The Western Cape Antiretroviral Programme

Monitoring Report

June 2006

Provincial Government of the Western Cape

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Provincial antiretroviral monitoring and evaluation team
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Synopsis

This report reflects on the past two years of antiretroviral service provision in the Western Cape, drawing together data from various sources to create a composite picture of the programme in the province. The first public sector patients accessed antiretroviral treatment (ART) in the Western Cape in 2001. This report covers routine data up until the 31 March 2006, based on the paper-based monitoring system implemented as the provincial minimum standard.

Rapid service expansion
By the time of the launch of the national programme to provide ART in April 2004, 2,327 patients were on ART at 16 sites in the Western Cape. In the past two years the number of sites has increased to 43, and the monthly enrolment of new patients exceeded 1,000 patients per month early in 2006. By the end of March 2006, a total of 16,234 patients were on ART in the province. In the 2005/6 financial year it is estimated that the number of patients accessing ART over the year represents 57% of those projected to be progressing to stage IV HIV disease in the same time period. The geographical distribution of ART service provision appears to be appropriate when compared to the estimated need for treatment by health district.

Unmet need
It is further estimated that between 7,000 and 10,000 patients died in the province in the last year without ever accessing ART. In order to keep this number constant or to reduce it, the monthly number of new patients enrolled onto ART in the province needs to double over the next five years.

Encouraging retention in care
By four years duration on ART, 7 out of 10 treatment-naïve adult patients are still in care. Without treatment almost all of these patients would have died in this time period. Looking just at those who are known to have died, cumulatively 15% of adult patients had died by four years duration on ART, although some of the patients lost to follow-up may in fact have also died. Of children followed up for three years, 8 out of 10 are still in care. These data suggest that if anything, most of the modelling of treatment numbers had underestimated the potential impact of the intervention in our setting.

Adherence so far appears to be good
Of those treatment-naïve adult patients who received viral load tests, over 90% achieved a viral load below 400 copies/ml at 6 months on ART, and 88% remained virologically suppressed at one year. The proportion with virological suppression to this level does not drop below 85% over the four years of follow-up, whilst of those adult patients who were followed up for the full four years, 17% had started second-line therapy by this duration on ART.

Trends between sites and over time
The main purpose of the monitoring system is to assist in programme management, and some indicators are starting to demonstrate differences between sites in the completeness of clinical follow-up (such as laboratory testing) as well as in the outcomes themselves. At the same time the rapid expansion of services has resulted in patients accessing care with less advanced disease in more recent years, which in turn has seen a decline in early mortality on the programme, from 13% in 2001 to 6% in 2005 in the first six months on ART. There has however also been an increase in the proportion of patients lost to follow-up as the services have expanded.

New clinical challenges are emerging

Whilst the routine information system focuses on information for programme management, a number of clinical research sites serve as sentinel sites for the province, which together with the adverse drug event reporting, provide a window into some of the clinical challenges that are emerging over time. Emerging issues include:

- substitutions to the first line regimen due to side effects are more commonly due to stavudine-related toxicity than had been anticipated, especially in women
- mortality is higher in very young children starting ART (< 1 year) compared to older children, although this could be a function of higher viral loads in these children
- the use of viral load measurements, coupled with targeted adherence interventions for patients with viral rebound, is a potent strategy for maintaining patients on first-line regimens, with over 70% of rebounding patients attaining virological suppression after the intervention
- the incidence of tuberculosis is greatly reduced in patients on ART compared to HIV-infected patients not on ART, but still remains much higher than in HIV-uninfected individuals, whilst patients with tuberculosis awaiting ART have a high mortality, suggesting early initiation of ART in these patients may be appropriate
- using a validated algorithm for smear-negative tuberculosis in HIV-infected individuals, tuberculosis treatment can be started on average three weeks sooner than if clinicians wait for culture results
- The adverse drug reaction reporting system is providing invaluable information on how adverse reactions are being managed and the clinical details of incident events

Efavirenz use is the most significant driver of antiretroviral drug costs

Out of an average R7,500 of earmarked funds spent per patient year on ART by the province in the past financial year, 40% was spent on antiretroviral drugs. Data from the drug depot demonstrate that over 70% of patients are on efavirenz-containing regimens, with efavirenz alone accounting for 49% of all antiretroviral drug expenditure in the province over the past two years.

Monitoring of programme performance will remain a major challenge

Whilst it is testimony to the commitment of all health workers involved in ART service provision in the province that near-complete data on the programme are available at this point, it is clear that with the rapidly increasing patient numbers, significant monitoring challenges lie ahead. The simple paper-based provincial standard has been shown to be a feasible and appropriate system, though cumbersome in bigger facilities. Although an electronic patient information system is nearing completion, this is likely to bring infrastructural and human resource challenges of its own.

Conclusion

This report has detailed the available output and outcome data for the antiretroviral treatment programme in the Western Cape over the past two financial years. The programme is having a dramatic impact on the health of those accessing it. Access appears to be equitable across districts. Enrolment capacity has increased steadily over this period, and it is feasible that the platform, with gradual expansion, will be able to initiate ART for most of those who need it over the coming years. The overall patient numbers accumulating on ART pose a huge service challenge however, and the increase over time in the proportion of patients lost to follow-up in the first six months on ART is an early signal pointing to the health system challenges in this regard. Whilst the location of ART within primary care services appears to have contributed to the success of the provincial programme to date, innovative approaches to sharing the service load across the entire primary care service platform are urgently required.

Introduction

Background to the provincial antiretroviral programme

Two full financial years have passed since the launch in this province of the national antiretroviral treatment programme in April 2004. Antiretroviral therapy (ART) as treatment for symptomatic patients infected with HIV was however available in the public sector in the province prior to April 2004 through a number of partnerships with academic institutions and non-governmental organisations. The first patients to begin ART in the public sector in the Western Cape started treatment in April 2001.

At the inception of the national programme, there were 16 sites already offering ART in the public sector, 5 at academic hospitals, 3 at regional hospitals, and 8 at primary care sites in the metropolitan area. Co-ordinated data collection from these sites began in earnest in April 2004, although some sites were able to contribute data prior to this date, which is included in the provincial database in order to discern temporal trends in enrolment and longer-term outcomes.

The number of sites providing ART in the Western Cape has increased to 43 (Figure 1) over the past two years. Many of the sites are primary care sites. Over 60% of patients receive ART at primary care sites in the province overall, and in the metropolitan area 75% of all patients receive care at primary care sites. A full list of sites is included in the monthly report for the end of March 2006 (Annexure A).

This report would not be possible were it not for the tireless work of the health workers who have fully owned this programme, and the many staff who support the treatment sites, including those who have patiently maintained the patient registers and ensured that monthly and quarterly reports have been completed.

The programme has been managed by the HIV/AIDS directorate at the Provincial Department of Health, with active participation by health managers from the City of Cape Town, and partners at academic institutions and NGO's. Clinicians from the programme come together from across the province every two months to discuss clinical issues facing the programme, whilst management of sites is shared between the directorate and regional managers.

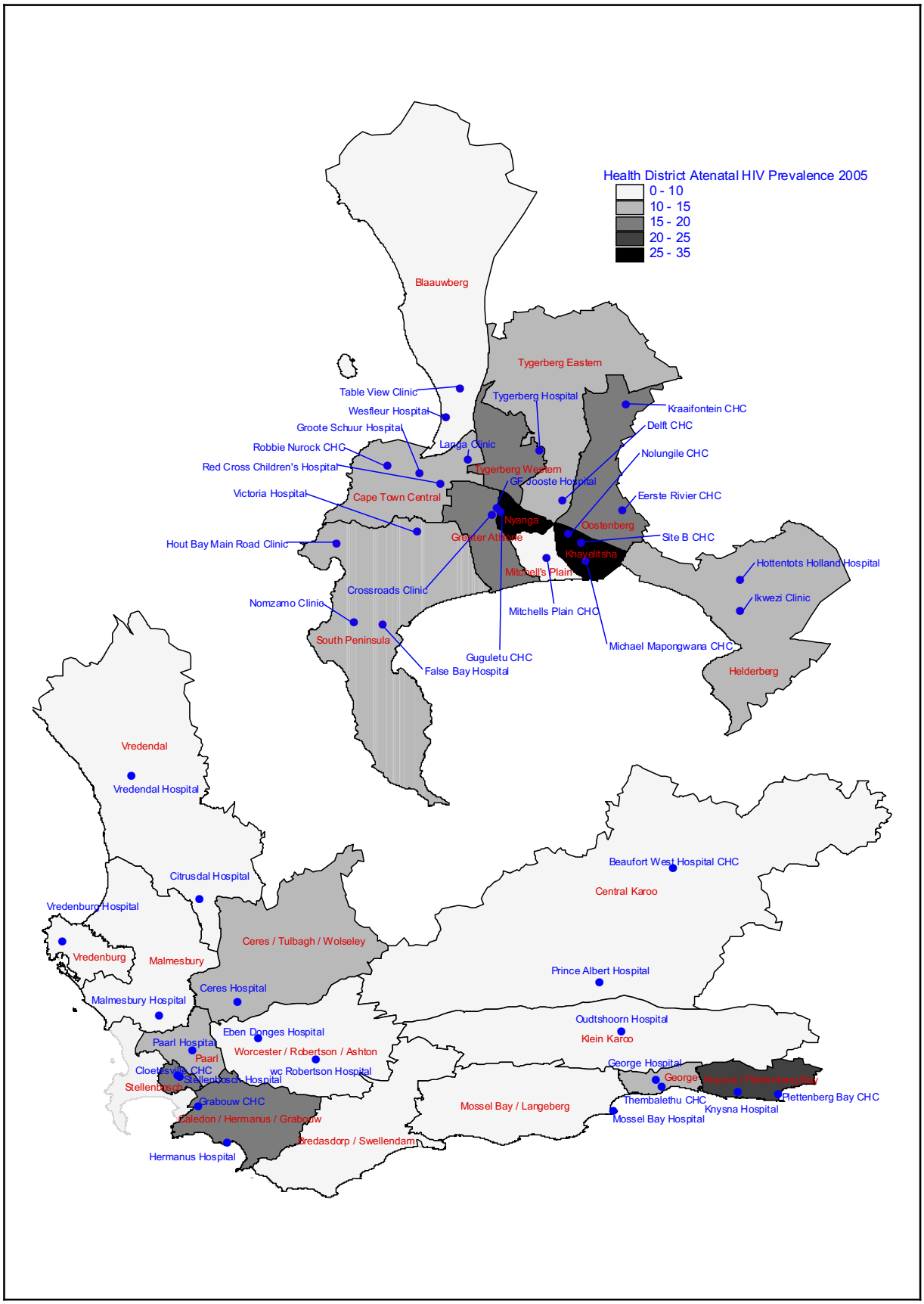


Figure 1. Antiretroviral treatment sites, a) City of Cape Town, b) Outside of Cape Town

Understanding the provincial burden of HIV care

It is important to recognise the context in which ART services are being developed in the Western Cape, as this emphasizes the future requirements for ART that the province will be facing, with implications for the most appropriate model of service delivery.

The Actuarial Society of South Africa maintain an integrated demographic and HIV model which is the *de facto* standard for estimating the size and composition of the HIV-infected population in the country. Key outputs are summarised below (Table 1). It is instructive to consider the implications for adults, bearing in mind that the same issues apply on a smaller scale for children. Currently it is estimated that around 250,000 adults are living with HIV in the Western Cape, and that 20,000 adult patients will develop symptomatic AIDS during the year 2006/7.

Table 1. HIV projections for the Western Cape

Western Cape HIV projections	2006	2007	2008	2009	2010	2011
Adults HIV infected	255,836	270,783	283,311	293,497	301,455	307,338
New infections over previous year	27,605	26,943	26,264	25,583	24,947	24,367
Entered Stage IV over previous year	18,018	20,206	22,002	23,368	24,307	24,851
Children HIV infected	11,453	12,960	14,358	15,605	16,660	17,499
Infected PMTCT previous year	2,993	3,058	3,082	3,073	3,036	2,979
Entered AIDS over previous year	2,073	2,273	2,466	2,623	2,726	2,769
Total number of patients newly eligible for ART	**20,091**	**22,479**	**24,468**	**25,992**	**27,033**	**27,620**

(Source: Adapted from ASSA2003 model)

The last line in this table provides a useful denominator for considering the enrolment of new patients. Without ART, the majority of these patients would die within a year. Some would argue that the private sector caters for some of this burden, since the model is a whole-population model. On the other hand, using projections of new stage IV patients is an underestimate of treatment need. The median CD4 count of patients who develop AIDS (Stage IV) is 126 cells/µl, which is significantly lower than the point of eligibility of 200 cells/µl. Currently this is a fair representation of when (in terms of disease advancement) on average patients are accessing ART in the Western Cape. With time however we should be seeking to treat patients sooner, increasing the size of this denominator.

At any point in time, the demand for care is also represented by patients who are already symptomatic, not just those who are newly symptomatic, resulting in this being a conservative denominator if considering coverage at a single point in time.

These figures will be reflected on again when presenting the data on patient enrolment.

The provincial monitoring system for ART

A system has been put in place for the clinical record-keeping and routine monitoring of the ART intervention (Figure 2). The clinical records, and the routine reports have been standardised. The overall approach is one of cohort monitoring, not dissimilar to that employed in the National Tuberculosis Control Programme. The province took a strategic decision to standardise on a system that could be implemented with immediate effect in all facilities as a minimum, allowing those facilities with additional resources to augment the system.

By force of circumstance this system had to initially be entirely paper-based,[1] comprising:

- Dedicated stationary for **clinical record keeping**, including a patient-retained record, a patient summary, and a visit summary designed to assist clinicians in providing optimal care to patients by integrating longitudinal data in a coherent manner.
- **Facility-based registers** as the minimum requirement for enumerating and documenting outcomes for all patients starting ART, allowing for up to 36 months of follow-up, and facilitating the extraction of routine reports
- Standardised routine **monthly and quarterly cohort reports**, as well as adverse drug reporting forms.
- A set of stock management and reporting **tools for pharmacists**

This system of cohort reporting was developed in consultation with the World Health Organization (WHO), who have included it as a country example in their guidelines on monitoring ART.[2]

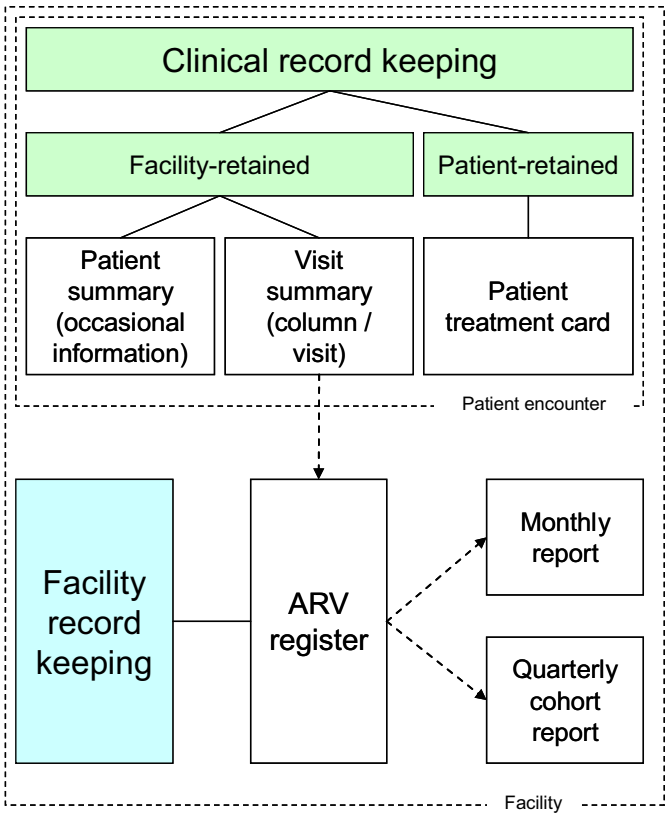


Figure 2. Routine information system for ART in the Western Cape

[1] The entire set of tools are archived on http://www.epi.uct.ac.za/artrollout
[2] Patient monitoring guidelines for HIV care and antiretroviral therapy (ART). Geneva: World Health Organisation; 2005. http://www.who.int/hiv/pub/guidelines/patientmonitoring.pdf

Although there are settings where electronic systems offer distinct advantages, the strategic decision to provide a paper-based minimum standard has ensured that outcome data is available from every single site over a period of two-years. Some facilities have augmented the system with electronic databases, and extract data in the standard formats from these databases. Currently the province is working on a provincial standard electronic patient information system to replace the disparate databases in those facilities that have implemented electronic systems. It is likely however that the paper-based system described here will continue to be used in smaller facilities for some time to come. There are also unique challenges not often appreciated that emerge when implementing electronic systems in primary care, which will be discussed further below.

A further important principle inherent in the monitoring system is one of restricting data collection to a minimum. Monthly data is used primarily to track patient numbers for the purposes of managing and anticipating human resource requirements, as well as ensuring that all facilities are meeting their targets. For this reason, the data elements collected monthly are only the total number of patients, and the total number of newly enrolled patients.

The quarterly reporting provides an opportunity to reflect on quality of care. It is restricted to treatment-naïve patients to ensure that outcomes are comparable between facilities. There is also a delay in reporting quarterly outcomes in order to give facilities a chance to ascertain all outcomes, such as loss to follow-up and outstanding blood results, prior to reporting.

Individualised data, where individual electronic patient records are held and verified for each patient, is restricted to what we term *sentinel* sites. It is preferable to get data of this quality from selected sites with motivated partners, than to attempt to verify data of this nature across the entire provincial programme. The types of data that are available from the sentinel surveillance system are demonstrated below. Overall though, a stratified approach to monitoring (Figure 3) has resulted in data of appropriate quality for the monitoring objectives being collected in each instance.

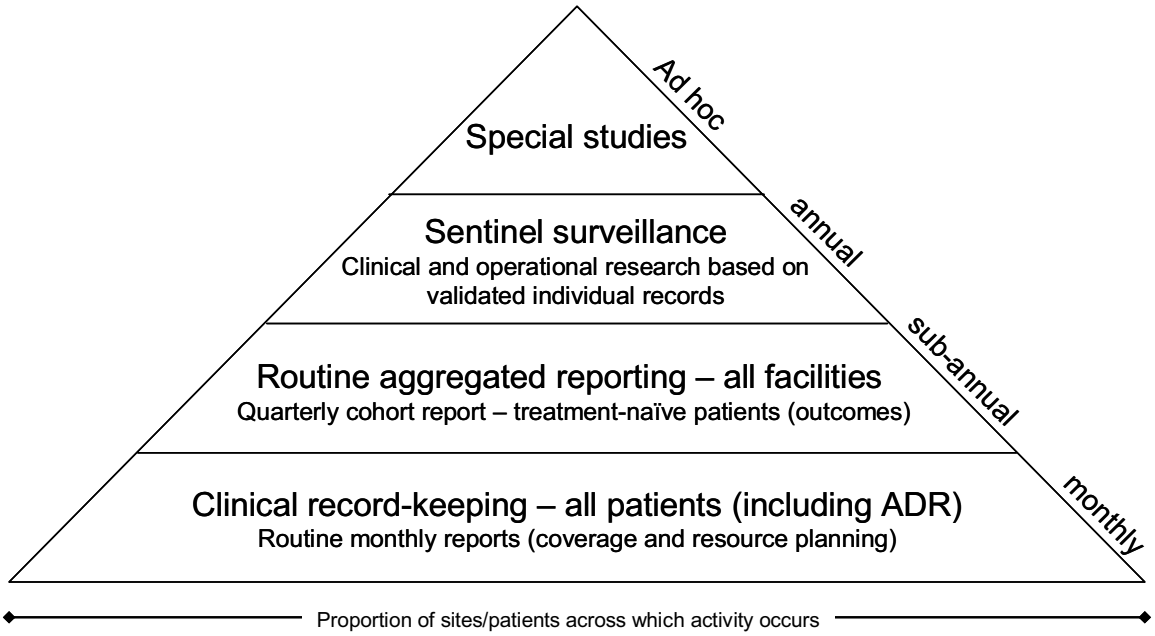


Figure 3. Stratified approach to routine monitoring of ART

Access to and distribution of care: Data from routine monthly reporting

The monthly reporting system provides feedback on the rate of enrolment and total ART patient load in the province. Complete reports are available dating back to the inception of the national programme. The monthly report for March 2006, including a site-by-site breakdown of treatment numbers is included as an annexure (Annexure A). The monthly totals aggregated across the entire province are listed for each month from April 2004 to June 2006 are included as a separate annexure (Annexure B).

At the end of March 2004, 2,327 patients were in care and on ART in the province, of whom 29% were children. The number of new patients enrolled per month since then has increased from 318 in April 2004 to 1121 in March 2006 (Figure 4a). There has been a seasonal decline in enrolment each December and January during this period.

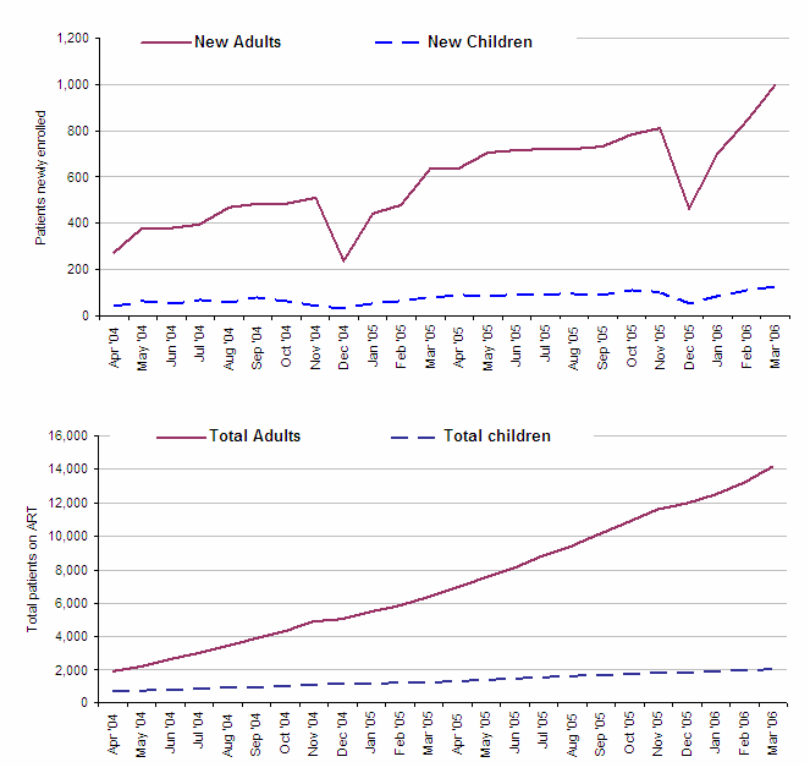


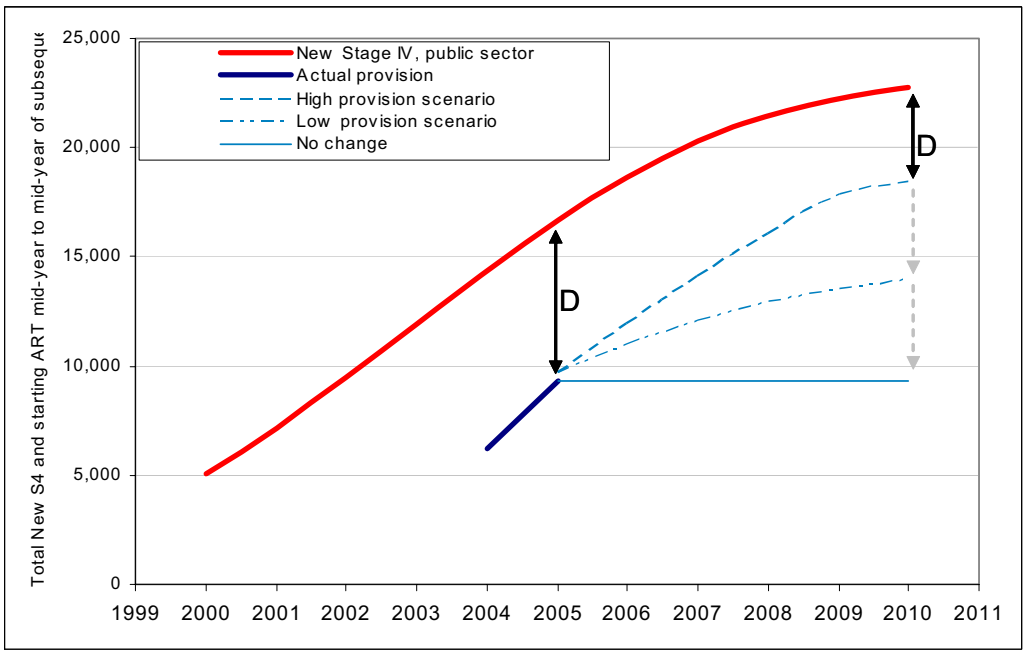
Figure 4. Patient enrolment (a) and total patients on ART (b) by calendar month

The total number of patients in care had increased to 16,234 by the end of March 2006, 14,201 (87%) of whom were adults. The higher proportion of children in April 2004 compared to current figures was the result of paediatric services in academic centres finding ways to provide ART prior to the inception of the national programme. Adult enrolment has subsequently increased at a faster rate than paediatric enrolment. Furthermore, the number of newly symptomatic children is constant or declining due to the prevention of mother-to-child transmission programme (which is estimated from routine data to have reduced vertical transmission to around 5% of infants of infected mothers since the introduction of dual therapy), whereas the number of newly symptomatic adults is increasing as a result of the natural progression of the epidemic in the province.

Comparing the enrolment of new patients to the projected number of new stage IV patients, it is estimated that currently 57% of this number have accessed ART in 2005/6 in the public sector. This does not accurately reflect the backlog in the number of patients requiring care at any point in time, since there are symptomatic patients in need of ART that have been

symptomatic for longer than a year. Using stage IV as a proxy for eligibility further underestimates the true requirement for ART.

Using this comparator for adults however (new stage IV), adjusted to reflect the public sector, Figure 5 demonstrates the potential requirement for ART in the province in terms of new adult patients enrolled. Currently it is estimated that around 7,000 adult patients are dying annually in the Province without ever accessing ART ('D' in the figure), whereas 9,687 newly symptomatic adults have accessed ART in the last year. To *maintain or reduce* the number of deaths in HIV-infected patients never having accessed ART over the next five years, the number enrolled each year will need to progressively double over the five years. If enrolment does not continue to increase or increases only modestly ("No change" and "Low provision scenario"), the number of patients dying without ever accessing ART could double.



D – projected deaths in patients who have never accessed ART

Figure 5. Coverage of projected WHO HIV stage IV adult patients accessing ART

Translating the enrolment into total numbers of patients on ART, it is anticipated that the province will have between 65,000 and 85,000 patients on ART by the end of the 2010/11 financial year in the public sector, depending on which of the trajectories described above (Figure 5) are followed. These estimates are based on an anticipated median survival in care for patient starting ART of between 6.3 and 8.8 years. Outcome data presented in the next section suggest that these assumptions are reasonable.

Looking at equity of provision across geographical areas, eighty percent of patients are treated in the metropolitan area. This compares closely with the proportion of symptomatic patients in the province projected to be in the City of Cape Town. The Provincial antenatal survey provides the opportunity to project treatment numbers by district, and there is a reasonable match between actual treatment provision by district and the projected need by district (Figure 6). There are some obvious distortions. The hospitals in Cape Town Central District for example, treat more patients than would be expected based on antenatal data.

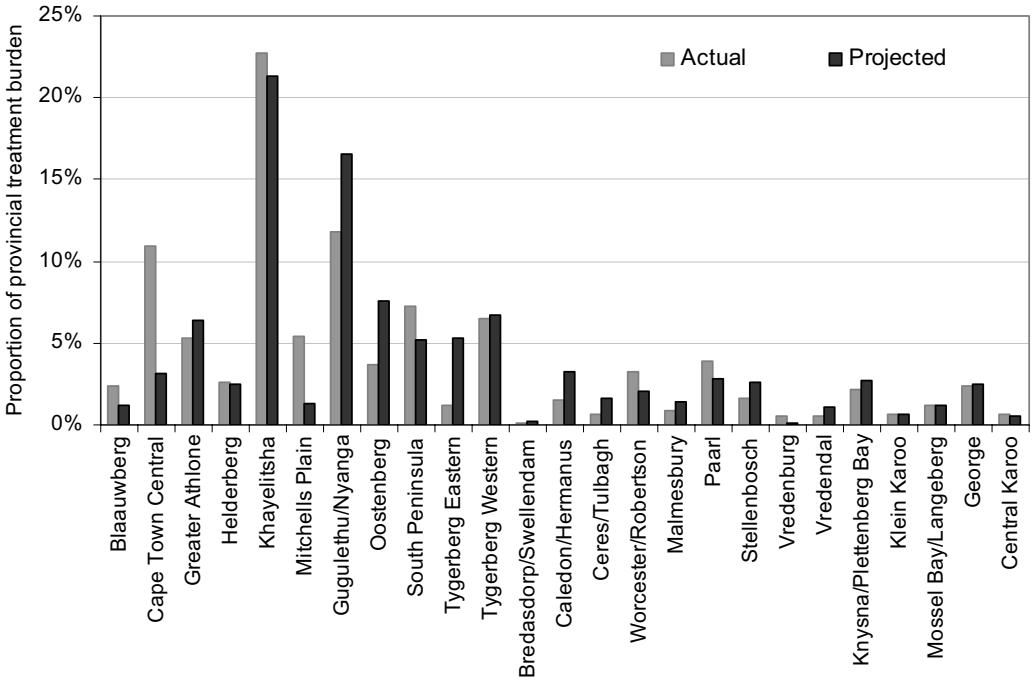


Figure 6. Actual versus projected proportion of treatment burden by district, March 2006

Patient profile and outcomes: Data from quarterly cohort reports

Description of the cohort system

Patients are entered into the antiretroviral register in the order in which they start ART. A quarterly cohort is defined as all patients starting ART in a particular quarter. A set of 11 data elements for each cohort are then extracted from the register at defined durations of follow-up, such as 3, 6, 12 and 18 months after starting ART. Since duration on ART is such a powerful independent determinant of outcomes such as mortality and viral load suppression, the cohort system enables indicators to be compared across facilities at the same duration of follow-up for each cohort.

The outcomes which the cohort system is designed to track include which patients are lost to care (death, loss to follow-up and transfers out), which regimens patients are on, and CD4 and viral load outcomes.

There are essentially four main uses of the cohort data:

1) Description of the characteristics of patients enrolling onto ART, including gender, CD4 count and treatment experience
2) Monitoring how the outcomes described above change as duration of follow-up increases
3) Comparing specific outcomes, at specific durations on treatment across facilities, districts or regions
4) Comparing specific outcomes or baseline characteristics in the same facilities, but at different calendar times – for example comparing outcomes at 6 months duration on ART in patients who started in 2004 compared to those who started in 2005

A composite table is included as an annexure (Annexure C) which demonstrates how baseline characteristics, changes with duration on ART, and changes over time can all be viewed in a single output.

As described earlier, cohort data is reported one quarter in arrears in order to allow for all outcomes to be fully described by the time of reporting. This is necessary as blood results are not always available immediately, and patient deaths and patients lost to follow-up are often only discovered by facilities some weeks or months after they occur when the facilities actively trace patients who have not presented for appointments.

Baseline characteristics of the cohort

This cohort report covers all patients started on ART by the end of 2005, reported in April 2006. Complete data prior to April 2004 is included for the largest sites that were operational before this date, with the result that cohort data goes back to patients starting ART in the second quarter of 2001.

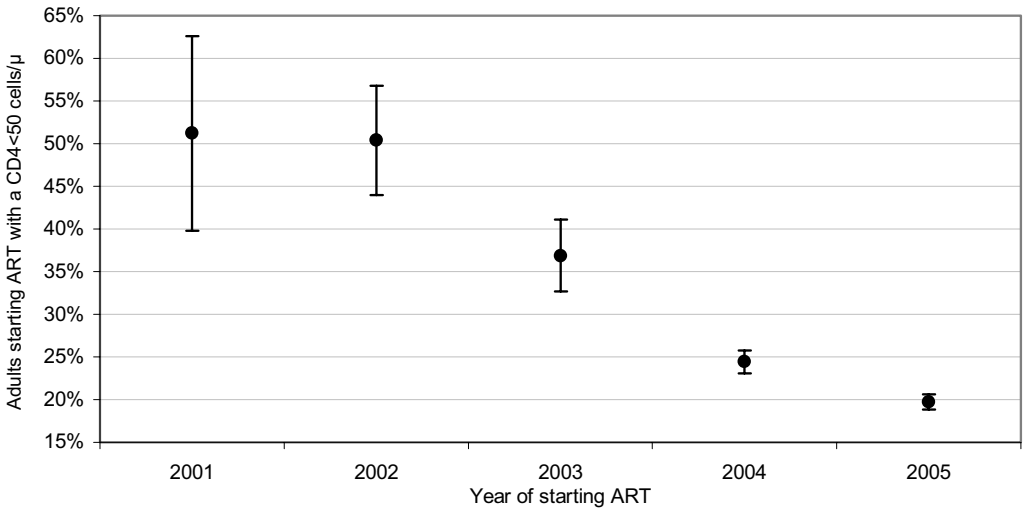
Overall, 12,587 adults and 1,709 children are included in this cohort report, totalling 14,296 treatment-naïve patients. This is a near-complete representation of all patients started on ART in the Western Cape Province by the end of 2005. Follow-up for the oldest quarterly cohorts extends to 48 months (4 years on treatment). A further 2.4% of patients were treatment experienced prior to starting ART, and are not included in this analysis.

A striking feature of ART treatment programmes in Southern Africa is the predominance of women, as has been the case in the Western Cape. The proportion of men starting ART has

remained around 30% over the five years of enrolment in the province, with a very slight increase over time.

The gender breakdown of children is not routinely recorded, but reviews of paediatric data reveal that the gender breakdown of children starting ART is roughly even.

As cohort reports are aggregate totals, the baseline CD4 count on enrolment is reflected by the proportion of patients starting ART with a CD4 count below 50 cells/µl, or 15% in the case of children. The rapid increase in enrolment over the last two years has resulted in patients accessing treatment with less immune suppression in the last two years than previously. This reflects a "catching-up" phenomenon. In 2001 and 2002, half the adult patients starting ART had a CD4 count below 50 cells/µl, whereas this has fallen to 20% in 2005 (Figure 7).



n	80	248	524	4041	7694
CD4 < 50 cells/µl	51%	50%	37%	24%	20%
95% CI	(40 - 63)	(44 - 57)	(33 - 41)	(23 - 26)	(19 - 21)

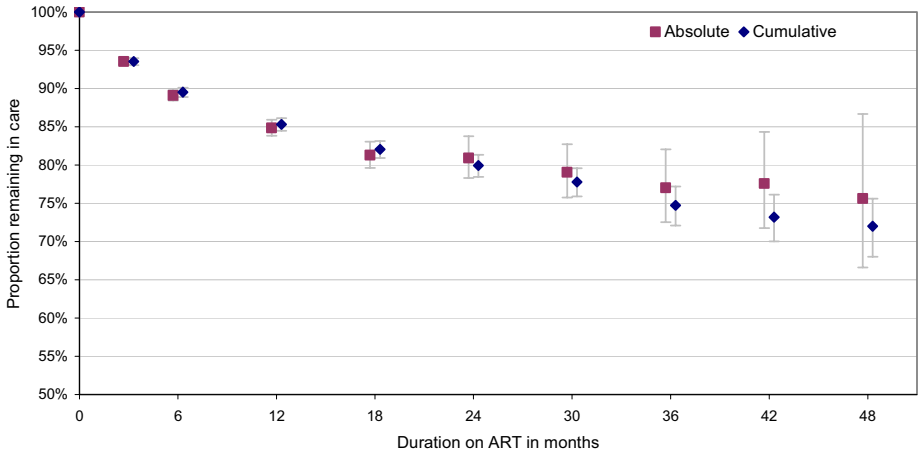
Figure 7. Adult CD4 count below 50 cells/µl on starting ART

Overall, 45% of children started ART with a CD4 count below 15% of total lymphocytes. There has been a decline over time in the proportion of children starting ART with more advanced immune suppression, but less dramatic than that observed for adults.

Outcomes by duration on ART

Survival and retention in care

After four years on ART, 76% of adults remain in care (Figure 8). The small proportion of patients transferring out are excluded from this calculation. For each duration on ART, this absolute estimate is based only on the data for those patients who started that number of months previously. Outcomes are however changing over time (see below), and it is possible to statistically include all the data in a survival estimate, known as the Kaplan-Meier method. Although we do not have individual data, we were able to convert count data to weighted survival data, and produce a cumulative estimate of retention in care. Using this latter approach, the estimate of retention in care is 72% at four years on ART and the confidence interval for this estimate is much narrower (95% CI 68.0% – 75.6%). In summary, it is reasonable to say that in the Western Cape, after four years on ART, 7 out of 10 adult patients remain in care.



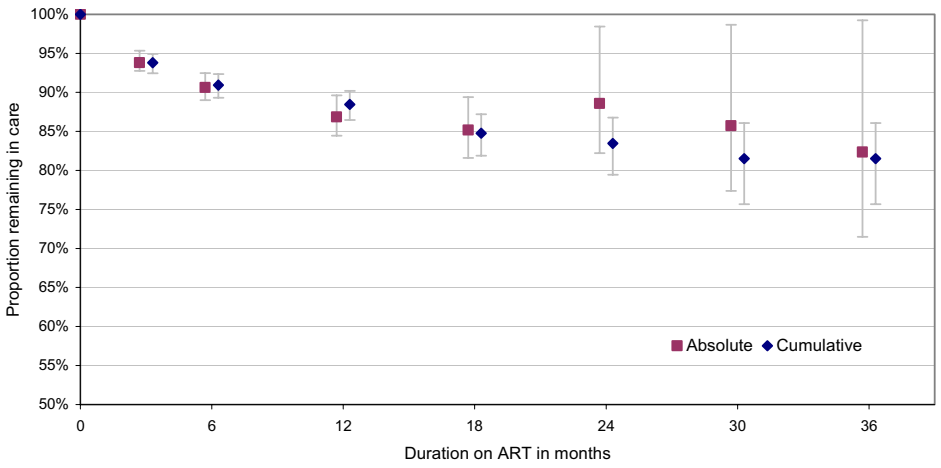
Total adults starting ART	12587	8341	4726	2167	852	561	328	189	80
Started before		30/06/2005	31/12/2004	30/06/2004	31/12/2003	30/06/2003	31/12/2002	30/06/2002	31/12/2001
Deaths since start - n(%)		545 (6.7)	397 (8.8)	239 (11.6)	131 (15.8)	96 (17.6)	60 (18.9)	36 (19.7)	18 (23.1)
Lost to follow-up since start - n(%)		340 (4.2)	286 (6.3)	148 (7.2)	27 (3.3)	18 (3.3)	13 (4.1)	5 (2.7)	1 (1.3)
Transfers out since start - n(%)		223 (2.7)	214 (4.7)	98 (4.7)	23 (2.8)	16 (2.9)	10 (3.1)	6 (3.3)	2 (2.6)
Remaining in care (absolute)		89.1	84.9	81.3	80.9	79.1	77.0	77.6	75.6
(95% CI)		(88.4 - 89.8)	(83.8 - 85.9)	(79.5 - 83.0)	(78.1 - 83.6)	(75.4 - 82.4)	(72.0 - 81.6)	(70.9 - 83.4)	(64.6 - 84.7)
Remaining in care (cumulative)		89.5	85.3	82.1	80.0	77.8	74.8	73.2	72.0
(95% CI)		(88.9 - 90.1)	(84.5 - 86.1)	(80.9 - 83.1)	(78.5 - 81.4)	(75.9 - 79.6)	(72.1 - 77.2)	(70.0 - 76.1)	(68.0 - 75.6)

Figure 8. Outcomes – adult retention in care, mortality and loss to follow-up

A similar analysis of paediatric outcomes (Figure 9) reveals 82% of children remaining in care after 3 years. If looking only at those children who have been in care for the entire three years, the estimate is the same.

In both adults and children starting ART, mortality is highest in the first 6 months on therapy, in line with what has been described in many similar settings, and in sentinel sites.

The definition of loss to follow-up is patients not seen in the services for 3 months or more. Although the 3 month window is useful from a reporting perspective (allowing full ascertainment of outcomes one quarter in arrears), it is by international standards a very tight definition of loss to follow-up, and a high proportion of these patients subsequently do return to care.



Total children starting ART	1709	1216	770	371	72	51	35
Started before		30/06/2005	31/12/2004	30/06/2004	31/12/2003	30/06/2003	31/12/2002
Deaths since start - n(%)		84 (7.4)	68 (9.8)	32 (9.3)	4 (5.7)	4 (8.2)	4 (11.8)
Lost to follow-up since start - n(%)		22 (1.9)	23 (3.3)	19 (5.5)	4 (5.7)	3 (6.1)	2 (5.9)
Transfers out since start - n(%)		84 (7.4)	77 (11.1)	27 (7.8)	2 (2.9)	2 (4.1)	1 (2.9)
Remaining in care (absolute)		90.6	86.9	85.2	88.6	85.7	82.4
(95% CI)		(88.8 - 92.3)	(84.1 - 89.3)	(81.0 - 88.8)	(78.7 - 94.9)	(72.8 - 94.1)	(65.5 - 93.2)
Remaining in care (cumulative)		90.9	88.5	84.8	83.5	81.5	81.5
(95% CI)		(89.3 - 92.4)	(86.5 - 90.2)	(81.9 - 87.2)	(79.4 - 86.8)	(75.7 - 86.1)	(75.7 - 86.1)

Figure 9. Outcomes – paediatric retention in care, mortality and loss to follow-up

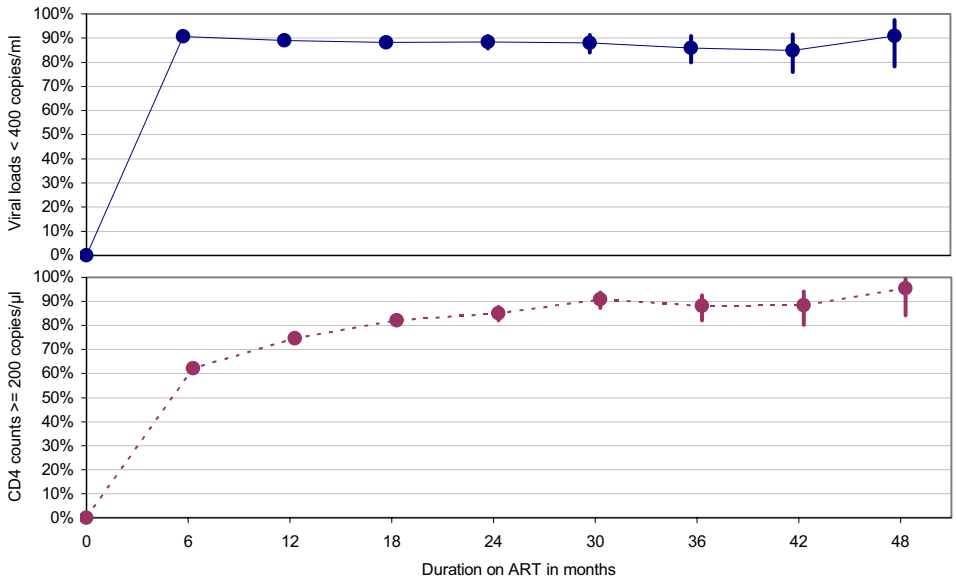
Laboratory outcomes and switching to second-line

The two laboratory tests that give an indication on the success of antiretroviral treatment are the viral load and the CD4 count. The cohort system uses a cut-off for each of these tests in order to allow the aggregation of results into two categories in each instance, which can be easily tabulated from a register. For viral load, the therapeutic goal is to attain virological suppression. The upper bound of the limit of detection for the tests used by the National Health Laboratory Service (NASBA EasyQ) is just below 400 copies/ml, which corresponds with the cut-off used in the cohort system. For CD4 counts, we monitor the proportion of patients attaining an absolute CD4 count above 200 cells/µl. This is the level above which prophylactic medication can be safely discontinued, and many opportunistic infections are much less likely to occur.

The first metric reported on here is the proportion of tests that are done when they should be done. This is an indication of the quality of care. To date, results are being received in the cohort system for four out of five patients who should be getting these tests. There is currently a slight drop-off in the test completion proportion as the duration on ART increases.

Looking at adult outcomes, of those tested, 90% of patients achieve virological suppression by 6 months on ART (Figure 10). Given that this is a treatment-naïve population, virological suppression should be attainable, and failure to suppress in the first six months is most commonly the result of adherence problems. Nevertheless 90% suppression compares very favourably with routine programmes in other settings. This proportion remains above 85% until 24 months on treatment. It is difficult to interpret the data beyond this duration, as by this time some patients have been put on second-line regimens, and the data system does not distinguish which viral loads are done in patients on first-line versus those on second-line. At 2 years duration on ART, 3.5% of adults were on second-line, rising to 17.9% at four years duration on ART. Combining all patients together, irrespective of the duration on ART, 1.3% of patients were reported to be on second-line regimens at the end of 2005.

At the end of the first year on treatment, 60% of patients had attained a CD4 count above 200 cells/µl, rising to 85% at 2 years and 95% at 4 years on ART.



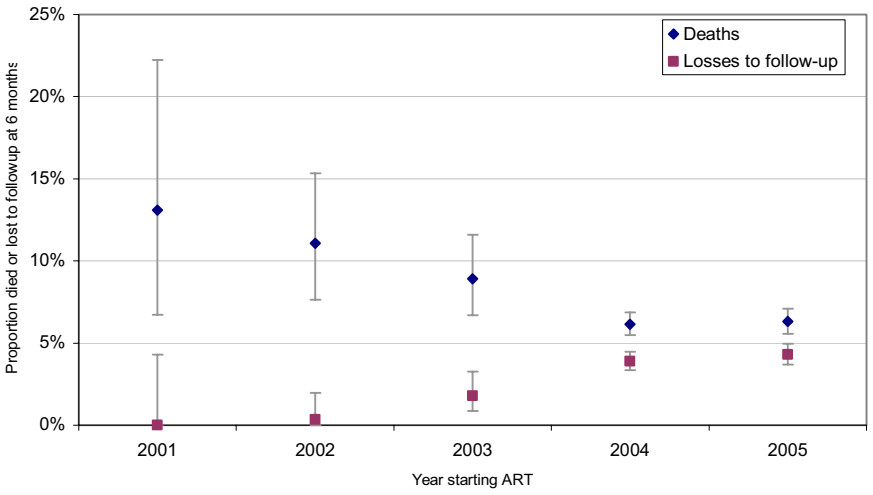
Viral loads done	5993	3331	1420	640	343	171	93	44
Completion %	84.2%	89.1%	85.4%	85.1%	82.9%	72.2%	66.9%	78.6%
Proportion <400 copies/ml	90.6%	89.0%	88.2%	88.4%	88.0%	86.0%	84.9%	90.9%
95% CI	(89.8 - 91.3)	(87.8 - 90.0)	(86.4 - 89.9)	(85.7 - 90.8)	(84.1 - 91.3)	(79.8 - 90.8)	(76.0 - 91.5)	(78.3 - 97.5)
CD4 counts done	5976	3336	1399	630	331	168	95	43
Completion %	82.5%	87.1%	82.1%	81.6%	76.8%	68.6%	66.9%	72.9%
Proportion>= 200 cells/µl	62.3%	74.7%	82.2%	85.1%	90.9%	88.1%	88.4%	95.3%
95% CI	(61.0 - 63.5)	(73.2 - 76.2)	(80.1 - 84.2)	(82.1 - 87.8)	(87.3 - 93.8)	(82.2 - 92.6)	(80.2 - 94.1)	(84.2 - 99.4)

Figure 10. Laboratory outc***o***mes for adults on ART

Although paediatric laboratory outcomes are not formally presented here (see Annexure C for more details), between 70% and 80% of children with follow-up viral load tests have levels below 400 copies/ml up until 3 years duration on ART. At 3 years duration on ART, 7.4% of children were on second-line regimens.

Changes in outcomes over time

As described above, as the rate of enrolment has increased in the province, so the patients have been less ill when starting ART, evidenced by the lower proportion with CD4 cell counts below 50 cells/µl at ART initiation. This, coupled with the expansion of the programme into different communities, has seen the mortality in the first six months on ART fall (Figure 11). At the same time, the increased numbers have strained the administrative, counselling and community follow-up capacity at many of the busiest clinics, with a consequent increase in the proportion of patients lost to follow-up. Some of the reduced recorded mortality can inevitably be ascribed to patients classified as lost to follow-up who have in fact died. It is also probable however that there has been a real impact on morbidity and mortality as a result of the “catching up”, as not all patients who are lost to follow-up are lost due to unrecorded mortality.



n	80	248	524	4041	7694
Mortality	13.1%	11.1%	8.9%	6.1%	6.3%
95% CI	(6.7 - 22.2)	(7.6 - 15.3)	(6.7 - 11.6)	(5.5 - 6.9)	(5.6 - 7.1)
Loss to follow-up	0.0%	0.4%	1.8%	3.9%	4.3%
95% CI	(0.0 - 4.3)	(0.0 - 2.0)	(0.9 - 3.3)	(3.4 - 4.5)	(3.7 - 5.0)

Figure 11. Changes over time in mortality and loss to follow-up at 6 months

Differences in outcomes across districts

Differences in outcomes between health districts are beginning to emerge, reflecting a combination of health service issues as well as different patient profiles. Two examples are included here as illustrative of the types of analyses that are fed back to districts. In the first example (Figure 12), the failure to document viral load results in patients eligible for follow-up tests at 12 months on ART is compared across health districts. Confidence intervals (95%) are included to assist in identifying where differences have statistical support. The upper and lower confidence bounds for the whole province are included for reference.

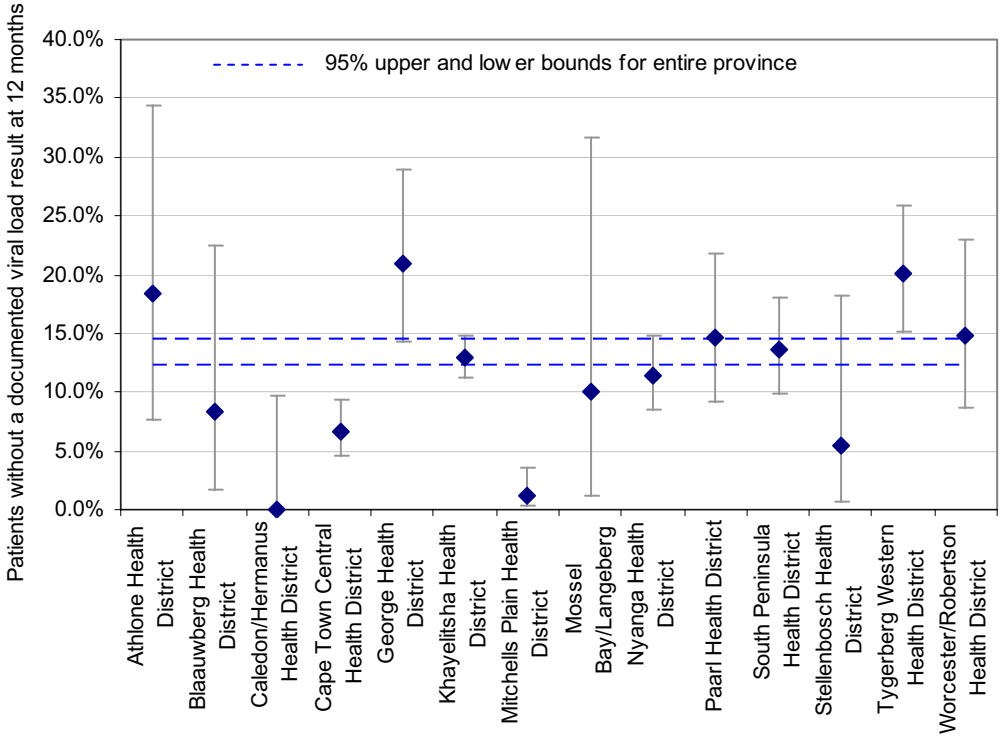


Figure 12. Failure to document viral load results at 12 months on ART by health district

From this analysis, it is possible to identify districts where viral load testing is reaching a higher proportion of patients. The local organisation of services and administrative systems are areas that can impact on this.

Looking at actual viral load results of those patients tested (Figure 13) also reflects on clinic functioning, especially on the quality and completeness of adherence interventions. Differences may also be related to the profile of patients at different sites, either clinical or socio-economic.

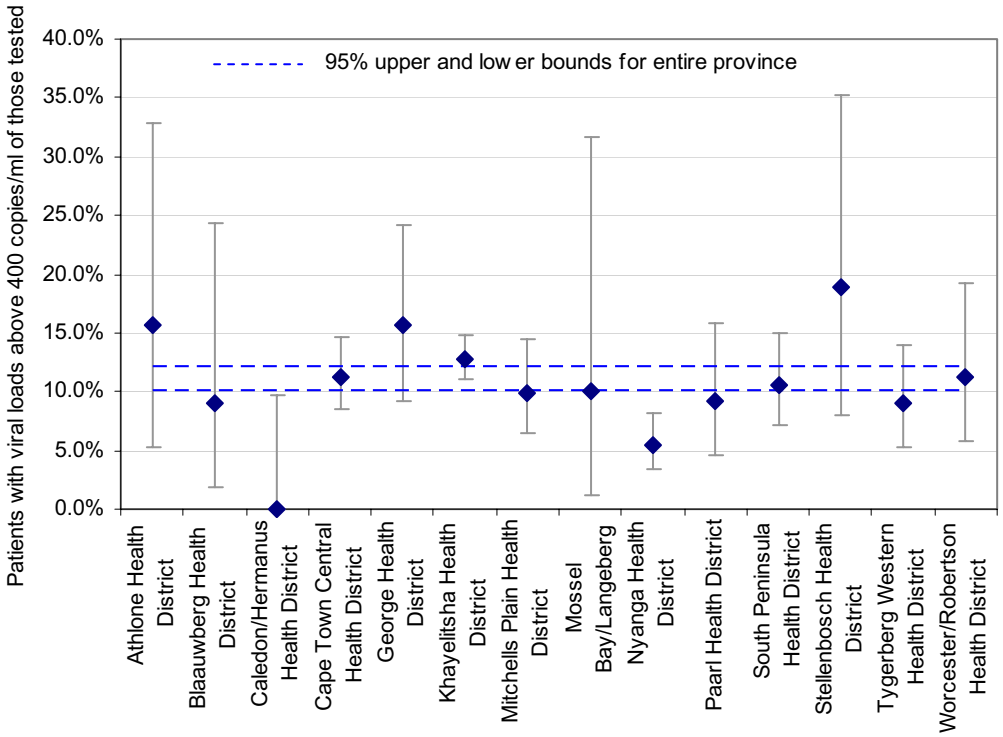


Figure 13. Viral loads above 400 copies/ml at 12 months on ART in those patients tested

Clinical challenges: Data from sentinel surveillance and pharmacovigilance reporting

Introduction

The Western Cape Department of Health is fortunate in having longstanding relationships with academic institutions and non-governmental organisations who have a keen interest in clinical and operational research in the area of HIV care interventions. Many of these initiatives predate the launch of the national programme, and provide the opportunity to both explore clinical issues with individualised patient data, and in instances where the programmes have been in operation for a few years, anticipate some of the medium and longer term clinical challenges.

Although the number of sites which collect their data in an electronic form is likely to increase, and that many sites do in fact currently collect electronic data, what distinguishes the sentinel sites is the ability to verify and validate the data collected to a level where it can be used for clinical research. It would not be feasible or necessarily a good use of resources to attempt to validate individual patient data to this extent across the entire province.

The sentinel sites, through the production of individualised cohort data, are able to answer a number of key questions, such as providing accurate estimates of the incidence of specified diseases, the durability and tolerability of individual drugs, and the patient and care factors that are associated with good or poor outcomes. At the same time, the Department of Pharmacology at the University of Cape Town, in partnership with the Department of Health, maintain a database of adverse drug events in patients on ART. The reporting format is adapted to the specific requirements of ART. Although ascertainment of events is not complete, the data provide the opportunity to detect new or infrequent events, and also provide important details on how events are managed after ascertainment, details which are often missing from the cohort databases.

In this section, a few recent contributions from sentinel sites that are part of the provincial programme and the adverse drug reaction reporting system are highlighted.

Early identification of viraemic patients can conserve first-line

Contributed by Catherine Orrell, Gugulethu ART clinic and the Desmond Tutu HIV Centre, UCT

In South Africa, the national ART programme supplies first- and second-line regimens free of charge, but thereafter offers no further treatment options. Only four nucleoside reverse transcriptase inhibitors are available as backbone therapy within the two available regimens. Treatment options following development of either drug toxicity or virological failure are often limited due to the high costs of alternative medications. Even within the limited options available, second-line therapy is on average three times more costly than first line.

For long-term health to be maintained within a framework of these limited ART options, it is important to maximise the clinical benefits derived from each regimen. High rates of switching of therapy would result in a large proportion of the ART treated population in South Africa quickly exhausting their treatment options. A balance must be maintained between switching early with resultant loss of regimens and continuing a failing regimen which may encourage development of viral resistance.

The experience of the team at Gugulethu suggests that use of regular follow-up viral load measurements coupled with an intensive peer-counsellor adherence intervention to manage initial virological breakthrough is associated with a low rate of confirmed failure, thereby

retaining individuals on first-line therapy and conserving more expensive second-line therapy for future use.

In our clinic, people who have a viral load of more than 1000 copies/ml at any time after treatment begins are targeted by the counsellors for an intensive adherence intervention. This includes repeating the initial 3 “treatment readiness” sessions”, training in the use of a pill box (supplied), use of a daily dosing diary and a series of home visits by a counsellor. They have a red sticker placed on their folders to alert all staff to the fact that they require more intensive input. Only once their viral load reaches lower than the detectable limit does the intensive intervention cease.

Over 32 months, 67 individuals (7.2%) had ≥1 follow-up viral load measurement of >1000 copies/ml, but only twenty people (2.2%) had been confirmed as virological treatment failures and had commenced or were shortly to commence the second-line treatment regimen. In essence, 71% of those with high viral loads returned to complete viral suppression after the intensive adherence intervention run by the counsellors.

To determine the likelihood of virological failure above >1000 copies/ml we plotted Kaplan-Meier proportion estimates. At 32 months on treatment, 20% of patients would be estimated to have a ≥1 viral load measurement >1000 copies/ml and receive the targeted adherence intervention. It was estimated that virological failure would subsequently be confirmed in 29% of these; comprising just 5.6% of the whole cohort. This corresponds to a rate of 2.2 per 100 patient years.

Recent studies in the developed world have noted that initial or primary virological failure (one elevated viral load) is more likely to be due to treatment interruption or poor adherence rather than viral resistance. Thus, management of initial virological failure using targeted interventions to improve adherence has the potential to have a positive impact on maintaining low rate of transfer to second-line therapy.

Use of viral load monitoring in community-based settings has been debated due to the expense. However, waiting for a decrease in the CD4 count or for an AIDS-defining illness, effectively delays recognition of virological failure and potentially increases the risk of developing viral resistance, thus limiting drug options further. At present all South African ART sites have access to viral load monitoring. Data from other programmes are needed to further evaluate different patient management strategies.

A public health approach to antiretroviral therapy requires optimal use of limited treatment regimens. In Gugulethu, the use of viral load measurements, coupled with a targeted adherence intervention, was associated with a low rate of virological failure and resulted in more than 95% of patients remaining on first-line therapy in this resource-limited setting. It is possible to conserve future ART options by maintaining the majority of individuals on first line regimens.

Challenges as a result of the high incidence of tuberculosis

Contributed by Steve Lawn, Gugulethu ART clinic and the Desmond Tutu HIV Centre, UCT

There is a huge burden of TB among patients entering the Gugulethu programme with 25% either already receiving treatment for TB or having active TB. Sputum smears for pulmonary disease have poor sensitivity and sputum culture is necessary in many cases. Patients with TB have a 2-3-fold greater mortality, but virological outcomes and CD4 recovery at 48 weeks are not compromised among survivors. Mortality risk is very high while patients with TB are waiting to start ART, suggesting patients should receive ART earlier than is happening at present. The risk of TB during ART decreases over 2 years as CD4 counts rise, but longer term risk of TB remains 5-10-fold higher than that among HIV-negative people in the community.

Contributed by Graeme Meintjes, G F Jooste Referral Unit and Department of Medicine, UCT

Diagnosing TB in patients with HIV is a constant challenge for clinicians, as the standard diagnostic test, a sputum smear showing acid-fast bacilli, is often negative in HIV-infected individuals in spite of them having active TB. In these patients with "smear-negative" TB, waiting for other tests such as cultures can take many weeks, and lead to significant delays in making a diagnosis and initiating TB therapy. A study conducted jointly by the Nolungile CHC in Khayelitsha, and the GF Jooste Hospital ART referral unit, tested an algorithm designed to facilitate clinico-radiological diagnosis of pulmonary TB (PTB) in HIV-infected smear-negative adult patients. Specific parameters such as weight, C-reactive protein, and haemoglobin were identified to be monitored in order to ascertain whether or not patients responded to empiric TB therapy.

Folders were reviewed for 58 HIV-infected adult patients with suspected PTB who were consecutively referred to the local TB clinic for outpatient TB treatment using this algorithm between February 2004 and April 2005. Thirty-two of the 58 patients (55%) ultimately had positive TB cultures (definite TB). Initiation of TB treatment occurred on average 19.5 days before the positive culture report. A further 21 patients (36%) demonstrated clinical improvement on empiric treatment (probable/possible TB). Two patients did not improve and subsequently died without a definitive diagnosis. Three patients defaulted treatment.

The algorithm allowed for earlier initiation of TB treatment in patients presenting with symptoms of PTB in this setting. The algorithm diagnosed TB reliably. It is likely that by reducing the delay in the initiation of TB treatment, morbidity and mortality in these patients was reduced. Adapting the TB algorithm that is in general use to specifically identify smear-negative TB is feasible and could result in a significant reduction in the diagnostic delay in HIV-infected patients with smear-negative TB.

Reasons for regimen substitutions

Contributed by Andrew Boulle, School of Public Health and Family Medicine, UCT

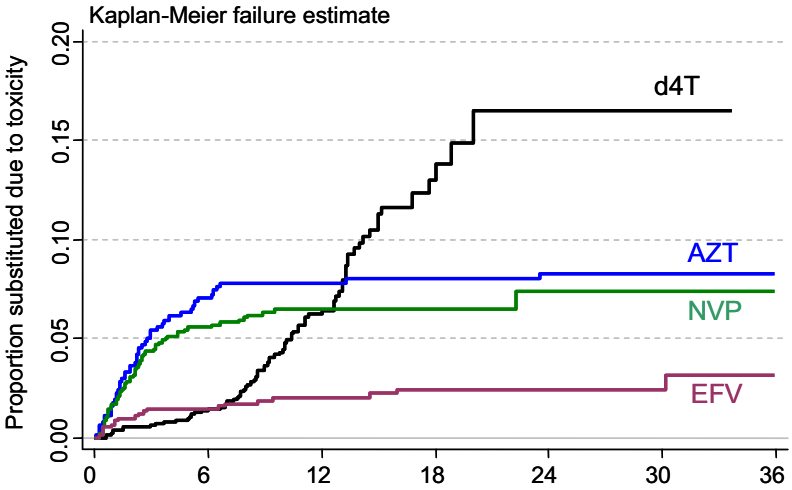
The Khayelitsha programme reported early in 2006 their findings on the rate of substitution of individual drugs due to toxicity as defined by the treating clinician. As the programme had started many patients on zidovudine (AZT) as first-line prior to the national programme, they were able to compare the rate of substitution in patients starting on this drug compared to on stavudine (d4T).

Of those patients who had been in care for three years, 70% were on the same regimen on which they started ART three years previously. The most frequent reason for changing therapy was due to contraindications such as concurrent tuberculosis (nevirapine substituted) or pregnancy or the desire for pregnancy (efavirenz substituted). Substitutions due to toxicity were the next most frequent reason for regimen changes, followed by switches to second-line due to virological failure.

In the first six months on ART, the most frequent toxicity-mediated substitutions were in patients on zidovudine or nevirapine. There were very few toxicity-induced substitutions of these drugs beyond six months on ART, with cumulatively 7.4% and 8.3% of patients having had the drug substituted by 3 years on ART respectively (Figure 14). Zidovudine was almost always substituted due to anaemia, whereas nevirapine was most commonly substituted due to raised liver enzymes, followed by rashes thought by the clinician to be associated with the drug.

In contrast, substitutions of stavudine due to toxicity were very few in the first six months on ART, increasing rapidly thereafter, surpassing substitutions to the other drugs. The most frequent reasons for toxicity-induced substitution of stavudine were peripheral neuropathy and symptomatic hyperlactataemia or lactic acidosis (SH/LA). In total 34 patients had

stavudine substituted due to SH/LA, with 31 of these patients being women, of whom 17 women weighed more than 75 kg at the start of therapy. A multivariate analysis revealed that compared to men weighing less than 60kg, women initiating ART above 75kg were 25 times more likely to develop SH/LA. This finding concurs with similar reports from elsewhere, including from McCord Hospital in Durban. As this condition is potentially fatal, and can be easily missed in a busy clinical setting, there is a strong rationale to consider alternative treatment regimens in this subgroup of patients.



	n							Changed by 36 months (%, 95% CI)
d4T	1228	1065	471	113	18	9	5	16.5 (12.0-22.6)
AZT	639	497	442	417	306	205	132	8.3 (6.3-10.9)
NVP	977	828	385	129	104	89	63	7.4 (5.4-10.1)
EFV	967	790	558	423	245	139	81	3.1 (1.8-5.5)

Figure 14. Regimen substitutions due to toxicity

Paediatric outcomes in a hospital setting

Contributed by Brian Eley, Red Cross Children's Hospital and School of Child and Adolescent Health, UCT

The Red Cross Children's Hospital have recently described the outcomes in children starting ART at their clinic by the end of 2004, and were able to look at predictors of poor outcomes at one year on ART.

Of 409 children commenced on HAART, 50.6% were < 2 years old, 62.7% had severe clinical disease and 76.6% severe immune suppression. After 1 year, 65.8% were alive and continued HAART at the hospital, 11.2% had been transferred to another antiretroviral site, 15.4% had died, 4.6% were lost to follow-up and treatment discontinued in 2.9%. Kaplan-Meier survival estimate for 407 children at 1 year was 84% (95% CI: 80-87%). On multivariate analysis, survival was adversely affected in children with WHO stage 4 vs stage 2+3 disease, age < 12 months and CD4 absolute count (per 100 cell increase). In a separate multivariate model including only children with an initial viral load (n=367), viral load ≥ 1million and taking a PI-based regimen were additionally independently associated with poorer survival, however young age was not a significant predictor of mortality, after adjusting for viral load. After 1 year of HAART 184/264 (69.7%) of children had a viral load < 400 copies/ml. Comparative analysis showed significant improvements in growth, immunological status and virological control.

In summary, the survival estimate of 84% after 1 year is reasonable in view of the clinical severity and the high proportion of children less than 2 years of age.

Adverse reaction reporting system

Contributed by Ushma Mehta and Tamara Kredo, Department of Pharmacology, University of Cape Town

As described above, the Provincial Government of the Western Cape in collaboration with the University of Cape Town and provincial clinical staff involved in HIV/AIDS treatment, has implemented an adverse drug reaction (ADR) reporting system for patients on antiretroviral medicines. The programme aims to improve the safety for patients using these and other medicines by monitoring the safety of these medicines in our local patient population. A report summarising the results of the ADR reporting system one year after its implementation is included below.

Objectives of the ADR reporting system

The objectives of the Western Cape antiretroviral pharmacovigilance system are to:

- Promote a culture of safety awareness and adverse drug reaction reporting
- Identify signals of previously unknown adverse drug reactions
- Identify preventable risk factors contributing to drug-related diseases in patients on antiretroviral medicines.
- Conduct operational research to identify and prevent system errors contributing to drug-related harm.
- Collaborate with the MEDUNSA pharmacovigilance unit and the MCC to comply with the pharmacovigilance requirements of the national HIV/AIDS comprehensive treatment plan.

About the Programme

The pharmacovigilance system focuses primarily on reporting of serious suspected adverse drug reactions using a specially designed form. This passive stimulated reporting system has been successfully piloted and is now being formalized throughout the province. The system involves completion of an ADR reporting form as well as a monthly null-reporting form. Guidelines on reporting are also provided for reporters.

Results

From March 2005 to the end of December 2006 172 reports were received from 23 facilities in the province. Figure 15 provides a synopsis of the monthly reporting rate since March last year. There were 146 adult reports (> 18 years) and 26 paediatric reports (<18 years).

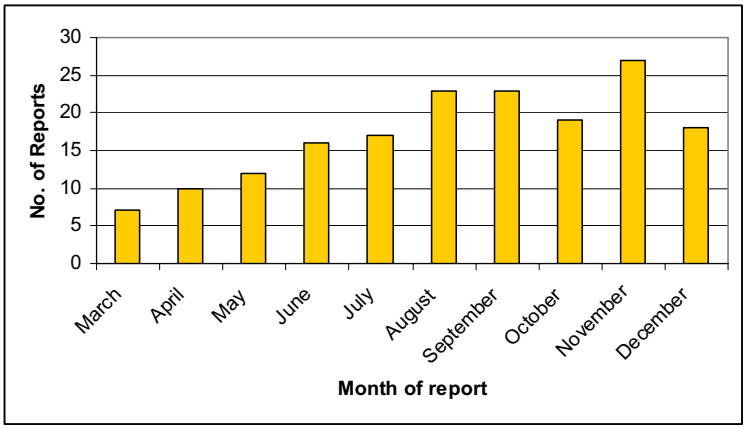


Figure 15. Number of reports received per month from March to Dec 2005

Adult Reports

Among adults (Table 2), reports were predominantly in females 109 (77%) and the median age of patients with suspected ADRs was 35 (Interquartile range 29 - 41). This is very similar to demographics of the patient population in the antiretroviral programme. Most of the reports (n=119) were with the efavirenz-based first line regimen (81.5%) and 20 (13.7%) with the nevirapine-based first line regimen.

Table 2. Frequency of ADR events reported in adults

Event reported	Number of events
Symptomatic hyperlactataemia	45
Death	36
Transaminitis/liver dysfunction	18
Lactic acidosis	15
Peripheral Neuropathy (severe)	12
Lipodystrophy	8
Anaemia	7
Skin reaction	6
Neuropsychiatric effects (EFV)	4
Pancreatitis	4
Cerebellar ataxia (EFV)	1

Deaths: Of the 36 reported deaths, 24 were due to the underlying disease and 5 were as a result of lactic acidosis with or without pancreatitis and hepatic steatosis. In addition deaths were reported in patients with liver failure (n=2), seizures (n=1) and a possible drug eruption (n=1). In 3 cases the cause of death was not specified.

Symptomatic hyperlactataemia and lactic acidosis: The number of SH/LA reports may be higher than the expected internationally reported rate taking into account the fact that not all cases have been reported from all facilities over the time period. Data from these reports, which is supported by the Khayelitsha analysis describe above, suggest that the rate of symptomatic hyperlactataemia may be higher in heavier women. The body mass indexes of patients reported to have metabolic complications were significantly higher compared to patients with non-metabolic adverse reactions. All cases of SH and LA occurred in adult patients on a stavudine-based-regimen.

Pregnancy reports: In nine of the reports, the patient was reported to be pregnant while taking HAART. Seven of these cases reported an efavirenz-based regimen, which is potentially teratogenic. Of these 9 cases the outcome of the pregnancy was unknown in 5. These cases will be followed up at the time of delivery. In 2 cases no congenital anomalies were noted at birth. One case of efavirenz hypersensitivity and one case of hyperlactataemia were reported. The pregnancy was ongoing at the time of the report in both these latter cases.

Cerebellar ataxia: There was 1 case of cerebellar ataxia associated with an efavirenz-based regimen. Based on the information in the report, it is unclear whether this is disease or drug-related and whether the ataxia could be attributed to acute dizziness. However, the patient recovered fully within a week of stopping efavirenz. There were 2 other reports of extreme dizziness warranting a regimen change. The diagnosis of cerebellar ataxia requires neurological confirmation. This potential signal needs to be strengthened with more detailed future reports.

Paediatric reports

Of the 26 paediatric reports, five deaths were reported, none of which were considered to be drug-related. In most of the paediatric reports, the adverse events could be explained by the patient's underlying condition. There were 2 cases of lymphadenitis after BCG vaccination,

and one case of lipodystrophy in a child on stavudine, didanosine and lopinavir/ritonavir since 2003.

Conclusions

- The pharmacovigilance programme has been extremely successful, thanks to the efforts of all the clinical staff participating in the programme.
- Despite our successes the system can be improved through more reports of better quality.
- Metabolic disturbances are the most commonly reported events, and are more frequently reported in heavier women. .
- No congenital anomalies associated with HAART have been detected and reported to date.
- The possibility of cerebellar ataxia associated with efavirenz use needs further investigation. Could this be disease or drug-related severe dizziness or a new signal?

Resource requirements

Expenditure on ART

Although delivering ART care draws on infrastructure and human resources that are already in place in many facilities, dedicated funding to employ staff, and fund drug and laboratory expenses specifically for ART, is derived from three major sources in the Western Cape. The largest source is from a national conditional grant that represents ring-fenced money allocated to specific HIV interventions including ART. The next largest source of funding for ART is from a grant awarded by the Global Fund for Aids, Tuberculosis and Malaria (GFATM) that has been in place for two out of an anticipated six years. Finally, the province has mobilised some resources from general provincial health funding to augment the ART programme. The total dedicated expenditure on ART in the 2005/6 financial year is summarised below (Table 3). In all, R91 million of dedicated funding was spent on ART in the province in this period, at an average cost per patient year on ART of R7,504.

Table 3. Dedicated funding for ART in 2005/6 in the Western Cape

	Conditional Grant	Global Fund	Provincial Earmarked	Total	%
Salary costs	20,816,938	9,465,163	6,359,907	36,642,008	*40%*
Antiretroviral drugs	26,766,023	10,038,642	-	36,804,665	*40%*
Laboratory investigations	8,164,896	2,620,032	-	10,784,928	*12%*
Other	1,529,393	5,367,524	-	6,896,917	*8%*
	57,277,250	27,491,361	6,359,907	**91,128,519**	*100%*
Patient years of treamtent provided during financial year				12,144	
Earmarked funds spent per patient year on ART				**R 7,504**	

Drugs and salaries accounted for 40% of this expenditure each, and with laboratories, comprise 92% of the dedicated expenditure on the programme.

Utilisation and ordering trends at the drug depot

Since July 2004, all pharmacies involved with the procurement and distribution of antiretroviral drugs as part of the treatment programme have submitted monthly drug reports to the Directorate: HIV/AIDS/STI & TB. These reports are collated into a single provincial report and provide a valuable source of information in terms of drug utilization. The information is also used to determine the future needs of the programme by inputting the historical usage into a forecasting tool, and assists the pharmacy with maintaining a continuous and uninterrupted supply of drugs at facility level.

Initially, it was thought that approximately 97% of patients would be on first line therapy and 3% would be on second line therapy. For first line therapy, an even split between stavudine 30mg and 40mg was expected, that zidovudine 300mg would only be used in pregnancy, and that the split between efavirenz 600mg and nevirapine 200mg would be roughly 70% to 30% in favour of efavirenz. Monitoring the usage of the drugs shows that 98.5% of patients are on first line therapy and only 1.5% of patients are on second line drugs. This is very close to the reported proportion of patients on second-line in the cohort reports. Furthermore, approximately 58.5% of patients are on stavudine 40mg and 3% of patients are on zidovudine 300mg as part of their first line regimen. The split between efavirenz 600mg and nevirapine 200mg is also higher than expected. There has also been a steady increase in the usage of lopinavir/ritonavir 133/33mg capsules, which cannot be explained by the number of patients on second line therapy alone. The majority of these “deviations” can be explained by drug toxicities being experienced and necessary within-regimen substitutions. By being able to identify these changes early, the province has been able to respond

timeously to the changing drug needs, thus ensuring a reliable and sustainable drug supply to patients. Since these changes also have a direct impact on the future drug choices for patients, highlighting them early has informed ongoing discussions on clinical aspects of the programme.

During the 2005/5006 financial year, the depot procured R40.82 million worth of antiretroviral drugs. Expenditure on adult treatment accounted for 84% of total expenditure – 77% on first line therapy and 7% on second line therapy. Of the total amount spent on adult first line therapy, a single drug, efavirenz 600mg, represents 64% of expenditure. Efavirenz 600mg also accounts for 49% of total drug expenditure for the financial year. Paediatric treatment accounts for 16% of total drug costs and nevirapine 10mg/ml, 24% of total expenditure on paediatric drugs.

From the patient data (monthly reports), a total of 125,552 treatment months for adults and 20,306 treatment months for children have been reported. This correlates well with the drug consumption data obtained from treatment sites. Using efavirenz 600mg and nevirapine 200mg as an indirect measure, a total of 119,649 treatment months of treatment were issued, the difference of around 6,000 treatment months in adults (4%) can be explained by patients on second line therapy who are not receiving these drugs and by the increased usage of lopinavir/ritonavir 133/33mg in the first line regimen in patients who are unable to use either efavirenz or nevirapine. At this stage, it is not possible to validate the data for paediatric drug consumption in the same manner, as children receive a combination of solid dosage forms as well as syrups.

Discussion

Enrolment and coverage
The rapid increase in the monthly enrolment of patients over the past two years can be directly linked to the number of treatment sites and the staffing levels in these sites. This increase has been appropriate in the context of HIV-related mortality in the province, with enrolment capacity set to increase even further. Although the service challenges of an ever-increasing patient population on ART are daunting, it is in many ways a remarkable achievement that the province is able to contemplate reaching levels of coverage that approach universal access targets. This expansion has had a favourable clinical impact on the programme in terms of how sick patients are when starting ART, with many clinicians anecdotally reflecting on the discernable reduction in the proportion of patients starting ART who are critically ill.

Service model
A key feature of the provincial programme is the high proportion of patients treated in primary care. The generally impressive treatment outcomes validate the feasibility of delivering the intervention in primary care settings, whilst there is a growing body of evidence of the desirability from a patient perspective of locating treatment within primary care sites. A more detailed exploration of the service model for ART in the province has been completed and is available as a separate report.[3]

Clinical outcomes
Retention in care at three and four years duration on ART demonstrates unequivocally the huge survival benefit conferred by the intervention. Most of the current simulation models to anticipate either patient numbers or the costs associated with ART have assumed a median of between 6 and 7 years survival on ART. The current data at four years where 7 out of 10 adult patients are still in care, suggest that these estimates are not over-optimistic, especially since many of the patients lost to care may well subsequently return to care given the very tight definition of loss to follow-up.

Notwithstanding this definition, a higher proportion of patients were lost to follow-up in the first 12 months on ART in 2005 compared to previously. It is probable that this is being affected by service capacity being reached, and clinic patient loads exceeding manageable numbers of patients in some clinics. It is clear that retaining patients in constant care will become increasingly difficult as the service continues to expand, highlighting the importance of adherence promotion extending beyond the health services.

Whilst we can never be vigilant enough about adherence promotion, the virological outcomes are encouraging, suggesting that at a population level the rates of viral rebound have not been alarming, and are not undermining overall programme success.

The monitoring system
The evolving length of follow-up, as well as gradual improvements in the quality of the cohort data, has resulted in the monitoring system starting to prove useful as a management tool, with geographical and temporal trends discernable. In spite of these gains, the lack of clarity as to who's role routine data management is at a facility level, as well as staff-turnover, result in the constant need for ongoing site support and training on the data system. As patient numbers increase, the paper-based system becomes increasingly cumbersome, and yet, to have near-complete data on over 14,000 patients, is testimony to the importance of keeping things simple initially.

[3] Pienaar D, Myer L, Cleary S, Coetzee D, Michaels D, Cloete K, Schneider H, Boulle A. Models of Care for Antiretroviral Service Delivery. Cape Town: University of Cape Town; June 2006

The experience to date with those sites that do maintain their own databases provides a window on some of the difficulties that will initially be faced as more and more sites adopt the electronic patient information system that is currently in development. Each month and quarter it is the sites with electronic databases that are usually the slowest to report, due to delays in data capture, data validation, importing of laboratory data, and the unavailability of highly skilled staff. Standardisation may alleviate some of these bottlenecks. At a facility level, the human resource requirements are likely to be similar to the current system – having a designated person responsible for completing the register prior to filing patient folders, is the stepping stone to ensuring that same-day data-capture is feasible.

Sentinel surveillance

Whilst keeping things simple has ensured that a minimum of information is collected reliably across all the sites, the flip-side is nurturing some sites that are able to validate electronically held individual patient data in order to address some of the clinical and operational research questions facing the provincial and national ART programmes. Partnerships with academic institutions are a necessary prerequisite for ensuring that the sentinel sites are able to meet these objectives, and have positive spin-offs back into the government programmes. Careful stewardship of these partnerships and research sites by government is still required to ensure that these objectives are met.

The Western Cape is fortunate in the wealth of expertise, as well as the existing cohorts that are able to address questions in advance of many of the newer sites. These cohorts are representative of the provincial population, being in the highest burden areas such as Khayelitsha and Gugulethu, or are the referral hospitals for these areas. Balancing the pressure to continually expand the services to meet the need, and maintaining the quality of follow-up in these sentinel sites is a constant challenge. Given the huge financial investment in ART, making an extra effort to ensure appropriate clinical guidance of the programme is likely to be a worthwhile investment. It is not guaranteed that others will be able to address these questions on our behalf if the sentinel surveillance in this province collapses.

The next two years

The monthly report demonstrates that already four sites in the province exceed 1,000 patients on ART. These are facilities in the highest burden areas which will become unworkable unless they are able to share the load with other health facilities in their districts. An active process is already underway to facilitate the expansion of the service platform in selected districts to include more facilities and to appropriately expand the role of other health workers such as nurses in the provision of ART.

Conclusion

This report has detailed the available output and outcome data for the antiretroviral treatment programme in the Western Cape over the past two financial years. The programme is having a dramatic impact on the health of those accessing it. Access appears to be equitable across districts. Enrolment capacity has increased steadily over this period, and it is feasible that the platform, with gradual expansion, will be able to initiate ART for most of those who need it over the coming years. The overall patient numbers accumulating on ART pose a huge service challenge however, and the increase over time in the proportion of patients lost to follow-up in the first six months on ART is an early signal pointing to the health system challenges in this regard. Whilst the location of ART within primary care services appears to have contributed to the success of the provincial programme to date, innovative approaches to sharing the service load across the entire primary care service platform are urgently required.

Annexure A: Monthly report for all facilities, March 2006

Western Cape Antiretroviral monthly summary - March 2006

		Newly enrolled			Total on ART		
		Adults	Children	All	Adults	Children	All
Academic Complex							
	Groote Schuur Hospital	16	7	23	396	290	686
	Red Cross Hospital	0	18	18	41	391	432
	Tygerberg Hospital	35	11	46	743	338	1,081
	Subtotal	***51***	***36***	***87***	***1,180***	***1,019***	***2,199***
Boland Overberg							
	Ceres Hospital	5	1	6	88	10	98
	Eben Donges Hospital	29	1	30	346	49	395
	Grabouw	6	1	7	65	11	76
	Hermanus	5	0	5	136	10	146
	Robertson	13	0	13	132	2	134
	Swellendam	5	0	5	17	1	18
	Subtotal	***63***	***3***	***66***	***784***	***83***	***867***
Metro District Health Services							
	Crossroads	36	36	72	445	55	500
	Delft	27	0	27	174	0	174
	Eersterivier	9	0	9	137	0	137
	False Bay Hospital	11	0	11	32	1	33
	Guguletu CHC	64	10	74	1,267	109	1,376
	Hout Bay Clinic	21	0	21	309	11	320
	Ikhwezi Clinic	16	0	16	88	0	88
	Kraaifontein	49	0	49	448	17	465
	Langa Clinic	23	0	23	726	28	754
	Masiphumelele CHC	23	0	23	355	19	374
	Michael M CHC	102	5	107	1,198	75	1,273
	Mitchells Plain CHC	29	0	29	884	1	885
	Nolungile CHC	52	3	55	846	94	940
	Robbie Nurrock	13	0	13	416	3	419
	Site B, Khayelitsha CHC	82	7	89	1,327	105	1,432
	Tableview	33	0	33	285	2	287
	Westfleur Hospital	8	1	9	94	4	98
	Subtotal	***598***	***62***	***660***	***9,031***	***524***	***9,555***
Metro Institutions							
	G.F. Jooste Hospital	24	0	24	480	0	480
	Hottentots Holland Hospital	20	6	26	301	35	336
	Victoria Hospital	19	0	19	410	47	457
	Subtotal	***63***	***6***	***69***	***1,191***	***82***	***1,273***
South Cape / Karoo							
	Beaufort West Hospital	19	1	20	74	22	96
	George Hospital	11	4	15	288	63	351
	Knysna	18	0	18	258	19	277
	Mosselbaai	20	0	20	189	12	201
	Oudtshoorn	11	0	11	90	14	104
	Plettenberg CHC	18	1	19	61	1	62
	Prins-Albert CHC	2	0	2	20	0	20
	Thembalethu CHC	9	0	9	40	0	40
	Subtotal	***108***	***6***	***114***	***1,020***	***131***	***1,151***
West Coast Winelands							
	Citrusdal Hospital	3	1	4	23	1	24
	Cloetesville DH	20	4	24	237	22	259
	Malmesbury Hospital	14	1	15	122	11	133
	TC Newman Hospital	58	8	66	481	150	631
	Vredenberg	14	0	14	72	4	76
	Vredendal	1	1	2	60	6	66
	Subtotal	***110***	***15***	***125***	***995***	***194***	***1,189***
Grand Total		**993**	**128**	**1,121**	**14,201**	**2,033**	**16,234**

Annexure B: Monthly reports summarised for the province April 2004 – June 2006

Year	Month	New Adults	New Children	Total started	Total Adults	Total Children	Total on ART
2004							
	Apr	275	43	318	1,935	706	2,641
	May	380	62	442	2,218	766	2,984
	Jun	381	51	432	2,611	800	3,411
	Jul	394	66	460	2,984	851	3,835
	Aug	469	60	529	3,416	917	4,333
	Sep	482	77	559	3,880	978	4,858
	Oct	484	64	548	4,298	1,030	5,328
	Nov	512	44	556	4,870	1,112	5,982
	Dec	235	29	264	5,075	1,140	6,215
2005							
	Jan	442	55	497	5,479	1,170	6,649
	Feb	480	62	542	5,860	1,221	7,081
	Mar	639	77	716	6,338	1,278	7,616
	Apr	636	90	726	6,951	1,337	8,288
	May	707	85	792	7,553	1,386	8,939
	Jun	714	89	803	8,142	1,440	9,582
	Jul	722	88	810	8,844	1,542	10,386
	Aug	720	94	814	9,457	1,638	11,095
	Sep	730	90	820	10,136	1,654	11,790
	Oct	782	109	891	10,855	1,732	12,587
	Nov	810	100	910	11,643	1,817	13,460
	Dec	465	54	519	11,987	1,834	13,821
2006							
	Jan	698	83	781	12,524	1,918	14,442
	Feb	840	113	953	13,259	1,975	15,234
	Mar	993	128	1,121	14,201	2,033	16,234
	Apr	852	82	934	14,982	2,085	17,067
	May	997	117	1,114	15,910	2,107	18,017
	Jun	990	116	1,106	16,749	2,192	18,941

Annexure C: Cohort Reports Q206

The cohort reports included on the next three pages demonstrate the data structure of the cohort reporting system. A cohort is defined by that group of patients starting ART in a particular quarter. These data are extracted from the patient register. Five data elements are documented for each cohort, and thereafter, a further 10 elements are collected for each cohort at each duration on ART, as follows:

Collected once per cohort
TOT - Number of treatment naïve patients starting ART (TOT)
MEN - Treatment-naïve adult men starting ART (MEN)
WOM - Treatment-naïve adult women starting ART (WOM)
EXP - Treatment experience patients starting ART in the same quarter (EXP)
CD50 - Number of treatment-naïve patients with CD4 counts < 50 on starting ART (CD50)

Collected at each follow-up duration for each cohort (3,6,12, 18 months ….)
FLR - Patients on the first line regimen
SLR - Patients on the second line regimen
STO - Patients in care but not on antiretrovirals when reaching the duration
RIP - Patients dying between the previous duration and the current duration
LTF - Patients lost to follow-up between the previous duration and the current duration
TFO - Patients transferred out between the previous duration and the current duration
VLD - Patients with a document viral load result at the current duration on ART
VLS - Patients with a document viral load < 400 copies/ml at the current duration on ART
CDD - Patients with a document CD4 count result at the current duration on ART
CDA - Patients with a document CD4 count >= 200/µl at the current duration on ART

A number of indicators can then be calculated based on these data (Table 4), as demonstrated in this report. The data and indicators can then be tabulated in different ways, depending on the analysis of interest (baseline characteristics, outcomes by duration, outcomes by site, outcomes by calendar period).

Table 4. Indicators in the cohort system

Indicators	*Indicator Formula*	*Description*
CD4<50prop	(CD4<50)/TOT	% CD4 counts less than 50 at baseline
Perc SL	SLR/(FLR+SLR+STO)	% on second-line regimen
Cum% in care	(TOT-LTF-RIP-TFO)/(TOT-TFO)	% remaining in care at x months
In care but stopped ARV's	STO/(FLR+SLR+STO)	% in care but stopped ART
Cum%died	(RIP) / (TOT-TFO)	Cumulative % of patients died
Cum%ltf	(LTF) /(TOT-TFO)	Cumulative % of patients lost-to-follow up
CD4 compl.%	CDD/(FLR+SLR+STO)	% CD4's done that should have been
CD4>200%	CDA/CDD	% CD4's above 200 of those done
VLDone	VLD/(FLR + SLR)	% viral loads done that should have been
VLSupp	VLS/VLD	% Viral loads < 400 of those done

* note that the TFO, LTF and RIP used in the formulas are the cumulative totals to that point, as opposed to the total in the most recent interval

The cohort reports included here have each quarterly cohort running vertically down the page. The analysis at each duration on ART for each column refers to the same number of patients who originally started ART. For example, of the 31 adult patients who started ART in the second quarter of 2001, at 48 months, 17 remained on first-line, 4 were on second-line and three were in care but not on antiretrovirals at the time. The aggregated outcomes at a particular duration on ART can be determined across multiple cohorts by looking at the horizontal totals. For example, by looking in the last column, of all the adults who ever reached six months on ART (10492), 93% remained in care at this duration.

Table 5. Adult Quarterly Cohort Report

Note: These are data aggregated across multiple facilities, and for the more recent cohorts, there are some instances where data for a particular facility at a particular duration on ART were not available at the time of reporting. This results in the total number of patients (the initial total) diminishing slightly in some instances as an individual cohort is followed vertically down the page. Ordinarily the entire column refers to the same group of patients who originally started ART.

Duration	Data	01Q2	01Q3	01Q4	01 Total	02Q1	02Q2	02Q3	02Q4	02 Total	03Q1	03Q2	03Q3	03Q4	03 Total	04Q1	04Q2	04Q3	04Q4	04 Total	05Q1	05Q2	05Q3	05Q4	05 Total	Grand Total
Baseline	TOT	31	28	21	80	50	59	58	81	248	90	143	132	159	524	593	971	1314	1163	4041	1652	1957	2116	1969	7694	12587
	CD<50prop	61.3%	42.9%	47.6%	51.3%	58.0%	42.4%	50.0%	51.9%	50.4%	42.2%	41.3%	29.5%	35.8%	36.8%	30.2%	23.9%	21.7%	25.0%	24.4%	23.3%	19.5%	18.0%	18.7%	19.7%	22.7%
	Male prop	32.3%	32.1%	19.0%	28.8%	30.0%	35.6%	29.3%	27.2%	30.2%	24.4%	32.2%	25.0%	34.6%	29.8%	30.0%	28.9%	30.6%	31.4%	30.3%	32.9%	32.8%	33.1%	31.9%	32.6%	31.7%
	Experienced prop															16.6%	3.5%	1.8%	2.4%	4.9%	0.8%	0.9%	1.4%	1.6%	1.2%	2.3%
3 mo	Initial Total	31	28	21	80	50	59	58	81	248	90	143	132	159	524	593	971	1314	1165	4043	1615	1957	2025		5597	10492
	On first-line	24	25	18	67	46	48	52	68	214	83	118	119	138	458	530	884	1198	1056	3668	1452	1771	1836		5059	9466
	On Second-line															3	5	6	4	18	7	3	2		12	30
	In care but stopped ARVs	4		1	5	2	1		4	7	4	7	3	4	18	10	19	19	18	66	21	23	41		85	181
	perc SL															0.6%	0.6%	0.5%	0.4%	0.5%	0.5%	0.2%	0.1%		0.2%	0.3%
	cum%died	9.7%	7.4%	9.5%	8.9%	4.0%	15.5%	10.3%	9.9%	10.1%	3.3%	11.2%	5.3%	8.8%	7.6%	6.0%	3.3%	3.5%	4.1%	4.0%	4.9%	4.4%	3.2%		4.1%	4.4%
	cum%ltf								1.2%	0.4%		1.4%	1.5%	1.9%	1.3%	1.4%	2.2%	2.4%	2.0%	2.1%	1.9%	2.4%	2.8%		2.4%	2.1%
	cum%in care	90.3%	92.6%	90.5%	91.1%	96.0%	84.5%	89.7%	88.9%	89.5%	96.7%	87.4%	93.1%	89.3%	91.0%	92.7%	94.5%	94.1%	93.9%	93.9%	93.3%	93.3%	94.0%		93.5%	93.5%
6 mo	Initial Total	31	28	21	80	50	59	58	81	248	90	143	132	159	524	593	971	1314	1103	3981	1615	1893			3508	8341
	On first-line	25	23	18	66	47	46	52	67	212	81	114	121	136	452	499	842	1120	927	3388	1355	1589			2944	7062
	On Second-line															6	6	9	6	27	6	5			11	38
	In care but stopped ARVs	2		1	3		1		4	5	3	5	1	3	12	5	14	22	17	58	30	25			55	133
	perc SL															1.2%	0.7%	0.8%	0.6%	0.8%	0.4%	0.3%			0.4%	0.5%
	cum%died	12.9%	14.8%	9.5%	12.7%	6.0%	19.0%	10.3%	11.1%	11.7%	6.7%	14.7%	5.3%	10.1%	9.6%	8.6%	5.3%	4.9%	6.4%	6.0%	6.9%	6.4%			6.6%	6.7%
	cum%ltf								1.2%	0.4%		2.1%	1.5%	2.5%	1.7%	3.3%	4.0%	5.0%	4.6%	4.4%	4.0%	5.3%			4.7%	4.2%
	cum%in care	87.1%	85.2%	90.5%	87.3%	94.0%	81.0%	89.7%	87.7%	87.9%	93.3%	83.2%	93.1%	87.4%	88.7%	88.1%	90.7%	90.1%	89.0%	89.6%	89.1%	88.3%			88.7%	89.1%
	CD4's done	25	23	18	66	44	44	49	64	201	73	102	115	130	420	447	791	1020	870	3128	1053	1104			2157	5972
	CD4's >= 200	9	15	10	34	23	21	25	35	104	41	57	72	79	249	245	488	677	540	1950	666	711			1377	3714
	CD4 compl.%	100.0%	100.0%	100.0%	100.0%	93.6%	95.7%	94.2%	95.5%	94.8%	90.1%	89.5%	95.0%	95.6%	92.9%	88.5%	93.3%	90.3%	93.2%	91.6%	77.4%	69.3%			73.0%	84.1%
	CD4>200%	36.0%	65.2%	55.6%	51.5%	52.3%	47.7%	51.0%	54.7%	51.7%	56.2%	55.9%	62.6%	60.8%	59.3%	54.8%	61.7%	66.4%	62.1%	62.3%	63.2%	64.4%			63.8%	62.2%
	Viral loads done	25	23	18	66	46	43	48	67	204	75	104	112	121	412	444	787	990	853	3074	1068	1155			2223	5979
	Viral loads<400	22	22	14	58	43	39	42	59	183	73	100	98	117	388	397	716	883	768	2764	966	1058			2024	5417
	VL completion%	100.0%	100.0%	100.0%	100.0%	97.9%	93.5%	92.3%	100.0%	96.2%	92.6%	91.2%	92.6%	89.0%	91.2%	87.9%	92.8%	87.7%	91.4%	90.0%	78.5%	72.5%			75.2%	84.2%
	VL supp%	88.0%	95.7%	77.8%	87.9%	93.5%	90.7%	87.5%	88.1%	89.7%	97.3%	96.2%	87.5%	96.7%	94.2%	89.4%	91.0%	89.2%	90.0%	89.9%	90.4%	91.6%			91.0%	90.6%
12 mo	Initial Total	31	28	21	80	50	59	58	81	248	90	143	132	159	524	593	924	1271	1086	3874						4726
	On first-line	23	23	16	62	46	44	49	65	204	79	112	114	128	433	450	717	977	826	2970						3669
	On Second-line	1			1			3	3	6						9	18	19	16	62						69
	In care but stopped ARVs	3		1	4				1	1	2	3	3	1	9	16	13	25	23	77						91
	perc SL	4.2%			1.6%			5.8%	4.4%	2.9%						2.0%	2.4%	1.9%	1.9%	2.0%						1.8%
	cum%died	12.9%	14.8%	19.0%	15.2%	8.0%	22.8%	10.3%	13.6%	13.8%	8.9%	16.8%	8.5%	14.7%	12.7%	10.3%	7.1%	6.8%	8.1%	7.8%						8.8%
	cum%ltf								1.2%	0.4%	1.1%	2.8%	1.5%	2.6%	2.1%	6.5%	7.4%	8.1%	7.3%	7.5%						6.3%
	cum%in care	87.1%	85.2%	81.0%	84.8%	92.0%	77.2%	89.7%	85.2%	85.8%	90.0%	80.4%	90.0%	82.7%	85.2%	83.2%	85.5%	85.2%	84.6%	84.8%						84.9%
	CD4's done	25	22	15	62	45	37	49	67	198	71	102	104	120	397	414	692	887	685	2678						3335
	CD4's >= 200	15	14	11	40	27	23	35	43	128	54	70	77	88	289	324	518	674	519	2035						2492
	CD4 compl.%	104.2%	95.7%	93.8%	98.4%	97.8%	84.1%	94.2%	98.5%	94.3%	89.9%	91.1%	91.2%	93.8%	91.7%	90.2%	94.1%	89.1%	81.4%	88.3%						89.2%
	CD4>200%	60.0%	63.6%	73.3%	64.5%	60.0%	62.2%	71.4%	64.2%	64.6%	76.1%	68.6%	74.0%	73.3%	72.8%	78.3%	74.9%	76.0%	75.8%	76.0%						74.7%
	Viral loads done	25	23	16	64	44	41	50	66	201	72	103	104	120	399	412	693	873	688	2666						3330
	Viral loads<400	21	20	12	53	38	34	38	59	169	64	94	96	116	370	359	629	770	613	2371						2963
	VL completion%	104.2%	100.0%	100.0%	101.6%	95.7%	93.2%	96.2%	97.1%	95.7%	91.1%	92.0%	91.2%	93.8%	92.1%	89.8%	94.3%	87.7%	81.7%	87.9%						89.1%
	VL supp%	84.0%	87.0%	75.0%	82.8%	86.4%	82.9%	76.0%	89.4%	84.1%	88.9%	91.3%	92.3%	96.7%	92.7%	87.1%	90.8%	88.2%	89.1%	88.9%						89.0%
18 mo	Initial Total	31	28	21	80	50	59	58	81	248	90	143	132	159	524	554	761			1315						2167
	On first-line	22	22	15	59	43	42	47	62	194	78	109	114	117	418	379	536			915						1586
	On Second-line	2	1		3	2	1	3	2	8			1	1	2	19	22			41						54
	In care but stopped ARVs	3		1	4	1	1	2	1	5	2	2		3	7	8	18			26						42
	perc SL	8.3%	4.3%		4.8%	4.4%	2.3%	6.0%	3.1%	4.0%			0.9%	0.8%	0.5%	4.8%	3.9%			4.3%						3.3%
	cum%died	12.9%	14.8%	19.0%	15.2%	8.0%	22.8%	10.3%	17.3%	15.0%	9.0%	19.6%	10.0%	17.0%	14.6%	12.1%	7.3%			9.4%						11.6%
	cum%ltf			4.8%	1.3%				2.5%	0.8%	1.1%	2.8%	1.5%	3.9%	2.5%	10.0%	11.3%			10.7%						7.2%
	cum%in care	87.1%	85.2%	76.2%	83.5%	92.0%	77.2%	89.7%	80.2%	84.1%	89.9%	77.6%	88.5%	79.1%	82.9%	77.9%	81.4%			79.9%						81.3%
	CD4's done	21	20	13	54	43	42	43	60	188	69	101	105	109	384	351	403			754						1380
	CD4's >= 200	15	16	10	41	34	29	30	50	143	54	83	91	84	312	291	345			636						1132
	CD4 compl.%	87.5%	87.0%	86.7%	87.1%	95.6%	97.7%	86.0%	93.8%	93.1%	88.5%	92.7%	91.3%	92.4%	91.4%	88.2%	72.2%			78.9%						84.1%
	CD4>200%	71.4%	80.0%	76.9%	75.9%	79.1%	69.0%	69.8%	83.3%	76.1%	78.3%	82.2%	86.7%	77.1%	81.3%	82.9%	85.6%			84.4%						82.0%
	Viral loads done	22	22	13	57	44	41	45	61	191	70	102	108	107	387	349	417			766						1401
	Viral loads<400	16	18	10	44	35	39	30	58	162	62	86	100	97	345	316	367			683						1234
	VL completion%	91.7%	95.7%	86.7%	91.9%	97.8%	95.3%	90.0%	95.3%	94.6%	89.7%	93.6%	93.9%	90.7%	92.1%	87.7%	74.7%			80.1%						85.4%
	VL supp%	72.7%	81.8%	76.9%	77.2%	79.5%	95.1%	66.7%	95.1%	84.8%	88.6%	84.3%	92.6%	90.7%	89.1%	90.5%	88.0%			89.2%						88.1%

Duration	Data	01Q2	01Q3	01Q4	01 Total	02Q1	02Q2	02Q3	02Q4	02 Total	03Q1	03Q2	03Q3	03Q4	03 Total	04Q1	04Q2	04Q3	04Q4	04 Total	05Q1	05Q2	05Q3	05Q4	05 Total	Grand Total
24 mo	Initial Total	31	28	21	80	50	59	58	81	248	90	143	132	159	524											852
	On first-line	21	21	13	55	39	41	40	60	180	76	98	110	108	392											627
	On Second-line	3	2		5	2	1	6	3	12		3	2	2	7											24
	In care but stopped ARVs	3		3	6	2	2	2		6	2	3		3	8											20
	perc SL	12.5%	8.7%		8.3%	4.9%	2.4%	13.0%	4.8%	6.3%		3.0%	1.8%	1.8%	1.8%											3.7%
	cum%died	12.9%	14.8%	19.0%	15.2%	10.4%	22.8%	12.5%	18.8%	16.6%	9.2%	21.3%	10.1%	18.4%	15.5%											15.8%
	cum%ltf			4.8%	1.3%			1.8%	2.5%	1.2%	1.1%	5.0%	3.1%	7.2%	4.5%											3.3%
	cum%in care	87.1%	85.2%	76.2%	83.5%	89.6%	77.2%	85.7%	78.8%	82.2%	89.7%	73.8%	86.8%	74.3%	80.0%											80.9%
	CD4's done	22	21	13	56	40	42	44	61	187	72	89	90	70	321											564
	CD4's >= 200	20	17	11	48	35	33	34	54	156	63	81	80	57	281											485
	CD4 compl.%	91.7%	91.3%	100.0%	93.3%	97.6%	100.0%	95.7%	96.8%	97.4%	94.7%	88.1%	80.4%	63.6%	80.5%											86.6%
	CD4>200%	90.9%	81.0%	84.6%	85.7%	87.5%	78.6%	77.3%	88.5%	83.4%	87.5%	91.0%	88.9%	81.4%	87.5%											86.0%
	Viral loads done	24	21	13	58	42	40	45	61	188	68	92	92	75	327											573
	Viral loads<400	17	17	11	45	33	38	38	58	167	61	85	86	62	294											506
	VL completion%	100.0%	91.3%	100.0%	96.7%	102.4%	95.2%	97.8%	96.8%	97.9%	89.5%	91.1%	82.1%	68.2%	82.0%											88.0%
	VL supp%	70.8%	81.0%	84.6%	77.6%	78.6%	95.0%	84.4%	95.1%	88.8%	89.7%	92.4%	93.5%	82.7%	89.9%											88.3%
30 mo	Initial Total	31	28	21	80	50	59	58	81	248	90	143			233											561
	On first-line	21	21	13	55	37	42	39	53	171	75	93			168											394
	On Second-line	1	2		3	4	2	6	2	14		3			3											20
	In care but stopped ARVs	4		2	6	2		2	2	6	2	3			5											17
	perc SL	4.5%	8.7%		5.2%	9.8%	4.5%	13.3%	3.6%	7.6%		3.1%			1.8%											4.8%
	cum%died	16.1%	14.8%	23.8%	17.7%	10.4%	22.8%	12.5%	23.1%	18.0%	9.3%	22.0%			17.2%											17.6%
	cum%ltf			4.8%	1.3%			3.6%	3.8%	2.1%	1.2%	7.8%			5.3%											3.3%
	cum%in care	83.9%	85.2%	71.4%	81.0%	89.6%	77.2%	83.9%	73.1%	79.9%	89.5%	70.2%			77.5%											79.1%
	CD4's done	21	22	13	56	37	41	32	56	166	60	49			109											331
	CD4's >= 200	18	19	11	48	35	38	27	53	153	57	43			100											301
	CD4 compl.%	95.5%	95.7%	100.0%	96.6%	90.2%	93.2%	71.1%	101.8%	89.7%	80.0%	51.0%			63.7%											80.0%
	CD4>200%	85.7%	86.4%	84.6%	85.7%	94.6%	92.7%	84.4%	94.6%	92.2%	95.0%	87.8%			91.7%											90.9%
	Viral loads done	21	22	14	57	39	43	38	56	176	60	50			110											343
	Viral loads<400	14	17	12	43	38	36	28	54	156	55	48			103											302
	VL completion%	95.5%	95.7%	107.7%	98.3%	95.1%	97.7%	84.4%	101.8%	95.1%	80.0%	52.1%			64.3%											82.9%
	VL supp%	66.7%	77.3%	85.7%	75.4%	97.4%	83.7%	73.7%	96.4%	88.6%	91.7%	96.0%			93.6%											88.0%
36 mo	Initial Total	31	28	21	80	50	59	58	81	248																328
	On first-line	21	20	13	54	36	40	32	52	160																214
	On Second-line	3	3	1	7	4	2	9	1	16																23
	In care but stopped ARVs	1		1	2		1	4	1	6																8
	perc SL	12.5%	13.0%	7.1%	11.5%	10.0%	4.8%	22.0%	1.9%	9.1%																9.7%
	cum%died	19.4%	14.8%	23.8%	19.0%	12.5%	22.8%	14.3%	23.1%	18.8%																18.9%
	cum%ltf			4.8%	1.3%	4.2%	1.8%	5.4%	7.7%	5.0%																4.1%
	cum%in care	80.6%	85.2%	71.4%	79.7%	83.3%	75.4%	80.4%	69.2%	76.2%																77.0%
	CD4's done	21	21	12	54	36	37	26	15	114																168
	CD4's >= 200	17	18	9	44	35	33	22	14	104																148
	CD4 compl.%	87.5%	91.3%	85.7%	88.5%	90.0%	88.1%	63.4%	28.3%	64.8%																70.9%
	CD4>200%	81.0%	85.7%	75.0%	81.5%	97.2%	89.2%	84.6%	93.3%	91.2%																88.1%
	Viral loads done	23	21	12	56	33	39	27	16	115																171
	Viral loads<400	19	19	10	48	31	32	24	12	99																147
	VL completion%	95.8%	91.3%	85.7%	91.8%	82.5%	92.9%	65.9%	30.2%	65.3%																72.2%
	VL supp%	82.6%	90.5%	83.3%	85.7%	93.9%	82.1%	88.9%	75.0%	86.1%																86.0%
42 mo	Initial Total	31	28	21	80	50	59			109																189
	On first-line	19	20	12	51	34	39			73																124
	On Second-line	4	3	1	8	4	3			7																15
	In care but stopped ARVs	2			2		1			1																3
	perc SL	17.4%	13.0%	7.7%	13.6%	10.5%	7.1%			8.8%																10.8%
	cum%died	19.4%	14.8%	33.3%	21.5%	12.8%	22.8%			18.3%																19.7%
	cum%ltf			4.8%	1.3%	6.4%	1.8%			3.8%																2.7%
	cum%in care	80.6%	85.2%	61.9%	77.2%	80.9%	75.4%			77.9%																77.6%
	CD4's done	14	20	13	47	28	20			48																95
	CD4's >= 200	12	18	9	39	28	17			45																84
	CD4 compl.%	60.9%	87.0%	100.0%	79.7%	73.7%	47.6%			60.0%																68.3%
	CD4>200%	85.7%	90.0%	69.2%	83.0%	100.0%	85.0%			93.8%																88.4%
	Viral loads done	17	20	13	50	21	22			43																93
	Viral loads<400	15	16	11	42	20	17			37																79
	VL completion%	73.9%	87.0%	100.0%	84.7%	55.3%	52.4%			53.8%																66.9%
	VL supp%	88.2%	80.0%	84.6%	84.0%	95.2%	77.3%			86.0%																84.9%
48 mo	Initial Total	31	28	21	80																					80
	On first-line	17	18	11	46																					46
	On Second-line	4	4	2	10																					10
	In care but stopped ARVs	3			3																					3
	perc SL	19.0%	18.2%	15.4%	17.9%																					17.9%
	cum%died	22.6%	15.4%	33.3%	23.1%																					23.1%
	cum%ltf			4.8%	1.3%																					1.3%
	cum%in care	77.4%	84.6%	61.9%	75.6%																					75.6%
	CD4's done	20	15	8	43																					43
	CD4's >= 200	18	15	8	41																					41
	CD4 compl.%	95.2%	68.2%	61.5%	76.8%																					76.8%
	CD4>200%	90.0%	100.0%	100.0%	95.3%																					95.3%
	Viral loads done	19	17	8	44																					44
	Viral loads<400	16	16	8	40																					40
	VL completion%	90.5%	77.3%	61.5%	78.6%																					78.6%
	VL supp%	84.2%	94.1%	100.0%	90.9%																					90.9%

Table 6. Paediatric Quarterly Cohort Report

Duration	Data	01 Total	02Q1	02Q2	02Q3	02Q4	02 Total	03Q1	03Q2	03Q3	03Q4	03 Total	04Q1	04Q2	04Q3	04Q4	04 Total	05Q1	05Q2	05Q3	05Q4	05 Total	Grand Total
Baseline	TOT	4	8	7	7	10	32	8	8	15	6	37	144	154	218	184	700	192	253	252	239	936	1709
	CD 15% prop	50.0%	87.5%	57.1%	57.1%	50.0%	62.5%	100.0%	37.5%	60.0%	50.0%	62.2%	36.1%	46.1%	49.5%	58.7%	48.4%	41.7%	48.2%	38.9%	34.3%	40.8%	44.8%
	Experienced prop												2.7%	2.5%	1.4%	2.6%	2.2%	2.5%	2.3%	1.6%	1.6%	2.0%	2.0%
3 mo	Initial Total	4	8	7	7	10	32	8	8	15	6	37	144	154	218	184	700	192	253	252		697	1470
	On first-line	3	8	6	7	9	30	8	8	13	5	34	136	137	196	166	635	171	231	223		625	1327
	On Second-line													1			1						1
	In care but stopped ARVs					1	1			1	1	2		1	2		3	1	4	3		8	14
	perc SL													0.7%			0.2%						0.1%
	cum%died	25.0%		14.3%			3.1%						4.2%	6.0%	7.0%	7.8%	6.4%	6.5%	4.1%	5.7%		5.3%	5.7%
	cum%ltf									6.7%		2.7%		0.7%	0.5%		0.3%	0.5%		2.0%		0.9%	0.6%
	cum%in care	75.0%	100.0%	85.7%	100.0%	100.0%	96.9%	100.0%	100.0%	93.3%	100.0%	97.3%	95.8%	93.3%	92.5%	92.2%	93.3%	93.0%	95.9%	92.2%		93.8%	93.6%
6 mo	Initial Total	4	8	7	7	10	32	8	8	15	6	37	144	154	218	187	703	192	248			440	1216
	On first-line	3	7	6	7	9	29	8	8	13	6	35	127	132	184	149	592	154	205			359	1018
	On Second-line													1			1						1
	In care but stopped ARVs					1	1			1		1		1	1		1	1	3			4	7
	perc SL													0.8%			0.2%						0.1%
	cum%died	25.0%	12.5%	14.3%			6.3%						7.9%	7.5%	9.2%	9.5%	8.6%	8.2%	4.4%			6.1%	7.4%
	cum%ltf									6.7%		2.7%	1.4%	2.0%	1.4%	2.4%	1.8%	1.2%	3.1%			2.3%	1.9%
	cum%in care	75.0%	87.5%	85.7%	100.0%	100.0%	93.8%	100.0%	100.0%	93.3%	100.0%	97.3%	90.7%	90.5%	89.4%	88.2%	89.6%	90.6%	92.4%			91.7%	90.6%
	CD4's done	3	6	4	5	7	22	8	8	13	6	35	96	105	149	126	476	117	154			271	807
	CD4's >= 200	2	2	1	3	5	11	3	6	10	5	24	56	77	82	63	278	66	83			149	464
	CD4 compl.%	100.0%	85.7%	66.7%	71.4%	77.8%	75.9%	100.0%	100.0%	100.0%	100.0%	100.0%	75.6%	78.9%	81.0%	84.6%	80.3%	76.0%	75.1%			75.5%	79.2%
	CD4>200%	66.7%	33.3%	25.0%	60.0%	71.4%	50.0%	37.5%	75.0%	76.9%	83.3%	68.6%	58.3%	73.3%	55.0%	50.0%	58.4%	56.4%	53.9%			55.0%	57.5%
	Viral loads done	3	7	6	6	7	26	7	6	10	6	29	85	112	156	132	485	126	153			279	822
	Viral loads<400	3	4	6	6	7	23	6	5	8	5	24	64	77	111	91	343	92	113			205	598
	VL completion%	100.0%	100.0%	100.0%	85.7%	77.8%	89.7%	87.5%	75.0%	76.9%	100.0%	82.9%	66.9%	84.2%	84.8%	88.6%	81.8%	81.8%	74.6%			77.7%	80.7%
	VL supp%	100.0%	57.1%	100.0%	100.0%	100.0%	88.5%	85.7%	83.3%	80.0%	83.3%	82.8%	75.3%	68.8%	71.2%	68.9%	70.7%	73.0%	73.9%			73.5%	72.7%
12 mo	Initial Total	4	8	7	7	10	32	8	8	15	6	37	144	154	218	181	697						770
	On first-line	3	7	6	7	7	27	8	8	13	6	35	124	116	169	119	528						593
	On Second-line													1	1	2	4						4
	In care but stopped ARVs					1	1			1		1		3			3						5
	perc SL													0.9%	0.6%	1.7%	0.8%						0.7%
	cum%died	25.0%	12.5%	14.3%		10.0%	9.4%						8.6%	8.8%	11.2%	12.2%	10.3%						9.8%
	cum%ltf					10.0%	3.1%			6.7%		2.7%	2.2%	3.6%	2.0%	6.1%	3.4%						3.3%
	cum%in care	75.0%	87.5%	85.7%	100.0%	80.0%	87.5%	100.0%	100.0%	93.3%	100.0%	97.3%	89.2%	87.6%	86.7%	81.8%	86.3%						86.9%
	CD4's done	3	7	6	7	6	26	8	7	9	2	26	99	88	142	115	444						499
	CD4's >= 200	3	5	6	6	4	21	5	6	9	2	22	57	60	114	80	311						357
	CD4 compl.%	100.0%	100.0%	100.0%	100.0%	85.7%	96.3%	100.0%	87.5%	69.2%	33.3%	74.3%	79.8%	75.2%	83.5%	95.0%	83.5%						83.6%
	CD4>200%	100.0%	71.4%	100.0%	85.7%	66.7%	80.8%	62.5%	85.7%	100.0%	100.0%	84.6%	57.6%	68.2%	80.3%	69.6%	70.0%						71.5%
	Viral loads done	3	7	6	7	6	26	8	7	13	6	34	108	98	146	116	468						531
	Viral loads<400	3	3	4	5	3	15	6	5	10	5	26	77	72	108	83	340						384
	VL completion%	100.0%	100.0%	100.0%	100.0%	85.7%	96.3%	100.0%	87.5%	100.0%	100.0%	97.1%	87.1%	83.8%	85.9%	95.9%	88.0%						88.9%
	VL supp%	100.0%	42.9%	66.7%	71.4%	50.0%	57.7%	75.0%	71.4%	76.9%	83.3%	76.5%	71.3%	73.5%	74.0%	71.6%	72.6%						72.3%
18 mo	Initial Total	4	8	7	7	10	32	8	8	15	6	37	144	154			298						371
	On first-line	3	5	6	7	6	24	8	8	13	6	35	119	106			225						287
	On Second-line		2				2			1		1		3			3						6
	In care but stopped ARVs																						
	perc SL		28.6%				7.7%			7.1%		2.8%		2.8%			1.3%						2.0%
	cum%died	25.0%	12.5%	14.3%		10.0%	9.4%						10.1%	10.5%			10.3%						9.3%
	cum%ltf					30.0%	9.4%			6.7%		2.7%	3.6%	7.5%			5.5%						5.5%
	cum%in care	75.0%	87.5%	85.7%	100.0%	60.0%	81.3%	100.0%	100.0%	93.3%	100.0%	97.3%	86.2%	82.0%			84.1%						85.2%
	CD4's done	3	6	4	4	5	19	4	5	8		17	104	76			180						219
	CD4's >= 200	3	5	4	3	4	16	3	4	8		15	68	62			130						164
	CD4 compl.%	100.0%	85.7%	66.7%	57.1%	83.3%	73.1%	50.0%	62.5%	57.1%		47.2%	87.4%	69.7%			78.9%						74.7%
	CD4>200%	100.0%	83.3%	100.0%	75.0%	80.0%	84.2%	75.0%	80.0%	100.0%		88.2%	65.4%	81.6%			72.2%						74.9%
	Viral loads done	3	7	6	5	6	24	6	7	11	6	30	104	84			188						245
	Viral loads<400	2	5	4	1	4	14	5	6	7	5	23	81	63			144						183
	VL completion%	100.0%	100.0%	100.0%	71.4%	100.0%	92.3%	75.0%	87.5%	78.6%	100.0%	83.3%	87.4%	77.1%			82.5%						83.6%
	VL supp%	66.7%	71.4%	66.7%	20.0%	66.7%	58.3%	83.3%	85.7%	63.6%	83.3%	76.7%	77.9%	75.0%			76.6%						74.7%
24 mo	Initial Total	4	8	7	7	9	31	8	8	15	6	37											72
	On first-line	3	5	6	6	6	23	6	8	13	6	33											59
	On Second-line		2				2	1				1											3
	In care but stopped ARVs																						
	perc SL		28.6%				8.0%	14.3%				2.9%											4.8%
	cum%died	25.0%	12.5%	14.3%		11.1%	10.0%																5.7%
	cum%ltf					22.2%	6.7%			13.3%		5.6%											5.7%
	cum%in care	75.0%	87.5%	85.7%	100.0%	66.7%	83.3%	100.0%	100.0%	86.7%	100.0%	94.4%											88.6%
	CD4's done	3	6	5	5	5	21	4	4	2	1	11											35
	CD4's >= 200	3	5	5	4	4	18	2	4	2	1	9											30
	CD4 compl.%	100.0%	85.7%	83.3%	83.3%	83.3%	84.0%	57.1%	50.0%	15.4%	16.7%	32.4%											56.5%
	CD4>200%	100.0%	83.3%	100.0%	80.0%	80.0%	85.7%	50.0%	100.0%	100.0%	100.0%	81.8%											85.7%
	Viral loads done	3	5	6	6	6	23	6	6	10	5	27											53
	Viral loads<400	1	3	5	5	4	17	6	5	8	4	23											41
	VL completion%	100.0%	71.4%	100.0%	100.0%	100.0%	92.0%	85.7%	75.0%	76.9%	83.3%	79.4%											85.5%
	VL supp%	33.3%	60.0%	83.3%	83.3%	66.7%	73.9%	100.0%	83.3%	80.0%	80.0%	85.2%											77.4%
30 mo	Initial Total	4	8	7	7	9	31	8	8			16											51
	On first-line	3	5	6	5	6	22	6	8			14											39
	On Second-line		1		1		2																2
	In care but stopped ARVs		1				1																1
	perc SL		16.7%		16.7%		8.3%																4.9%
	cum%died	25.0%	12.5%	14.3%		11.1%	10.0%																8.2%
	cum%ltf					22.2%	6.7%	14.3%				6.7%											6.1%
	cum%in care	75.0%	87.5%	85.7%	100.0%	66.7%	83.3%	85.7%	100.0%			93.3%											85.7%
	CD4's done	2	5	3	3	3	14		1			1											17
	CD4's >= 200	2	4	3	3	2	12		1			1											15
	CD4 compl.%	66.7%	83.3%	50.0%	50.0%	50.0%	58.3%		12.5%			7.1%											41.5%
	CD4>200%	100.0%	80.0%	100.0%	100.0%	66.7%	85.7%		100.0%			100.0%											88.2%
	Viral loads done	3	6	5	5	3	19	3	3			6											28
	Viral loads<400	3	3	4	5	2	14	3	2			5											22
	VL completion%	100.0%	100.0%	83.3%	83.3%	50.0%	79.2%	50.0%	37.5%			42.9%											68.3%
	VL supp%	100.0%	50.0%	80.0%	100.0%	66.7%	73.7%	100.0%	66.7%			83.3%											78.6%
36 mo	Initial Total	4	8	7	7	9	31																35
	On first-line	3	5	6	5	6	22																25
	On Second-line		1		1		2																2
	In care but stopped ARVs		1				1																1
	perc SL		16.7%		16.7%		8.3%																7.4%
	cum%died	25.0%	12.5%	14.3%		11.1%	10.0%																11.8%
	cum%ltf					22.2%	6.7%																5.9%
	cum%in care	75.0%	87.5%	85.7%	100.0%	66.7%	83.3%																82.4%
	CD4's done	1	2	2		1	5																6
	CD4's >= 200	1	1	2		1	4																5
	CD4 compl.%	33.3%	33.3%	33.3%		16.7%	20.8%																22.2%
	CD4>200%	100.0%	50.0%	100.0%		100.0%	80.0%																83.3%
	Viral loads done	3	5	5	4	3	17																20
	Viral loads<400	3	2	4	4	2	12																15
	VL completion%	100.0%	83.3%	83.3%	66.7%	50.0%	70.8%																74.1%
	VL supp%	100.0%	40.0%	80.0%	100.0%	66.7%	70.6%																75.0%