The Senegalese Antiretroviral Access Initiative : an introduction

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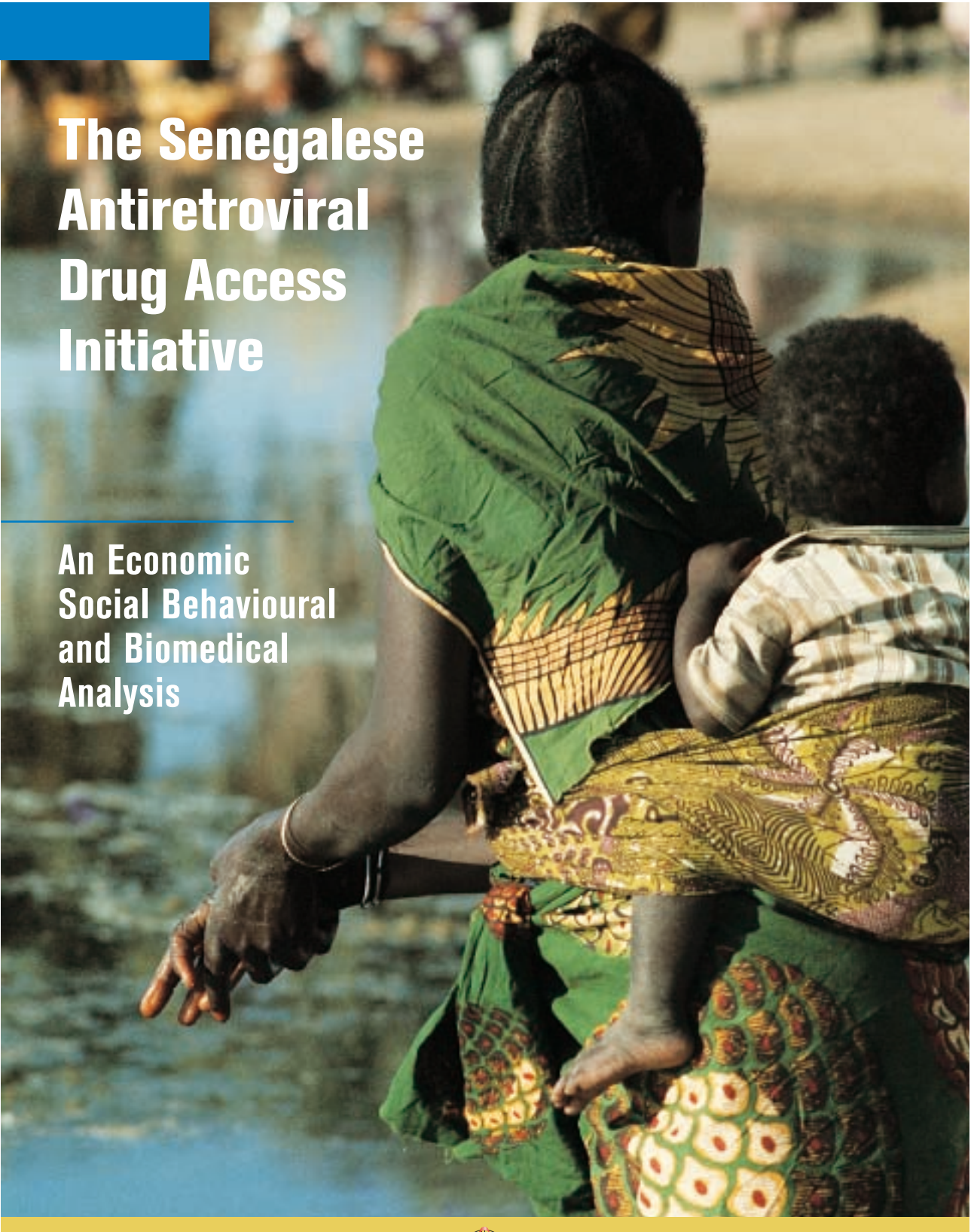
The Senegalese Antiretroviral Drug Access Initiative

An Economic Social Behavioural and Biomedical Analysis



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The Senegalese Antiretroviral Access Initiative: An Introduction

I. Ndoye, B. Taverne, A. Desclaux, I. Lanièce, M. Egrot, E. Delaporte, P. S. Sow, S. Mboup, O. Sylla, M. Ciss

In 1998, Senegal became the first sub-Saharan African country to establish a public antiretroviral (ARV) distribution programme, creating the Senegalese Antiretroviral Access Initiative (ISAARV) with government backing. The same year, two other African countries — Uganda and Côte d'Ivoire — also set out to provide access to ARVs under the UNAIDS Drug Access Initiative, with technical support from UNAIDS.

The establishment of a governmental ARV access programme at that time testifies to the attention Senegal paid to combating HIV, attention that translated into strong political will, sustained by international recognition of Senegalese virology work and by Senegal's success in prevention, which was internationally proven with the report on the country's prevalence stability [8].

In 1998, however, the introduction of such a programme presented numerous challenges: the cost of medicine was extremely high relative to national and individual resources; international consensus advocated AIDS prevention over treatment for Southern countries; and no international institution would agree to finance the treatments. Four years later, when the necessity for ARV access in Southern countries is internationally recognised,[1] and in light of its positive results, ISAARV — once considered a gamble — has proven to be farsighted.

A rough sketch of the prevailing international context at the time of ISAARV's creation is essential to understanding the programme's innovative nature; the account below will elucidate public health issues surrounding an ARV treatment access programme in a Southern country. A description of Senegal's epidemiological and health situation will then precede a summary of national strategic principles. An introduction to ISAARV's general organisation, a broad outline of how it functions, and an analysis of its evolution from 1998 to 2002 will follow.

[1] Cf. United Nations, Resolution adopted by the General Assembly, August 2001, A/RES/S-26/2, 18 pp.

History

Programme Issues and International Context

The announcement in 1996, at the XI International Conference on AIDS in Vancouver declaring the effectiveness of highly active antiretroviral therapy (HAART) sparked fervent determination among associations, public-health officials, and leaders in the scientific community to distribute these therapies in Africa. Given the prevailing international scepticism at the time, which regarded the proposition unrealistic, a challenge was posed.

In Africa, commitment to treatment manifested itself notably in the organisation of an international scientific consultation in Dakar in September 1997. Participants at the consultation defined prerequisites for antiretroviral treatment distribution and specified optimal therapeutic protocols [3].[2] At the International Conference on AIDS & STDs in Africa (ICASA) in Abidjan in December 1997, some heads of state brought political support to the discussion, announcing the forthcoming implementation of ARV treatment programmes in a number of African countries. The announcement, however, was not met with general consent.

The establishment of ARV access programmes raised public health problems, relating particularly to 1) insufficient scientific knowledge at the time regarding the effectiveness of these therapies, both for the long term as well as within the health-care context of Southern countries; 2) the complexity of treatments, presumably requiring lifelong adherence and requiring heavy medical follow-up; 3) the need for well-developed health infrastructures to implement these treatments; as well as 4) the high cost of the medications. Like other health programmes, ARV access programmes must prove that they can fulfil the four requirements of public health: equity, optimum cost-effectiveness, accessibility and acceptability for those affected, and sustainability.

For the decision-makers and backers, the primary obstacle concerned the cost of such programmes relative to the budgets of African states [6, 7].[3] ARV treatment, according to some economists, would swallow up the total health budgets of some countries. This argument was sometimes raised to single-handedly quash all reflection on the development of treatment programmes. In addition, in the context of the 1990s, when the functioning of African health systems was seen as requiring "the contribution of populations to health costs" and "cost recovery," as generalised under the "Bamako Initiative," it was considered essential that patients contribute to the purchase of their antiretroviral treatment. Obviously, though, very few people would be able to pay the necessary sums (between US$7000 and US$10,000 per person per year). This called into question the equity and sustainability of programmes, introducing the possibility that efforts towards North-South equity, in the end, only increased the disparity between social classes in Southern countries.

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[2] See [3], with the support of ANRS, ICASA, the European Union, IAS, IMEA, ORSTOM, PNLS/MST of Côte d'Ivoire, PNLS/MST of Senegal, SAA, Secretary of State of the Coopération Française, UNAIDS, WHO.

[3] In 1998, the ratio of ARV treatment cost per person to per capita GNP (were all patients needing treatment actually receiving state-financed ARV multi-drug therapy) is estimated at 12.9% in West Africa, while it is lower than .1% in Western Europe ([7] p. 2206). See also [6].

For the clinicians, the risk of these treatments' failing was high, due in particular to problems in drug adherence, as scientific publications in 1997 showed to be the case in developed countries.[4] Close medical follow-up therefore appeared to be indispensable. Medical response to treatment failures or side effects should be quick. Adherence to antiretroviral multi-drug therapy was crucial, more so than for any other treatment.

For epidemiologists and virologists, difficulties in monitoring, along with inadequate prescriptions by insufficiently trained health professionals and the uncontrolled trafficking of ARV in the informal market, represented a significant risk in the emergence of viral resistances. They feared that the establishment of an ARV access programme would promote inappropriate usage with serious virological consequences.

Public health officials, for their part, feared that these programmes would work to the detriment of other programmes, particularly HIV prevention and testing or treatment of opportunistic infections. Accessibility to HIV testing and to treatment of opportunistic infections was considered by some actors to be a necessary prerequisite for a HAART access programme.

And finally, the pharmaceutical manufacturers declared their position, publicly neutral, seeking to avoid the debate on the price of medications which would inevitably reflect badly on their pricing in Northern countries.

These various fears corresponded to real public-health problems but should have been viewed in a rapidly evolving context likely to change with the emergence of new, less expensive treatments or, conversely, by the discovery that the available ARVs are less effective in the long term [5].

In view of the obstacles, the most cautious attitude was clearly to postpone the creation of ARV access programmes, as was recommended by the main international institutions, who maintained that prevention, because of its cost-effectiveness, was the only imaginable solution for Southern countries. At the same time, other actors in the fight against AIDS argued that the establishment of HAART access programmes would advance testing, prevention, and treatment of opportunistic infections.

When Senegal's National AIDS Control Programme (Programme national de lutte contre le sida; PNLS) committed to ISAARV, strategic choices were determined by what would enable the system to avoid the pitfalls outlined below.

Epidemiological Indicators of HIV Infection and PNLS Objectives and Resources

Since the onset of the epidemic, Senegal has had a low prevalence — under 2% among adults — which appears to be stable.[5] This situation can be attributed in part to the promptness and pertinence of prevention efforts, which were implemented on a national level. This expanded, multi-sectoral response considerably increased condom use in non-marital sex and improved treatment of sexually transmitted infections.[6]

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[4] See the numerous papers presented at the Geneva International Conference and also [9].

[5] Conseil national de lutte contre le sida, République du Sénégal, "Plan stratégique 2002–2006 de lutte contre le sida."

[6] "Acting Early to Prevent AIDS: The Case of Senegal." Best Practices, UNAIDS/99.34E.

Estimated number of people with HIV/AIDS at the end of 2000

Adults	80,000
Women	35,000
Children (under 15)	3000
Adult prevalence	1.4%
New infections	5500
Orphans	20,000
Deaths	5000
Cumulative deaths	30,000

Source: *Bull. Epi. HIV du Comité national de lutte contre le sida du Sénégal,* n° 8, décembre 2000.

In 1998 the PNLS laid out the four following objectives: 1) strengthen prevention efforts (community mobilisation, prevention of blood transmission, improved treatment of sexually transmitted infections, prevention of mother-to-child transmission); 2) improve care for people with HIV; 3) monitor the epidemic's development and evaluate the impact of interventions; and 4) develop operational research.

PNLS budget assessment, 1998 to 2001, in millions of CFAF

	1998	1999	2000	2001
State (total)	375	460	525	1290
Development partners	1165	2430	1997	2156
ISAARV (state)	250	250	300	600
Percentage of state	66%	54%	57%	46%

Source: PNLS 2002

The Groundwork

In early 1998, the PNLS established an antiretroviral multi-therapy intervention programme called the Government Antiretroviral Treatment Initiative. This programme, implemented with 250 million CFAF in government funds, was designed to finance the drug treatments and clinical and biological monitoring of 50 patients for the year 1998. PNLS created a number of administrative organs to manage the initiative. In addition to the PNLS, the following partners participated in the programme: the Ministry of Health, three health-care facilities chosen for patient care — the Infectious Diseases Unit (Services des maladies infectieuses) and Ambulatory Treatment Centre (Centre de traitement ambulatoire) of Fann Teaching Hospital and the Internal Medicine Unit (Service de médecine) at Principal Hospital — and the Sidak Project (IMEA/IRD/ANRS/Coopération française), which provided technical support and scientific monitoring.

Senegal: principal socio-demographic and health indicators

Demographics	
Population (estimated 2000)	9,200,000
Percentage of the population under age 20	57%
Health standard	
Rate of infant mortality	63.5/1000
Rate of infant-juvenile mortality	143/1000
Life expectancy at birth*	53 years
Total fertility rate	5.2 children/woman
Economy	
Per capita GDP (1996–1998)**	US$545
Poverty rate (adults earning less than 392 CFAF/day)	65%

Source: Ministère de la Santé, Direction des études, de la recherche et de la formation, "Enquête Sénégalaise sur les Indicateurs de Santé, 1999," juin 2000.

* Epidemiological Fact Sheets on HIV and STI, Senegal, 2000, UNAIDS.

** République de Sénégal, "Troisième conférence des Nations unies sur les pays les moins avancés: mémoire présenté par le Sénégal," février 2001

Various ISAARV-related research programmes funded by ANRS, IRD, MAE, and the EU

–Evaluation and support of antiretroviral multi-drug therapy among Senegal's HIV-1 patients (1999–2000), ANRS Project 1215.

–ANRS Trial 1204/IMEA 011: ddI/3TC/efavirenz once daily (1999–2001).

–ANRS Trial 1206/IMEA 012: Evaluation of tolerance and effectiveness of a first antiretroviral treatment combining Zerit® 40, twice daily, and Videx®, Stocrin®, once daily (2000–2002).

–Multi-centre study on accidental blood exposure (2000–2002), ANRS Project 1224.

–Social aspects, adherence, and impact of ISAARV on the medical system (1999–2001), ANRS Project 1216.

–ARV Availability in Senegal: An Anthropological Approach (2000–2002), ANRS Project 1242.

A pilot programme was launched, a strategy in keeping with Recommendation 17 of the Dakar-Abidjan Consensus.[7] It was of modest size, compared to its Ugandan and Ivorian counterparts, but would be expanded if the results from the first group of patients demonstrated the programme's feasibility, accessibility, acceptability, and effectiveness. The innovative and experimental nature of the Senegalese Initiative, combined with the will to set up treatments as quickly as possible for the patients needing them, encouraged a pragmatic approach to the programme's development.

[7] "The planned introduction of antiretroviral drugs in Africa requires the completion of a pilot phase in numerous countries, which will create a means by which to specify, in the context of local conditions, the terms of their use and provide data necessary for the drafting of national directives," "Les traitements antirétroviraux dans la prise en charge thérapeutique de l'infection par le VIH en Afrique sub-saharienne: Déclaration de consensus de Dakar-Abidjan," 1997, 3 pp.

Economic accessibility to the programme was considered from the outset a major issue. Out of concern for equity and social justice, a system of subsidising HAART was established to avoid a selection of patients based on their ability to pay for the medication. The subsidy amount granted to each patient was determined by their resources.

Whereas the initial framework — particularly regarding therapeutic protocols and the terms of clinical and biological monitoring — was defined on the basis of international recommendations and was presented in a number of reference documents [1, 10], the details regarding access and the programme's other social aspects were clarified pragmatically, as individual cases, difficulties,[8] and ethical questions emerged on the ground.

The technical capacity available in Dakar and the competence of its research institutions created favourable conditions for the development of such a project. Nevertheless, the approach was bold, and in 1998, the PNLS was relying on a future reduction in drug prices for the project's continuation beyond the three years initially planned. The scientific support brought to the pilot project by research institutions was simultaneous with the project's implementation, but the financial support of international backers was only obtained afterwards.

Senegal: principal health-care system indicators

Resources and infrastructure (1999)	
Hospital/population ratio	1 hospital for 545,800
Clinic/population ratio	1 clinic for 175,000
Health centre/population ratio	1 health centre for 11,500
Human resources (1999)	
Doctor/population ratio	1 doctor for 17,000
Nurse/population ratio	1 nurse for 8700
Women of childbearing age/midwife ratio	1 midwife for 4600
Financial Resources (2001)	
Health care budget	25.5 million CFAF
Proportion of health expenses in the national budget	8.24%
Health-care funding sources	
State	53%
Partners	30%
Population	11%
Local government	6%

Source: Conseil national de lutte contre le sida, République du Sénégal, "Plan stratégique 2002–2006 de lutte contre le sida."

General Organisation

Institutional Organisation

ISAARV, born of government will, was entrusted to the National AIDS Control Committee (Comité national de lutte contre le sida; CNLS) for its implementa-

[8] These were described in a preliminary study conducted in November 1998, three months after the programme's implementation [4].

tion. Instead of creating a separate institution or handing the project over to experts, ISAARV administrators had practitioners who would execute the programme — doctors, biologists, virologists, pharmacists, social workers — as well as civil society representatives and PLWA, involved in the programme's definition and planning. Most of these actors belonged to clinic-counselling, epidemiological, ethical, or legal CNLS groups.

This strategy of involvement was dictated by budgetary constraints and fulfilled two functional requirements: it could optimally adapt the project and its procedures to difficulties that would emerge in practice, and it could adapt the terms of treatment to scientific advancements, available drugs, and treatment costs in this rapidly changing field

ISAARV Institutional Organisation

Four committees were created to run ISAARV.

A first committee defines the project's direction and serves as the Initiative's control and monitoring organ. Issues relating to organisation, resource management, and personnel, as well as the evaluation of virological, bio-clinical, public-health, and social aspects; of the status of medicine and reagent stocks; and of negotiations relating to medicine or reagent purchasing, are all raised in the course of the committee's monthly meetings. Decisions are taken collegially, after discussion and agreement among committee members.

From the start of enrollments, this committee, now the Eligibility Committee (Comité d'éligibilité; CE), is responsible for patient recruitment. The committee statutorily comprises 20 people (doctors; biologists; pharmacists; Medical Association, Pharmacists' Association, and Dental Surgeons' Association representatives; religious and legal representatives; representatives from the Ministries of Finance, Public Health, and Social Action; psychologists/psychiatrists; and representatives of PLWA, social workers, NGOs, partners, and the Office of the Prime Minister). In the future, this committee will also be responsible for patient follow-up care, but the more precise "Eligibility and Follow-Up Committee" has not yet officially replaced the original denomination.

The Medical Committee (Comité medical technique; CMT) defines and periodically revises the programme's medical aspects (enrolment criteria, therapeutic protocols, monitoring of adverse reactions, etc.). In monthly meetings, it reviews the medical files of patients who will be recommended for treatment and gives its opinion on the accuracy of the combination therapy chosen by the clinician. This committee groups prescribing doctors, biologists, and pharmacists.

A Welfare Committee (Comité technique pour les aspects sociaux; CTAS) defines options relating to non-medical aspects of project access, and provides support to follow-up. It coordinates social surveys among patients recommended for treatment. The committee consists of PNLS health professionals (pharmacists, psychiatrists, etc.) and social workers.

The Drugs and Reagent Management and Supply Committee (Comité de gestion et d'approvisionnement en medicaments et réactifs; CGAMR) is responsible for managing, in addition to drug supply, the organisation of dispensation sites and relations with wholesalers, who imported the drugs before the creation of ISAARV.

Finally, an independent structure, in the form of a foundation, was envisaged to handle the collecting of private funds for the programme. It has not yet, however, come into being.

Functional Organisation

ISAARV was designed to be accessible to anyone needing antiretroviral treatment, whatever their nationality or socioeconomic status, provided that they lived in Senegal. From the beginning, the criterion of nationality, with its concomitant sensitive political issues, was eliminated in favour of residency. This was done also to assure optimal medical follow-up for the patient — which was considered impossible for a patient living outside the country — and to avoid making an "open call" to patients in neighbouring countries who would be prepared to travel to Senegal for less expensive medicine.

Criteria and channels for patient recruitment

The introductory medical criteria for treatment were based on the Dakar Consensus of 1997, revised in October 2000.[9] So, for adult patients (the only patients enrolled in ISAARV's first year), the criteria were as follows:

–patient is asymptomatic with a CD4 count of less than 350/mm^3 with a viral load greater than 10,000 copies/ml, or
–patient is symptomatic stage B with a CD4 count of less than 350/mm^3 or stage C (1993 CDC classification). A Karnofsky index of less than 70 and the presence of certain clinical signs are the exclusion criteria.

Similarly, the criteria for administering treatment to children and for establishing protocols for their care — prevention of mother-to-child transmission and prophylactic treatment of accidental blood exposure, initiated in June and July 2000, respectively — were modelled on international recommendations adapted to Southern countries and to the drugs available in Senegal. These were also revised in October 2000.[10]

Patient access procedures and itineraries

Patients are initially recruited and treated at three facilities: the Infectious Diseases Unit of Fann Teaching Hospital and its Ambulatory Treatment Centre, and the Internal Medicine Unit of Principal Hospital. Doctors selected patients at one of the three sites based on immunovirological and clinical criteria (see above). After the CMT reviews the patient's clinical file, a social worker completes a survey with the patient, which is designed to assess the patient's economic resources and the quality of his or her social support (familial, relational); identify others in the household who may be HIV-positive; and ensure that the patient understands the constraints of the treatment. The resources considered include both salaries and revenues as well as supplementary resources (social insurance, employer contribution, family support). After CTAS studies the survey results, the patient's complete file (bio-clinical and social), is rendered anonymous to guarantee equitable consideration by the CE. The CE then discusses the file, endorses the decision for treatment, and sets the amount of financial contribution to be asked of the patient in accordance with a pricing grid (see Table 1 in Chapter I.1).

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[9] "Africa: Antiretroviral Treatments for People Infected with HIV. Updated Recommendations," October 2000. ANRS, IMEA, IRD, Société africaine contre le sida (African Society Against AIDS), UNAIDS, PNLS-Senegal, PNLS-Côte d'Ivoire, IAS (ANRS, ed., French and English versions).

[10] Cf. footnote 9.

In a subsequent consultation, the doctor informs the patient of the CE's decision; if the contribution amount seems feasible to her or him, the patient is included in the programme once s/he reads an information letter and signs an informed consent.

The clinical and para-clinical follow-up of ARV treatment is overseen by the programme and thus costs nothing to the patient. Treatment of intercurrent infections, however, as well as possible associated biological tests, are the patient's responsibility, according to the variable terms of the treatment sites. In addition, supplementary fees (transportation to consultations, certain supplementary tests, etc.) are not paid for by the Initiative.

Patients are asked about the programme's economic accessibility each month when they pay for their treatment.

Medical and psychosocial monitoring

Patients' medical follow-up is given in medical consultations on Day 1, 7, 14, 30, and then monthly, based on the patient's bio-clinical log. During each consultation, the doctor writes a prescription, a copy of which he keeps. The patient then goes to the pharmacy, where the prescription is filled and the pharmacist discusses treatment with the patient, filling out an adherence follow-up log. The patient gives his financial contribution to the pharmacist.

Patients' social follow-up was intended to comprise several meetings, which was not possible beyond the first 180 patients enrolled. The patients had access to group discussion and information sessions, which were held monthly at one of the sites. Social intervention consisted mainly of adherence support in the discussion and information sessions and in the socioeconomic surveys, which were required to access ISAARV. These discussion and information sessions were not, however, regular or large enough for all patients to benefit from them. PLWA associations, which were less involved in drug-adherence support, did not develop support groups until after the pilot project had ended.

The entire system guarantees patient anonymity and confidentiality of treatment through the use of codes. Only the doctor and social worker know patients' names.

A number of problems emerged in the programme's early months, mostly relating to economic issues: a high proportion of rejections of patients in lower socioeconomic groups, and enrolled patients stopping treatment after a few months. These difficulties suggested that the way in which the initial social surveys were carried out allowed for overestimates of patients' financial capacities; discussion was reopened on the initial strategy for treating poor patients and ensuring programme equity. In addition, the proposed support measures could not be set up for a number of reasons, mainly due to the workload of programme personnel (in particular the social workers), who are public-health employees and did not have extra time to lead programme activities.

Development

From Pilot Project to National Programme

Following the XIII International Conference on AIDS in Durban in 2000, which marked a turning point in mobilising Northern institutions for treatment access in the South, the CNLS planned an expansion of ISAARV. This expansion included first, the enrolment of patients from two clinical trials[11] and patients from a mother-to-child-transmission prevention programme, and then the enrolment of new patients and decentralisation through the opening of new recruiting sites. This growth of ISAARV, defined in the 2000-2003 action plan in September 2000,[12] was made possible by the drop by about 75% in ARV prices, announced October 2000 and in effect for patients in November 2000.

This development was not independent of the change in the economic environment or in international strategy. The HAART access programme in Abidjan experienced problems (related to patient procedures and inclusion deadlines) and poor results in terms of treatment effectiveness (in particular with the formerly used two-drug regimens and with frequent interruptions due to economic reasons [2]); other HAART access programmes in African countries (Uganda, Kenya) held patients responsible for treatment costs; and new programmes, in the process of being developed, have not so far obtained any real results. And so, the Senegalese pilot programme was internationally considered a success, and UNAIDS encouraged its replication. In 2000, missions were organised for advocates of HAART access programmes in other West African countries to learn from the Senegalese experience. At the end of 2000, ISAARV was being promoted in neighbouring countries because of its relatively unusual nature, even though it involved just 166 patients.

ISAARV's expansion announced at the end of 2000 answered simultaneously to CNLS's own national strategy and to international expectations, all while taking advantage of the results of negotiations with pharmaceutical firms. Development of ISAARV and of a sufficient monitoring and support structure, maintenance of acceptable drug adherence, and improvement of equity in ARV access were challenges for the programme's second phase. It was now clear that ARV use was feasible in pilot centres — university hospitals that are specialised and competent in clinical research. The next step was to set up HAART access in non-university health-care structures likely to attract a greater number of patients: as was emphasised by P. Piot, "before treating tens of millions of Africans who are affected, start with the thousands."[13] In terms of feasibility, the challenge was no smaller than in the first phase.

Developing the System

At the end of 2000, the passage from ISAARV's pilot phase to expansion phase was announced by the CNLS, which presented its 2000–2003 action plan. Some elements of the initial system were reviewed and refined, but the expan-

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[11] ANRS 1204/IMEA 011 and ANRS 1206/IMEA 012.

[12] Ministère de la Santé/PNLS, 2000. ISAARV. Plan d'action 2000-2003. Rapport. Dakar, septembre 2000, 31 pp.

[13] "Un fonds unique contre le sida," Libération, jeudi 26 avril 2001, p. 19.

sion did not call into question the aforementioned structure. The four administrative organs defined in the first phase would remain in place, and their staff would be enlarged to include new service professionals.

The programme expansion applied initially to the city of Dakar, which saw the opening of new prescription and dispensation sites. First, a site was opened at the Social Hygiene Institute (IHS) for adult patients. Albert Royer Children's Hospital, the paediatric unit of Principal Hospital, and the paediatric clinic at Guediawaye Health Centre were then involved in children's treatment, while the maternity wards of Principal Hospital, Le Dantec Teaching Hospital, and Guediawaye Health Centre were entrusted with the treatment of pregnant women. The protocol for treating children and pregnant women, as defined by the International Therapeutic Solidarity Fund (Fonds de solidarité thérapeutique internationale; FSTI) in the framework of a prevention of mother-to-child transmission (PMCT) programme, was implemented.

The operation was to be extended across ten regions of the country. On December 1, 2001, the first decentralised site was opened in Kaolack; the other nine were to be established over the following years. The number of ARV-prescribing doctors in ISAARV went from 9 in 1998 to 24 in early 2002.

Treatment Protocols for ISAARV's Expansion

Adults

The treatment protocols for adults were revised. Dual therapies were no longer recommended. The biological criteria for enrolment did not change, but were reduced: viral load was no longer required.

Initially, triple therapies consisting of 2 NRTI + 1 NNRTI or 2 NRTI + 1 PI were thought to have comparable effectiveness. Combinations including 1 NNRTI were of particular interest because they appeared to have better patient adherence.

The choice of an NRTI cocktail among the four products available at the end of 2000 (zidovudine, didanosine, lamivudine, and stavudine) took into account drug interactions (zidovudine-stavudine is the only combination not recommended) as well as side effects (neurotoxicity, anaemia, etc.).

A second treatment option was considered in case of treatment failure among adherent patients or in case of intolerance to treatment; side effects, possible major mutations (indicated by genetic characterisation), and expected increased resistance were taken into account.

In case of an interruption of HAART, the same schema is reintroduced if the interruption concerned all molecules in the cocktail. If the interruption was only of one or two of the drugs, the continuation of these molecules is discussed according to the results, viral load, and research on viral mutation (if possible).

Particular attention was given to medicinal interactions likely to occur with treatments for opportunistic infections, in particular with anti-tuberculosis treatment.

It was recommended that treatment of HIV-2 patients follow the same enrolment criteria, with a multi-drug therapy of 2 NRTI + 1 PI; the NNRTI were excluded because of natural resistance.

Children

When ISAARV was extended to children in July 2000, patient criteria were:

–any symptomatic child at stage B or C, whatever the CD4 count;
–asymptomatic or paucisymptomatic (N or A) children over 12 months with a CD4 count lower than 15%; and
–infants (under 12 months) whose HIV diagnosis was confirmed by two positive PCR; in practice, this mainly includes children in the PMCT programme whose HIV-positive status was fixed before the age of 4 months.

Viral load therefore, it is important to note, does not play any role in treatment initiation.

Pregnant women

To prevent mother-to-child transmission, the protocol decided upon was: oral AZT treatment for the mother starting at the 34th-36th week of amenorrhoea and AZT orally every three hours during childbirth (or intravenously if necessary), followed by treatment of the newborn for six days. An alternative treatment of nevirapine can be given at the time of birth and for the newborn if the mother was unable to take AZT in due course.

Accidental blood exposure

Finally, a network for reporting and treating accidental blood exposure was set up, accompanied by the wide dissemination of information to health centres about the treatment programme. A preventative triple therapy could be given for one month according to a specific protocol for evaluating the probability of transmission.

Access and Follow-up in the Second Phase

The patient route is the same as that in ISAARV's first phase, though patient access was transformed by the implementation of new pricing and the availability of new treatments (following the objective to accelerate the inclusion of new patients). Simplified monitoring tools were finalised in November 2001 for clinical follow-up and in January 2002 for psychological follow-up.

Increase in Patient Enrolment

In the first 39 months of ISAARV's operation, the pattern of recruitment varied with treatment access procedures (Figure 1)

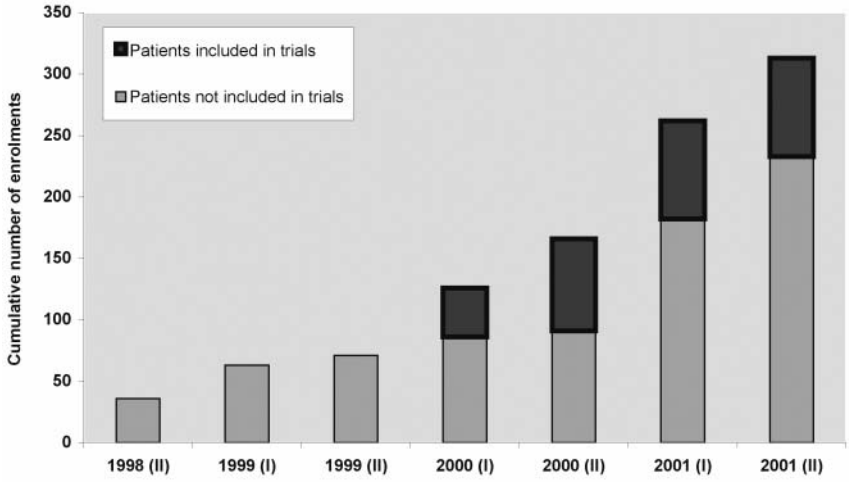

Figure 1

Recruitment in ISAARV's first 39 months (August 1998 to October 2001).

The reduction of ARV prices on the international market played a decisive role in the acceleration of new patient enrolment: the treatments became more affordable for patients, and were available in greater quantities for the programme. In the 27 months prior to the price slash, three-quarters of new patients outside clinical trials had entered ISAARV in the first 12 months; recruitment had slowed down. Once the new pricing took effect, enrolment accelerated and continued to do so throughout 2001: the number of new patients tripled monthly in the 12 months following the price reduction.

"Off-Programme" Treatment

The Biomedical Sector

Before ISAARV was initiated, some patients were already taking ARV treatment. The few people who could afford to do so travelled to Northern countries for treatment by doctors there. In Dakar, 20 patients managed to pay between 80,000 to 320,000 CFAF monthly for the purchase of drugs[14] prescribed by doctors already involved in AIDS treatment. Patients bought the medicines at one of three wholesalers or in a few private pharmacies, or received them through donations.

Some of these patients enrolled in ISAARV upon its launch or in the following years. Others continued with their initial means of treatment (purchasing drugs at ISAARV dispensing sites) and from then on were considered "off programme" — because they could not benefit from the state subsidy as a result of their relatively high economic level, or because of their foreign residency, concerns over privacy, or, less commonly, ignorance about the programme access criteria. From 2000 to 2002, the number of off-programme patients fluctuated by

[14] From "improved" mono-therapy (Videx®, Hydréa®, chloroquine), which was prescribed by a few clinicians at the start of ARV access, to triple therapies with protease inhibitors.

between 20 and 30. Enrolment in ISAARV, meanwhile, went from 80 in April 2000 to 450 in April 2002. "Off-programme" patients therefore, whose numbers remained stable, came to represent a smaller percentage of patients obtaining ARVs through the ISAARV system (from 25–30% in 2000 to less than 7% in 2002).

The doctors prescribing medicines to "off-programme" patients are ISAARV clinicians, corporate doctors, and some doctors with private practices:

–Most (seven) of the doctors are from ISAARV, and have therefore been involved in treating HIV for several years; their reputations are good and their consultations attract many patients.

–Corporate doctors provide another institutional framework for care of patients taking HAART. The doctors of seven large Dakar businesses participated in AIDS training in 2000, and since 2002, four of them have been actively involved in treatment. Some patients coming from countries in which these companies are established (CAR, Chad, Mali, etc.) and others living in Senegal were integrated into ISAARV. Corporate doctors prescribing ARVs and ISAARV clinicians are well acquainted and exchange information via an informal network.

–Some doctors practicing in the private sector devote part of their medical work to AIDS. The private doctors who prescribe HIV testing refer patients to ISAARV in case of seropositivity. In early 2002, only two were prescribing HAART extensively; a third was doing so infrequently.

The Traditional and Neo-Traditional Medical Sector

In addition to biomedical treatment, most patients turn to traditional and neo-traditional medicine. This health service is very diverse; it should not be misunderstood but will not be discussed here. A research programme is expressly pursuing the subject, which will be covered in future publications.

Conclusion

ISAARV was profoundly innovative, a pioneer among programmes introducing HAART in Africa. In 1998, it was born of the joint vision of politicians and public health decision-makers, while the AIDS association movement played a marginal role in the programme's launch. Its development was progressive, guided by the monitoring of various operational research projects and gradually incorporating new resources that came with the involvement of new partners (EU, FSTI, IDA, ESTHER, and the Global Fund to Fight AIDS, Tuberculosis and Malaria). The pharmaceutical industry also agreed early on to employ preferential pricing for the Initiative, and then renewed some price reductions in the wake of UNAIDS's ACCESS Initiative.

With its pilot experience widely successful, ISAARV transformed in its third year into a large-scale public-health programme with the objective of treating thousands of patients in all the regional capitals of Senegal by the year 2006. Maintaining quality treatment in these less-than-favourable circumstances is the challenge ISAARV faces in its second phase.

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ISAARV in Context: A Time Line

		International context	PNLS/ISAARV
1996	July	XI International Conference on AIDS in Vancouver (Canada). Demonstration of effectiveness of HAART and advocacy for its use in Southern countries	
1997		Drafting of recommendations for the use of HAART in Africa	
	June	Announcement of UNAIDS Initiative in four pilot sites (Uganda, Chile, Côte d'Ivoire, Vietnam)	
	September		Dakar Workshop drafts recommendations for the use of HAART in Africa
	November	Official launch of pilot phase of UNAIDS Initiative	
	December	X ICASA in Abidjan; Announcement of public involvement by heads of state Creation of FSTI	Presentation of Dakar recommendations at ICASA (Abidjan)
1998			Development of Senegalese HAART access programme Definition of clinical and biological follow-up protocol
	June	XII International Conference on AIDS in Geneva (Switzerland)	
	August	Start of recruitment in Abidjan under UNAIDS Initiative	Start of recruitment Methodological support
	October		Mission to assess social aspects Definition of social support measures
1999	June	Suspension of enrolment in UNAIDS Initiative in Abidjan	
	November	XI ICASA in Lusaka (Zambia) Resumption of enrolment for UNAIDS Initiative in Abidjan	Presentation of ISAARV in Lusaka

2000	January		Start of enrolment for ANRS 1204/IMEA 011 Presentation of ISAARV to ECI (Enhancing Care Initiative) Symposium
	May	Launch of the Accelerating Access Initiative (ACCESS) by the World Bank, WHO, UNFPA, UNICEF, and UNAIDS	Start of FSTI's PMCT programme
	June	Announcement of ARV price reduction to the Global South by five pharmaceutical companies Paris Workshop	
	July	XIII International Conference on AIDS in Durban (South Africa)	Presentation of ISAARV results in Durban
	October	Within ACCESS, pricing agreements with four pharmaceutical firmsinvolving, for Africa, Senegal, Rwanda, and Uganda Workshop for revising Dakar clinical recommendations UNAIDS and the World Bank promote ISAARV in other African countries	First ISAARV price reduction Beginning of enrolment in ANRS 1206/IMEA 012 Drafting of 2000-2003 ISAARV plan of action and announcement of its expansion
2001	January		Meeting on ISAARV's 2001 decentralisation into five regions
	February	CIPLA offers a triple therapy for US$600 (420,000 CFAF) per year to Southern governments	Establishment of simplified tools for social follow-up Opening of a second dispensation site (IHS)
	April	End of Pretoria trial WTO-WHO workshop on financial accessibility to HAART	
	June	Extraordinary session of United Nations General Assembly in New York to define a global strategy to fight AIDS	
	October		International workshop in Dakar on social aspects of HAART (Gorée Workshop)
	December	XII ICASA in Ouagadougou (Burkina Faso); Gorée 2001 recommendations, social aspects, HAART's role in the treatment of PLWA in Africa	Presentation of ISAARV results in Ouagadougou Announcement of decentralisation HAART access