Providing HIV Services including Antiretroviral Therapy at Primary Health Care Clinics in Resource-Poor Settings:

The experience from Khayelitsha

ACTIVITY REPORT

2003

Médecins Sans Frontières (MSF)

Infectious Disease Epidemiology Unit,
School of Public Health and Family Medicine, University of Cape Town

MEDECINS SANS FRONTIERES

UNIVERSITY OF CAPE TOWN

TABLE OF CONTENTS

Introduction

In February 2000 Médecins Sans Frontières (MSF) and the Health Department of the Province of the Western Cape initiated a comprehensive service for persons infected with HIV in Khayelitsha. In May 2001 this site became the first public sector service to provide antiretroviral therapy (ART) in South Africa.

The aim of this project was to show the effectiveness, feasibility and acceptability of treating persons infected with HIV, including the provision of ART, in a primary health care setting. In order to show that it was more affordable to use generic versions of antiretroviral drugs, MSF sought and received a section 21 authorisation of the Medicines Control Council to use generic antiretrovirals in September 2001. The use of generic antiretrovirals started in January 2002.

MSF sought the technical assistance of the Infectious Disease Epidemiology Unit of the School of Public Health and Family Medicine at the University of Cape Town (UCT) to provide support and to evaluate this programme.

This report describes the epidemiology of HIV and development of services in Khayelitsha, including the ART programme, and reports on adherence**,** clinical response, survival and occurrence of adverse events in patients on ART until the end of June 2003.

Evolution of the HIV epidemic in Khayelitsha

The prevalence of HIV is measured by the annual antenatal HIV seroprevalence surveys conducted at public sector services. In Khayelitsha over 95 % of pregnant women are tested for HIV at antenatal clinics as part of the Programme for the Prevention of Mother to Child Transmission (PMTCT). The Khayelitsha, Western Cape Province and National HIV seroprevalence rates for the past 3 years are presented in table 1.

Year	National	Western Cape	Khayelitsha
2000	24.5% (23.4-25.6%)	8.7% (6.0-11.4%)	19.3% (18.0-20.6%)
2001	24.8% (23.6-26.1%)	8.6% (5.6-11.6%)	23.2% (21.1-25.3%)
2002	26.5% (25.5-27.6%)	12.4% (8.8-15.9)	24.7% (22.6-26.8%)

Table1. HIV prevalence in South Africa, Western Cape Province and Khayelitsha district with 95% confidence intervals.

The antenatal seroprevalence rate in Khayelitsha is one of the highest in the Western Cape. As shown in figure 1, the rates in Khayelitsha reflect national levels of infection rather than those of the Western Cape. As the prevalence has increased in the Western Cape overall, the rate of increase has slowed nationally and in Khayelitsha.

Evolution of voluntary counselling and testing (VCT) services

The PMTCT programme was started by the Health Department of the Province of the Western Cape in January 1999 and the first large scale services for VCT were established at antenatal clinics. At the beginning of 2001 most testing was done at these services.

During 2002 VCT services were extended to general primary health care services and in particular tuberculosis, family planning and sexually transmitted disease services. As a result of this increased access, 16 024 people were tested in 2003. Of these 4928 (31%) were found to be infected with HIV as shown in figure 2.

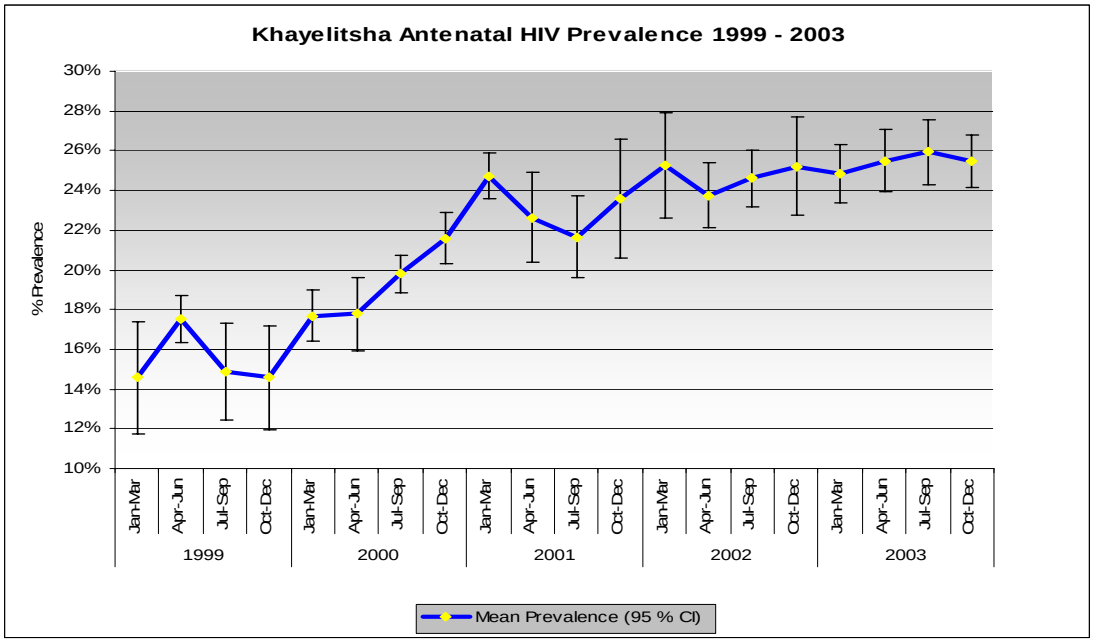
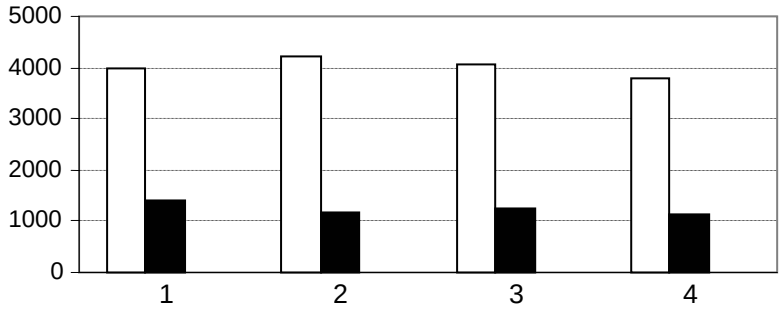


Figure 1: HIV Prevalence rate as measured by the PMTCT programme from 1999 to 2003.



	1	2	3	4
Number tested	3981	4213	4057	3773
Number positive	1416	1157	1232	1123
Percent positive	36%	27%	30%	30%

Figure 2: Number of tests conducted at VCT services and the number of positive tests in Khayelitsha in 2003.

HIV services

In April 2000 a comprehensive service for persons infected with HIV was started at 3 clinics in Khayelitsha. From April 2000 to Jan 2004 there were 5,049 consultations for new patients and 48,097 consultations for follow-up visits. As can be seen in figure 3 the number of consultations has increased from 2,000 per quarter in 2001 to 6,000 per quarter in 2003 (figure 3). In April 2003 the Provincial Department of Health provided 3 additional nurses for these services but this increase in personnel has not been sufficient to deal with the increased numbers. As a result, from the end of 2002 the waiting period for new patients to be seen at the clinics has increased.

An attempt is being made to refer patients in stages I and II to the general primary care services. Since 2002, formal training has been provided twice a year with the objective of developing HIV capacity in all services and fifty nurses from the Khayelitsha district have been trained. Because of shortages of staff and the large number of vacant posts the objective has not been achieved, as the personnel that have been trained have not been allocated to services where HIV-infected patients are seen. Attempts are being made to address this issue.

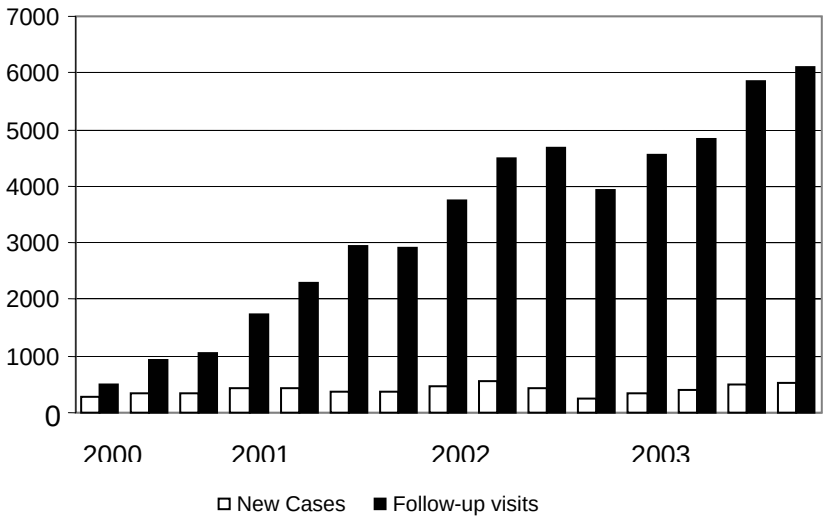


Figure 3: Number of consultations for new patients and number of follow-up visits at 3 HIV services in Khayelitsha April 2000 – December 2003.

Despite the increase in the number of people tested and an increasing number of HIV-infected patients identified, there has not been a corresponding increase in the number of new patients coming to the HIV services. Figure 4 shows the number of new patients seen at HIV services as a proportion of the number of people testing positive for HIV from April 2002 to December 2003 in Khayelitsha.

Pic 1. People waiting for consultation in an HIV/AIDS clinic.

Evolution of HIV treatment entry points

In 2001 many new patients arriving at HIV services had been tested in the PMTCT programme. With the increase in testing in other services, the proportion of patients arriving from the PMTCT programme has decreased and in 2003 more patients coming to the HIV services were tested at the TB, Family Planning, STI and general PHC services (figure 5).

As more patients have come from services other than PMTCT the profile of new patients, in terms of disease advancement, has changed. As can be seen from figure 6 more patients with advanced HIV disease are entering the HIV service than previously, as indicated by the median CD4 cell count of patients coming from referral hospitals and TB services. These patients are generally sicker, are more likely to acquire opportunistic infections and are in more urgent need of antiretroviral therapy. More nurses are required to provide prophylaxis and to treat opportunistic infections and in particular TB.

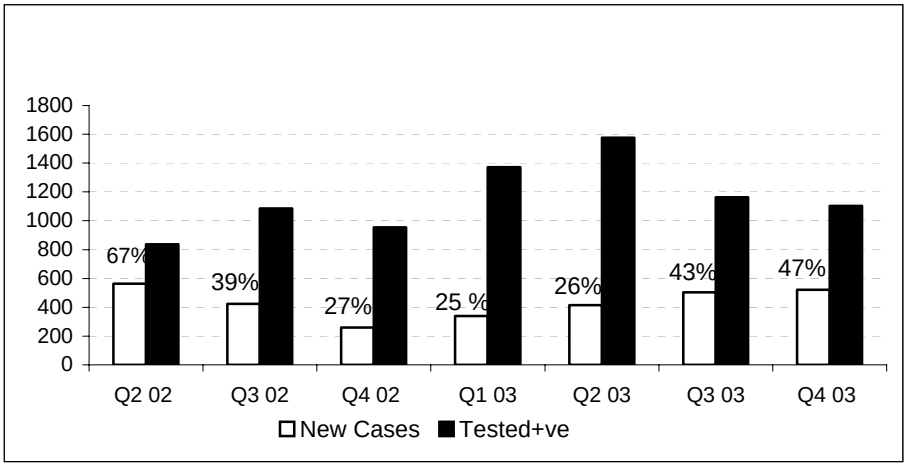


Figure 4. Number of new patients attending HIV services and number of people testing positive for HIV by quarter (from April 2002 to December 2003).

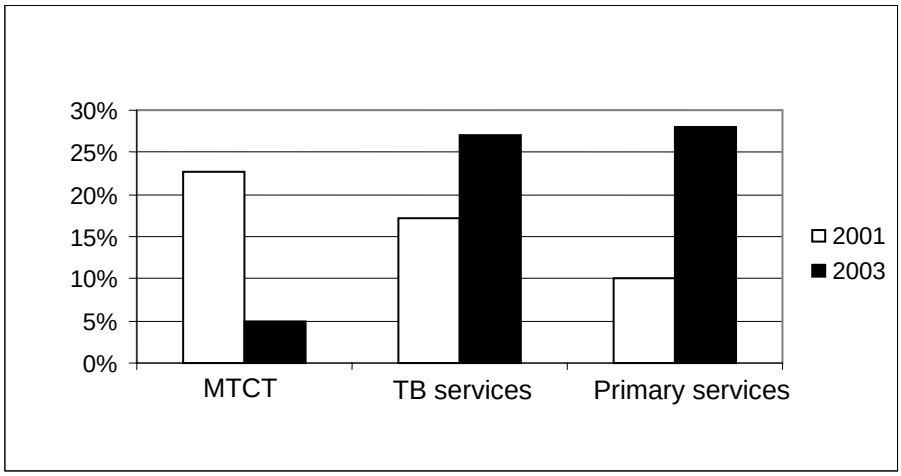


Figure 5: Evolution of referrals to HIV clinics from TB, MTCT and general primary services between 2001 and 2003.

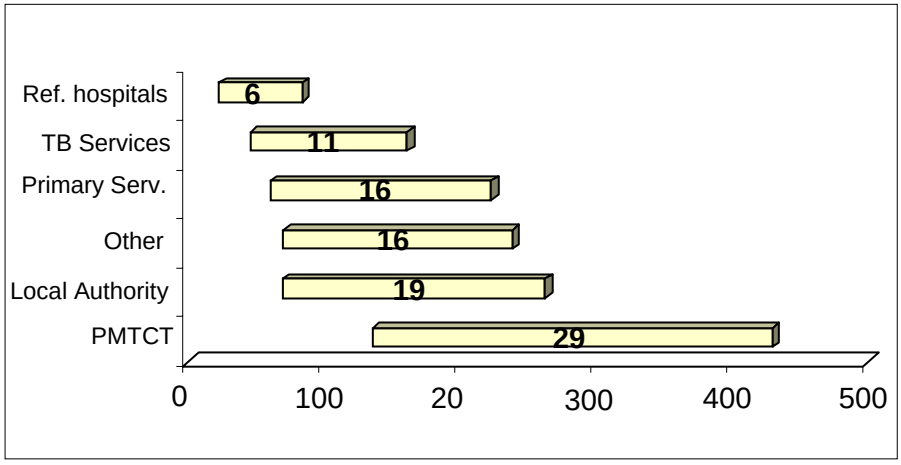


Figure 6: Median CD4 cell count on admission to HIV services according to source of referral (with inter-quartile range).

Integration of TB and HIV services

In many countries including South Africa the increasing HIV and TB epidemics have impacted significantly on already weakened public sector services. Khayelitsha has the highest annual TB incidence and one of the highest HIV prevalence in the Province. In 2002, the district accounted for 20% of the TB case load for the metropolitan area of Cape Town. TB is the second most common opportunistic infection (after oral candidiasis) seen and the commonest cause of mortality in HIV-infected patients. Thirty six percent of patients with HIV stage IV acquire TB each year.

As VCT has been promoted at TB services, there has been a steady increase in the identification of dually infected clients. As new models for HIV care are being developed, and ART is provided, every effort should be made to determine the optimal model for TB and HIV care. There is a strong overlap of activities and relationship between TB and HIV services. By integrating TB and HIV care, the available human and financial resources can be optimally used. Efficiency gains can also be anticipated by the use of a common information system and a single set of records. A single venue and a comprehensive consultation should result in less waiting time for patients. In addition there is usually more donor support for HIV programmes and this should benefit the TB programme. For these reasons there are strong arguments for some form of integration of HIV and TB services. A model for the integration of these services is being tested at Site B in Khayelitsha.

The Site B TB and HIV clinics were gradually integrated during 2003. The TB staff have been trained in HIV care including screening and staging of patients and management of opportunistic infections. Some of the TB staff have also had training on antiretroviral treatment. In addition the HIV staff have a better understanding of the TB programme. The integration of the HIV and TB services will be evaluated and the benefits and constraints will be monitored as the pilot project proceeds.

Extra-pulmonary TB is more common in HIV disease. Over the past two years extra-pulmonary TB has increased in Khayelitsha from 490 cases in 2000 to 926 in 2002 – a 90% increase. A review of a consecutive sample of 109 HIV-positive patients with TB showed that 49% of them had negative sputum smears (direct microscopy) but the culture of their sputum was positive for MTB. The current emphasis of the TB programme to focus on the detection and cure of new smear positive pulmonary TB is challenged by HIV. The development of new guidelines together with training may be necessary.

Antiretroviral therapy (ART)

Initiation of ART

In May 2001 the first patients were started on ART at the HIV services. By the end of 2001, 100 patients were initiated on ART and 300 by the end of 2002 (17 months since inception). The enrolment was accelerated and an additional 400 patients were placed on ART in 2003 (33 months since inception) reaching a total of 776 patients, including 84 children, by the end of 2003 (figure 7).

The median CD4 cell count of patients at the initiation of ART differs across clinics (figure 8). The low CD4 cell count of patients being initiated on ART at Site B clinic (where TB and HIV services have been integrated) may indicate that there is a backlog of very sick patients there. This may be linked to the fact that people with TB are being tested for HIV at an advanced stage of disease. The objective is to place patients on ART before their CD4 cell counts drop to very low levels and the risk of serious opportunistic infections and immune reconstitution with the initiation of ART increases. Many studies, including this programme have shown that patients with CD+ cell counts below 50 cells/μl have a significantly lower probability of survival.

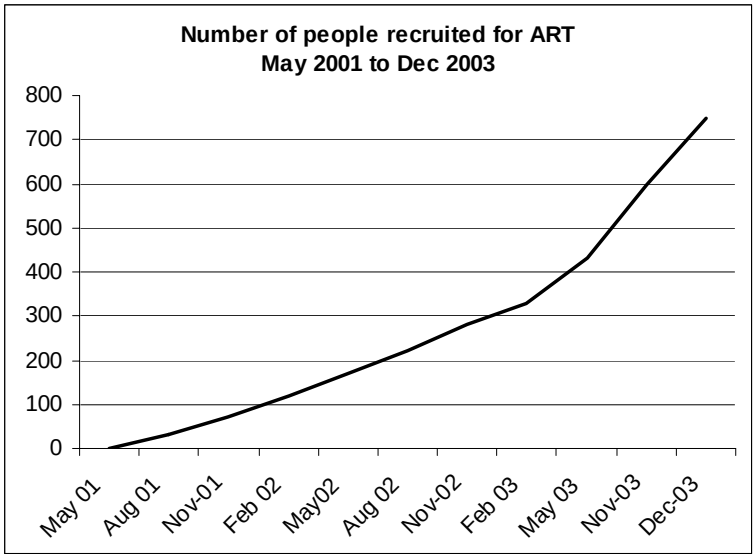


Figure 7: Number of patients recruited for ART from the initiation of the programme to December 2003.

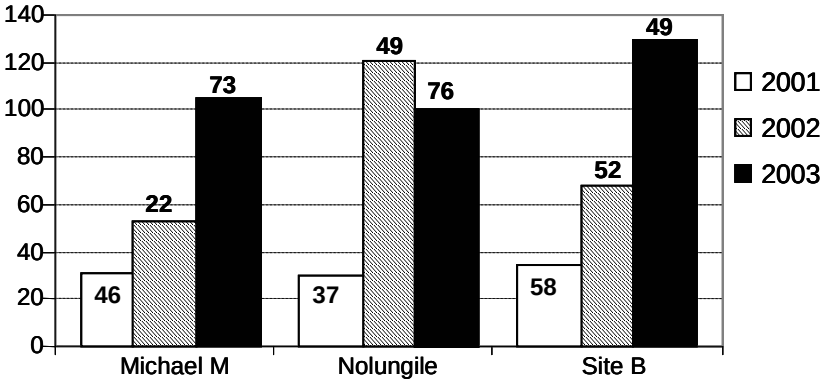


Figure 8: Baseline CD4-cell counts of patients at initiation of ART in 2001, 2002 and 2003 per clinic.

Simplification of procedures for starting ART treatment

According to the World Health Organization classification, patients in stage III and with a CD4 cell count of less than 200/μl, and all patients in stage IV are eligible for ART. Initially in Khayelitsha, after the patient had been counselled about ART, a clinic worker conducted a home visit to verify the patient's residence in Khayelitsha and disclosure to at least one person. The patient was presented to a committee of community representatives responsible for the final decision on readiness for enrolment. The committee included persons living with HIV/AIDS, counsellors and a private general practitioner.

Although procedures were simplified and in 2003 the number of patients presented to the committee doubled, the process was still too slow to keep pace with the numbers presenting and needing ART. Enrolment procedures were therefore further simplified and decentralised in the following way:

- Each of the 3 HIV services enrol patients independently following the same protocol.
- Committees at each services meet twice a month to assess preparedness for enrolment.

- The home visit is only conducted if information is not known with regard to disclosure, place of residence and/or social support
- The duration of the period that patients have to attend the service (in order to assess the potential for good adherence) has been reduced from 3 months to 4 to 6 weeks, during which period the patient should present “on time” to at least 4 visits.

ART regimens

First-line	Second-line
Stavudine (d4T) and Lamivudine (3TC) and Nevirapine (NVP) or Efavirenz (EFV)	Zidovudine (AZT) and Didanosine (ddI) and Lopinavir/ritonivir (LPV/r)

Table 2: ART regimens for adults

During 2003, the programme progressively switched from AZT/3TC/NVP or EFV as first line to d4T/3TC/EFV or NVP (table 2). The new regimen simplifies monitoring and eliminates the side effects of AZT. EFV has been increasingly used since 2002, having less side-effects than NVP, even for women of child-bearing age if under injectable family planning. However since the end of 2003 NVP has been used in preference to EFV for the following reasons:

- Fixed dose combinations (FDC’s) with NVP are available whereas FDC's with EFV are not.
- Generic equivalents of NVP are as much as 80% cheaper than EFV.

Nelfinavir (NFV) has been replaced by LPV/r in the second line regimen. We are considering including tenofovir (TDF) in our second line regimen, especially for patients who have been on AZT and 3TC in their first line regimen.

Clinical response to ART

By the end of 2003, 776 people had been started on ART. A detailed analysis of all adult patients naïve to prior ART, who started ART between 29 May 2001 and 31 December 2002 has been published (*AIDS* 2004, 18: 887-895).

Table 3 presents the baseline characteristics of the 287 adults started on ART during that period. The median period of was 14.9 months.

More women than men were started on ART. At initiation the median CD4 cell count of patients was 43 cells/µl and 52% had a prior AIDS diagnosis. The median weight gain at 6 and 12 months duration on treatment was 5.0 kg and 9.0 kg respectively.

The percentage of patients with undetectable HIV RNA measurements was 89.2%, at 6 months, 84.2% at 12 months, and 69.7% at 24 months. By 24 months the median gain in CD4 cell count, compared to baseline, was 288 cells/µl.

Pic 2. At initiation of treatment, patients are shown how to prepare their pillbox.

Baseline	
Number starting ART	287
Women	201 (70%)
Median CD4 cell count (IQR)	43 (IQR 13-94) cells/µl
Viral load (mean log10 copies/mL)	5.18 (SD 0.68)
Follow-up (months)	
Duration of follow-up (all)	13.9 (IQR 9.2 - 18.1) months
Survival at 24 months	86.3 (95% CI 81.7 - 89.8)%
Median CD4 cell count gain at 24 months	288 (IQR 181-470) cells/µl
Patient retention on 31 July 2003	
Patients lost to follow-up	1
Transferred out	3
In care but stopped ART	6
Alive but no longer in care	3
Initial antiretroviral regimen	
AZT/3TC/EFV (%)	n=173 (60)
AZT/3TC/NVP (%)	n=108 (38)
Other	n=6

Table 3: Baseline characteristics of patients starting ART prior to the end of 2002.

Patient retention and survival

At the end of July 2003, one patient from the cohort was lost to follow-up, 3 patients had moved to a different province, 6 patients were still attending the service but had stopped ART while 3 patients had stopped attending the services altogether but were known to be in good health. These results demonstrate that a cohort of patients initiated on ART in a resource-limited setting in a developing country can be retained. The fact that only one patient was lost-to-follow-up, and so few others left care, is remarkable.

Thirty-eight patients died after starting ART and 71% of deaths occurred before 3 months duration on ART. The cumulative probability of survival was 86.3% at 24 months. Estimates of survival stratified by initial CD4 cell count were 81.8% for those initiating treatment with a CD4 cell count of less than 50 cells/µl and 91.4% for those with initial CD4 cell counts above this value (Figure 9).

The excellent retention of patients and high percentage of patients with undetectable viral loads could be related to services being situated within the primary care setting close to patients' homes and family environment as well as to the careful preparation of patients. A paradigm focused on preparation rather than selection is better suited to the aggressive targets for the scaling up of ART in countries with large epidemics (such as in South Africa), where the view of ART as a very expensive rationed intervention is rapidly changing.

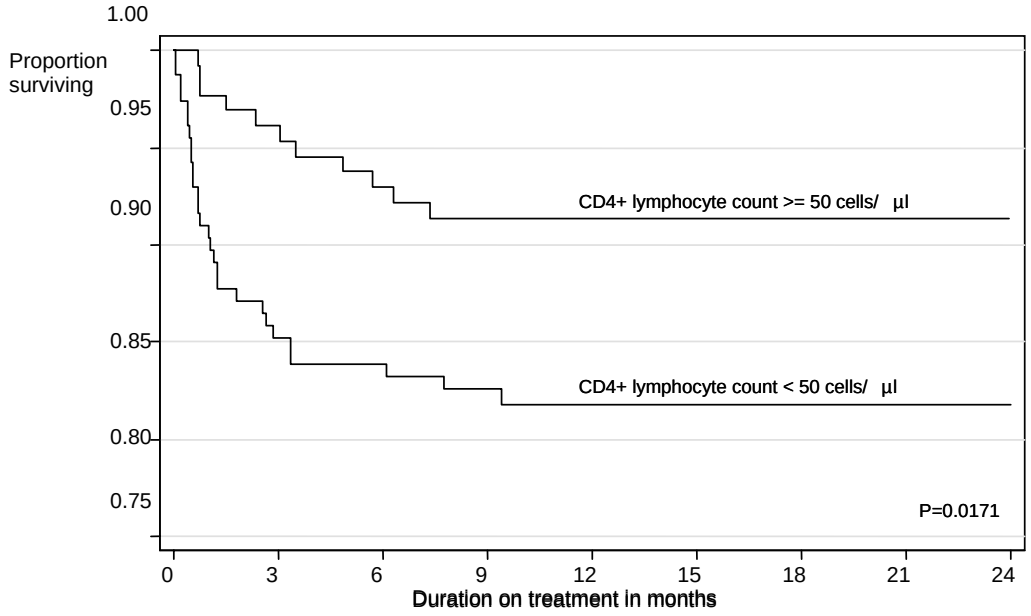


Figure 9. Survival of adults on antiretroviral treatment stratified by initial CD4 cell count.

Regimen durability

In the same cohort, most changes in individual antiretroviral drugs were due to adverse events attributed to NVP (9%), AZT (5%) and EFV (1%) and most changes occurred soon after treatment was started (Table 4). For all regimens combined, 8% of patients had a change to their first regimen cumulatively by 24 months as a result of intolerance. A further 4% of patients switched from NVP to EFV due to a new episode of tuberculosis and 1% from EFV to NVP due to pregnancy or a wish to become pregnant.

	zidovudine	nevirapine	efavirenz	all
Number ever to start on antiretroviral	285	114	197	287
Number changed due to side-effects	12	10	2	23
Time to change in days: Median	53	20	day 8 & 262	42
Percentage changed by 24 months	5	9	1	8
Number changed due to contraindications	0	10[†]	3[±]	13

[†] Changed due to a new episode of tuberculosis, [±] Changed due to pregnancy or desire for pregnancy

Table 4 :Changes to the initial treatment regimen.

With standardised regimens, monitoring and clinical management algorithms antiretroviral treatment can be safely utilised in resource-constrained settings.

Cost-effectiveness

The Health Economics Unit at UCT has examined the cost-effectiveness of providing ART. The costing study demonstrated that per life-year gained, the costs of ART are marginally less than the costs of providing appropriate care in the absence of ART. This indicates that in economic terms the intervention is technically efficient, and should be pursued if the resources exist.
(ftp://ftp.hst.org.za/pubs/research/arvcost/)

Children on ART

Children began to be enrolled for ART in November 2001. Eighty one children have been started on ARV and 53% were boys. The median age at enrolment was 4 years of age. Five children died (6%) and 3 stopped ART. Twenty five percent of children were referred from tertiary hospitals, specifically to access ART. Table 5 shows first and second line ART regimens for children.

First-line	Second-line
Stavudine (d4T) and Lamivudine (3TC) and Nevirapine (NVP) or Efavirenz (EFV if more than 3 years of age)	Zidovudine (AZT) and Didanosine (ddI) and Lopinavir/ritonivir (LPR/r)

Table 5: ART regimens for children.

Fifty four percent of children were started on AZT/3TC/EFV; 34 % on AZT/3TC/NVP; 8 % on d4T/3TC/EFV and 4% on d4T/3TC/NVP. The mean duration on ARV treatment was 10.4 months. Sixty eight percent of children had never been exposed to ART, 1% had accessed ART previously and for the rest, previous exposure to ARV was not stated.

The median change in weight between baseline and 3 months was 1kg, and between baseline and 6 months 1.2kg. The most impressive change is in the behaviour and activity of children. Before the initiation of ART children were apathetic and unhappy but once on ART they became playful and full of energy. A detailed analysis of outcomes on children on ART is being prepared with several other sites treating children.

Referral networks

A referral network has been instituted with specialists at JF Jooste and Tygerberg Hosptials for adults and children respectively. Advice is given telephonically and specialists attended difficult cases at Khayelitsha services on a regular basis during 2003. Mechanisms have been identified to refer patients more easily and patients are referred back to our services with clear referral letters. This has improved quality of care and eliminated delays.

Adherence support: Strategies and outcomes

Since the start of ART treatment in 2001, a strong patient-centred adherence support system, promoting patients' understanding of their therapy, has been implemented. Through this programme, patients learn about the principles of ART, the drugs prescribed, the adverse events and the monitoring tests required. It also facilitates the engagement of patients in supportive environments where they share their experiences and concerns about disclosure, discrimination, challenges to adherence, and other aspects of their status and their therapy.

The components of the adherence support programme are:

- Individual support: Patients are requested to select someone close to them (a relative, a neighbour or a friend) as a treatment assistant (TA). The TA is aware of the patient's status and treatment, and is expected to provide support to the patient in his own environment. The TA participates with the patient in the enrolment process for treatment initiation in the clinic, where he learns the basic principles of antiretroviral therapy. Besides TAs, the clinics provide individual support through adherence counsellors.

- Peer support: At the clinics there are support groups for people on ART, and outside the clinics community education programmes. Critical to this is the partnership of the dedicated HIV services with civil society. In this partnership health services commit to keep people healthy and civil society commit to break the silence about HIV. The intensive work of the Treatment Action Campaign on awareness about AIDS, rights of people with HIV and treatment has been essential to promote a shift towards a more open community in Khayelitsha.
- Material support: This is directly related to the medication, such as pill-boxes, recall charts and side effects charts. Others are more general informative material, in the form of pamphlets, posters, and newsletters.
- Other strategies: Video-shows, songs, drama and memory work are also used.

In May 2003 the Khayelitsha ARV programme celebrated its second anniversary having reached 400 people on treatment. The Khayelitsha community had by then succeeded in demonstrating that treatment is feasible in resource-limited settings and that people with HIV accept the constraints linked to the drugs if appropriate support is given. However, it also marked a shift in the understanding of the programme from the first pilot site to the first “roll-out site” in South Africa. This new situation implies: (1) large numbers of people on ART, (2) different support requirements of people who have initiate treatment than of those on treatment for longer periods, and (3) a need to facilitate physical and psychological well-being after a period on ART.

With this in mind during 2003 the adherence programme has been adapted and new counselling guidelines defined. The programme has (1) standardised counselling in the three services; and (2) has taken account of the evolving support needs of patients on therapy for different periods of time. Implementation of the guidelines is ongoing. By the end of 2003, all clinics had started separate support groups for patients on treatment for less than 3 months, 4 to 6 months and more than 6 months. The content of the support first covers self-acceptance and disclosure, introducing social skills at a later stage, and moving towards re-integration in society. The last stage is facilitated by creating a social environment increasingly open about HIV/AIDS.

Pic 3. People on treatment celebrate the 2nd anniversary of the ARV programme in May 2003.

MSF conducted a prospective study to evaluate adherence to ART at 1, 3 and 12 months after initiation of treatment. All patients enrolling in the programme between May 2002 and May 2003 were included in the study. Patients were rated as highly adherent if they had taken 95% of their doses, moderately adherent if they took between 80 and 95% of doses and poorly adherent if less than 80%, over a recall period of the 4 days previous to the interview. The preliminary results indicate that 90% of patients reported high adherence levels at 1, 3 and 12 months (Figure 10). Being a woman, over 25 years of age and with a level of education of Standard 8 or above, were associated with higher adherence levels. During 2004 the study will be expanded to look at determinants of non-adherence for people who have been on ART for more than one year.

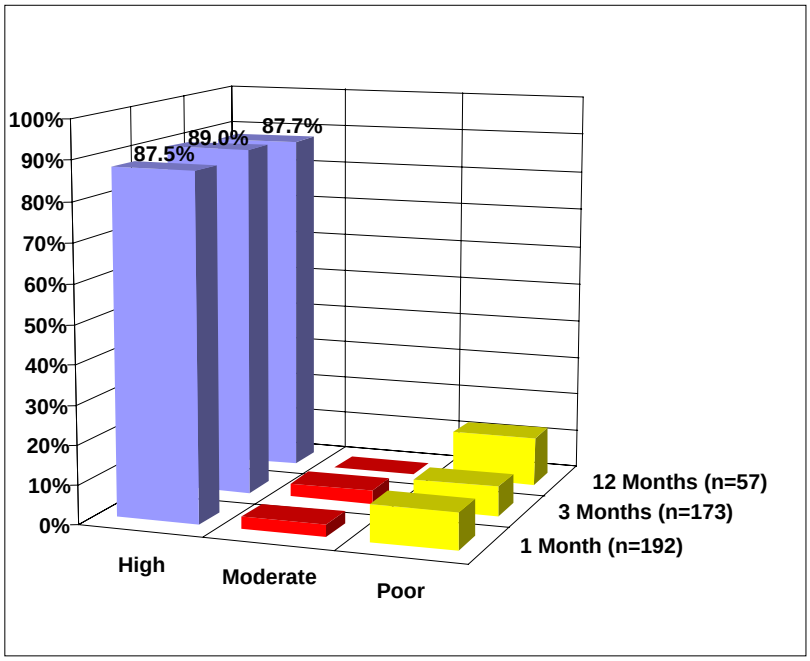


Figure 10. Self-reported adherence to ART at 1,3 and 12 months after treatment initiation.

Access to generic ARV drugs

In late 2002, the most generic ARVs used in the Khayelitsha clinics were still being sourced from the Brazilian state manufacturer Far Manguinhos. In October 2002, MSF received authorisation from the Medicines Control Council (MCC) of South Africa to expand procurement to other manufacturers, particularly Ranbaxy and Cipla. These companies had submitted registration dossiers to the MCC, and, therefore, their products will eventually be fully registered. In order to develop procurement channels that could be used by other programmes in South Africa, MSF attempted to import ARVs from these sources.

During 2003, MSF imported generic versions of ARVs from Cipla (table 5). Ranbaxy was reluctant to supply generic ARVs due to patent barriers. However early in 2004 a shipment of Ranbaxy nevirapine will be supplied. The difference in price between the Cipla generic versions and the patented formulations has diminished significantly between December 2002 and December 2003. In the case of lamivudine, the price of the patented version is now even cheaper. Nevertheless, it needed an important amount of pressure for GSK announced two consecutive price reductions for its products during 2003. The prices of paediatric formulations however remained largely unchanged.

Boehringer Ingelheim, originator manufacturer of nevirapine, did not reduce the price of this drug during 2003. With the reduction in the price of nevirapine by Cipla, the difference in price between the two products has become even larger during 2003.

	December 2002			December 2003		
	Price[1] Cipla	Price Original drug	Ratio O/C	Price Cipla	Price Original drug	Ratio O/C
Lamivudine 150 mg	126	234	1.86	88	69	0.78
Lamivudine oral solution	2.0 (100 ml)	7.45 (240 ml)	1.55	2.0 (100 ml)	6.73 (240 ml)	1.40
Zidovudine 100 mg						
Zidovudine oral solution	1.53 (100 ml)	7.9 (200 ml)	2.58	1.53 (100 ml)	7.1 (200 ml)	2.32
Lamivudine 150 / zidovudine 300	292	621	2.13	197	237	1.20
Nevirapine 200 mg	208	438	2.11	124	438	3.53

Table 5. Generic versions of drugs purchased during 2003 and the difference in price between December 2002 and 2003, comparing the Cipla generic version (C) and lowest price offered by the originator companies (O). 1: Prices in USD/month (excl. VAT). Source: Untangling the web of price reductions, December 2002 and December 2003 (http://www.accessmed-msf.org).

In August 2003, Aspen Pharmacare launched the first locally produced ARV: Stavudine. Since then, MSF has procured this ARV, given that its price is competitive with other alternatives available in the market.

Due to the savings associated with using generic ARVs, MSF identified the need to facilitate access to these drugs for other programmes. Therefore, in February 2003 MSF and other partners created the Generic Antiretroviral Procurement Project (GARPP). In December 2003, GARPP was fully licensed as a wholesaler of drugs in South Africa.

During 2003, the number of generic versions of ARVs registered by the MCC increased dramatically (table 6). MSF prioritised the procurement of registered ARVs instead of using only those allowed under the section-21 authorisation. However, many fixed-dose combinations (FDCs), particularly 3-in-1 FDCs, and affordable paediatric formulations are still not registered, which imposes a serious limitation for wide access to ARVs.

January 2003	**December 2003**
lamivudine 150 mg, Cipla	lamivudine 150 mg, Cipla
zidovudine 100 mg, Apotex	lamivudine 150 mg, Thembalami
zidovudine 100 mg, Garec	zidovudine 100 mg, Apotex
	zidovudine 100 mg, Garec
	zidovudine 100 & 300 mg, Cipla
	zidovudine 100 & 300 mg, Thembalami
	lamivudine/zidovudine, Cipla
	lamivudine/zidovudine, Thembalami
	Stavudine 20, 30 & 40 mg, Aspen
	Stavudine 20, 30 & 40 mg, Cipla
	nevirapine 200, Thembalami

Table 6. Generic versions of ARV drugs registered by the MCC at the beginning and at the end of 2003.

Prevention of mother to child transmission (1999 – 2003)

The large proportion of pregnant women accepting HIV testing in Khayelitsha (over 95% for 2002 and 2003) proves the success of the PMTCT programme. Since its initiation, 31,346 women have been tested (overall acceptance rate: 84% since inception), 7,043 of them being positive.

Initially the Thai regimen was used, with AZT (600mg/day) provided from 36 weeks of gestation and during labour. This regimen has been adapted: AZT is now given from 34 weeks, and NVP to late bookers and all women arriving in labour who have received less than 2 weeks of AZT.

In October 2003, in keeping with international protocols, the regimen was changed to the "Ditrame-plus" regimen with AZT and NVP given to all mothers and babies. This regimen, together with exclusive formula feeding has shown to reduce mother-to-child transmission to less than 5%. Since late 2003, the CD4 cell count is determined as women enroll in the PMTCT programme. The plan is to offer triple therapy to women presenting with CD4 cell counts of less than 200 cells/μl. The organisation of services to provide triple therapy will be decided once the numbers of women with low CD+ cell counts has been established.

In 2002 a survey was conducted to determine the feeding practices of mothers on the PMTCT programme and the results became available in 2003. A sample of 113 women was interviewed on choice of feeding practice. Over 95% of women did not breast fed at all. Most women (63%) stated that they themselves took the decision not to breast feed in order to protect their child. Although the overwhelming majority of women chose formula feeding the incidence of diarrhoea is low and has not increased since the introduction of the PMTCT programme. Almost 40% of women had not disclosed to anyone in their household and over 50% had not disclosed to the father of their child. Focus groups were held with a smaller sample of women to understand the social constraints HIV-infected women face in making their feeding choices. The main reasons given by women to their families and those around them for not breast feeding included the fact that they had a caesarean section, tuberculosis, high blood pressure, “bad milk”, problems with feeding the previous child, or that they were employed. Although the PMTCT programme had been running for 5 years, the low rate of disclosure of HIV status indicates that stigma around HIV is still high. The burden of having to conceal their status and lie about the reason for formula feeding is heavy.

In 2003 a seroprevalence survey was conducted, using the polymerase chain reaction (PCR), to identify the rate of mother to child transmission in infants over 6 weeks of age, born to HIV-infected mothers in Khayelitsha. The preliminary results from the consecutive sample of 535 mother/infant pairs show a transmission rate of 8.8% (95% CI 6.2 – 11.4). The response rate was 80%. Fifty one percent of mothers were referred to secondary hospitals for delivery and 24% of births were by caesarian section.

From 2000 to mid-2003, MSF provided technical support and training for the programme. These responsibilities have been taken over by the district TB/HIV coordinators.

Simelela rape survivors clinic

In 2002, a dedicated centre providing comprehensive post rape care, was established at Jooste Hospital (*Thuthuzela* Centre) for women, 14 years and older, to serve the areas of Khayelitsha, Guguletu and Manenberg. More than 50% of the clients are from Khayelitsha.

In September 2003, MSF, together with the Provincial Administration of the Western Cape and other partners, opened the *Simelela* Rape Survivor’s Centre in the Site B Clinic to support the follow-up of women from Khayelitsha and seen at the *Thuthuzela* Centre. The *Simelela* Centre aims to provide forensic and counselling services, establish a referral service to the HIV clinic at the Site B clinic and to develop community interventions to decrease rape and to support victims of rape. It is an integrated service including the police, the justice system and social services. All cases reported to the police are referred to the district surgeon who refers them for counselling. Children

are followed at the *Simelela* Clinic. All patients seen within 72 hours of the rape are counselled, tested for HIV and given Post Exposure Prophylaxis, if they are not HIV-infected.

The number of patients attending the *Simelela* Rape Survivor's Clinic has increased since it started in mid-September. During the last 4 months of 2003 eightyeight women were seen at the *Simelela* Centre, 77% of whom were less than 15 years of age. A possible reason for the large number of children may be that women are more likely to bring in their children than to come themselves if they were raped. Most women were tested for HIV.

Community mobilisation for treatment & prevention

The stigma associated with HIV and discrimination against people with HIV is still very prevalent in South Africa. By addressing fear and facilitating openness about HIV a supportive environment that allows communication about infection, treatment and prevention, and endorses positive attitudes towards the infected, can be achieved. This is the principle of project *Ulwazi* (Xhosa for 'Knowledge'), a project that started in 2001, involving patients from the HIV/AIDS services and the PMTCT programme, in education and awareness campaigns in communities. The project is sponsored by MSF and developed by the Treatment Action Campaign (TAC).

Although, a treatment literacy project, *Ulwazi* aims to educate and promote awareness. In 2002, *Ulwazi* set up a mobile exhibition called *Yazinzulu-i-HIV* (Xhosa for 'Know more about HIV'). The exhibition contained banners with pictures and life stories of people with HIV. Persons infected with HIV are portrayed at home, at work, in the clinic or performing other daily activities. In 2002 and 2003 the exhibition was displayed in community halls and libraries in Khayelitsha and other townships in the country. Local schools, churches, leaders and NGOs were invited to participate in workshops, video sessions and discussions on human rights, prevention and treatment.

In 2003, MSF and TAC designed a 'Treatment Bus' similar to the mobile community libraries accepted by communities. In 2004 the bus will move through communities, starting in Khayelitsha, portraying people on ART and their stories. It will engage local networks of AIDS activists and other AIDS related organisations in treatment literacy and counselling, stressing the importance of openness and pre-vention. It will also disseminate information on services.

Pic 4. March for treatment. Cape Town, Feb'03.

In 2003 the tensions caused by the government's AIDS policy made the TAC concentrate efforts on treatment advocacy and political action. Countless workshops took place, calling for immediate community action in the form of marches, pickets, rallies and even civil disobedience to demand that the government provide treatment for persons infected with HIV. The opening of parliament on 14 February 2003, saw the largest march ever when almost 10,000 people marched to demand treatment.

The availability of ART can break the cycle of fear and misinformation as HIV is no longer seen as a life-threatening disease. It also demonstrates that people infected with HIV can live quality lives with family and friends. At community level, exposure to persons on ART facilitates openness and helps confront the fear and the stigma.

Community survey on knowledge of HIV and availability of services

A population-based survey on HIV risk behaviour and factors influencing risk behaviour was completed in March 2004 in Khayelitsha. Interviews were conducted with 800 men and 800 women between the ages of 14 and 49 years. The results of this survey are expected in June 2004. The results will guide further prevention activities in Khayelitsha.

Conclusions

The Khayelitsha programme has shown that a well-run HIV programme can succeed in resource-limited areas. HIV has been tackled on a number of fronts by including HIV prevention, PMTCT, the provision of services for persons infected with HIV, integration with TB services and by the provision of ART. Each of the components compliments the other.

VCT services have been extended to a number of services and increasing numbers of people are being tested. With the extension of VCT to TB and STI clinics many more infected persons have been identified and therefore every effort should be made to first extend services to these clinics.

The PMTCT programme is accepted by the overwhelming majority of pregnant women in Khayelitsha. It also provides support to infected mothers and referral to HIV services. The low rate of mother to child transmission is evidence of the success of this programme.

More people are accepting the HIV service, as indicated by the increasing numbers. This is expected to increase even further as the roll-out extends and as the results of this ART programme become known. This will place increased demands on services and services will have to increase the number of patients initiated on ART to 30 per clinic per month in 2004.

The results of the ART programme are of importance due to the paucity of data from similar settings. Clinical and biological parameters show a reduction in morbidity and mortality including those patients who initiated therapy at a late stage of disease. Strategies need to be identified to improve survival for those with extensive immune suppression at presentation.

With a patient-centred approach, careful patient preparation and a strong support program involving specifically trained lay counsellors and peer support mechanisms, good adherence to treatment is achievable. Investment in good counselling services and providing a career-path for ART-trained counsellors is a key enabler of patient retention and good clinical outcomes.

Nurses working in a primary care setting, if properly trained and with support from doctors, can diagnose and treat most opportunistic infections and deliver ART in line with standardised protocols. This is reassuring given the challenges of providing sufficient staff for the intervention.

Given the backlog in providing ART and the late stage of disease at presentation, it is inevitable that the first treatment sites in the national roll-out plan will predominantly be at hospitals. There can be little doubt however, that we need as quickly as possible to move towards strengthening primary care services so that people can be treated at this level, both from the patient and health services point of view. A good referral network is essential to ensure quality care. These initiatives should ensure that primary care services generally are improved and bolstered.

It is not only the provision of ART at primary care which has ensured these results. It is also the location within the framework of a comprehensive HIV/AIDS service, where patients develop a relationship with the service over time and when appropriate are started on ART within the same service, rather than being started on ART at specialised referral services.

Community activism has been essential for the success of the programme in Khayelitsha, and this too is much more easily linked to services if they are located within communities. The role of organisations such as the Treatment Action Campaign (TAC) is critical.

This programme represents one of the first attempts to integrate ART as part of a comprehensive government response to HIV/AIDS, in one of the most marginalised urban communities in South Africa. To date over 1 000 patients have been started on ART indicating that the large scale roll-out of ART can work, if well planned and supported.

Challenges

Although the Khayelitsha programme was recognised in 2003 by the World Health Organization as one of the models for an integrated HIV programme, new constraints are emerging in 2004 and the programme will have to find new solutions and adapt to the new challenges.

The first major challenge is to cope with the demands of the scaling-up programme. Initially the plan was to place 300 persons on ART. At the end of 2003 there were over 700 people on ART and the target for the end of 2004 is 1,700. This requires a substantial increase in the number of patients enrolled each month, while at the same time ensuring that quality is maintained and that outcomes remain good. This can be achieved if patients are placed on ART before they have extensive immune suppression.

The availability of dedicated and well trained health staff appears to be the biggest constraint and the most difficult to overcome. The objective of scaling-up can only be achieved if HIV care is integrated into existing services rather than creating new services. Because of the large proportion of patients dually infected with TB and HIV, an obvious point of integration is with TB services. Operational research needs to be conducted to identify the best model for the delivery of HIV services, including the management of patients with early stage disease.

The Khayelitsha programme has been integrated into the provincial scale-up plan. Much has been learnt from Khayelitsha and programme is well represented on the provincial HIV task team. Over the next 3 years the challenge will be to transfer responsibility for the Khayelitsha programme to the Western Cape Department of Health.

New challenges are emerging in Khayelitsha that other programmes will soon face, and finding solutions to these questions is the basis of the current research. This includes developing approaches to identify and support patients who are not adherent to ART and identify when to change therapy due to resistance and treatment failure.

Although ART greatly reduces the incidence of TB (by over two-thirds in Khayelitsha), the overall burden of TB remains extremely high and novel approaches are required to identify TB.

Drug formulations and especially drug suspensions can make providing ART for children very difficult and may compromise adherence. Simplified approaches to treating children need to be developed.

With additional support ART can be provided and can lead to an improvement in primary care services generally. Given the huge threat to society posed by HIV, the challenge is now to expand HIV services and ART and particularly in rural areas. MSF has formed a partnership with the Eastern Cape Department of Health and the Nelson Mandela Foundation to demonstrate the feasibility of providing comprehensive HIV services including ART in rural settings, with 30 patients having started ART in Lusikisiki. Given that the effectiveness of the intervention is no longer in doubt, the research emphasis within this project will be more directly focused on the systems of service delivery with further simplification and emphasis on nurse-based services.

Cape Town 2004/04/26