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Public health

Access to antiretroviral drugs in Brazil

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Since 1996, the Brazilian Ministry of Health has guaranteed free and universal access to antiretroviral treatment for people living with HIV/AIDS. Implementation of this policy has had political, financial, and logistical challenges. I have investigated the history and context of antiretroviral policy in Brazil, the logistics of the drugs' distribution, and the government's strategies for acquisition of the drugs. Many antiretrovirals used in Brazil are produced domestically; the remainder, including some of the most expensive drugs, are purchased from abroad. Although the Brazilian policy of antiretroviral distribution has had notable success, it remains threatened by the high cost of acquisition of drugs, which has led to disputes with international pharmaceutical companies over prices and patents. Whether or not the Brazilian model of guaranteeing access to antiretroviral treatment for people living with HIV/AIDS can be applied in other countries or regions, much can be learnt from the country's experience.

Free and widespread distribution of antiretrovirals through the public-health system continues to be one of the best-known parts of the Brazilian National AIDS Programme, whose other components include education and prevention, epidemiological monitoring, and development of partnerships between government and society to broaden the response to the HIV/AIDS epidemic.[1,2]

At the moment antiretroviral treatment is totally subsidised by the Brazilian Ministry of Health. Although the government is responsible for the purchase of antiretrovirals, domestic manufacture of some of these drugs—by private and public laboratories—is presented by the Brazilian Ministry of Health as a fundamental strategy for maintenance of the distribution programme.[3,4] In 2001, this local production of antiretrovirals, and implications for patent laws, generated great attention to the way that Brazil is confronting the HIV/AIDS epidemic.

The viability of the Brazilian distribution programme of antiretrovirals owes much to mobilisation of society.[5] Groups representing people living with HIV/AIDS; gays, lesbians, and transvestites; feminists; and religious organisations have been especially active. Their role—for example, in advisory committees created to guarantee public participation in government, and in non-governmental organisation forums and networks of people living with HIV/AIDS—has contributed greatly to maintenance and expansion of the rights of these people in Brazil, and for continuity of the government's response to the epidemic.[1]

The profile of the HIV/AIDS epidemic in Brazil has three main trends—the increase of HIV-1 infection in poor people and in women, and spread of the epidemic to regions outside large urban centres.[2] The increase of HIV-1 infection in women has also led to a rise in the rate of vertical transmission of HIV-1.[2]

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According to official data from the Brazilian Ministry of Health, the number of people who are infected with HIV-1 in the country is estimated to be around 597 000,[4] with 222 356 people with AIDS registered between 1980 and September, 2001.[6] Of these individuals, 162 732 were male and 59 624 female, and about 50% (107 104) have died.

Brazilian policy about access to antiretrovirals

Free distribution of drugs for treatment of people living with HIV/AIDS is not new in Brazil. In 1988, the Brazilian public-health system began to distribute drugs to treat opportunistic infections, and in 1991, began to offer zidovudine.[7] However, Brazil did not commit itself to free and widespread distribution of antiretrovirals through the public-health system until 1996.[4,7] In November of that year—in an unusual measure—the Brazilian President, Fernando Henrique Cardoso, signed a law establishing free distribution of drugs to people living with HIV/AIDS.[4]

Since the present policy of coordinated distribution of antiretrovirals began, the number of people living with HIV/AIDS receiving treatment has steadily increased. An estimated 35 900 individuals received these drugs in 1997; 55 600 in 1998; 73 000 in 1999; 87 500 in 2000; and 105 000 in 2001.[4] Government spending on antiretrovirals has also followed an upward trend: US$34 million in 1996; $224 million in 1997; $305 million in 1998; $336 million in 1999; and $303 million in 2000.[4] In 2001, the costs for these drugs reached $232 million.

From the perspective of the Brazilian government, there are at least two arguments for continuing the distribution programme. First, the clear effect of antiretroviral treatment in reduction of deaths, and second, the substantial reduction in hospital admissions and treatment costs associated with opportunistic infections. For example, in 1995–2000 after introduction of new antiretrovirals, such as saquinavir and ritonavir, the number of deaths from AIDS in the municipality of São Paulo fell by nearly 54%, and by 73% in the municipality of Rio de Janeiro.[4] The reduction of costs of hospital admissions and of treatment of opportunistic infections was also great. For 1997–2001, cost savings throughout Brazil have been estimated, by the Ministry of Health, to be close to $1·1 billion.[4]

After the announcement of the distribution of antiretrovirals through the public-health system in 1996,

the number of new AIDS cases reported in Brazil for that year exceeded expected values by about 40% (Pedro Chequer, coordinator of the Brazilian National AIDS Programme in 1996, personal communication).[8] This rise means that another effect of the distribution of antiretrovirals has been a reduction in under-reporting of AIDS cases. However, other factors could have contributed to this fall as well, since measures to guarantee access to treatment were accompanied by improvements in the notification system as a whole, in particular, in epidemiological surveillance. But government distribution of antiretrovirals has clearly had an important role. Many people who had a private doctor changed to the public-health system to receive free treatment. Others, who had not yet been diagnosed, decided to be tested on the basis of information about the effectiveness of the drugs and their availability free of charge.

Other benefits of the distribution programme include improvements in quality of life of people living with HIV/AIDS, in particular, the social recognition gained when the government defended their rights to treatment, and thereby their value and importance to society as a whole. In this respect, the distribution programme has helped to avert what one Brazilian activist called—in less favourable times—the "civil death" of people living with HIV/AIDS.[9]

Logistics of antiretroviral distribution

Beyond its financial aspects, the distribution programme has logistic and strategic considerations that, in a country the size of Brazil, cannot be understated.[5] In 1988, the Unified Health System (Sistema Único de Saúde or SUS),[10] was established to offer free comprehensive health care to the entire population, irrespective of employment status or access to other forms of health insurance. This structure was an important factor in implementation of a distribution programme for drugs for AIDS. Also important is the country's ability to train personnel in diagnosis and treatment of HIV/AIDS, to strengthen public clinical laboratories, and to establish criteria for administration of antiretrovirals.[2] On this last point, independent advisory committees have aided the Brazilian National AIDS Programme in developing and regularly updating recommendations and guidelines for treatment of different target groups.

Part of this logistical challenge was to develop a strategy to both distribute and monitor antiretrovirals through the public-health system. Key aspects of this strategy included definition of locations at which people could receive drugs, creation of a system to track distribution of drugs, and establishment of a network of laboratories for clinical examinations.[4]

Presently, there are 424 sites around Brazil at which patients could receive antiretrovirals.[4] These sites, called AIDS Drugs Dispensing Units (ADDU) are located in public hospitals or health centres. To be eligible to receive treatment, a patient must be enrolled at the unit, and a doctor from the public-health system must follow-up the patient and issue prescriptions. There are three main ways a patient can be diagnosed and enter the system: by being tested at an anonymous site (Centro de Testagem e Aconselhamento, CTA),[11] and referred to a public hospital or outpatient centre to be enrolled; by being tested in a public hospital and enrolled there; or by being tested in a private clinic and enrolled in a public hospital afterwards.

At many ADDUs, patients now receive a magnetic card that must be presented to receive treatment. In 2001, according to the Brazilian National AIDS Programme, about 65% of patients were using cards.[4] The card helps to track patients' prescriptions, especially in units with high enrolment. In some ADDUs—eg, in large cities such as São Paulo—at least 2500 people can be registered and receive treatment.

In 1998, the National AIDS Programme began to implement a system, known as the Sistema de Controle Logístico de Medicamentos (SICLOM; computerised system for control of drug logistics), which registers distribution of antiretrovirals, helping to maintain needed stocks of drugs at ADDUs and to track prescriptions.[12,13] Every unit needs at least one computer running SICLOM, and usually one staff member is responsible for its operation. SICLOM automatically checks every prescription issued by a doctor to establish whether it falls within Brazilian guidelines for antiretroviral treatment. At the end of every day, prescription information from all ADDUs is sent via modem to the National AIDS Programme in Brasília. There, after synchronised transmission of data, the system generates a report showing any errors or problems at the units or in the prescriptions. For example, from November, 1999, to January, 2000, SICLOM detected and rejected 9% of prescriptions as being outside the guidelines for antiretroviral treatment.[12,13] In 5·1% of these rejected prescriptions, if the patient had used the drug, he or she could have developed serious side-effects.[12,13] Data for errors in prescriptions are used to establish where further training for health providers is needed.

Since appropriate application of antiretroviral treatment depends on accurate patients' data, the Brazilian Ministry of Health established, in 1997, a network of public laboratories at which patients could receive CD4 and viral load tests free of charge.[14] For 2001, the Ministry expected to do about 400 000 tests at the centres, at a total cost of around US$18 million.[4] In 2001, 138 public laboratories around the country were equipped to do the tests.[4]

Another computer system—Sistema de Controle de Exames Laboratoriais (SISCEL; system for control of laboratory examinations)—gathers data from these public laboratories and sends it via the internet to the National AIDS Programme in Brasília.[14] SISCEL tracks test results and generates graphs of changes in CD4 and viral load for use by clinicians. SISCEL and SICLOM, which continue to be developed, are key factors helping to overcome logistical challenges to delivery of antiretroviral treatment in Brazil.

Centralisation of patients' information in the two databases raises the question of confidentiality, since names of individuals have to be linked to prescriptions for antiretrovirals and clinical test results. Measures to protect confidentiality include limitation of database access to authorised users with passwords, a mandate that names should not be divulged, and restriction of access to clinical data to the doctor looking after the patient. Until now, the procedure has not generated objections from advocacy groups of people living with HIV/AIDS nor have there been any public reports of violation of confidentiality.

Local production of antiretrovirals

Together with guaranteeing free and widespread access to antiretrovirals, Brazil has favoured domestic production of these drugs to reduce costs (figure). The high cost of purchasing antiretrovirals is the factor that, more than any other, could threaten the feasibility and maintenance of the Brazilian programme.

By 1999, 47% of antiretrovirals (19% of expenditure) were acquired from domestic firms, of which 92·5% were state-run laboratories and 7·5% private companies. 53% of antiretrovirals (81% of expenditure) were acquired from international pharmaceutical companies.[4] In 2000 and 2001, domestic share of this production increased. In 2001, 63% of antiretrovirals (43% of expenditure) were produced by domestic firms, and 37% (57% of expenditure) by international companies.[4] By the end of 2001, Brazil was producing seven of 13 antiretrovirals used to treat people with HIV/AIDS in Brazil.[4] The remainder have to be purchased on the international market, and it is there that Brazil has sought to negotiate the best possible prices with international pharmaceutical companies.

AP/Douglas Engle

Brazilian worker checks quality of AIDS drug that is distributed for free

Brazil and international pharmaceutical companies

Citing high costs charged by international pharmaceutical companies, Brazil has threatened to break patents on certain antiretrovirals if companies do not reduce prices. Such a measure, called compulsory licensing, would be admissible under Brazilian patent law, given certain circumstances.[15] It must be emphasised, however, that despite such threats, and since Brazil implemented the TRIPS (trade-related aspects of intellectual property rights) agreement[16] in 1996, compulsory licensing has not been applied, and no patent has been violated. Nonetheless, the threat has remained an important negotiating tool. For example, in February, 2001, Brazil announced it was considering breaking patents for nelfinavir (Roche) and efavirenz (Merck) if manufacturers did not reduce their prices. Negotiations ensued, and Merck agreed to reduce the price of efavirenz by 60%.[17] Reductions offered for nelfinavir however were deemed inadequate.

In August, 2001, the Brazilian government announced that it intended to break Roche's patent and to produce nelfinavir domestically at the government-run laboratory Far-Manguinhos.[17] They argued that 28% of the annual budget for antiretrovirals was being spent on this drug alone.[17] At the end of August, 2001, however, Roche agreed to reduce the price of the drug, and plans to break the patent were ended.[18]

Brazil's willingness to threaten compulsory licensing of drugs has evoked both support and challenges. In February, 2001, the World Trade Organization (WTO) accepted a request by the USA for a panel questioning the compatibility of Brazilian patent law—and specifically provisions for compulsory licensing—with the TRIPS agreement.[3] In April, 2001, in what could be perceived as a sign of support for the Brazilian position, the 57th session of the UN Human Rights Commission approved a resolution, proposed by the Brazilian delegation, establishing access to medical drugs during pandemics—such as HIV/AIDS—as a basic human right.[19] In June, 2001, shortly before the UN General Assembly Special Session on HIV/AIDS, the USA withdrew the WTO panel against Brazil.[20]

In November, 2001, the WTO, at its fourth ministerial conference, released a declaration allowing use of compulsory licensing in cases of national public-health emergencies.[21] This declaration not only strengthened the Brazilian position but also suggested that the transnational movement for access to drugs for HIV/AIDS could lead to poor nations being able to acquire necessary drugs.

Despite these gains, it remains unclear up to what point the Brazilian government will be able to continue to negotiate acceptable terms for purchase of antiretrovirals, especially since important new drugs arrive on the market, and because the number of people needing them continues to rise.

Conclusions

The Brazilian policy of offering free and widespread access to antiretrovirals for people living with HIV/AIDS has received support from non-governmental organisations,[22] health-professional organisations, networks of people living with HIV/AIDS, international bodies such as the Joint UN Programme on HIV/AIDS (UNAIDS), and national and international media.[23] I have briefly outlined some of the most important factors and challenges for this aspect of the Brazilian response to the AIDS epidemic. Other features that merit further analysis include relation, within the Brazilian National AIDS Programme, of prevention to treatment; adherence by people living with HIV/AIDS to treatment protocols within the public-health system; role of patients' and advocacy organisations in creation of settings making possible the antiretroviral policy; and political factors that both lend support to and threaten the distribution programme within Brazil. Similarly, the rise of infection in poor people questions whether populations with the greatest social exclusion in Brazil are genuinely being included within the public-health system, and thus diagnosed and treated for HIV/AIDS.[24]

In conclusion, the Brazilian response to the HIV/AIDS epidemic merits being seen as an example of one developing nation's determination to meet the treatment needs of people living with HIV/AIDS. Although local realities could make it difficult to apply the Brazilian model to other countries, much can be learnt from Brazil's experience. At the same time, the country's commitment to free and widespread access to

antiretroviral treatment warrants further study with respect to its effectiveness, dynamics, and sustainability.

Conflict of interest statement

After over 10 years of experience working in AIDS policy and the non-governmental organisation (NGO) sector, I worked from December, 1999, to January, 2001, at the Ministry of Health, National AIDS Programme, in Brasília, first directing the liaison office with NGOs, and later working in the Office of International Cooperation. This experience offered valuable insight to the subject of this article, but in no way otherwise affected the content or positions expressed. Since February, 2001, I have been a visiting scholar at the University of California at Berkeley School of Public Health. During this time, I have also assisted the National AIDS Programme and the School of Public Health in establishing a formal cooperative training agreement under the Fogarty International AIDS Training Programme.

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Viewpoint

The need for resources for clinical research: the European Society of Cardiology calls for European, international collaboration

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Much of the progress in disease management achieved over the past 50 years in medicine has been driven by an open and fruitful collaboration between academia and industry, particularly in clinical research.[1] However, over time, the status of clinical research has deteriorated. Interest in clinical research and academic medicine is declining among doctor-scientists. Basic research has become disproportionately well funded by comparison with clinical research. Furthermore, the cost of clinical trials has greatly increased, and in particular industry-driven research has become more motivated by rapid return on investment. As a result, many areas that are of little commercial interest remain unfunded. Cardiovascular medicine is no exception to this trend.

The European Society of Cardiology (ESC) felt the need to address this issue and, to this end, in June, 2002, it invited a group of key cardiovascular specialists for a Policy Conference at its headquarters, the European Heart House, in Sophia Antipolis, France. Clinical investigators from the academic world met with representatives from non-industry and industry driven contract research organisations (CROs), industrial research divisions, European medical research councils, health authorities, the US National Institute of Health (NIH), the Directorate General XII of the European Commission, European Heart Foundations, the European Science Foundation, editors in chief of prominent medical journals, and the leadership of ESC for 2 days of intense debate. At the conference, important areas of clinical research that require improvement in Europe were identified. Here, we summarise the discussions that took place and, although we provide no magic solutions, address important areas in which action should, and could, be taken.

Hurdles to clinical research

The first major hurdle to clinical research is a lack of competent doctor-scientists. Clinical research is threatened by an increasing shortage of doctors adequately trained in research. Scientific education has attained decreasing priority, while clinical training and skills have been emphasised. Support for clinical research from governmental and institutional funding agencies seems to be in decline, whereas investment in basic research is rising. Tighter control of health-care resources and more restricted budgets have limited opportunities for clinical research and, perhaps more importantly, have reduced the number of reasonable career openings, particularly in academic hospitals.[2]

This situation is aggravated by a gradual reduction in the amount of European funding for research compared with the USA, Japan, and Canada, where the share of the gross national product (GNP) devoted to research is 2·6–2·8%. By contrast, investment in research in Europe remains at about 2% of the GNP. Promises by EU nations that this proportion will be increased to 3% have yet to be fulfilled. By contrast, industry-driven research in Europe is not subject to the same constraints as elsewhere. However, the industry has become increasingly independent of academia through the recruitment of its own researchers and investigators, and via provision of its own facilities. This independence has placed the industry in a dominant position over academia, whose relations with the industry are ever more complicated and sometimes contested.[3–5]

The decreasing numbers of doctor-scientists and the increasingly limited possibilities offered by academic medicine must be addressed. This situation can only be improved by political decisions at national and European levels, and by re-establishing a true collaboration between academia and the industrial world, paying respect to each other's genuine responsibilities and obligations.

The second hurdle is the cost of clinical research, especially industry-driven clinical trials. The cost of a randomised cardiovascular trial depends greatly on its complexity and duration, and can hence vary from €5000 to €10 000 per patient. Outsourcing the handling of clinical trials to profit-making CROs, and payment of significant honorariums to investigators add to these costs (table). Academia-driven clinical randomised trials use simplified organisational procedures at lower costs. Networks of university-based clinical researchers can undertake supervision, data monitoring, and processing themselves, rather than having to contract out to a profit-making CRO. Reimbursement to hospitals and trialists can be considerably decreased. Such initiatives should make it possible to do high quality clinical trials at a cost of €500 per patient, a 10–20-fold saving compared with industry-driven research. But even with such a low per-patient cost, academic-driven clinical research remains difficult to fund.

	Number of patients to be enrolled		
	100	1000	10 000
Costs (€ per patient)			
Trial organisation	1000	1000	1000
Investigator fee	3000	2500	2000
Monitoring of patients	2100	1500	1200
Data management	800	800	800
Other	4000	3000	2000
Total cost per patient	10 900	8800	7000

Estimated budget of industry-driven clinical trials

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