

Ministry of Health - Brazil
National Drug Policy

Brazil
February 2001



Foreword

The Brazilian HIV/AIDS drug policy has been highly debated and criticized, particularly at the time of its implementation by the national authorities in the early 90s. The dearth of trained health professionals and the poor structure of the health services, the lack of laboratories capable of monitoring the infection, and the patients' capacity of adhering to treatment were hotly questioned. National and international experts and health professionals, managers of programs of prevention and care of people living with HIV/AIDS, staff responsible for the budgetary and financial execution of public monies and international organizations argued amid reports of treatment assessment and cost-benefit studies and projections both favorable and contrary to the implementation of a such a costly policy for the State.

However, fortunately, reality not only corroborated our policy; over and above, the statements of its most optimistic defenders were outdone by their remarkably positive results. The quality of the government-provided services is reflected by the significant improvement in the health status and in the control of the infection among people living with HIV/AIDS. To this more immediate consequence of the antiretroviral regimens recommended by the Brazilian Ministry of Health one must add several social, economic and political benefits, both palpable and yet to be achieved, without precedent in the history of Public Health in our country.

At the present time, the success of the program for the free and universal distribution of these drugs to every patient who needs them cannot be doubted. In addition, its repercussion may contribute to the global debate on the access of people living with HIV/AIDS to antiretroviral treatment, with strong priority to the poorest countries, which bear the heaviest brunt of an epidemic that, according to UNAIDS data, was responsible for 5.3 million new infections and 3 million AIDS deaths in 2000 alone.

The so-called developing countries suffer from the lack of public resources, social problems and political oppression. AIDS has shown, in bright and sharp colors, all the contrasts unveiled by the epidemic in these countries when its threat does not elicit a response or is not tackled with the responsibility, competence and a humanist and solidary planning that are necessary.

This document retraces the most recent history of the unquestionable advances in laboratory care and in the treatment of HIV infection and assesses its development from the perspective of the unique Brazilian experience in the efforts for the prevention and control of the epidemic.

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AIDS drugs policy in Brazil

Background

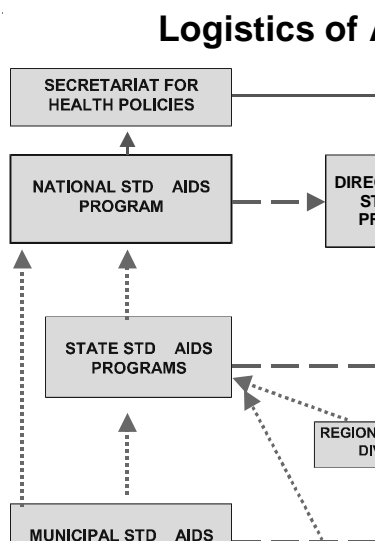
The Brazilian population is estimated at 169,5 million people. From 1980 until September 2000, 196,016 AIDS cases were reported to the National STD and AIDS Program (NAP) of the Ministry of Health (MoH). 146,472 of them are males and 49,544 females; 6,856 are children. It is estimated that HIV infects 536,000 Brazilians. Since 1996, the incidence rate has stabilized around 14 cases per 100,000 population. The number of new cases reported in the last five years was approximately 22,000 per year.

The Ministry of Health's policy for the care of people living with HIV/AIDS includes, among several other initiatives, the structuring of a Laboratory Network for the Quantification of Viral Load and CD4+ and CD8+ cell counts, the organization of health care services, the support to the organization of People Living with HIV/AIDS and to projects carried out by Non-Governmental Organizations, and the creation of a program for the free and universal access to antiretroviral drugs through the public health network.

This program, begun in the early 90s with the distribution of AZT capsules, was expanded and consolidated in 1996 by a Congressional Bill, sanctioned by the President, that guarantees every patient the access, free of direct costs, to all the medication required for his/her treatment, including protease inhibitors (since December 1996), following treatment criteria and guidelines set forth by the MoH. The Ministry thus created two advisory committees, with the mandates to define a Consensus on the Recommendations and Guidelines for the Use of Antiretroviral Therapy in Adolescents and Adults and a second similar consensus on treatment for children. The committees meet periodically at least once a year, to review the recommendations and adjust them to the updated scientific knowledge and the availability of new drugs.

Infrastructure of the system for HIV+ patient care

The following flowchart summarizes the functioning of the AIDS drugs logistic system. Brown arrows indicate the procurement flow within the MoH, which starts with the programming of needs, done by NAP; green arrows demonstrate the programming of distribution; blue arrows the different drug flows from delivery from the manufacturers to dispensation to the patient; and red arrows show the flow of information from the patient to the NAP, which includes data essential for the distribution and procurement programming.



NAP has developed a Computerized System for the Control of Drug Logistics (SICLOM), with the following main characteristics:

- Nationwide patient register
- Registration linked to the individual drug dispensing unit
- Validation of the register and dispensation, using MoH criteria.
- Computerization of the dispensing units
- Certification of the ARV prescription through a magnetic card
- Patient information on the appropriate use and storage of drugs
- Daily replication of data to the NAP by telephone data transmission

There are currently 424 AIDS drugs dispensing units in Brazil. SICLOM has been implemented in 111, including some of the largest ones, and covering 65% of the distribution clients in Brazil. A managerial module for SICLOM is now being developed by NAP.

362 hospitals are accredited (AH) for HIV/AIDS care. In addition, there are 69 day hospitals (DH), 52 projects of home therapeutic care (HTC) and 148 specialized care services (SCS). The following maps show their distribution throughout the country.

**Aids drugs dispensing u
Brazil, 2001.**

**Distribution of Accredited
Hospitals (AH) for HIV/AIDS
Brazil. AIDS I and AIDS II**

**AIDS I:
Nº AH = 338**

AIDS II:

**Distribution of Day Hospitals
for HIV/AIDS care.
Brazil. AIDS I and AIDS II**

**AIDS I:
Nº DH = 49**

**AIDS II:
Nº DH = 60**

**Distribution of Home The
Care Projects (HTC) on H
Brazil AIDS I and AIDS II**

**AIDS I:
Nº HTC = 33**

**AIDS II:
Nº HTC = 52**

**Distribution of specialize
services (SCS) on HIV/AI
Brazil. AIDS I and AIDS II**

**AIDS I:
Nº SCS = 76**

**AIDS II:
Nº SCS = 148**

Concomitant to the drug distribution policy, NAP has endeavored to strengthen the country's public laboratories and implement the National Network of Laboratories for T CD4+ Lymphocyte Counts (70) and for HIV Viral Load Quantification (63). This network carries out the tests required for the indication of antiretroviral therapy and chemoprophylaxis of opportunistic infections, as well as for the appropriate monitoring of patients under treatment. In 2001, 422 thousand viral load tests and 422 thousand T CD4+ lymphocyte counts are foreseen, corresponding to a total expenditure of approximately US\$ 18 million (unitary costs of US\$ 15 per CD4+ test and US\$ 29 per viral load test).

**National network of laboratories
for TCD4+ lymphocyte counts
viral load quantification -**

**Viral load = 63 Lab.
T CD4+ = 70 Lab.**

Costs: US\$ 18 million

National production, procurement and distribution of drugs

Domestic AZT production began in 1993 by the private company Microbiológica. In the following year, AZT production by the public sector was begun by LAFEPE, Laboratório do Estado de Pernambuco. Domestic AIDS drugs production comprises 7 antiretrovirals: zidovudine (AZT), didanosine (ddl), zalcitabine (ddC), lamivudine (3TC), stavudine (d4T), indinavir and nevirapine. The current list of antiretrovirals provided by the MoH includes 12 drugs (5 nucleoside analog reverse transcriptase inhibitors-NRTI, 3 non-nucleoside analog reverse transcriptase inhibitors-NNRTI, and 4 protease inhibitors-PI), in 25 pharmaceutical presentations.

Public laboratories manufacturing antiretrovirals are: Far-Manguinhos/FIOCRUZ/MoH, Fundação para o Remédio Popular/SP, Laboratório Farmacêutico do Estado de Pernambuco, Fundação Ezequiel Dias/MG, Indústria Química do Estado de Goiás, and Instituto Vital Brasil/RJ. Far-Manguinhos provides 40% of the antiretrovirals used in Brazil. Six Far-Manguinhos-produced drugs - zidovudine, didanosine, lamivudine, zidovudine+lamivudine and zalcitabine - have been approved in bioequivalence tests and thus are eligible for licensing as a generic drug. The bioequivalence testing of indinavir and nevirapine is in its final phases.

The quality control of the antiretrovirals distributed by the MoH is done by: (1) statement (mandatory) from the competent health authority of the country where the product is manufactured, certifying that the plant complies with the Good Manufacturing Practices (GMP); (2) preliminary inspection of the pharmaceutical plant before the first delivery of the product; (3) monitoring of the production of the first batches; (4) analysis of batches purchased, in the early phases of the provision contract, at laboratories accredited by the National Health Surveillance Agency/MoH; and (5) starting in 2001, mandatory bioequivalence testing for all drugs purchased. Bioequivalence tests, proving the interchangeability of the drugs, are a recent achievement of the Brazilian National Drug Policy, guaranteed by the 1999 Generic Drugs Bill. The Brazilian bioequivalence process comprises pharmaceutical, clinical, analytic and statistical testing. Clinical studies are carried out mainly by the quantification of the drug or its active metabolite in the circulation (most commonly in blood, plasma or serum samples) of healthy volunteers, who receive the drugs being tested and the reference drugs at different times, in single or multiple dose regimens. This is a complex study and it requires a research project document, experimental protocol, free and informed consent form, and approval by the Committee of Ethics in Research (CER).

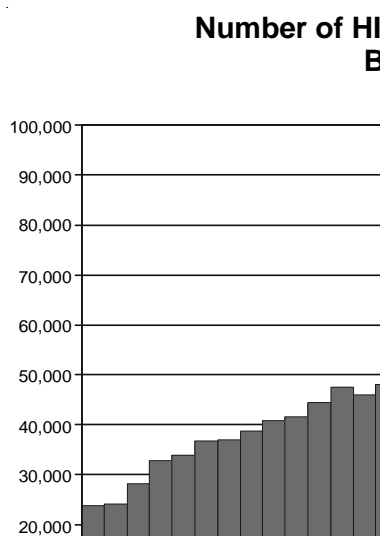
Year of first distribution	
1991	
1992	
1993	
1996	
1997	

It is important to highlight that while the Federal Government is responsible for ARV drugs, the procurement and distribution of drugs for the treatment of opportunistic diseases is decentralized to the states and municipalities.

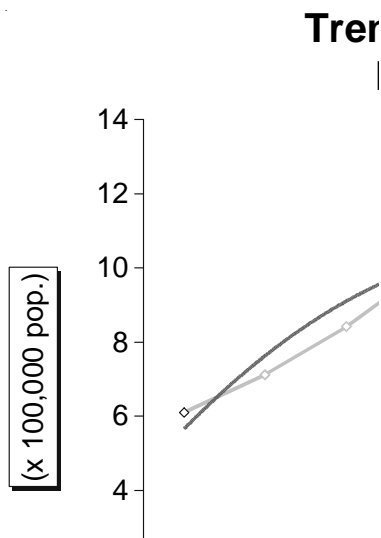
Impact of the antiretroviral therapy

Under the current recommendations, antiretroviral treatment is indicated for all symptomatic patients, asymptomatic patients with significant laboratory findings and HIV+ pregnant women for the reduction of vertical transmission.

There are currently 95,000 infected individuals on antiretroviral treatment; 95% are adults and adolescents and 5% are children under 13 years old. As a comparison, in January 1997, approximately 23,000 people were benefiting from the free access policy.



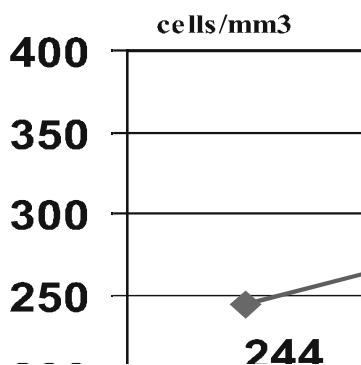
Nowadays the antiretroviral drugs policy guarantees a longer survival for HIV+ individuals, minimizing the impact of the epidemic on the population groups infected, particularly the productive age ones. Moreover, the universal access program, together with other initiatives, such as the more widespread use of chemoprophylaxis for the main opportunistic infections and the different types of care available (Day Hospital and Home Care), has decreased the need for hospital admissions, with the consequent reduction of costs, as well as the frequency of opportunistic infections. As for the decrease in deaths, the past few years have seen a marked reduction in AIDS-related mortality. In 1995, the AIDS death rate was 12.2 per 100,000 population; in 1999, it had dropped to 6.3/100,000 population, a 48.3% reduction. In large urban centers such as São Paulo and Rio de Janeiro (with more than 31% of the known AIDS cases in the country), the decrease in mortality has been even more marked, of approximately 70% (SP - 54%, Rio - 73%) in the period 1995-2000 (data up to August 2000).



In addition, a 60-80% decrease in the frequency of the main opportunistic conditions associated with severe immunodeficiency in patients with HIV/AIDS, such as cryptococcosis, cytomegalovirus and Kaposi's Sarcoma, has been observed in the major services caring for these patients. According to data from the Center of Treatment and Reference in STD/AIDS of the São Paulo State Health Secretariat (CRT/AIDS-SP), new cases of tuberculosis in HIV+ individuals seen at this institution, a condition with an estimated risk approximately 800 times higher than in the general population, have decreased approximately 76% in the period 1996-2000.

Another figure reflecting the impact of the Brazilian policy of universal access to antiretrovirals is the phenomenon of partial immunological reconstruction promoted by the treatment. This is demonstrated by the evolution of the mean T CD4+ cell count in HIV+ patients on antiretroviral therapy. Recent MoH data show that in patients on antiretrovirals, the mean counts of these cells have shown a progressive rise (from approximately 244 cells/mm³ at the beginning of treatment to 372 cells/mm³ after 18 months of treatment). This improvement seems to have a significant contribution to the reduction of the frequency and severity of the opportunistic conditions associated with HIV/AIDS and undoubtedly is an indicator of the better quality of life of HIV+ patients seen in the public health network.

Evolution of near ARV therap Brazil,



As to costs, some studies have shown that the price of antiretroviral therapy is largely offset by the reduction of costs with drugs for the treatment of opportunistic infections and with the ensuing hospitalizations. The analysis of data at the MoH has shown a significant drop in the number of hospitalization/patient; it estimated that approximately 234,000 AIDS-related hospital admissions were prevented in the period 1997-2000, with a savings of US\$ 677 million for the Unified Health System. In the case of cytomegalovirus, for instance, a condition affecting individuals at an advanced stage of HIV infection and that may cause blindness, data on the use of ganciclovir for its treatment show a 69% decrease in the period 1997–1999; in the past two years, this meant a savings of approximately US\$ 34 million.

Adherence to antiretroviral therapy

Combined antiretroviral therapy not only contributes to a longer life span for HIV+ individuals but also to a better quality of life, directly related to a better physical and emotional status. Thus these individuals, mostly in the economically active age group, can remain productive and therefore do not divert Social Security funds for the payment of illness aid, retirement pensions for disability reasons, and other such benefits.

It is clear that patient adherence to multiple doses therapeutic regimens is fundamental to the clinical management of this disease, since non-adherence to antiretroviral treatment is directly linked to the development of viral resistance, the consequent therapy failure and the emergence of multiresistant viral strains.

A study carried out in São Paulo has shown that certain characteristics of users' groups are risk factors for non-adherence, particularly less than 4 years of schooling and lack of personal income.

The history of HIV+ individuals is a record of overcoming obstacles, mainly those related to adjustments of lifestyle and issues pertaining to the stigma of the disease. One critical moments is the beginning of treatment, when the need to accept the condition and to establish a reliable rapport with the physician and the health services are clearly seen.

The health services have an extremely important role in overcoming treatment-related difficulties, and their dialogue and negotiation abilities are crucial. Antiretroviral adherence in Brazil seems very similar to that seen in first-world countries.

However, the rates achieved everywhere are still far from the desired levels. A study on adherence that defined adherence as taking 80% or more of the total prescribed doses has shown 69% adherence among more than one thousand patients interviewed. Similar studies carried out in Baltimore (202 patients), London (114 patients) and San Francisco (388 patients) have obtained similar rates (60%, 75% and 78%, respectively).

Comparative resu

Site
Sao Paulo/Brazil
Baltimore/USA
London/UK
San Francisco/USA
Madrid/Spain

Expenditures with drugs

The Federal Government's expenditures with the purchase of antiretrovirals was approximately US\$ 34 million in 1996, US\$ 224 million in 1997, US\$ 305 million in 1998, US\$ 336 million in 1999, US\$ 303 million in 2000; it is estimated that they will reach US\$ 422 million in 2001. These expenditures corresponded to 0.24% of the MoH budget in 1996, 1.18% in 1997, 1.82% in 1998, 2.93% in 1999, 2.84% in 2000, and are estimated to correspond to 2.92% in 2001. In terms of GIP, they have ranged between 0.004% in 1996 to 0.06% in 1999. In spite of the increasing number of patients on treatment and increasing proportions of patients on more complex and more expensive regimens, an overall reduction of expenditures with drug purchase is expected.

Antiretroviral dr

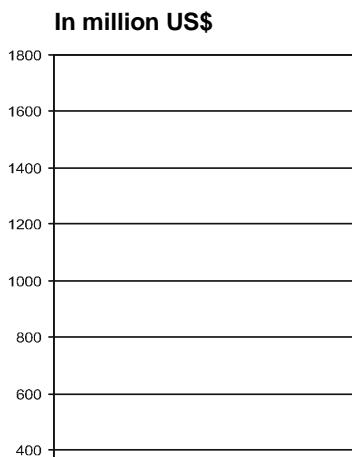
Year
1996
1997
1998
1999
2000
2001*

* estimated data

The prices of antiretroviral drugs purchased by the MoH have shown a declining trend over the past few years, largely due to the MoH investments to foster the production by public-sector manufacturers and to the policy of price negotiation in the case of single exclusive manufacturers. The most significant drop is seen in the price of drugs already produced domestically, both by private national companies and especially by public manufacturing laboratories, which had an average 72.5% decrease in the period 1996–2000.

The most striking individual falls involve indinavir, from US\$ 2 to US\$ 1.34 per 400 mg capsule (-33%); nevirapine, from US\$ 3.04 to US\$ 1.28 per 200 mg tablet (-58%) ; didanosine, from US\$ 1.85 to US\$ 0.51 per 100 mg tablet (-72%); lamivudine, from US\$ 2.90 to US\$ 0.83 (-71%) per tablet; the greatest drop was shown by zalcitabine, from US\$ 1.55 to US\$ 0.08 per 0.75 mg tablet (-95%).

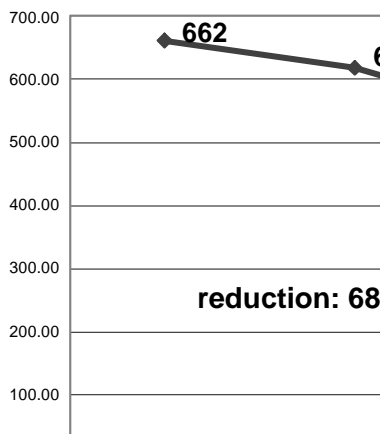
Corr



In 1999, 47% of antiretroviral drugs, accounting for 19% of the expenditures, were purchased from national companies (92.5% from public laboratories and 7.5% from private ones); 53% of the antiretrovirals, corresponding to 81% of the expenditures were purchased from multinational pharmaceutical companies. (It is interesting to point out that, in 1999, some drugs that are manufactured domestically were still provided by multinational companies, which reduced their prices and won governmental bids). In 2000 (preliminary data), 57% of the antiretrovirals, corresponding to 44% of the expenditures, were purchased from national companies and 43%, corresponding to 56% of the expenditures, were purchased from multinational pharmaceutical companies.

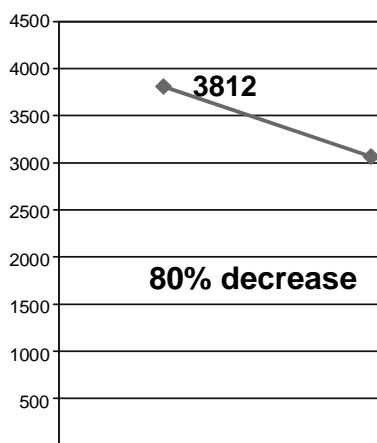
This reduction of antiretrovirals' prices in Brazil decreased the costs of AZT chemoprophylaxis for the control of HIV vertical transmission (ACTG 076 complete) from US\$ 662 in 96 to US\$ 208 in 2000 (68.6% variation).

Costs of AZT chemop



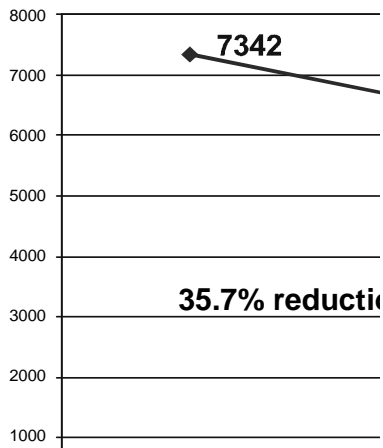
The mean weighted cost of double NRTI therapy dropped more markedly, from US\$ 3,812 per patient/year in 1996 to US\$ 763 in 2000 (80% variation).

Mean weighted cost (ii)



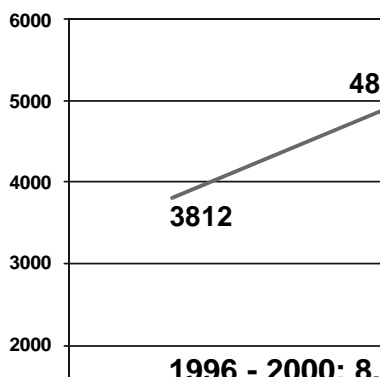
The reduction of the mean weighted cost of triple regimens including PIs (US\$ 7,342 in 97, US\$ 4,717 in 2000) or NNRTIs (US\$ 4,584 in 98; US\$ 3,009 in 2000) has varied between 35.7% and 34.4% and can be accounted mainly by the decreased costs of nucleoside analogs.

Mean weighted cost (in



The mean weighted cost per patient/year on ARV therapy showed a significant increase between 1996 and 1997, associated with the beginning of PI distribution; on the other hand, between 1997 and 2000 there was a drop of approximately 15% (US\$ 4,858 in 1997; US\$ 4,137 in 2000), in spite of the proportional increase in the number of patients using more complex and expensive therapeutic regimens.

Mean weighted c



Cooperation between Brazil and other developing countries

A considerable part of the success achieved by the Brazilian drug distribution program is due to the development of quality generic antiretroviral drugs by Brazilian manufacturing laboratories, at costs significantly below those practiced in the international market. The Brazilian expertise in AIDS drug manufacturing was offered to developing countries, particularly in Africa, during the XIII International AIDS conference held in Durban, South Africa, in July 2000. In a spirit of cooperation and national solidarity, Brazil can, at the present time, promote the transfer of technology for the establishing of industrial antiretroviral drug manufacturing poles, including the training of technical staff. So far some countries, like South Africa and Uganda, have shown an interest in obtaining the Brazilian technology and others, like Chile, Burkina Faso, Barbados and Guatemala, in direct drug purchase, through point cooperation actions.

