

Anticipating future challenges to ART provision in South Africa: reflections on the Khayelitsha ART programme

The Khayelitsha ART programme has been in existence for five years. The emerging challenges are indicative of challenges other districts will face in the future. The number of adult patients started on ART annually in Khayelitsha has increased from 80 to 1 500. The gap between need and provision has narrowed, with a concomitant increase in the baseline CD4 count at ART initiation. Over time, adherence preparation has become less intensive, but the patient-centred approach has been retained. Consultations and staffing (especially doctors and counsellors) have increased substantially over four years, without deterioration in clinical outcomes. To keep up with projected demand, the service needs to quadruple enrolment over the next five years. This will only be possible by utilising the full breadth of the primary care system and by integrating TB/HIV/ART care at each service point.

Antisipering van uitdagings vir antiretrovirale voorsiening in Suid-Afrika: oorwegings van die Khayelitsha ART-program

Die Khayelitsha ART-program bestaan reeds vir vyf jaar. Die uitdagings wat ervaar word, dui op probleme wat ander distrikte in die toekoms sal ondervind. Die aantal volwasse pasiënte wat jaarliks met ART by Khayelitsha begin, het van 80 tot 1 500 toegeneem. Die gaping tussen behoefte en voorsiening het vernou, met 'n gepaardgaande toename in die basis-CD4-telling by ART-inisiasie. Na verloop van tyd is voorbereiding vir terapietrou afgeskaal, maar die pasiëntgesentreerde benadering is behou. Konsultasies en personeel (veral dokters en voorligters) het oor vier jaar beduidend toegeneem, sonder agteruitgang in kliniese resultate. Om met die geprojekteerde vraag tred te hou, moet die diens in die volgende vyf jaar vervierdubbel. Dit is slegs moontlik deur gebruik te maak van die volle spektrum van die primêre sorgsisteem en geïntegreerde TB/MIV/ART-sorg by elke dienspunt.

Three-drug antiretroviral therapy (ART) has been the standard of care for patients with advanced human immunodeficiency virus type 1 (HIV-1) since 1996 in well-resourced countries. Uptake in these countries was widespread, and substantial reductions in mortality and morbidity were observed soon thereafter (Egger *et al* 2002, Hogg *et al* 1999, Sterne *et al* 2005).

In South Africa, however, the country with the highest number of people living with HIV-1, ART only became officially available in the public sector in April 2004, a full eight years later (NDoH 2003). The nature of the health system and an evolution in the way the intervention has been conceptualised for poor countries have meant that, from a service perspective, ART as implemented in South Africa has important differences from the experience in well-resourced countries.

In well-resourced countries, patients with HIV are typically treated by super-specialist infectious diseases clinicians, as outpatients of specialised units in hospitals. In South Africa, by contrast, ART is seen as a service that should be available in primary care; the mainstay of care provided is generally by nurses and counsellors, and medical support by medical officers, seldom with specialist training. Another important difference is in the clinical protocols — whereas in well-resourced countries, treatment is highly individualised and the threshold for changing therapy is very low, the protocols developed by the World Health Organization (WHO) for developing countries are highly standardised, and there is generally a higher threshold for changing therapy (WHO 2004).

A further defining feature of ART in the South African setting and related settings is the strong emphasis on patient adherence and structured adherence programmes (Coetzee *et al* 2004a, NDoH 2003). This developed in part as a form of activism to counter the perception that African patients would not be able to take these drugs without being poorly adherent, leading to the development of widespread drug resistance, and partly due to careful planning in order to attain the best possible outcomes.

Given these important differences, the medium- and long-term challenges of the intervention in South Africa are yet to emerge in most provinces, with much of the early experience having been focused on setting up the services and rapidly enrolling patients in care. Clinical

and health service insights gained from interventions in better-resourced countries are of limited application to the South African context. Against this backdrop, the experience of the early ART projects in South Africa needs to be considered as a window through which to observe some of the pending challenges, and as a test-bed for solutions to these challenges.

This paper seeks to describe the way the service has changed over time in Khayelitsha, largely as a result of increased demand and consequent enrolment, and to reflect on the challenges that lie ahead if it is to meet the ongoing demand.

1. Structure and methods

The paper begins with a description of the programme's evolution, followed by a presentation of temporal changes in patient enrolment and in the key metrics of patient outcomes — retention in care and virological suppression. The discussion reviews emerging challenges to the programme and then focuses on the most important challenge, which is providing an appropriate service platform to keep pace with the projected demand for ART.

The description of the programme evolution is based on a prospective cohort analysis of all treatment-naïve adult patients enrolled in care over the first four years of the programme, stratified by year of ART initiation. All such patients who started ART between May 2001 and 31 December 2004 are included in the analyses by duration on treatment. Product-limit estimates (Kaplan-Meier) of retention in care were determined for all patients irrespective of subsequent discontinuation of therapy. Patients who had not attended services for three months or more after their last scheduled appointment and who could not be traced were classified as lost to follow-up, and statistically considered as failures on their last recorded visit to the clinics.

Baseline characteristics at enrolment in ART are described as proportions or medians. Virological suppression is described as the proportion of patients with viral loads below 400 copies/ml, with binomial confidence intervals. The hypothesis that outcomes had changed over time tested statistically with Cox proportional hazards regression (retention in care) and the *chi*-square test for differences in proportions (virological suppression at six months).

Projections for Khayelitsha are based on modelled national projections from the ASSA2002lite model (ASSA 2000), crudely scaled to the population of Khayelitsha, together with the Cape Town Antiretroviral Costing Model (Boulle *et al* 2004, 2003).

2. Evolution of the Khayelitsha programme

2.1 History of the Khayelitsha programme

Khayelitsha has been a test-bed for antiretroviral-related interventions since 1999. It was in this year that the Western Cape (WC) provincial government embarked on the first public sector programme to routinely provide antiretroviral-based intervention for the prevention of mother-to-child transmission (PMTCT). Based at the two midwife-staffed obstetric units (MOU) in the township, the intervention comprehensively covered the entire population of over 400 000 residents. Pregnant women were offered counselling and testing; received the drug zidovudine from 34 weeks of pregnancy, and more intensively during labour (a regimen that had recently been demonstrated to be effective in Thailand), and were offered free formula milk after delivery to encourage replacement feeding, thereby minimising the risk of transmission via breast milk (Abdullah *et al* 2001).

It was at this time that the international non-governmental organisation (NGO) *Médecins sans Frontières* (MSF) opened an office in Khayelitsha and offered assistance to the PMTCT programme. As a group with an advocacy agenda lobbying for antiretroviral interventions to be available in poor countries, MSF chose Khayelitsha for a number of reasons:

- the WC provincial government was already exploring antiretroviral-based interventions, and
- the township represented one of the more challenging service environments, with endemic poverty and unemployment (40%), a long history of under-resourced health services, and the highest HIV-1 burden in the province.

Together with the WC provincial government, MSF opened three dedicated primary care-based clinics (infectious diseases) in 2000, focusing primarily on HIV and sexually transmitted infections (STIs). These clinics were located within the existing community health centres (CHCs)

in the township. They initially focused on establishing a patient base and introducing dedicated care for opportunistic infections. A strong emphasis was placed on nurse-based care, with each clinic initially being primarily staffed by a doctor-nurse-counsellor team. ART was offered for the first time in May 2001 (WHO 2003).

2.2 The adherence model

Initially, the level of contestation concerning the feasibility of ART was such that the programme design was extremely cautious with respect to adherence promotion. The concept of patient-centredness in the approach to adherence promotion has remained central from the beginning of the programme, however.

The process of preparing patients for therapy initially involved structured three-session facility-based counselling, the nomination of a self-selected treatment supporter, participation in a support group, a home visit to validate social circumstances and residency, and the signing of a contract with the services (Coetzee *et al* 2004b, NDoH 2003). The demand for ART initially outstripped the availability of treatment slots. A combination of sicker patients jumping the queue and delays associated with the preparation regime resulted in patients commencing treatment with extremely advanced disease — the median CD4 cell count of those starting treatment was below 50 cells/ μ l in the first two years (Coetzee *et al* 2004c).

The structured counselling still pertains, support groups and treatment supporters are still encouraged but not mandatory, while home visits are reserved for patients with identified social problems. For patients who are already eligible for ART on biological grounds, the time elapsing from the first visit to the commencement of ART has fallen dramatically, often being less than a month.

2.3 The care team

In the early days of the programme, the care team in each clinic consisted of one doctor, one nurse and one counsellor. Over time, this has changed. First, the team was expanded to include an extra nurse and an extra counsellor. As the WC provincial government took over staff recruitment and employment, however, they were more successful at appointing doctors than nurses. The team at each clinic has therefore

tended to become doctor-driven as the service has expanded further. Currently each clinic has on average four counsellors, two nurses and three doctors. The patient load across the three clinics has increased over time from a combined 1 500 consultations per month to around 7 000 by the end of 2004.

2.4 Temporal trends in patient outcomes

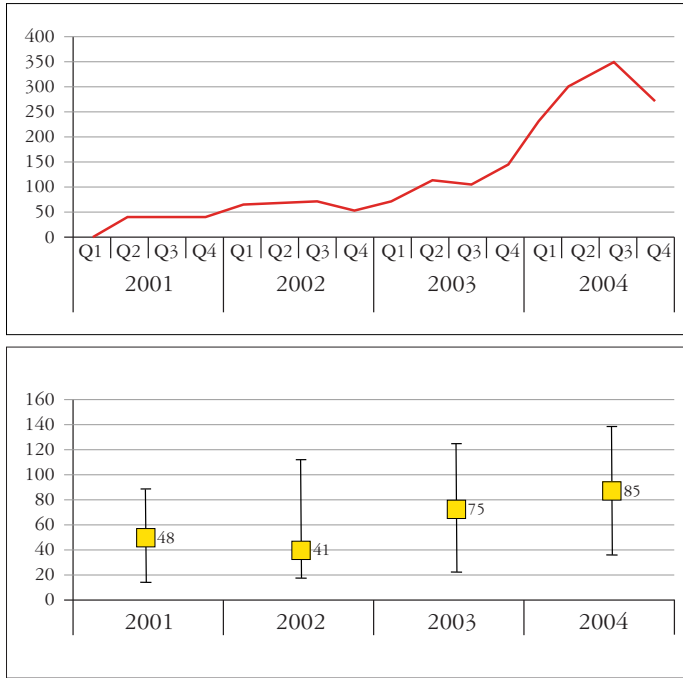
The clinical outcomes of the programme in Khayelitsha have been described elsewhere (Coetzee *et al* 2004d, Jelsma *et al* 2005), and it is not the intention of this paper to present them again. What is important to reflect on here, however, is the stability and evolution of these findings over time.

When the PMTCT programme started in 1999, the proportion of women attending their first antenatal consultation who were HIV-infected on testing was 14%. By the last quarter of 2004, this had risen to 27%, and in fact the antenatal survey for 2004 reflected an even higher proportion than this (WCDoh 2004). The services have, therefore, been delivered in the context of an epidemic that is both large and young, with the majority of those who are HIV-infected having been infected in the last five years.

The CD4 count of those starting ART was initially very low (for the reasons described above) but has increased rapidly along with the rate of enrolment of patients (Figure 1).

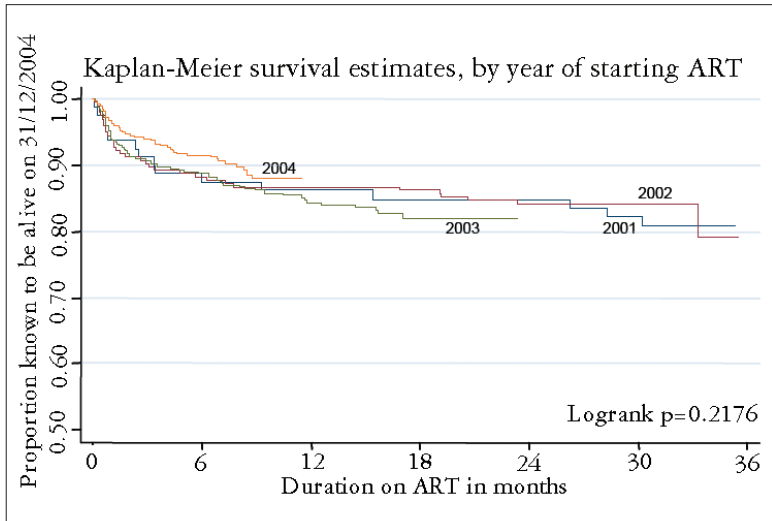
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Figure 1: Evolution in enrolment in ART (above) and in the median baseline CD4 count over time for patients starting ART (below)



The survival rate of treatment-naïve adults has not deteriorated as the programme has expanded. In fact, because the baseline CD4 count has risen in recent years, retention in care has improved in the most recent annual cohort (2004 — Figure 2). This is corroborated by multivariate Cox proportional hazards modelling in which the year of ART initiation is not strongly associated with estimates of retention in care after controlling for the baseline CD4 cell count.

Figure 2: Proportion of patients remaining alive and in care by duration on ART



Nor was there any deterioration in the proportion of patients with virological suppression at six months duration on ART when compared to patients starting ART in different years (Table 1, $p=0.445$).

Table 1: Evolution in virological suppression at 6 months duration on ART by year of initiation

Year	n	<400 cps/ml	95%	CI
2001	62	87.1%	76.1%	94.3%
2002	153	90.8%	85.1%	94.9%
2003	282	92.6%	88.8%	95.3%
2004	320	92.8%	89.4%	95.4%

2.5 Challenges to service delivery as a result of increasing need

Gaining an understanding of the number of people in need of ART at the district level is a complex undertaking, given the paucity of district-level parameters for modelling (including HIV prevalence, migration, fertility, and mortality). The potential demand for ART in Khayelitsha may be roughly estimated by applying estimates derived for South Africa as a whole, scaled to the population of Khayelitsha. For the purposes of gaining a broad understanding of the likely scale of the need for ART, this approach is reasonable; alternative approaches are not possible, given the lack of data.

The most recent version of the Actuarial Society of South Africa's (ASSA) Aids and Demographic Model (ASSA2002lite) was used to model the HIV epidemic in the South African population, utilising default assumptions (ASSA 2000). This model has been widely used for projecting the HIV epidemic in South Africa (Bradshaw *et al* 2004, Groenewald *et al* 2005), with good agreement with other methods. The model was rerun with varied parameters to match the estimated antenatal prevalence between 1999 and 2004 with that observed in the PMTCT services in Khayelitsha. These values estimate a less mature epidemic and slightly fewer people in the advanced stages of HIV when compared to the outputs produced using the default parameters.

The proportions of the population infected with HIV in these two models (with the default assumptions and the modified assumptions) were then extrapolated to the Khayelitsha population based on an estimated 2001 population of 400 000 (Demarcation Board 2002). The mid-point of the estimates produced by these two approaches was utilised in the figures. The numbers of patients starting ART were fed into the Cape Town Antiretroviral Costing Model, which assumes a median retention in care of six years for patients starting ART.

The number of patients requiring ART in Khayelitsha is estimated to be between 3 000 and 4 000 each year over the next ten years. The current provision is for around 1 500 new patients each year.

Were enrolment to remain constant (for instance, with no change in the capacity of the services to enrol new patients), the gap between those in need of treatment and those receiving it would once again widen

dramatically (see Figure 3). At the same time, the total number of patients accumulating on treatment would approach 7 000 by 2010 and 12 000 by 2015.

If the enrolment were to be increased (doubled over the next two to three years) in order to keep up with the demand, then the total number of patients accumulating on treatment would reach 12 000 in 2010 and 18 000 in 2015.

If the services in Khayelitsha are to keep up with the need for treatment, the enrolment of new patients has to double over the next two to three years and the total number of patients in care is likely to rise at least four-fold over the next five years. The consequent health service challenges are obvious.

Concomitant with the service expansion has been a shift in the case-mix seen at the HIV services. Initially, around a quarter of all consultations were for patients on ART or being prepared for ART. These patients now comprise more than half of all consultations. The crowding out of care for patients not yet eligible for ART requires that other services, such as those for tuberculosis and acute care, be able to provide appropriate chronic care for HIV-infected patients not yet eligible for ART.

3. Discussion

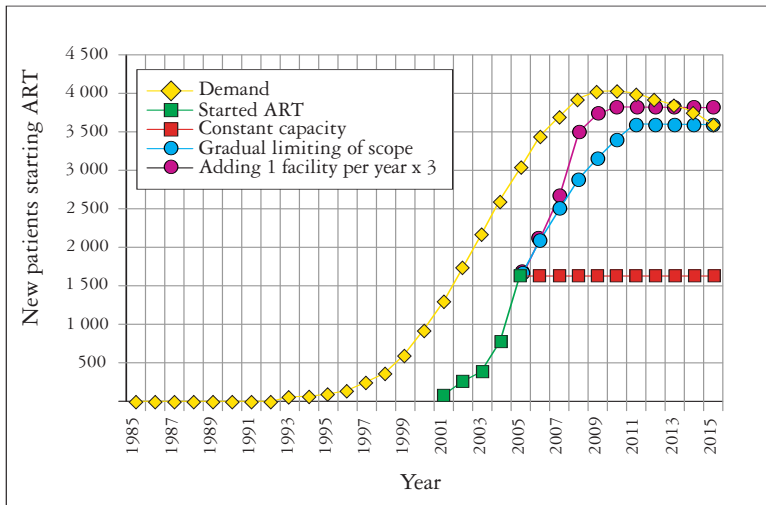
The existing service platform for dedicated HIV care in Khayelitsha consists of three facilities linked to provincially run CHCs. These are currently operating at full capacity with respect to both their staff and their physical infrastructure. As in any service, there is some potential for incremental improvement in efficiency and, linked to this, the physical space available for service delivery could be expanded. It is unlikely, however, that this configuration could accommodate a four-fold increase in patients on antiretrovirals, let alone the anticipated increase in patients not yet eligible for ART.

The alternative approach to dealing with increasing patient numbers would be to expand the service platform by bringing on board other clinics that currently offer only a limited HIV service. There are seven TB clinics in Khayelitsha, all of which could be enhanced to provide a more complete HIV service, including antiretrovirals. The advantages

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of integrated TB/HIV care have been widely argued (Coetzee *et al* 2004e, Corbett *et al* 2006). Logistically, the higher number of clinics providing the service is offset by the manageability of smaller patient numbers at each facility. These approaches are reflected in Figure 3. In this figure, new patients enrolling for ART are reflected on the y-axis, and the year of enrolment on the x-axis. The demand is reflected by the yellow line and the projected numbers actually enrolled under three scenarios by the remaining lines.

Figure 3: Projected demand, enrolment to date, and treatment gap should enrolment remains constant over time or the rate of enrolment is expanded



This paper has explored the changing nature of the HIV services in Khayelitsha, where enrolment has increased rapidly in recent years. Anti-retroviral care has started to dominate pre-ART HIV chronic care; there has been a massive increase in the number of consultations and a shift in the staffing profile but until now, clinical outcomes have remained relatively constant.

The service has become disproportionately doctor-based and is physically constrained by the facilities in which it is located. The concerns relating to a doctor-driven service are premised on a more general concern that, due to human resource constraints, using less skilled cadres of health workers is advantageous (see Kober & Van Damme 2004). Expansion within the existing facilities is possible, but is unlikely to meet the demand of doubling enrolment and quadrupling the overall patient load. At the same time, genuine concerns are being expressed by providers about the ability of the clinics to function optimally when they exceed a certain size.

There is a danger that planners will view the scaling-up of the ART programme as a scaling-up to a certain fixed service level. Experiences with PMTCT in the Western Cape, which was able to attain complete coverage, are not a fair comparison — with the number of live births being relatively constant — as the number of patients on ART is constantly increasing.

Service planning needs to anticipate constant expansion, using the full breadth of the primary care service where possible, in order to meet the demand for care. Any tailing-off in enrolment, or even a levelling-out, would likely be to widen the treatment gap once again (see Figure 3, where constant enrolment is contrasted with increasing enrolment, represented by the red line).

One of the other concerns about failing to expand the service platform for HIV on an ongoing basis is that the Khayelitsha experience has shown how, over time, the ART service can crowd out the service for patients not yet on ART. It is estimated that a small fraction of those testing HIV-positive through Voluntary Counselling and Testing (VCT) services actually take up a referral to a dedicated HIV service, demonstrating how many opportunities of enrolling HIV-infected patients in dedicated HIV care services are missed.

One of the locally proposed solutions to this challenge is a two-tier HIV service in primary care. The first tier would be nurse-run, and would be responsible for clinical staging and the management of stable patients on ART. The second tier would be doctor-run, initiating patients into ART and dealing with complications. At face value this solution seems coherent. There are, however, a number of constraints to the effective implementation of such a service configuration.

Firstly, a two-tier primary care service for life-long care makes huge demands in terms of the level of integration of information systems, clinical protocols and referral systems, and this is not yet in place. Secondly, patients develop a relationship with a certain set of health care providers and a facility — we do not yet know what effect the referral of patients to a different service would have on adherence. There are not as yet working models of down-referral (the process of referring stable patients to a less-intensive level of care) from which we could determine its impact on adherence. There are also clinical reasons to be concerned about two-tier primary care systems. It is only through the exposure to delivering ART that providers learn the importance of timely referral, as well as some of the complications and the importance of diagnosing them. Similarly, staging and treating opportunistic infections is clinically probably more complex than starting antiretrovirals in patients who are well, and yet there is a tendency to assign this task to nurses with limited clinical training and to under-utilise the scarce skills of doctors by assigning them to patients who are doing well on antiretrovirals.

In conclusion, the services in Khayelitsha have done remarkably well in catching up with the backlog in antiretroviral provision to the current extent (Figure 3, solid lines). This is evidenced by the increase in the median baseline CD4 count of those starting ART. The challenge is to continue with the rapid expansion of the service. This may not be possible within the confines of the existing service platform, so innovative solutions are required on a district-wide basis, utilising the full array of available primary-care facilities. If successful, this will probably see a doubling in the number of new patients starting on ART every month, and a quadrupling of the total number of patients on ART over the next five years. This is a sobering reflection of the challenges that lie ahead in other districts and, from a planning perspective, it is imperative that the service capacity for antiretroviral provision be expanded on an ongoing basis. Failure to do so would result in an unacceptable widening of the already wide treatment gap.

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