



ANTIRETROVIRAL THERAPY IN PRIMARY HEALTH CARE:

SCALING-UP IN TWO HEALTH CENTERS IN KIGALI, RWANDA



© Julie Rémy

November 2007



CONTEXT

MSF in Rwanda: towards HIV care

Médecins Sans Frontières (MSF) has been active in Rwanda since 1991. After the phase of emergencies (genocide, war), the programs were redirected towards support of the health districts and «intermittent» emergencies. By the end of the 90's, the projects were reoriented. In 2000, a mental health program was launched to provide psychological support to 3 Kigali-based associations supporting women traumatized by war and genocide, often widows infected/affected by HIV. A HIV sensitization project in primary schools (Kigali, Cyangugu) was started the same year. Throughout these projects, it became clear that, in Rwanda at that time, the majority of activities in the field of HIV/AIDS were directed towards prevention efforts. Two exploratory missions were done in 2000 and 2001, confirming the lack of medical care for people living with HIV/AIDS (PLWHA) and drawing attention to the extent of the HIV epidemic (estimated prevalence rates of 16.3 % in Kigali, 1998¹). The active demands of the health authorities and various Rwandan HIV-associations to engage in the medical and psychosocial care of PLWHA, confirmed the need to launch a HIV treatment program. Kigali was chosen for several reasons:

- High prevalence rates in certain sectors of Kigali with HIV being a major cause of mortality in Kigali
- A network existed of community partners and local initiatives, requesting support
- The opportunity of a vertical program integrated into the existing functional health structures

A team consisting of a medical coordinator and a nurse were sent to Kigali in November 2001. The project was developed and formally approved by the national authorities by April 2002. With the decentralization (in 2002), further direct contacts with health authorities were mainly with the local administration.

Response towards HIV in Rwanda (at that time)

Though national programs against HIV were in place since the end of the eighties, the activities were obviously hampered during the years following the genocide and resulting national turmoil. Subsequently, the national program for HIV was given new life. The centralized approach, centered on the PNLS (Programme National de Lutte contre le SIDA) in the Ministry of Health, was modified in 1997 with decentralization and adoption of a multi-sectoral approach. In 2001, the PNLS was replaced by two separate national services:

- the CNLS (Commission Nationale de Lutte contre le SIDA) was put in place, under the authority of the Presidency, mainly focusing on general policy, coordination and resource mobilization. Similar structures were organized at district and provincial level.
- TRAC (Treatment and Research AIDS Center) was founded, under the authority of the Ministry of Health, and mainly working on medical and technical issues (guidelines, training, monitoring) and surveillance.

The CNLS strategic plan for 2002-2006 emphasized the need to enhance HIV care and treatment to individual patients including antiretroviral treatment (ART) and psychosocial care, and pointed out the need for partnerships, coordination and alignment of all activities within the multi-sectoral approach². In 2003, a Ministerial instruction detailing the modalities of ART was published, ensuring free ART for the poorest.

Since then, the combination of political commitment, well-functioning national services and the application of external financial and technical support in a constructive way, have resulted in a fast scaling-up of various activities in the HIV field, ranging from prevention to ART. The outcomes achieved in this MSF project reflect the favorable context of collaboration that has developed in Rwanda within the field of HIV.

SCALING-UP OF ART WITHIN A HEALTH CENTER-BASED PROGRAM

The project was launched as a pilot program within a limited geographical region and with a close link to the community. It aimed to develop a model of care that was integrated within and adapted to the existing health structures, taking into account the lack of medical doctors in Rwanda at that time. The program was planned for 5 years, with potential extension to other parts of the country according to the needs. Building on the experience of MSF ARV programs launched since 2000-2001 in Kenya and South-Africa, the aim was to provide comprehensive care through a continuum of care, by providing medical and psychosocial care at various levels starting from the community level, towards health center (HC) and hospital level. Access to care was a central issue, with the program mainly reaching out towards the most excluded and stigmatized people, and aiming to reduce barriers to their care. The scope of the program included IEC, VCT/PMTCT, counseling services and psychosocial support, family-planning, OI prophylaxis and treatment, hospitalization and ART. The whole package of care was provided free of charge. In addition to traditional prevention activities, the program hoped to have an indirect positive impact on prevention efforts by reducing the stigmatization of PLWHA and through IEC activities within the ART program, linked to the community.

² CNLS Strategic Plan 2002-2006 (p83-87; p90-93)

First phase: organizing care at the various levels (2002-2003)

The HIV program started in April 2002 at three levels: with the Home Based Care (HBC) program, in two health centers (Kimironko and Muhima HC) and in Muhima district hospital. With the latter being transformed into a maternity service, Muhima HC was replaced by Kinyinya HC in 2003.

1. Community-based: home-based care program (HBC)

The objectives of the HBC program were to increase the access and quality of medical care for PLWHA in need and provide social support for and improve the quality of life of severely affected PLWHA. Nine HIV/AIDS associations, mainly working on solidarity and social issues, were selected to join the efforts. Volunteers were selected and trained in medical and psychosocial care of PLWHA. Through their knowledge of their area, bed-ridden people were approached, HIV-testing was discussed and medical care was provided with support of nurses on the field. Severe cases were referred to the health centers or were given palliative care.

The role of MSF in the HBC program was limited to

- training of the volunteers and provision of basic equipment and incentives
- organization and follow-up of medical activities through field nurses
- ensuring the link to the health centers and care there
- negotiating nutritional support (WFP)
- capacity building of the associations: logistics; organization; material

All PLWHA had the chance to join one of the associations, after which they got the support of a trained and supervised volunteer, providing regular visits at home. The volunteers provided domestic help, participated in basic daily nursing of patients, followed-up the adherence to treatment and gave psychosocial support to the patients and their families.

The first field activities started in July 2002. By December 2004, around 120 volunteers were active, supported by 3 field-nurses. Each volunteer followed between 4-10 people. From 2002 to 2004, 1450 patients were reached through the associations, with 370 followed at home.

The HBC-program has played an important role in fighting isolation and stigmatization. The volunteers, serving as positive role-models of people living with HIV, helped to make HIV discussable within the community and to raise issues like testing of the partner and children.

With the roll-out of ART, the number of patients requiring palliative care diminished dramatically. As the capacity of the associations increased, MSF support was gradually reduced. It ended in 2004 and was redirected towards the health centers, where the launch of the ART program had significantly increased the need for a psychosocial support program.

Table 1. Chronogram of the HIV/ART program (2002-2007)

1. Organizing care at multiple levels (4/2002- 9/2003)

- Home based-care program
- Health center-based care: Kimironko Health center (KMK); Muhima Health center (later on Kinyinya HC (KNN))
 - Construction and rehabilitation works
 - Launch of VCT/PMTCT and basic HIV care
- Hospital-based care: Muhima District hospital (KNN medical unit later on)
- Psychosocial emphasis: collaboration with MSF mental health program

2. Introduction of Medical Care, ART and capacity building (10/ 2003-12/2004)

- Launch of ART upon arrival of MD: KMK (10/2003); KNN (01/2004)
- Capacity building:
 - investment in nurse-based care (skills-building)
 - building hospitalisation capacity in KNN
- Psychosocial emphasis:
 - discussion and support groups in the HCs
 - training on psychosocial impact of HIV (including children's' issues)

3. Scaling-up (2005)

- Involving nurses in care with continuous medical training and supervision
- Launch of community support groups
- Psychosocial emphasis: children psychosocial support program

4. Consolidation and increased autonomy of the HCs (2006-2007)

- Further training for the entire health care staff
- Addressing long-term issues of the ART program: toxicity, adherence,...
- Training of HC staff in organizational aspects: stock-keeping, reporting,...
- Autonomy for community support groups

5. Hand-over of the project (2007)

2. Health-center based care: Kimironko and Kinyinya HCs

Kimironko HC is an urban state run health center with a catchment area of around 25 km² covering a population of about 75 000 people. Kinyinya HC is a semi-rural health center, located at the outskirts of Kigali with a small local population.

Initially, support was given by MSF-B to the health centers in terms of renovating and constructing buildings, sponsoring the care and medications for the HIV positive patients and providing financial incentives to the health-center staff. Training sessions for the nurses in diagnostic skills and treatment of OIs due to HIV were organized, and an HIV consultation process for OI prophylaxis and treatment was put in place. In collaboration with TRAC, the VCT and PMTCT services were launched. The activities in the HCs were aligned with the HBC and IEC activities. Overall, the first phase of the program consisted of building the infrastructure and capacity within the HC to provide basic HIV care.

3. Hospital-based care

With Muhima turned into maternity service for the CHUK, no district hospital existed in Kigali at that time. Given the urgent need for additional hospitalization capacity, activities were transferred from Muhima to Kinyinya health center, with the aim to transform it into an «upgraded» HC, accepting patients from the whole of Kigali, while awaiting the construction of the district hospital. This relatively large health center, that had been functioning as district hospital more than a decade before, was at that time only using 30 % of its operational capacity. Apart from the VCT/PMTCT and HIV care program, the capacity of KNN HC was expanded with 45 «medical» beds, a laboratory, an upgraded pharmacy and a medical doctor. On indication, transfer and follow-up of patients to the university hospital was organized.

4. Political commitment

In this first phase, basic care was organized within the existing (health) structures, in close collaboration with the district health services. It is in this same period that the strong political commitment at the national level towards HIV was evidenced, setting the stage for the scaling-up of the national ART program.

Second phase: antiretroviral treatment and capacity-building (2003-2004)

By the end of 2003, an MSF doctor, later joined by a district doctor, was sent to each HC, to launch the ART program. From the onset, a strong emphasis was put on psychosocial support and treatment for children and pregnant women. A lot of time and energy was invested in theoretical and practical training, gradually training all staff in HIV care (see below). Responding to the increased work-load, the district services substantially increased staffing at the health centers.

Table 2. Support provided by MSF

Logistics

- › construction, expansion and rehabilitation works
- › expansion of the laboratory service
- › provision of transport (patients, samples, drugs)
- › expansion of the pharmacy: drugs and organizational support
- › accountancy services
- › data monitoring/reporting

Training and supervision

- › nurse capacity building: theoretical and bed-side training
- › supervision and mentoring by the physician

Psychosocial support

- › psychosocial team: psychologist/IEC responsible
 - counseling caregivers and children
 - support and discussion groups
 - individual psychological follow-up
 - training of staff on psychosocial support
- › nutritional support, community involvement
- › community support groups

Financial/Human resources

- › financial incentives for staff for extra work in training and scaling-up
- › training and increased involvement/responsibility

Collaboration

- › negotiated support from World Food Program and the Global Fund

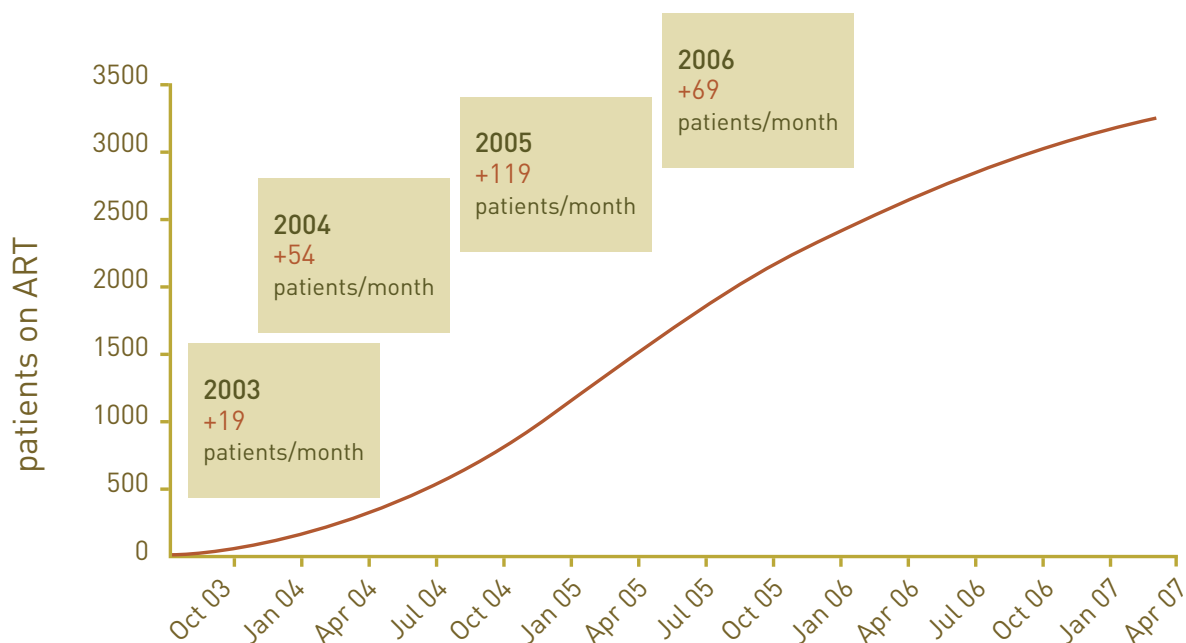
Technical support (national HIV program)

- › participation in technical working groups, workshops and conferences

By the end of 2004, the antiretroviral program in the HCs was well-functioning, the hospitalization capacity had increased and a psychosocial support program was in place, including adult and children support and discussion groups. At that time, 5000 PLWHA had entered the program (KMK and KNN together) and 737 patients had been started on ART, 15.5 % of them children.

Third phase: scaling-up of the ARV program (2005)

With the high number of patients in (urgent) need of ARV and the limited number of services available at the launch of the project, the program aimed for a rapid scaling-up, within a vertical program. In 2005, the number of patients started on ART (in both HCs combined) increased to 119/month and by the end of the year 2089 patients received treatment (see Figure 1). As reflected in the mapping of the localization of our patients, Kinyinya was accessible for a large part of the city of Kigali (see Figure 2).



Several factors have facilitated the scaling-up within a health-center based program:

Capacity building: capitalizing on nursing resources

The dramatically increased work-load during scaling-up implied increased involvement of nurses in providing HIV care. From the onset, skills-building of the (nursing) staff was emphasized. Ongoing training and supervision were provided by a combination of MoH and MSF physicians, who were ultimately responsible for the medical care. Nursing staff received theoretical and bed-side training in comprehensive HIV care and ART, gradually increasing their knowledge and confidence. The approach towards managing side-effects of ARVs was standardized through basic protocols, and indications for referral to the physician were clarified. As the program matured, physician involvement decreased gradually. Given the emphasis on psychosocial support and pediatric issues from the launch of the program, HC staff were sensitized to these subjects at an early stage, and their skills improved through practical training.

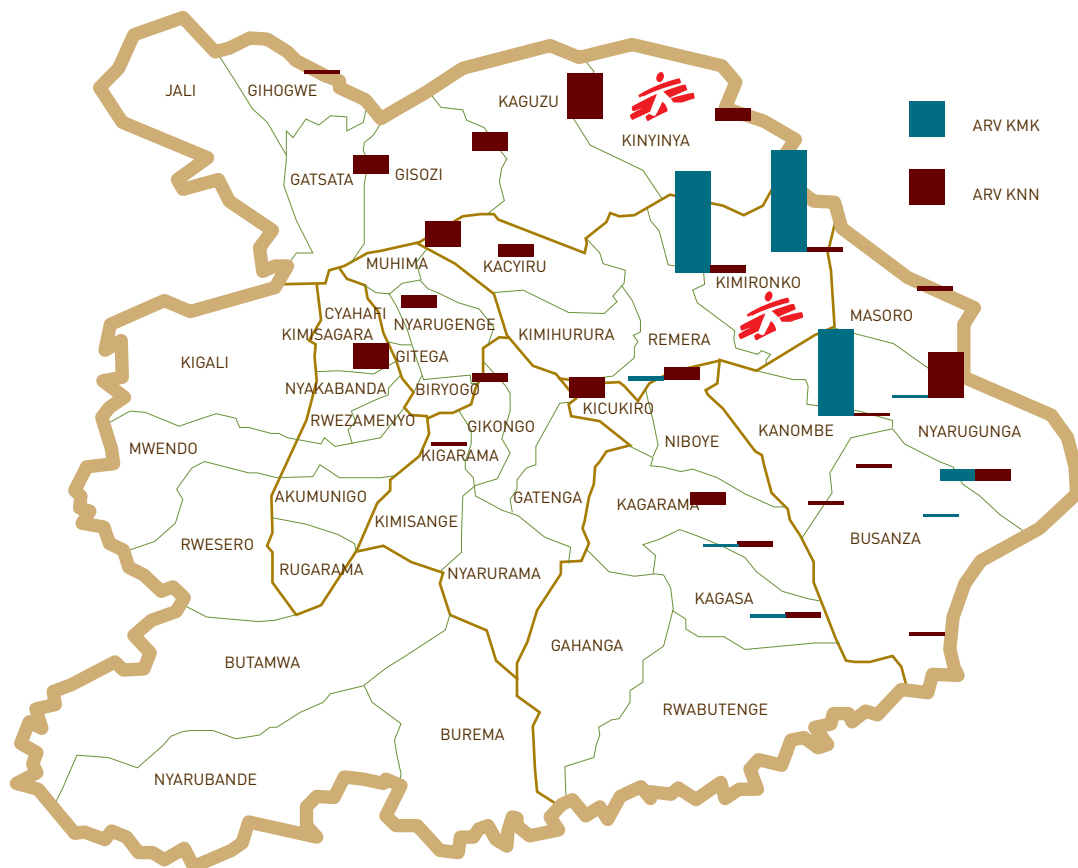


Figure 2. Geographic distribution of patients on ART in KNN and KMK (2005)

The increase in government health care staff at the health centers has been a critical factor to meet the increased demand. Whereas the KMK health center had 7 trained nurses before the launch of the HIV program in 2002, this had increased to 28 by the end of 2004, when scaling-up began. Overall, around 40-50 % of the entire staff's time was dedicated to HIV care. Table 3 summarizes the staffing (and who provided the salaries) for the HIV care program by 2005. Retention of the government staff was facilitated by performance-based financial incentives, continuous training and promotion of responsibilities for the staff in the program. There was considerable energy and time spent on training and supervising the nurses, especially early in the program, but in our experience, this investment in capacity-building paid off in the end. When scaling-up began, the program was running smoothly and the role of the MSF team decreased gradually.

Table 3. Human resources for HIV care/health center (2005)¹

HIV care service	MoH	GF	MSF	Total
OI consultation (nursing staff)	3			3
ARV consultation (nursing staff)	2			2
Pharmacy ARV (nursing staff)	1		0.5	1.5
Pharmacy OI (nursing staff)	2			2
VCT/PMTCT/ANC (nursing staff)	4			4
Hospitalization (nursing staff)	2			2
Social assistant	2		1	3
Follow-up of referrals (nursing staff)			0.25	0.25
Psychologist			0.25	0.25
IEC			0.25	0.25
MSF MD			1	1
District MD			1	1
HIV lab-technician		0.25	1	1.25
Receptionist		2		2
Accountant		1		1
Data entry clerk			1	1
Total	16	3.25	6.25	25.50

¹ With differences in HR between KNN and KMK HC, the numbers give an average estimate

Partnerships

Through the Global Fund to fight AIDS, Tuberculosis and Malaria (GF), support was provided at various levels including construction work, contributions to the common basket for ARVs and CD4 counts, nutritional support, human resources and material. This funding helped substantially in scaling-up the activities in the HCs. The World Food program provided additional nutrition support for the PMTCT and ART program. The common basket system, launched at the end of 2004, further facilitated scaling-up activities of ART implementers. As mentioned above, the results within this program reflect the successful scaling-up of the national program, with the support of all the different partners.

Community-based support groups/Community involvement

While the psychosocial support program was localized in the HCs when the ART program was started, this was gradually moved to the community by the launch of community support groups, leading to decreased work-load in the HC and engaging the community in care. The idea of these groups was for PLWHA to organize themselves into small groups, consisting of around 20 people living in the same area, promoting solidarity and breaking down discrimination and social isolation. In addition, this maintained a link with the community through the group leaders, identified by their colleagues. They were invited regularly to report on their activities, received continuing training and support and were involved in IEC and tracing of lost to follow-ups.

Whereas it can be challenging to organize home-visits for all patients within a HIV program, these visits have played an important role to improve the individual care for PLWHA and to build links with the community.

Fourth phase: solidifying the services and increasing autonomy (2006)

With the scaling-up of ART at the national level, the influx of patients into the ART program in KNN and KMK gradually leveled off. During 2006, the services/activities were solidified and a strong emphasis was put on continuous training, aiming to have all the nurses trained in ART care and rotating through the different HIV services. This facilitated integration of the HIV program within the other health center services and sensitized the staff in all service areas to the HIV issues. This was a distinct advantage over having only a few specially-trained HIV nurses providing limited coverage. Specific attention was given to ongoing problems like long-term toxicity and adherence. At the same time, the support provided by MSF could gradually be diminished and the HCs, linked with the newly built district hospital and supported through

the national program, gradually became more autonomous in all the aspects of the ART program.

Table 4. Scaling-up of HIV services at the KMK and KNN health centers¹

HIV program	2002	2003	2004	2005	2006
VCT					
Tested	1435	3187	6659	5754	5759
% HIV+	23.0	29.1	36.1	30.0	20.4
PMTCT					
Tested	1148	2458	3171	3727	3853
% HIV+	13.1	12.8	14.5	14.8	11.1
Consultation HIV					
Total	486	6814	33.569	45.609	39.100
OI	486	6660	25.419	30.535	23.290
ARV	-	154	8150	15.047	15.810
Total on ARV	-	58	733	2089	2970

¹ Data for both health centers combined

TREATMENT OUTCOMES OF THE PATIENTS ON ART

Between October 2003 and December 2006, 2970 patients received ART through KNN and KMK health centers. With data analyzed by July 2007, all patients had been on treatment for at least 6 months.

Table 5. Characteristics of patients started on antiretroviral treatment (n=2970)

Age at start (years) ^a	35 (29 – 41)
Sex (male/female) ^b	917/2053 (31/69)
Clinical WHO-stage (n=2957) ^b	
WHO stage I	193 (6.5%)
WHO stage II	839 (28.4%)
WHO stage III	1673 (56.6%)
WHO stage IV	252 (8.5%)
Baseline weight in kg (n=2664) ^a	54 (46-60)
Baseline absolute CD4 counts (n= 2753) ^a	162 (94-231)
ART regimen ^b	
d4T/3TC/NVP	2467 (83.1%)
d4T/3TC/EFV	223 (7.5%)
AZT/3TC/NVP	199 (6.7%)
AZT/3TC/EFV	63 (2.1%)
Other	18 (0.6%)
Time on ART (years) ^b	1.8 (1.0-2.3)

a Values are expressed as median (Inter Quartile Range (IQR))

b Values are expressed as N (%)

The baseline characteristics are described in Table 5. The median age at start was 35 years, 69 % were female. The majority of patients were started with a WHO stage III/IV, and a median baseline CD4 count of 162 cells/ μ l. The generic fixed-dose combination of d4T/3TC/NVP was

the most frequently used treatment regimen. The median time on ART was 1.8 years, with 74 % taking ART for more than 1 year.

By July 2007, 2457 patients were still receiving treatment through the program. Two hundred and eleven have been transferred out (7.1 %), 146 died (4.9 %). Overall, 156 patients (5.3 %) have been reported lost to follow-up, mainly patients previously receiving care in KNN. Kaplan-Meier analysis showed that 93.6 % were still alive at 3 years of ART. With failure defined as death or lost to follow-up, 86.9 % of patients were still in care by 3 years (Table 6). Clear improvements in CD4 counts and weight were seen. Viral load was < 40 copies/ml and < 400 copies/ml for 83.6 % and 89.4 % of the patients respectively. Currently, 19 patients have been started on second line therapy.

Table 6. Outcomes of the patients on ART

Started on ART	Active cohort	Transferred out	Death	Lost-to FU ^a	
2970 (100 %)	2457 (82.7 %)	211 (7.1 %)	146 (4.9 %)	156 (5.3 %)	
	Baseline	6 mo	12 mo	24 mo	36 mo
Survival (%) ^b	100	97.1	96.1	95.0	93.6
In care (%) ^c	100	94.8	92.4	89.8	86.9
CD4 count (abs)	162	261	286	336	352
IQR	(94-231)	(173-397)	(185-435)	(218-500)	(210-559)
Weight gain (kg)	-	+ 1.5	+ 1.9	+ 2.0	+ 3.0
IQR	-	(-0.5;+3.6)	(-0.8;+4.7)	(-1.5;+5.4)	(-1.0;+7.0)
Viral load	Months on ART	< 40 c/ml	< 400 c/ml	< 5000 c/ml	
(N=1425)	17 (IQR 14-24)	1191 (83.6%)	1274 (89.4%)	1336 (93.7%)	

a Defined as not coming to their last scheduled visit for more than 2 months

b Kaplan-Meier survival estimates: failure defined as death

c Kaplan-Meier survival estimates: failure defined as death or lost to follow-up

Whereas, in the early years of the program, very few patients were lost to follow-up, their numbers had increased significantly from 2006 on (of all 156 patients lost to follow-up over the 4 years, 68 % of these occurred in 2006-2007). Around 30 % of these were patients on treatment

for > 1 year, and had good clinical and immunological outcomes, making mortality as reason for lost to follow-up less likely. Feed-back from the community support group leaders point out that a substantial number are still under care, but have moved to another center, often closer to home. However, 43 % of all patients lost to follow-up were on ART for < 6 months. Since the first few months on ART have a relatively high mortality rate, a certain number of these cases can be expected to be unreported deaths.

Toxicity of the stavudine-based first line ARV regimens

With the high number of patients started on a stavudine-containing regimen, the assessment of long-term complications of ART was part of the routine medical follow-up. A standardized approach was developed for diagnosis and management of mitochondrial toxicities (symptomatic hyperlactatemia/lactic acidosis (SH/LA), lipoatrophy and neuropathy)

Table 7. Severe toxicity with d4T and/or nevirapine-containing first-line regimens

Drug related toxicity	Events (%)	Rate /1000 py	Patients with toxicity-related drug substitution (%) ^b			
			6 mo	12 mo	24 mo	36 mo
Nevirapine (n=2667)						
Toxicity all	170 (6.4)	39	6.0	6.4	6.9	7.2
Skin toxicity	131 (4.9)	30	4.9	5.1	5.3	5.4
Liver toxicity	40 (1.5)	9	1.1	1.3	1.6	1.8
Stavudine (n=2694)						
Toxicity all	448 (16.6)	107	2.6	8.6	22.5	35.4
Neuropathy	206 (7.6)	49	2.3	6.0	9.8	12.1
SH/LA ^a	85 (3.2)	20	0.2	2.0	4.5	6.0
Lipoatrophy (La)	180 (6.7)	43	0.0	1.0	9.2	19.8
SH/LA and/or La	248 (9.2)	59	0.3	2.6	12.9	24.2

a Symptomatic Hyperlactatemia/Lactic Acidosis

b Kaplan-Meier estimates, time to first severe toxicity (ie requiring treatment change) at specified months on ART

Of the 2694 patients that started on a d4T-containing first line regimen, therapy was changed due to d4T-related toxicity for 448 patients (16.6 %). In total, 7.6 % of the 2694 patients changed for severe neuropathy, 3.2 % for lactic acidosis and 9.2 % for moderate/severe lipoatrophy. Whereas in the first year therapy changes were mainly due to neuropathy, lipoatrophy was the most frequent long-term side-effect (Figure 3).

Nevirapine-related toxicity was less frequently seen, mostly occurring within the first months on ART. For the 2667 patients starting on a nevirapine-containing regimen, therapy was changed due to NVP-related toxicity for 170 patients (6.4 %), mainly presenting with skin toxicity (Table 7).

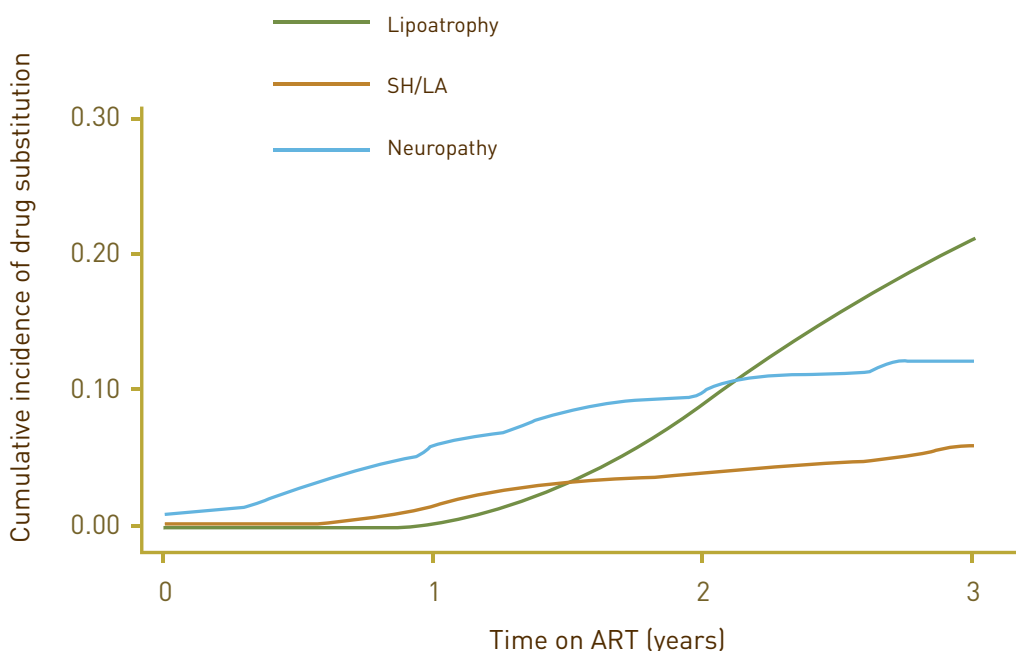


Figure 3. Substitution of stavudine due to drug toxicity

Monitoring ART: discordant treatment responses

Whereas on average the CD4 count increases when viral replication is inhibited by ART (and vice versa), considerable variability at the individual level has been documented. In particular, discordant responses (ie opposite immunological and virological responses) have been frequently observed, both in high and low-income countries.

Most of the viral load results came from adult patients. With virological success defined as a viral load < 40 copies/ml (> 1 year on ART) and immunological success as an increase in CD4

count > 50 cells/ml from baseline at the time of viral load measurement, we observed combined immunological and virological success in 65.6 % of cases and combined failure in 4.7 % of the adult patients (concordant responses), see Table 8. Twelve percent of all adult patients had immunological success despite a detectable viral load. Importantly, virological suppression (success) without immunological recovery was seen in 17.7 % of patients (discordant responses in 29.7 %). This type of treatment response has been frequently observed in both high and low-income countries and remains poorly understood. With virological success defined as a viral load < 1000 copies/ml, discordant responses were still seen in 24.7 %. Interestingly, the CD4 response for children on ART differed to some extent: almost all showed an increase in CD4 count, even when having active viral replication.

Table 8. Virological-immunological outcomes on ARV treatment (n(%)) ¹

Threshold	ADULTS		CHILDREN		Total
	VL < 40	VL ≥ 40	VL < 40	VL ≥ 40	
Immunological success	661 (65.6)	121 (12.0)	95 (68.8)	32 (23.2)	909 (79.4)
Immunological failure	178 (17.7)	47 (4.7)	7 (5.1)	4 (2.9)	236 (21.6)
Total	839 (83.3)	168 (16.7)	102 (73.9)	36 (26.1)	1145 (100)

¹ Viral load was routinely performed after at least 1 year of ART

The frequent occurrence of discordant responses illustrates the limitations of the CD4 count for monitoring the treatment response. If no viral load testing had been available, a large number of patients with immunological failure, despite virological success, might have been started on second-line ART incorrectly. In contrast, since there is no other proven strategy to enhance immune recovery and these patients are considered to have a relatively favorable prognosis despite the limited immune recovery, they should be continued on their current regimen. On the other hand, some patients have a steady increase in CD4 count despite a detectable viral load. They run the risk of developing and transmitting drug-resistant virus.

PROVIDING ANTIRETROVIRAL TREATMENT FOR CHILDREN

By the end of 2006, 315 children (≤ 15 years) had been started on HAART, constituting 11 % of the total ARV cohort. With a very low rate of mortality and lost to follow-up, the overall outcomes are even better than for adults.

Psychosocial support as key to successful ART-scaling up for children

Since 2000, the MSF mental health program in Rwanda had been working with women who were victims of violence during the genocide. A substantial number of them were HIV-infected, and so the issue of HIV infection in their children with associated problems of testing and disclosure was well known by the team. The need to address psychosocial issues in HIV care resulted in a collaboration between the mental health team and the HIV program. We believe that this focus on psychosocial issues for PLWHA in general and for children in particular from the onset of the program has been a key factor for the successful scaling up of the paediatric HIV/ARV program (Table 9). By gradually adapting over the years to the problems encountered within the program, the current psychosocial program for children took form and several lessons were learned.

VCT for children: overcoming barriers by addressing the psychosocial needs of caregivers

From the onset, the need of the patients to express themselves on issues concerning HIV was evident. Caregivers themselves were distressed by their own (recent) HIV diagnosis. They were reluctant to discuss testing of their children, since they felt guilty, fearing the reaction of the child to their own and the child's disclosure, and being worried about the health and future of the child. From the start of the program, support and discussion groups were organized for the caregivers, designed to increase acceptance of their own HIV positive status, a prerequisite for discussing testing of their children. In addition, prior to starting ARVs, individual in-depth counseling sessions were held to discuss testing of children in detail. Subsequently, the health center-based support groups were transformed into community-based support groups, within which issues like testing of partners and children were discussed amongst peers.

Table 9. Psychosocial aspects of the pediatric HIV program

Caregiver-centered approaches

- organization of discussion/support groups – at health center and in community
- family-based approach to identify eligible children
- individual counseling (pre-ART)
- psychosocial issues addressed in follow up care

Child-centered approaches

- adapted counseling for children for disclosure and ART (child-adapted tool)
- designated days for children's clinics
- child support groups
- integrated care, including disclosure, with their caregivers

Health-staff centered approaches

- discussion groups for health care staff
- training on psychosocial implications of HIV
- practical training by psychosocial team (check-lists,...)
- supervision and mentoring

Building confidence: training health care staff on child-specific issues of HIV

Early in the program, several barriers were observed for the medical staff to test children, essentially related to a 'fear of the result'. There seemed to be a lack of confidence and skills in discussing an HIV-positive test with the parents and the children. Consequently, training sessions were organized for the medical staff. Apart from formal training on counselling and the psychosocial aspects of HIV in general, discussions with the health care staff were organised to address the issue of testing of children (why, when, how?). Through these sessions and discussions, medical staff progressively felt more convinced of the need and confident in how to test children of HIV-positive adults.

Adequate disclosure: prerequisite for good adherence

In our experience, adults and children were generally not well prepared when they came for testing of the child. Few children knew exactly why they were there, had little knowledge of HIV and rarely knew about the status of the caregiver. However, the children preferred to be informed about their and their caretaker's status from the caretaker and felt cheated when they were not told the truth. Consequently, we tried to involve the caretaker as much as possible during disclosure. Caretakers were first counselled on why it was important to talk openly with their children about HIV, why their active participation was important for the child, how the child might react, and how they should respond to questions. During disclosure, we tried to have the caregiver explain their and the child's status, supported by the counsellor. The use of a booklet explaining HIV provided a common language around HIV (Figure 4).

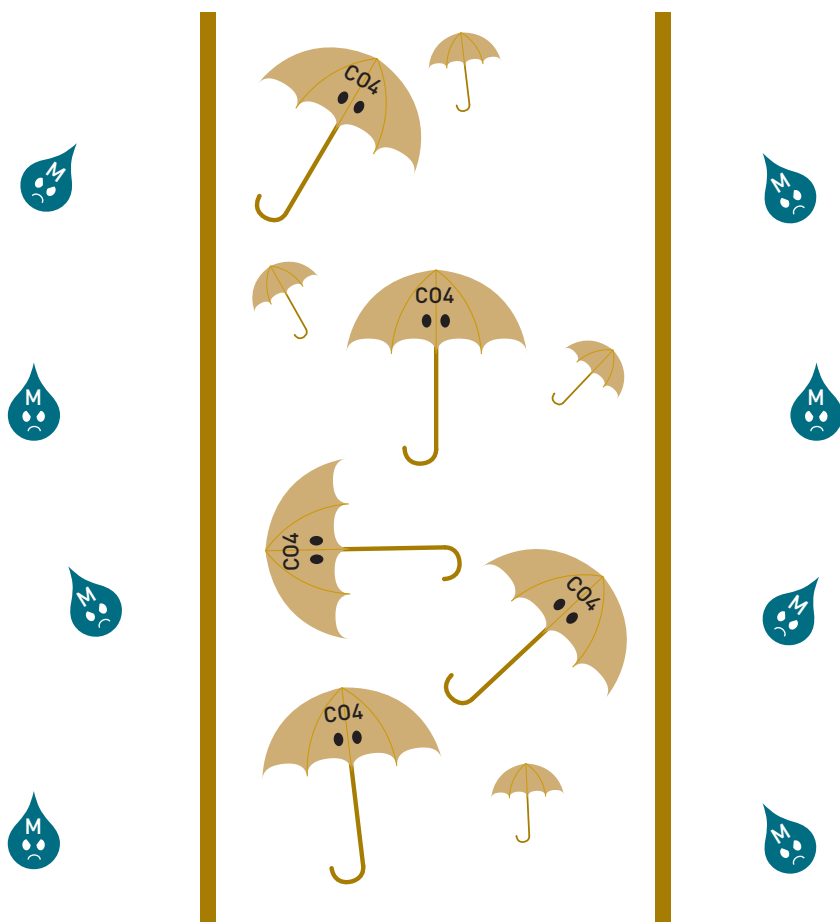


Figure 4. Picture from the tool used to explain HIV/AIDS to children.

The CD4 cells (umbrellas) protect against the rain (diseases).

Testing of children was done on a separate day, ensuring that enough time was available for every child, making the environment/event more child-friendly and facilitating on-site training of health care staff in counseling of children. Individual disclosure was considered when the child was above 6 years of age.

Children support groups - active involvement of the children

To increase the acceptance of the HIV diagnosis and to address the psychosocial well-being of the children after testing, support groups for children were organized by the psychosocial team. These groups created an environment where the children could express themselves, raise their questions and worries and develop a positive attitude towards life with HIV. Most of the issues discussed were raised by the children themselves and reflected their deeper feelings: HIV (what, why and how?), life and death, sexuality, manipulation in the parent-child relationship and discrimination. This was done in several ways including open discussions, games, fairy-tales and drawings



© Julie Rémy

For the time being, around 18 groups with 200 children have been organized, meeting every 4-6 weeks. These groups were open to all children, irrespective of taking ART, and were organized according to age (7-11; 12-14; 15-18). Caregivers were invited to participate in some of these sessions to ensure they were aware of the children's knowledge and feelings towards their diagnosis. If individual problems were identified through the groups, individual follow-up was offered. More recently, the child support groups were combined with the medical consultation, while at the same time a support group for caretakers was taking place.

Treatment outcomes of the children on ART

Over a period of more than 3 years, 315 children were started on ARVs, with a median age of 7.2 years (Table 10).

Table 10. Characteristics of children started on antiretroviral treatment (n=315)

Age at start ^a	7.2 (4.5 – 10.4)
< 3 years ^b	38 (12%)
3 – 4.9 years ^b	51 (16%)
5 – 14.9 years ^b	226 (72%)
Sex (male/female) ^b	157/158 (50/50%)
Clinical WHO-stage ^b	
WHO stage I	43 (13.7%)
WHO stage II	145 (46.0%)
WHO stage III	115 (36.5%)
WHO stage IV	12 (3.8%)
Weight for age (z-score) (n=293) ^a	-1.9 [-3.0;-0.9]
Baseline CD4 count % (n=282) ^a	14% (9-18)
< 15 % ^b	158 (56.0%)
15-25 % ^b	118 (42%)
> 25 % ^b	6 (2.1%)
Baseline absolute CD4 counts (n= 302) ^a	345 (229-572)
ART regimen ^b	
d4T/3TC/NVP	281 (89.2%)
d4T/3TC/EFV	6 (1.9%)
AZT/3TC/NVP	19 (6.0%)
AZT/3TC/EFV	9 (2.9%)
Time on ART (years) ^a	2.0 (1.2-2.6)

^a Values are expressed as median (Inter Quartile Range (IQR))

^b Values are expressed as N (%)

Approximately 25 % were less than 5 years of age, 7 were started before the age of 18 months. Sixty-one percent were in WHO stages I and II at treatment initiation with a median baseline CD4 count of 14 %. The vast majority started on d4T/3TC/NVP, with adult FDC tablets used for 282 children. The remaining 33 commenced syrup formulation. By the time of analysis, all but five had changed to tablets. The median time on ART was 2 years.

Clinical, immunological and virological outcomes (Table 11)

To date, 84 % (265) are still alive and being followed up in the clinics. Thirty (9.5 %) have been transferred to another ART program. Eight (2.6 %) have died, only 12 (3.8 %) were lost to follow-up. Of the 8 deaths, 2 were clearly not linked to HIV. Kaplan-Meier estimates showed a probability of remaining in care of 94.7 % and 92.9 % at 12 and 24 months respectively (with failure defined as death or lost-to follow-up). CD4 results and the Weight-for-age Z-scores (WAZ) all showed progressive improvement over the treatment interval. Most viral load results were obtained between and 15 and 23 months after treatment commencement and were available for 88 % by 18 months (n=174). Viral load was less than < 400 copies/ml in 82.8 % of children and showed satisfactory viral suppression in 86.8 %.

Table 11. Clinical, immunological and virological outcomes

Started on ART	Active cohort	Transferred out	Death	Lost-to follow up ^a	
315 (100 %)	265 (84.1 %)	30 (9.5 %)	8 (2.6 %)	12 (3.8 %)	
	Baseline	6 mo	12 mo	24 mo	36 mo
Survival (%) ^b	100	96.8	94.7	92.9	92.9
N	315	297	258	152	40
CD4 count					
< 5 years (%)	16	30	32	33	35
IQR	(12-19)	(23-35)	(26-34)	(28-36)	(28-40)
N	84	59	48	39	7
≥ 5 years (%)	13	25	26	29	29
IQR	(9-17)	(18-29)	(21-32)	(24-34)	(19-33)
N	198	175	117	80	24
WAZ	-1.9	-1.6	-1.6	-1.5	-1.5
IQR	(-3.0;-0.9)	(-2.6;-0.8)	(-2.6;-0.7)	(-2.5;-0.6)	(-2.7;-0.6)
Viral load	Months on ART	< 40 c/ml	< 400 c/ml	< 5000 c/ml	
(N=174)	18 (15-23)	127 (73.0%)	144 (82.8%)	151 (86.8%)	

a Defined as not coming to their last scheduled visit for more than 2 months

b Kaplan-Meier survival estimates: failure defined as death or lost-to follow-up

For 13 children among whom viral loads were detectable, a second sample was available after adherence counseling. The median time from first viral load collection to the repeat sample was 5.8 months (IQR 2.7-8.8). Four out of the 13 positive viral loads became undetectable and one decreased significantly. Two children were switched to second line treatment. For the remaining children, adherence problems were still being addressed or criteria to switch were not met.

We only had complete data on clinical attendance as an indirect measure of adherence to therapy. Allowing a delay of up to two days (accounting for the security stock), we defined excellent, good and poor adherence as being punctual for > 95 %, 80-95 % or < 80 % of the visits respectively. Poor adherence was observed for 5 % of the children, with the majority having excellent (49 %) or good (46 %) adherence.

Safety and tolerance

Drug toxicity resulted in therapy changes for 26 children (8.3 %). Toxicity was mainly related to NVP, requiring treatment change to EFV (n=24). Sixteen cases were due to grade 3-4 skin manifestations of which two were Stevens-Johnson syndrome occurring within 1 month of therapy. Both have recovered. Five early changes (within 3 months) were made for severe hepatitis, 4 children showing clinical signs, 1 child having asymptomatic grade 3 hepatotoxicity. An additional three children were changed late (median 9 months) due to symptomatic hepatitis. We observed an additional 11 children with grade 2 and 3 with grade 3 liver toxicities, mostly occurring within the first months of ART. In general, these were transient and well tolerated and did not require treatment change. Stavudine was changed for one child with severe neuropathy; two cases of lipoatrophy were reported (one requiring treatment change). No lactic acidosis or anemia requiring treatment change was observed. In contrast, a high occurrence of lactic acidosis and lipoatrophy was observed within the adult population.

CONCLUSION AND LESSONS LEARNED

This program offers reassuring evidence that health center-based ART programs can provide high quality care and suggests a way forward in scaling up ARV treatment. A combination of factors has probably contributed to the overall good outcomes of the program.

The localization in **health centers** and the link with the community has facilitated access and acceptability of testing and care. In addition, the program aimed to minimize barriers to care and to address the various needs of PLWHA by providing free **comprehensive medical care** (including nutritional support and OI treatment and prophylaxis) and through a strong **psychosocial emphasis** within a family-based approach. The **community** has progressively played an increased role in IEC activities, adherence and psychosocial support. A lot of energy was put into **training and mentoring of the nursing staff**, however, this allowed fast scaling-up to

occur and facilitated integration of the HIV care program into the health center services. This experience shows that an ART program relying extensively on trained nurses can maintain excellent outcomes during scaling-up, given investment in human resources, training and supervision.

The combination of all these factors also helps to explain the high number of children being tested and their overall good treatment outcomes. This experience shows that providing pediatric ART within a health-center based program can be very effective and safe. It also demonstrates that there is a significant burden of HIV illness in children, besides that from PMTCT sources, that is readily identifiable through their HIV+ caregivers, given a program that makes it a goal. This requires that psychosocial support programs, addressing both the needs of the children and caregivers, are considered an essential part of HIV/ART programs.

We think that this kind of program could be replicated in other settings and is sustainable. The success of the program depended, to a large extent, on the commitment of the national services and the success of the national HIV program. External support of this HC-based program by MSF was targeted at certain areas such as logistics, training and psychosocial support. This support decreased gradually over the last year, with standards of care remaining high and MSF is handing over the project to the Ministry of Health at the end of 2007.

MAJOR REMAINING CHALLENGES

1. Although excellent clinical and immunological responses have been observed on current WHO first-line regimens, the stavudine-based regimens are associated with important toxicity. This could limit the future success of these regimens and calls for better tolerated ones.
2. A significant number of patients can be expected to experience treatment failure within the near future, pointing out the need for a widely available, affordable and well-tolerated second-line therapy. Access to viral load testing is important to correctly decide on the need for second-line treatment.
3. Long-term adherence and acceptance problems can be expected (in particular for adolescents), calling for close follow-up and a pro-active approach.
4. The long-term success of this program will require (amongst others) several factors:
 - a. long-term political commitment
 - b. ongoing financial resources and investment in human resources
 - c. continuous and increasing community involvement
 - d. low barriers of access to care
 - e. strong focus on the psychosocial aspects of HIV
 - f. special attention/support for children



Rue Dupré 94
1090 Brussels
Belgium
info@brussels.msf.org