the final numbers may still increase and indicate a less marked reduction.

This decrease has been observed even with zidovudine monotherapy, despite the poor provision of proper prenatal care: between 1995–1998 an estimated 17% of pregnant women received appropriate treatment as
recommended by the NACP. In recent years, however, there has been some improvement: in the first half of 2000 there was a 78% increase in the number of pregnant women who received intravenous zidovudine during delivery [16], although percentages for the country as a whole are still low.

Pregnant women
The prevalence of HIV infection in pregnancy is estimated to be between 0.4 and 0.6% [15,17]. The MoH promotes counselling and volunteer testing for all pregnant women, and ensures that treatment will be provided for those found to be HIV positive. A remaining obstacle is that approximately 40% of HIV-infected women reach delivery without having had proper prenatal assistance. In an attempt to remedy this situation, the MoH has recently acquired 300 000 rapid HIV test kits that will permit the detection of the virus and treatment of the mother with zidovudine immediately upon presentation during delivery and of the newborn after delivery. Early detection of perinatal infection has also substantially changed the natural history of paediatric AIDS, resulting in both decreased mortality and also an improvement in the quality of life for the children’s families. The survival of parents has saved thousands of children and teenagers from being orphans; this alone represents social gains that by far outweigh the cost of the programme.

The strategy used by the government has curbed medication costs. Expenses for the three phases of the AIDS Clinical Trials Group Protocol 076 regimen (zidovudine to the mother, orally during pregnancy from the 14th week on and intravenously during labour, and to the newborn orally for 6 weeks), for example, has fallen to US$208 in 2000, from US$662 in 1996, a decrease of 69% [16]. This saving permits the allocation of funding to replace breastfeeding, as well as other activities that are crucial to reach the successful results planned. These activities include: educational programmes for pregnant women and the public, through courses, print-ads, videos, radio and TV advertising; courses and technical manuals for health professionals, targeting better prenatal care and care for HIV-exposed or infected children.

In a recent edition of these manuals, ART is recommended for pregnant women, based on CD4 cell counts and viral load. With the current recommendation against breastfeeding, as well as criteria for birth delivery, mother-to-child transmission rates are expected to fall below 3%, as has been the case in many industrialized countries.

It is hard to carry out an isolated assessment of the impact of each of these actions on the epidemic in Brazil, because other actions, such as universal access to highly active antiretroviral therapy (HAART) discussed below, have probably also had a substantial impact on the epidemic. However, our data indicate that the earlier growth in the epidemic was reduced by these interventions (Fig. 5) [18].

Civil society organization
One of the keys to the successful Brazilian response to AIDS was strong social mobilization. Homosexual individuals were the first to mobilize active non-governmental organizations (NGO) to fight the epidemic. HIV-positive individuals and individuals with AIDS facing unremitting prejudice at the time began to denounce all forms of discrimination, and fought for their dignity on the streets, in the workplace, and at public health assistance units. They adamantly rejected civil disenfranchisement. Minority group movements, and community and religious associations joined in these efforts, and by the year 2000, the number of NGO involved in the fight against AIDS in Brazil was nearly 450 [19]. These organizations serve as advocates for HIV-positive and AIDS-infected individuals by providing educational programmes and maintaining support homes for patients who have been excluded from society. Some NGO provide care to children who are AIDS orphans; others, prison assistance. Still others focus on the assertion of human and civil rights.

Although these NGO have been criticized as ineffectual instruments of their sponsors, such criticism is not warranted; they are active and effective. Their strength and effectiveness was recently demonstrated when Brazil undertook to make HIV medications more affordable. The influence of Brazilian NGO was credited world-wide.

Recognition of the efforts of the NGO in turn led to better partnerships between them and the Brazilian government. In recent years, those partnerships were enhanced and consolidated when the NACP established interventions in specific population groups as
their primary objective. The NGO were then able to coordinate initiatives with local institutions and served as effective bridges between them and the government. As a result of these partnerships, in the period between 1993 and 1997, approximately US$18 million was allocated to 427 community projects carried out by NGO, advancing the dissemination of information, infection prevention and public assistance throughout the country. At present, the NGO/AIDS groups working with the MoH number 175. In the past 3 years, 1780 projects have benefited from their support (see Table 2). The focus now is on better integrating the work of the NGO with that of state and municipal HIV/STD coordination centres.

Antiretroviral therapy

Until the late 1980s, the therapeutic approach towards HIV/AIDS patients was limited to the treatment of opportunistic complications. By 1988, the MoH had started, in a limited way, to supply public health network locations with some of the medications used for that purpose.

By 1991, ART was also made available. However, in the period when only monotherapy or dual treatment with nucleoside analogues was available, few patients in Brazil were receiving ART; slightly over 20,000 patients were being treated as of the end of 1996.

In that year, with the arrival of protease inhibitors, ART became more effective for patients but more challenging for physicians to administer. It was at that point that two crucial developments occurred. First, in December 1996, federal law 9313 mandated the free provision of ART through the public health system, and second, the ART Support Committee was created. This group of specialists was charged to meet periodically, usually once a year, to discuss and formulate guidelines and recommendations on ART, and revise them as necessary. At the present time, guidelines determine that ART should be offered to any individual with AIDS-related symptoms or a CD4 cell count of 200 cells/µl or less. ART is also allowed when the CD4 cell count is between 200 and 350 cells/µl if the patient is motivated to start treatment and his physician considers it advisable. It is important to note that the ART Support Committee acts with total independence from the MoH, and its guidelines are driven strictly by scientific criteria and best judgement.

In subsequent years, all ART medications registered in Brazil became increasingly accessible. At present the
available formulary comprises 15 different medications (Table 3) and 30 different formulations. A ‘HAART’ regimen is preferred, comprising three medications, but those already receiving dual therapy with a good response are able to continue to receive their current regimen. As of December 2000, 78% of patients were receiving triple therapy, 20% were receiving dual therapy, and 2% were taking four antiretroviral drugs (Fig. 6) [20].

As expected, the number of public health system patients being treated increased to 105 000 in 2001 [21]. This figure represents approximately 99% of patients under treatment in Brazil.

Full and free access to treatment obviously led to increased costs for the NACP. Such high allocations for a single disease (over US$200 million in 2001) have not escaped heavy criticism. Growing costs nearly threatened the continued viability of the programme, but thanks to government intervention to reduce the costs of ART medication and the cost-effectiveness of medication as a component of the total cost of AIDS patient care, the programme remains in effect.

ART medication costs were brought under control by MoH investment in Brazilian owned manufacturers, which today supply 50% of all ART medications used in the country. Fig. 7a shows the impact of that measure [21]. In addition, the government undertook successful price negotiation with multinational pharmaceutical companies, exclusive manufacturers of certain medications, securing reductions of 60%, for example, for efavirenz and lopinavir/ritonavir.

The result was a 48% annual cost reduction per ART patient from US$4860 in 1997 to US$2530 in 2001. As shown in Fig. 7b, the cost per patient–day fell from US$13.41 in 1997 to US$8.51 in 2000. But for these price reductions, costs would probably have reached unsustainable levels. If ART costs in Brazil had remained at Canadian or United States costs as of the year 2000, the total bill would have been US$471 million or US$792 million, respectively, instead of US$258 million. Finally, in answer to critics of the

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<tr>
<th>Table 2. Projects of non-governmental/AIDS organizations in Brazil supported by the Ministry of Health in the period 1999–2002.</th>
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<td>(a) Number of projects and targeted public</td>
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<tr>
<td>General public</td>
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<td>Population in poverty situation</td>
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<td>Population in rural and urban establishments</td>
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<td>Children and adolescents</td>
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<td>Children and adolescents in social risk situation</td>
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<tr>
<td>Women</td>
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<tr>
<td>Adult confined population</td>
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<tr>
<td>Truck drivers</td>
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<tr>
<td>Homosexual individuals</td>
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<tr>
<td>Indigenous population</td>
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<td>Mineral mines and extractives reserves</td>
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<tr>
<td>Injection drug users</td>
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<td>Drug users</td>
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<td>HIV/AIDS carriers</td>
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<td>Handicapped individuals</td>
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<td>Health and education professionals</td>
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<td>Sex professionals</td>
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<td>Female sex professionals</td>
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<td>Total</td>
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<tr>
<th>Year</th>
<th>Projects</th>
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<tr>
<td>1999</td>
<td>347</td>
<td>4924933.96</td>
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<tr>
<td>2000</td>
<td>523</td>
<td>7974267.28</td>
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<tr>
<td>2001</td>
<td>704</td>
<td>15023803.60</td>
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<tr>
<td>2002 (to May)</td>
<td>206</td>
<td>3201374.24</td>
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<tr>
<td>Total</td>
<td>1780</td>
<td>31124377.08</td>
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US$ – UNDP conversion R$2.50.

Table 3. Antiretroviral therapy medications distributed in Brazil by the Ministry of Health in 2002.

| • Zidovudinea | • Ritonavir |
| • Didanosinea | • Saquinavir |
| • Zalcitabineb | • Nelfinavir |
| • Lamivudineb | • Amprenavir |
| • Stavudinea | • Nevirapinea |
| • Abacavir | • Delavirdine |
| • Indinavir | • Efavirenz |
| • Stavudinea | • Lopinavir/r |

a Generic version available.
high allocation of AIDS funding, as a proportion of total government expenses, total ART expenses in 2002 were 1.5% of the MoH total budget, less than 0.05% of Brazil’s gross domestic product [22].

For the proper assessment of the cost-effectiveness of ART it is important to recognize that good control of HIV infection results in savings in other AIDS care, such as hospitalizations, diagnostic procedures, outpatient and day-hospital assistance, medications for opportunistic infections, and other more difficult to quantify costs such as absenteeism from work, financial hardships for patients and families, and foregone expenses for public assistance to children who would otherwise have been orphaned.

Although not exclusively ART-related, the mortality rate reduction has been impressive. Fig. 8 shows the mortality rate changes in Brazil [23], with a clear reduction after 1996, when HAART became freely available. With respect to hospitalization reduction, the MoH estimates that in the period between 1996 and 2001 the average admissions per patient per year dropped from 1.65 to 0.28, with 358 000 hospitalizations having been prevented, and resulting in savings of more than US$1 billion [23]. Savings were also realized on treatment for opportunistic infections. Fig. 9a shows the number of annual cases in São Paulo, of tuberculosis, the most widespread opportunistic infection in Brazil [24]. In the period between 1996 and 2001, a 71.2% reduction was reported for new patients. The most dramatic reduction of 54.5% in 1996–1997 coincided with the first widespread availability of HAART.

The occurrence of other opportunistic infections was similarly affected. Fig. 9b shows the number of new cases at the Emilio Ribas Institute of Infectology Day Care Hospital, in São Paulo (the institution that provides the greatest HIV/AIDS assistance in the country) of cytomegalovirosis and neurocryptococcosis for the period 1995–2000. Here, too, the reduction in new cases is evident.

Overall data for the country show that as early as 1997–1998 a reduction in expenses for Pneumocystis carinii infection was 61%, and for Mycobacterium avium complex, the figure was 81%. Another example of cost reduction by ART is in the use of ganciclovir at the Emilio Ribas Institute of Infectology. In 1996, 32 980 vials were used, and in 2001 this number fell to 7200
vials, even though more patients were being followed at that time at the Institute (R. M. C. Florim, personal communication).

Even putting aside the humanitarian mandate to care for individuals with HIV/AIDS, from a strictly economic point of view, the expense of full and free ART has been counterbalanced by the savings realized in overall AIDS care costs.

Laboratory network

Once the government undertook to provide ART to all citizens, it was necessary to create a network of laboratories to perform lymphocyte subset counts and plasma viral load testing. At the time, few public laboratories were capable of performing such tests; capacity was not equal to the anticipated demand.

The MoH implemented an ambitious programme to have laboratories prepared for the tests throughout the country. A laboratory network for CD4/CD8 cell counts, and another for plasma HIV/RNA quantitation were created, with allocations for laboratory staff training, equipment purchase, and the provision of reagents. Several problems immediately became apparent, such as deciding which equipment and reagents to use, coping with daunting costs, competition between companies, and the urgency with which a large well-trained laboratory network had to be established. There are currently 80 CD4/CD8 cell laboratory units and 65 viral RNA laboratory units, most with overlapping capabilities in Brazil. An external quality control programme was also established, both as a local initiative and also as a result of international cooperation.

More recently, the first steps have been taken towards instituting a network for ART resistance genotyping. Twelve laboratories are already participating, and three others are being trained. As only 6000 tests have been purchased, the genotyping effort is limited to patients reporting their first on-treatment virological failure, defined as an elevation of the viral load greater than 0.5 log from nadir or between two consecutive results. This effort is also limited by the requirement that screening and prioritization can only be performed by experienced professionals who are accredited by the HIV/STD national programme for indication and results interpretation. Genotyping results are provided to applicant physicians, with specialists’ recommendations for therapeutic changes based on the results.

With regard to HIV primary resistance monitoring, the MoH position now is that rates are still too low to justify the high investment that would be needed for routine genotyping. Should an ongoing pilot study...
monitoring recently infected individuals reveal a higher frequency of transmitted drug resistance in the future, that position may change.

Final considerations

We are hopeful that the description of Brazil’s experience will prove useful to other nations in their fight against AIDS, and may contribute to reduce the marked differences in the AIDS-related mortality rate between Brazil and other developing countries with similar economic situations that are severely affected by the epidemic (Fig. 10) [25]. Our experience is most likely to be adaptable in Latin America, where cultural and economic similarities to Brazil lend themselves to comparable efforts. However, we want to make it very clear that we do not propose a ‘Brazilian Model’. Each country must fashion its own response in consideration...
of its own peculiarities, economy, politics, and social and cultural values. This is a field in which Antonio Machado’s verses are fully apropos:

‘Caminante, no hay camino
Se hace camino al andar’.a

The Brazilian experience does prove, however, that if there is political willingness, multisectional action involving committed professionals, and strong civil society mobilization, even in countries constrained by limited resources, AIDS can be effectively countered and its expansion contained.

aWayfarer, there is no way,
A way is opened up as fared on’.

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References


Other information on this matter of possible interest to the reader are available at URL: http://www.aids.gov.br