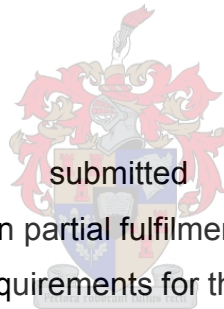


Exploring programme design, evaluation of programme performance
and describing the clinical outcomes of a public sector based ARV
treatment programme in a semi-rural area in the Western Cape over the
past 6 years. (2004-2010)

by

Dr Cornelis Johannes (Nelis) Grobbelaar
MBChB, DipHivMan(SA)



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University of Stellenbosch

Supervisor

Dr Dirk Hagemester

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Abstract

Background: A national roll-out of antiretroviral therapy in the public sector was started in 2004, and Paarl was one of the first sites to start these services in the Western Cape. Operational research is required to guide the continuous improvement of such services. This research aimed to describe the characteristics of the treatment cohort started at TC Newman CDC's ARV clinic in Paarl, to determine the retention in treatment rate and to assess the clinical and virological outcomes.

Methods: A retrospective descriptive and observational study was done at the TC Newman ARV clinic in Paarl. All adult HIV positive patients that were started on antiretroviral therapy in the given time period were included. Patient and treatment data had been collected in an electronic database (e-register) and were extracted and analysed.

Results: Starters: Out of the 2469 patients that were enrolled for ARV treatment between February 2004 and December 2010, 2254 started locally (the rest transferred in). 64% of them were female (decreasing rate over the years). Strugglers: By June 2011 51.5% of patients were still on ARVs, 6.9% patients had died, 16.7% had been 'transferred out' and 24.7% were reported as 'Lost to Follow-up'. 40% of the attrition of the cohort occurred in the first 6 months, 70% in the first 18 months. Stayers: Of the 1172 patients retained after start at TC Newman CDC, 1023 (87.3%) were still on Regime 1 and 149 (12.7%) on Regime 2.

Conclusions: The results of this treatment cohort (mortality, treatment retention and regimen durability) equal those in other published treatment cohorts, although very limited comparable data are available. However, the high 'lost to follow-up' rate is of concern and needs further investigation. Changes in the programme structure and environment tend to have an immediate effect on initiation numbers of new patients.

Declaration

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List of abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ARV	antiretroviral
ART	antiretroviral therapy
AZT	Azidothymidine (Zidovudine)
CDC	Community Day Centre
DoH	Department of Health (South Africa)
HAART	highly active antiretroviral treatment
HIV	Human immunodeficiency virus
HREC	Health Research Ethics Committee
MSF	Medecins sans Frontieres
NACOSA	National AIDS Convention of South Africa
NGO	non-governmental organisation
NNRTI	non-nucleoside reverse transcriptase enzyme inhibitor
PEPFAR	President Emergency Plan for AIDS Relief (United States)
PCP	PneumoCystisjirovecii pneumonia
PI	Protease Inhibitor
PMTCT	prevention of mother-to-child-transmission(of HIV)
VCT	voluntary counselling and testing
WHO	World Health Organisation

1 Introduction

HIV infected individuals suffer from the chronic complications of immunodeficiency. The clinical symptomatology presentation of HIV/AIDS touches almost all possible medical disciplines and HIV/AIDS can ideally be 'practised' by all medical practitioners. This has not happened because of the growing complexity of the subject, intensive research underlining new treatment strategy, and the dynamics of the disease unmatched by other clinical conditions. The system for providing clinical HIV management and the use of highly active antiretroviral therapy (ART) forms the foundation of what is referred to as "HIV medicine." ART is a life-long intervention and determining the long-term outcomes and impact of treatment programmes is necessary to monitor and improve programme performance.

In 2003 around 400 000 people were estimated to be receiving antiretroviral therapy in low-income and middle-income countries.(1) At the end of 2008, more than 4 million people were receiving ART, representing a 10-fold increase in 5 years and a 35% increase in 1 year. (2) In view of the enormous scale and need for ART a simplified programmatic approach has been adopted to facilitate delivery of treatment.(3)

With this dramatic expansion in HIV medicine, concerns have been raised that expanding access to ART in resource-poor settings will lead to 'antiretroviral anarchy' characterised by poor adherence to therapy, widespread viral resistance to medications and ultimately poor clinical outcomes. (4)

A number of programmes in resources-poor settings have demonstrated the feasibility of providing ART services (5,6) and have shown that in these instances outcomes in these programmes parallel outcomes in Europe and North America. (7,8)These services were provided by dedicated staff working in the field of "HIV medicine" and were linked to specialists and sub-specialists.(9)The good programmatic outcomes achieved by small, focused ART services, may be difficult to maintain as programmes grow in size and get integrate into general care. (10,11)

A systematic review of 33 patient cohorts, totalling 74 289 patients, from 13 African countries reported that only between 46 and 85% of patients remained in care at two years.(12) Rosen concluded that retention varies widely across programs and programs that have achieved higher retention rates can serve as models for future improvements. (12)

Determinates of outcomes and the effect of differences in the health delivery system on outcomes, have not been studied in detail in resource limited settings. Understanding these issues is important to guide the development of effective ART programmes.

In 2004 antiretroviral therapy was implemented at selected state health sector sites in the Western Cape. Since the implementation of ART, services for HIV-infected people have undergone a rapid change. Medical specialists and sub-specialists initially offered ART in tertiary institutions. Within 6 years, the ARV program expanded successfully to primary care

facilities and the services are largely driven by non-specialised doctors. With the increasing need and demand for ART it has become appropriate to expand services to include nurse clinicians. (8)The model of providing ART has changed in response to the changing needs of the local community, the health system and the availability of resources.

This research aimed to document the development of the ART service and to review the changing patterns in outcomes and patient survival among patients attending a public sector community-based ART service. The TC Newman CDC's ARV clinic was one of the first clinics to be accredited in the Western Cape that was not directly linked to an academic hospital. A standardized monitoring system to track the number of patients starting ART and to determine four key outcomes (those who are alive and on ART, those who are dead, those who have transferred out to another facility and those who have been lost to follow-up) was set up. The data collected was used to describe the characteristics of the treatment patient cohort groups started at the facility.

2 Methods

2.1 Setting

The Cape Winelands District is centrally located in the Western Cape Province, the largest sub-district in the Cape Winelands is Drakenstein. The area is known for towns such as Paarl, Wellington, Gouda and Saron and it comprises an area of 1 538 km². The agriculture industry plays a significant role in the region's economy and Paarl serves as an agricultural service centre for the surrounding intensive farming areas.

The Drakenstein Local Municipality has a population of 194 231 (2006) which is expected to decline by -0.2 % per annum to reach 192 336 by 2010. The population is predominantly coloured (64 %) and black (22%) with a small white population (14%). Half of the population is under the age of 30, with males and females evenly split.

Total unemployment stood at 22.8 % in 2001, comparing poorly with the district average of 18.4%. When seasonal unemployment is considered unemployment increases to 24.1%

The Drakenstein sub-district record high levels of TB prevalence (1 196 TB cases per 100 000) and low TB cure rate (69 % in 2005) (13)

The proportion of the population infected by HIV/AIDS remains high and stable at 5.4% from 2005 –2010. (The population figures are based on the ASSA Demographic and AIDS Model 2003)

In 2008 19 433 people (10 % of population) were tested for HIV at state clinics in Drakenstein, 2 136 people tested positive for HIV. 4 099 pregnant woman were tested for HIV with 462 testing positive (11%) In 2008 it was reported that only 24 patients of the 2 136 people tested positive for HIV were under 15 years. tested positive for HIV. (14)

2.2 Medical facilities and health care:

Most HIV+ residents rely on health services delivered by the state. There are 18 primary care HIV clinics within the sub-district; each clinic has staff able to provide voluntary testing and counselling, together with prophylaxis and outpatient management of common HIV opportunistic infections. TC Newman (Paarl) and Wellington community day centres (CDC) give support to the primary health care clinics. Patients requiring inpatient care are referred to a local 250-bed secondary care hospital or a local 80-bed TB hospital.

2.3 Development of ART services

Paarl was one of the national pilot sites for implementing the Nevirapine based PMTCT programme in 2001.

A dedicated HIV/AIDS service for HIV infected adults and children were established in January 2003 at TC Newman CDC. A full package of prophylaxis, treatment of opportunistic infections and palliative care was provided.

The National Minister of Health launched The Operational Plan for the Comprehensive Care, Management and Treatment of HIV and AIDS in South Africa in November 2003 which for the first time allowed for the widespread provision of an antiretroviral service for patients who needed them in the public sector.(15,16)

Up till then the only patients who were started in the Western Cape on antiretroviral treatment, in the public sector, were those managed by Non-governmental organizations (MSF and Hannan-Crusaid) and as part of clinical drug trials in tertiary academic hospitals. These programmes observed encouraging results in providing ARV treatment at primary health care level in the public sector and confirmed that ARV treatment is a feasible and a cost-effective intervention and can significantly reduce the morbidity and improve the survival rates of people living with HIV/AIDS.(6,9,17)

Initially, the plan was to provide a service where the expertise and infrastructure was already in place to provide patients with immediate access to ART. There were a lot of patients waiting for ARV treatment at the dedicated HIV/AIDS clinic at TC Newman (Paarl), but the staff had no experience in providing antiretroviral treatment. With the support of Non-governmental organisations and the back-up tertiary academic hospitals the first patients were started on ARV treatment in February 2004 in Paarl.

In February 2004 the ARV treatment site in Paarl was the only service available for people living in the West Coast Winelands region. Patients travelled up to 300 kilometres to get ARV treatment. The need to provide equitable access to ARV treatment for all patients in the region stimulated/resulted in the opening of satellite ARV sites and service points in the sub-district. Mobile teams from TC Newman ARV clinic provided training, mentoring and clinical support to the new sites.

By February 2005 373 patients were receiving ARV treatment at 5 different sites in the district. Stable patients on ARV were transferred out from TC Newman to the sites in neighbouring towns. By February 2006 more than a 1 000 patients had been started on ARVs and by February 2007 2115 patients received ARV treatment in the region.

By now most patients from outside Paarl were seen at clinics closer to them, but all patients from Paarl were seen at T C Newman hospital. The infrastructure needs of the ARV clinic at TC Newman became a big concern. As the clinic became more and more saturated, a bottleneck in patient enrolment was created and patient retention was undermined. In order to relief the TC Newman ARV site 4 satellites ARV sites were started at the 4 biggest “feeder” primary care clinics at the end of 2007. A cluster of ARV service sites was created in Paarl since 2008. In February 2011, 7 years of providing ARV treatment at T C Newman CDC and in Paarl was celebrated.

2.4 Clinical Care, protocols and documentation:

Enrolment and treatment of patients followed the National Ministry of Health ART guidelines. (16)

Clinical services are provided by a team comprising of doctors, nurses, pharmacy staff and counsellors with good continuity of care. Reasonable referral networks exist with the local hospitals and other primary care services such as Tuberculosis services.

Doctors are mainly responsible for treatment initiation, regimen changes and dealing with specific problems, while nurses provide most of the routine patient follow-up for those on ART, according to standardized protocols.

Standardized flowchart algorithms for the management of adverse events and virological failure guide doctors and nurses in safely monitoring patients and advise when and how to change treatment. (15)

The clinical protocol stipulates that patients begin treatment:

WHO clinical stage 4 or have a CD4 lymphocyte count of < 200/ μ l

In December 2009 the protocol was modified to also include pregnant women and patients co-infected with tuberculosis with CD4 lymphocyte counts of <350/ μ l or a clinical stage 3 or 4 disease. Since August 2011 all patients with CD4 lymphocyte counts of <350/ μ l qualify for treatment.

Additional criteria: Nominating a treatment assistant to assist with adherence

Receiving a home-visit to verify the family environment

Evidence of disclosure

Attendance on time for at least 3 previous appointments.

The consultation frequency for those on ART is determined by the clinical protocol: fortnightly until 2 months on ART, monthly until the first year on ART, and the 2-3 monthly thereafter. Patients are seen more frequently if clinically indicated.

A strong patient-centred approach is used to promote adherence. This includes a comprehensive counselling infrastructure providing for one-on-one individual counselling with trained lay-counsellors and regular support groups.

2.5 Study design and methodology

2.5.1 Research Question

What are the outcomes in patient survival, patient retention and virological control of HIV+ patients enrolled in the ARV programme since February 2004 up to December 2010 at TC Newman CDC, Paarl, Western Cape?

2.5.2 Aim

The aim of this study was firstly to identify available data, to analyse the data and to evaluate the outcomes of a state health care (semi-urban, non-academic) ART programme in the Western Cape.

Secondly, the aim was to contribute to the continuous improvement of the quality of care and the development of the programme design.

2.5.3 Objectives

The objectives were to

- collect information on the rate of enrolment and characteristics of patients enrolled on ART (“the Starters”)
- determine the proportion of patients retained on ART (“the Strugglers”)
- assess the clinical and virological outcomes of the patients started on ART (using six annual cohorts) – (“the Stayers”)
- give recommendations for monitoring outcomes in future.
- develop suggestions for the improvement of the model of care.

2.5.4 Study design

This is a retrospective descriptive study. Clinical records of patients were reviewed and information together with laboratory results was transferred to a data basis.

2.5.5 Research population and sample

All adult HIV positive patients enrolled on antiretroviral treatment at the T C Newman CDC in Paarl Patients who were 18 year or older when they started their treatment were included. Women who received ARVs solely for the prevention-of-mother-to-child-transmission during pregnancy were excluded. The complete treatment cohort in the given time period was included and no sampling was performed.

2.5.6 Data Source and analysis

When the data capturing for the project was started in 2010, a paper based system was in place by which clinical information, out of patient records, was transferred to a paper register. Data needed for the study was captured from the paper register and transferred into an excel database

The growing number of patients created a complex amount of data, and the delay between the occurrence of an outcome event and its documentation on the paper based register undermines the quality of data required for the study. A “live” electronic data capturing system was introduced during 2010. Data from the paper register was “back-captured” onto the electronic register, and after completing the back-capturing of the data, the paper register was discontinued.

With the new electronic data capturing system, information was directly (‘live’) transferred from the patient file to the electronic register. It was possible to transfer data captured in the electronic register to Excel Datasheets. At the end of June 2011, the data in the electronic register of all the patients enrolled at TC Newman ARV clinic since February 2004 up to December 2010, were transferred to an Excel Datasheet. A digital file of the data sheet, without the patient names, is available.

The results of the study are based on analysing the data transferred out of the electronic register. To help with the interpretation and visualisation of data, Tableau software® was used.

2.5.7 Describing the results

ARV services at TC Newman CDC have undergone a rapid change since their inception in 2004. Quality improvements were implemented at regular intervals, resulting in a need to document the impact of the changes made on patient outcomes.

As one example, a new way of categorising the differing needs of patient attending the ARV clinic was introduced to the clinic in 2009 by Dr David Pienaar, then director in the Western Province HAST management team. The demand on patients to attend health facilities for drug pick-ups and clinical assessments needed to be reduced by either reducing follow-up visits to once every 2 or 3 months or by providing decentralized ART services. To help staff identifying patients ready for decentralizing and reduced visits to the clinic the following terms were created:

- *Starters*: refers to new patients at the clinic and during their first year on ARV treatment,
- *Strugglers*: refers to all those patients in “danger” of getting lost to the programme and those lost to the programme
- *Stayers*: refers to all the patients that are “stable” on ARV treatment.

In accordance with this concept, the results of this study will be presented in three sets of data, each focusing on a “different group of patients” and the processes in the services supporting the groups of patients.

2.5.8 Ethical considerations

The research proposal was approved by the Health Research Ethics Committee (HREC) of the Faculty of Health Science, University of Stellenbosch.

Operational research focusing on patient retention and virological outcomes has been done before in different settings, but limited information is available on outcomes in resource limited setting. Understanding determinants of virological outcomes and patient retention in different operational setting is important to guide the development of effective ART programmes. Through improvements based on the outcomes of this research, the study can benefit the individuals on treatment and future patients entering the treatment programme. This is a retrospective study and thus no clinical risks for participants are foreseen.

All information was collected and handled in a strictly confidential way. Members of the clinic staff collected the data, and after collecting the data the information was anonymous. No names or other individual identifiers were used in the discussion of results.

Given the retrospective nature of this research, obtaining informed consent from the subjects was not feasible and a waiver of consent had been obtained from the ethics committee.

3 Results

3.1 Objective 1: Patient enrolment into the ARV programme (*The starters*)

The aim of this set of results is to describe, develop an understanding of and evaluate the factors affecting the enrolment of the patients into the ARV programme. This analysis included 2469 adult patients who were enrolled for ART at TC Newman CDC from 1 February 2004 until 31 December 2010. The study population included all adult patients that were ever enrolled at TC Newman, no one was excluded.

3.1.1 Enrollment of patients

Patients who were enrolled into the programme were either 'New' (a patient starting ARV treatment for the first time) or 'Transferred In' (a patient already on ARV treatment who moved in from another clinic). The term 'enrolled' will be used when referring to patients both 'New' and 'Transferred In'. The term 'starter' will be used when referring to 'New' patients only.

Table 1: Number of patients enrolled annually for ART at TC Newman ARV clinic

	2004	2005	2006	2007	2008	2009	2010	Total
New	189	263	422	427	251	334	368	2254
Transferred in	20	20	30	41	39	32	33	215
Total	209	283	452	468	290	366	401	2469

Table 1 shows that only 215 of the 2 469 patients ever enrolled at TC Newman CDC were 'Transferred In'. The majority (91%) of the patients were started newly on ART at TC Newman CDC. The ratio between 'New' and 'Transferred In' patients remained fairly constant over the 6 years.

Table 2: Number of 'New' patients enrolled annually for ART at TC Newman by gender

	2004	2005	2006	2007	2008	2009	2010	Total
Women	127 (67%)	184 (70%)	271 (64%)	283 (66%)	165 (66%)	201 (60%)	209 (56%)	1440 (64%)
Men	62	79	151	144	86	133	159	814
Total	189	263	422	427	251	334	368	2254

On average two thirds (64%) of the patients started on ARVs were women.

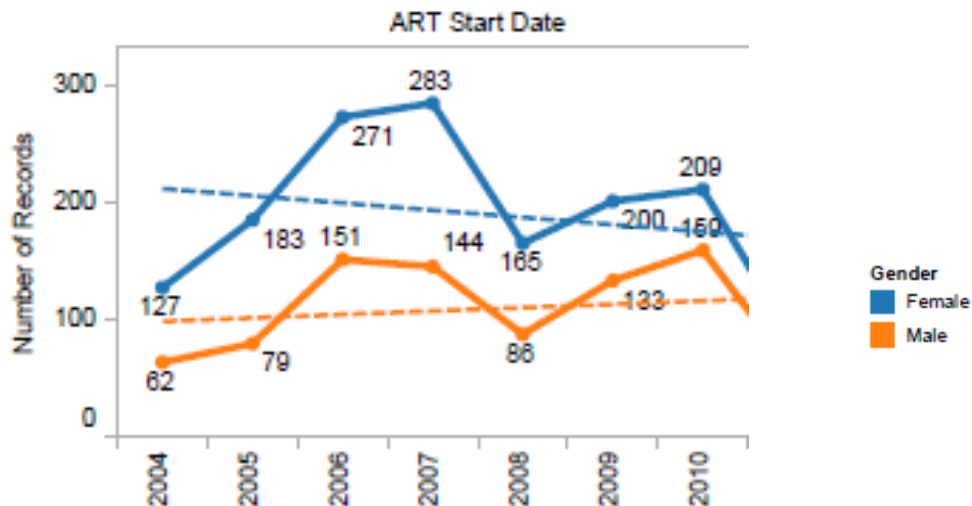


Figure 1: Number of patients started on ART annually at TC Newman ARV clinic from January 2004 to December 2010 divided into female and male patients

An interesting trend seems to be developing over the seven years, where the first five years were marked by an average of 66.6% of the patients started being women and in the last two years this percentage has dropped to under 60%. This trend would justify further investigation.

Table 3: Number of patients enrolled for ART TC Newman by age intervals

Age (years)	ART Start Date							Grand Total
	2004	2005	2006	2007	2008	2009	2010	
15-19	1					2	2	5
20-24	2	3	6	3	7	20	27	68
25-29	20	15	37	45	49	67	71	304
30-34	82	156	91	90	53	78	88	638
35-39	35	34	112	130	78	80	80	549
40-44	33	33	86	75	44	47	46	364
45-49	13	22	54	50	29	36	41	245
50-54	12	11	41	37	11	16	24	152
55-59	4	3	12	25	11	9	15	79
60-64	4	3	9	6	5	7	4	38
65-69	3	2		4	3	3	2	17
70-74			4	3		1	1	9
75-79		1						1
Grand Total	209	283	452	468	290	366	401	2469

When looking at the age demographics, it shows that 48% of patients are between the ages of 30-40 years old. Furthermore, 85% of the patients are between 25 and 50 years old.

Table 4: Number of patients enrolled for ART at TC Newman by gender and age

Age	Gender		
	Female	Male	Grand Total
15-19	4	1	5
20-24	48	20	68
25-29	229	75	304
30-34	450	188	638
35-39	354	195	549
40-44	224	140	364
45-49	112	133	245
50-54	70	82	152
55-59	36	43	79
60-64	15	23	38
65-69	6	11	17
70-74	5	4	9
75-79	1		1
Grand Total	1554	915	2469

Men on treatment are older than the women on treatment (Table 4).

3.1.2 Rate of patient recruitment

The rate at which patients are enrolled can be related to a lot of known and unknown factors. Some of these issues can be site and time specific or can be generalised issues such as access to the clinic, number of patients in need of ART treatment, the protocol, number of staff, and turnover of professional staff, infrastructure needs, the opening of new ART services points and the use of temporary employed staff

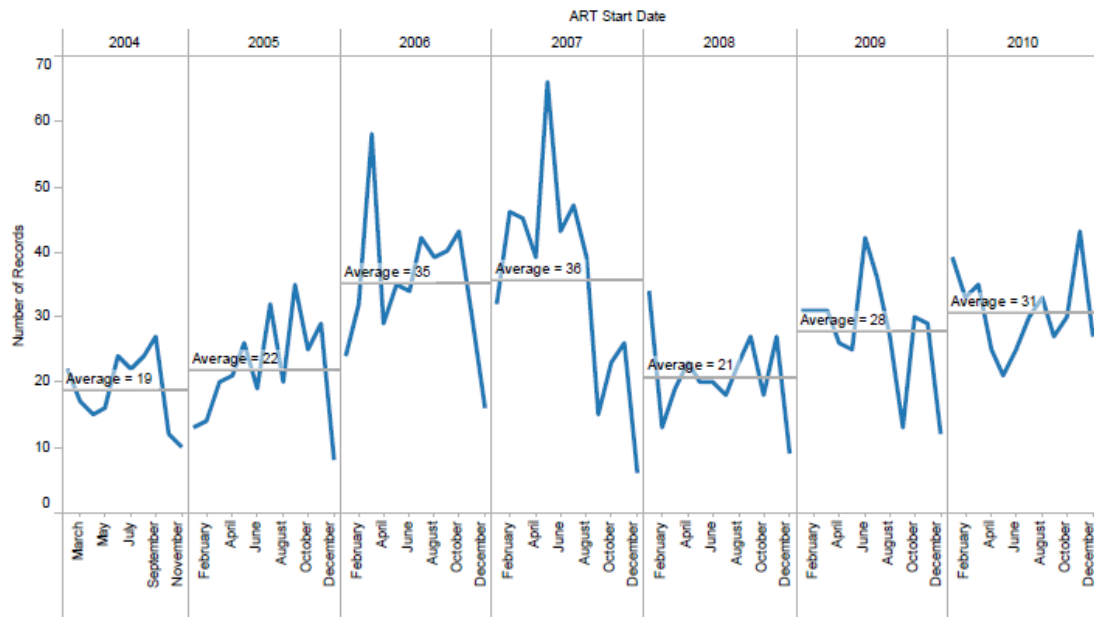


Figure 2: Number of patients started on ART per month at TC Newman ARV clinic, with annual averages

Figure 2 summarises the average number of patients started at TC Newman CDC on an annual basis.

3.2 Objective 2: Programme retention and outcomes (The strugglers)

The aim of this set of results is to describe, develop an understanding, and evaluate the outcomes of patients after they were initiated on ARV treatment. Only one outcome per patient was documented. Outcomes were divided according to the four following definitions:

- On ART: The patient received ARV treatment and care at the clinic during the past 3 months.
- Died: The patient died after starting on ARV treatment.
- Lost to Follow-up: No documentation for the patient receiving ARV treatment and care in the last 3 months. If the patient returns and starts with treatment or information about the patient's outcome is received (e.g. death or transfer-out are reported) the lost to follow-up patient's outcome status would be changed.
- Transferred/Moved Out: The patient was transferred to another ARV clinic or moved to another town.

Table 5: Outcomes as reported by the end of June 2011 of patients enrolled in the ARV programme at TC Newman

• Outcome	Number of patients	% of total patients enrolled
On ART	1272	51.5 %
Died	171	6.9%
Lost to Follow-up	612	24.8%
Transferred/Moved Out	414	16.8%
	2469	100%

By June 2011 (Table 5), 171 (6.9%) patients had died after enrolment into the ART programme at TC Newman CDC, 51.5% of patients were still on ART, 16.7% Transferred/Moved Out and 24,7% of patients were reported as Lost to Follow-up. Retention in care (On ART + transferred (moved out)/total number of patient enrolled) was 68.2%

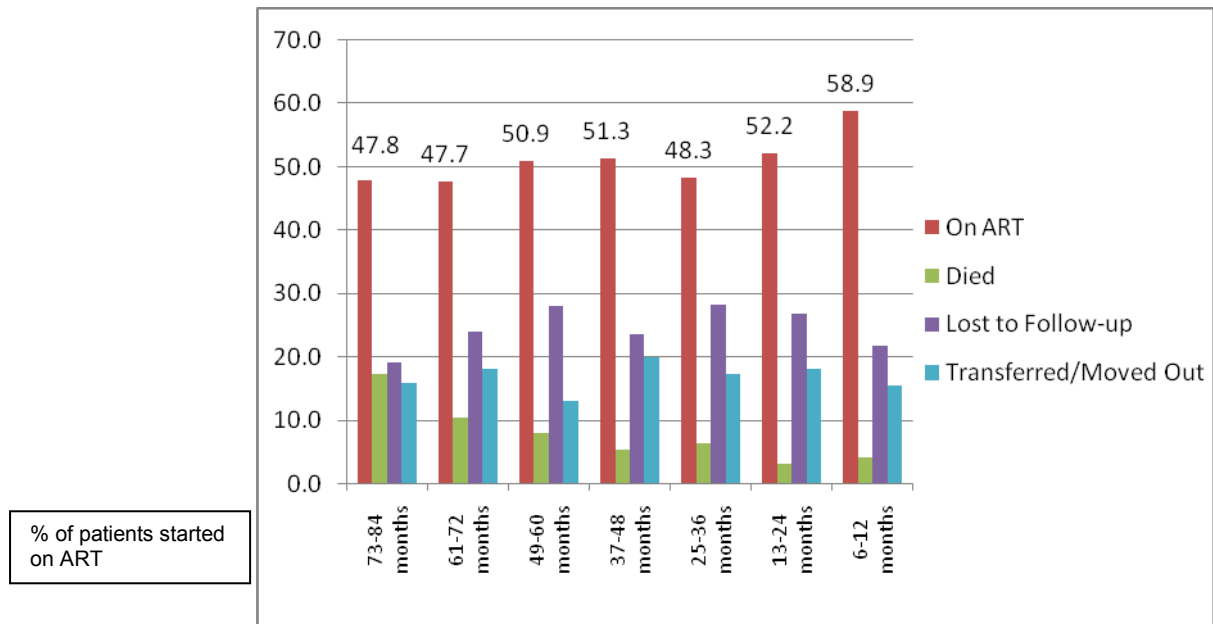


Figure 1 Time on treatment as a variable against outcomes of patients enrolled into ART

Table 6: Time on treatment as a variable against outcome.

Outcome	2004	2005	2006	2007	2008	2009	2010	Total
On ART	100 47,8 %	135 48.2%	230 51%	240 51.2%	140 48.2%	191 52%	236 58%	1272
Died	36 17.2%	29 10.2%	36 8%	25 5.3%	18 6.2%	11 3%	16 3.9%	171
Lost to Follow-up	40 19.1%	68 24%	127 28%	110 23.5%	82 28%	98 26.7%	87 21.6%	612
Transferred/Moved out	33 15.7%	51 18%	59 13%	93 19.8%	50 17.2%	66 18%	62 15.4%	414
Retention in care (On ART + Transferred/moved out)	63.5%	66.2%	64%	71%	65,4%	70%	73.4%	

Analysing time on treatment as a variable against outcomes (refer to Figure 3 and Table 6), it was found that 17,2 % of the patients enrolled into treatment in 2004 had died, while only 3% of the patients started in 2009 died. Only 19.1% of the patients started in 2004 were lost to follow-up, while 28% of patients started in 2008 were lost to follow-up. There was no significant difference between the numbers of patients transferred out per year. The data show no clear change in outcome trends with variation of time on treatment.

Table 7: Gender as a variable against outcomes of patients enrolled at TC Newman

Outcome	Female	% of Females	Male	% of Males	Total	% of total
On-Art	834	53.6%	438	47.8%	1272	51.5%
Died	82	5.2%	89	9.7%	171	6.9%
Lost to Follow-up	388	24.9%	224	24.4%	612	24.7%
Transferred/Moved out	250	16%	164	17.9%	414	16.7%
Total	1554		915		2469	

Analysing gender as a variable against outcomes was found that 9.7% of males had died and 5.2 % of females died. (Table 7)

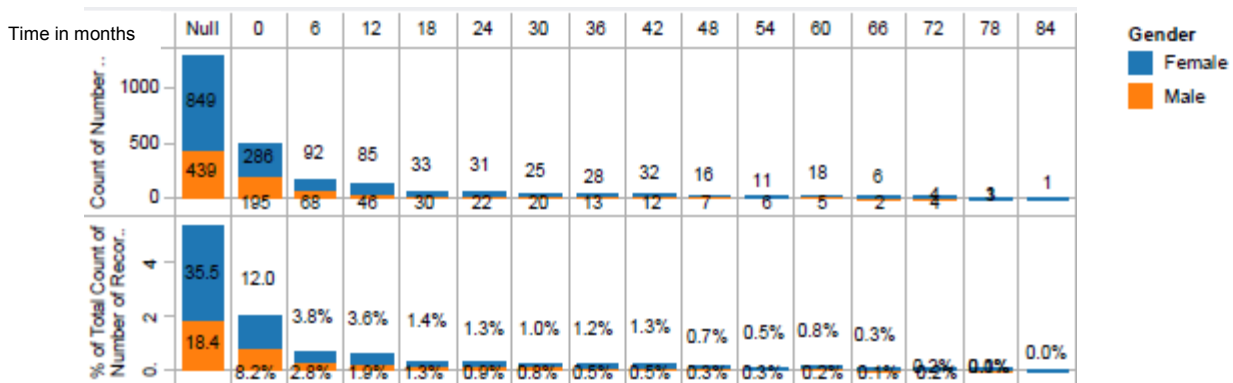


Figure 2 Total number of patients not on treatment at the end of June 2011 as a function of time in months after initiation of ART. (Null = patients still on ART)

Figure 4 illustrates that of all the patients not on treatment anymore, 43% left (either Died, Lost to Follow-up or Transferred/Moved Out) the programme between 0 to 6 months after treatment initiation and 70 % left between 0-18 months after treatment was started.

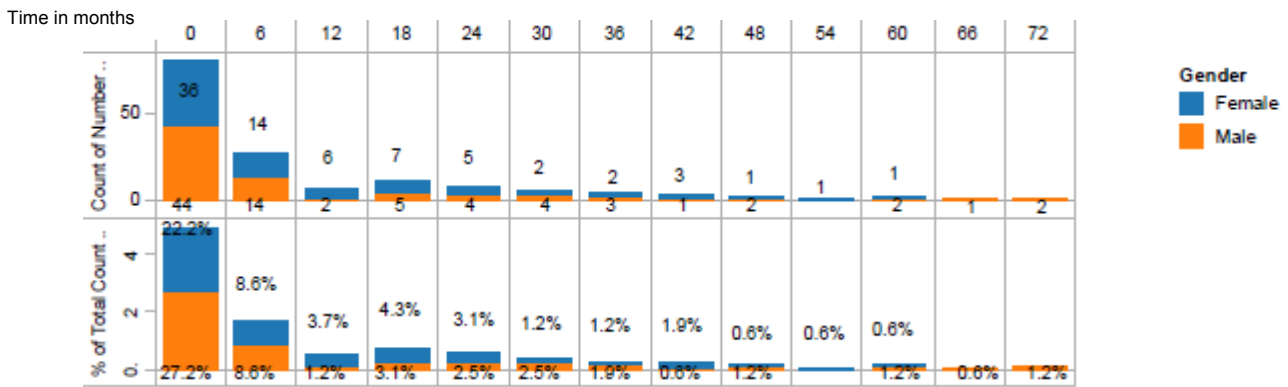


Figure 3 Summary of time since ART initiation of patients who died

Figure 5 shows that 49.4% of all patients who died did so in the first 6 months after treatment initiation and another 17,2% died between 6 and 12 months on treatment.

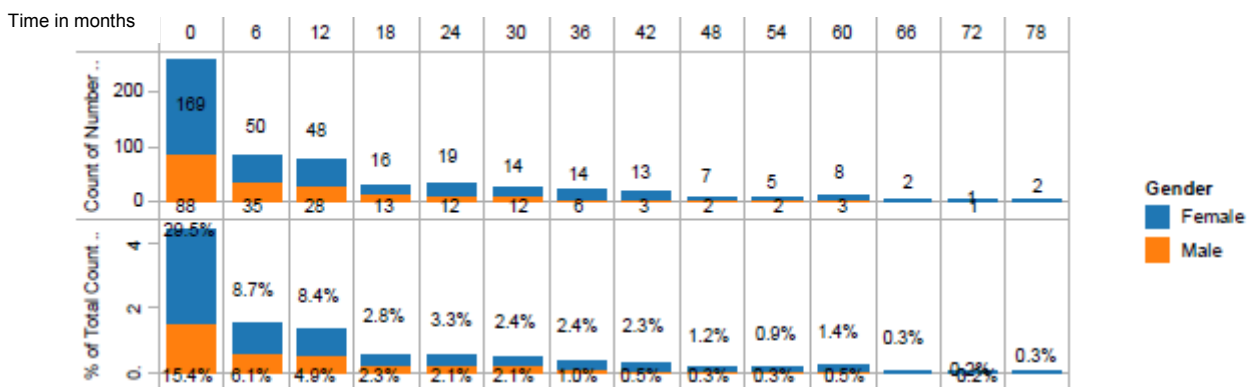


Figure 4 Summary of time since ART initiation of patient who were Lost to Follow-up

The primary reason for patients not staying in the programme was Lost to Follow-up (refer to Figure 6), 44.9% of patients became lost to follow-up within 0-6 months, 14,8% between 6-12 months and another 13.3 % between 12-18 months

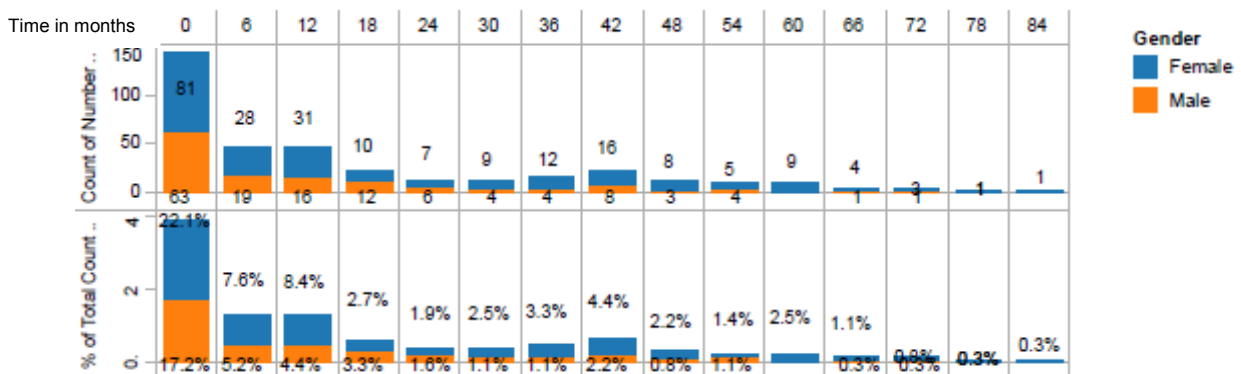


Figure 5 Summary of time since ART initiation of patients who Transferred/Moved Out

.The patient who Transferred/Moved Out showed a similar pattern (Figure 7).

3.3 Objective 3: Regimen 1 durability and “On-treatment virological suppression” (The stayers)

The aim of this section is to describe, understand and evaluate programme performance of the patients that are on ARV treatment at the clinic. Of the 2254 patients that started on ARV's, 1172 (51.9%) patients were still on treatment at the end of June 2011. Regime 1 Durability and “On-treatment virological suppression” are determinates to evaluate the performance of the clinic in providing care to patients on treatment.

To analyse this group only patients that were started on ARV treatment at TC Newman were included. Patients remaining on treatment were grouped together, based on the ARVs they were receiving. Patients were classified as: on Regime 1 or as a patient on Regime 2. Regime 1 is (NNRTI based) and is used as starting regime. Regime 2 is a “PI based” second line regime and is used for patients who have failed Regime 1.

At the end of June 2011, of the 1172 of the patients started at TC Newman CDC 1023 (87,3%) were still on Regime 1 and (149)12.7% on Regime 2

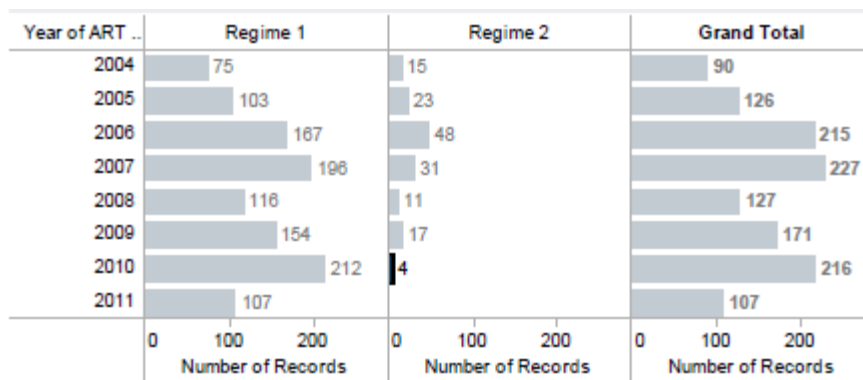


Figure 6 Time on treatment and number of patients on Regime 1 and Regime 2

Table 8: Patients still on Regime 1 as percentage of all patients still on treatment after specified time

Time in months	73-84	61-72	49-61	37-48	25-36	12-24	6-12
% of patients	83, 3%	81,7%	77,6%	86,3%	91,3%	90%	98%

Figure 8 and Table 8 illustrate time on treatment as a variable against number of patients on Regime 1. Even with the increase in time the % of patients on treatment on Regime 1 stayed high compared to the number on Regime 2.

Table 9: Outcomes of viral load testing of the patients on treatment

Number of patients on treatment	Viral load not done	Lower than Detectable level VL	Detectable
1172	215	911	153
	18.3%	85.5%	14.3%

On-treatment virological suppression rates are important determinates of programmatic outcomes. Patients on treatment were grouped together, according to the last recorded viral load measurements. The groups were classified as: No Viral load recorded, Viral loads < 400 copies/ ml = LDL, Viral loads > 400 copies/ml = Detectable

Viral loads were not reported on 18.3% (Table 9) of the patients remaining in treatment. 85.5% of the viral loads done were 'Lower than Detectable Levels'. Of the patients with Detectable Viral loads, 6.6% were on Regime 1 and 6.5 % on Regime 2.

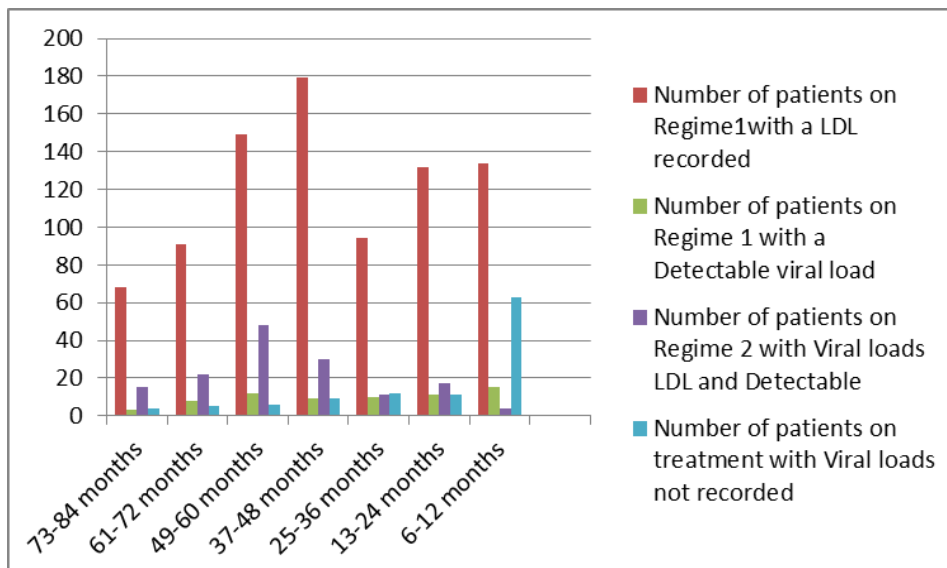


Figure 7 Summary of time on treatment of patients on Regime 1 and Regime 2 and Viral load control

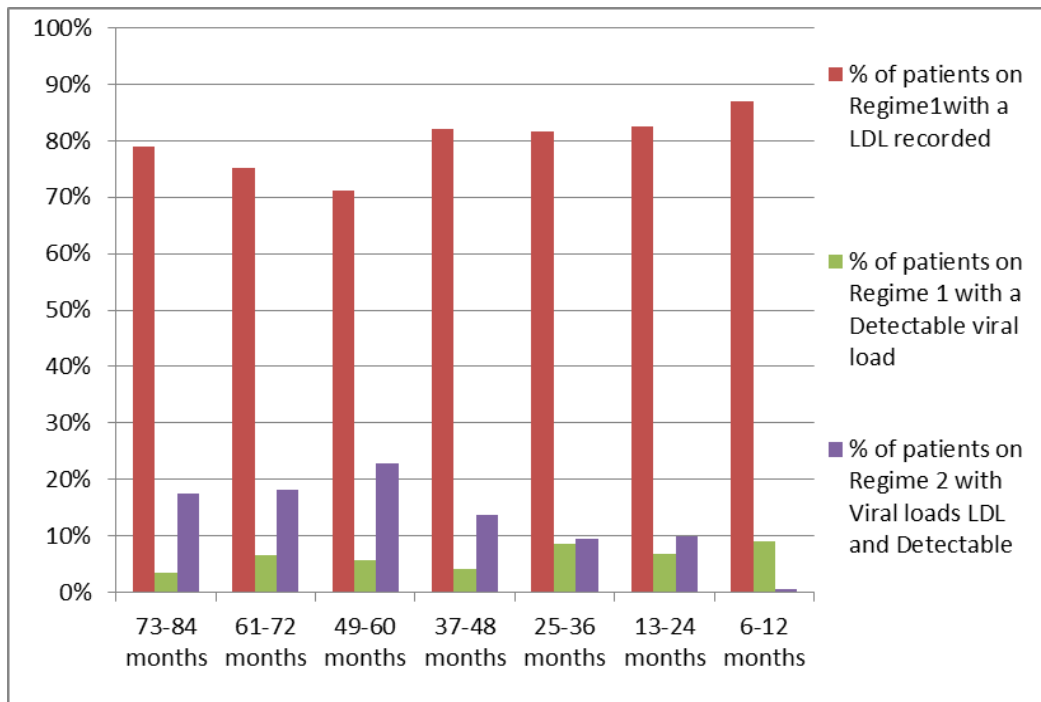


Figure 8 Percentage of patients on Regime 1 and Regime 2 and Viralological outcomes.

Figure 9 and 10 demonstrate good durability of Regime 1 over time.

4 Discussion:

Over time the quality of data capturing and analysing data became an increasing concern for the staff and management of the clinic. In the absence of curative treatment, lifelong follow-up of patients on ART is required to monitor adherence, treatment response and adverse effects. A growing amount of increasingly complex information needs to be reviewed at each visit, and new data must be added to the record.

Cornell studied data collection and data quality at 11 ART programs in South Africa and concluded that although South Africa has implemented the largest treatment programs in the world, the ability to monitor the programs closely has not kept pace with expansion. (18)

Foster suggested that promoting appropriate and sustainable databases and systems to trace patients should be a priority in the context of scaling up ART. (19) Electronic databases can play an important role, particularly as numbers of patients in ART sites increase, but for this to work adequate human resources and staff training are essential.

In line with above recommendations and to facilitate the collection of good-quality data and the transition from a paper based register to an electronic data based register a full time data capture was employed during the period of data collection for the study. The extra staff member helped in reducing the pressures facing the clinic and ensured a complete set of data.

4.1 Objective 1: Enrolment of patients “The Starters”

Access to antiretroviral therapy expanded rapidly in the sub-district and compare well with the 10 fold expansion in 5 years of ART in low- and middle-income countries reported in 2009. (2)

4.1.1 Proportion of transferring in

The ARV service at T. C. Newman CDC was one of the first ARV sites in the more rural areas of the Western Cape. It was expected that a lot of patients on treatment will be transferred to the “new” site. It was also argued that transferred in patients are a “difficult group” to integrate into the “culture” of the clinic, because they were not part of the standard patient education programme. In conclusion the proportion of “transferred in patients” at the TC Newman CDC is small compared to the number started at the clinic. It is unlikely that

the” transferred in patients” have a significant impact on the functioning and outcomes of the clinic.

4.1.2 Gender distribution

Data disaggregated by gender shows that about 60% of adults who were receiving ART in low- and middle income countries were women. (2) At TC Newman 62.9% of the patients started on ARV were women. In the first 5 year 66.6 % of the patients started at the clinic were women, the last two years the percentage has dropped to 58%. This trend justifies further investigation in order to identify and support strategies that enhance men’s acceptability of ART services.

Studies had shown that men are less likely to access treatment, present with more advance stages of HIV disease and have a higher risk of defaulting. (20) (21)

4.1.3 Age distribution

It is the young adults in the population that are the worst affected by HIV with 48 % of the patients at the clinic between the ages of 30-40 years. Staff working in the ARV clinics needs to adjust to the needs of the younger adult, like reproductive health needs and the need for flexibility to accommodate the working adult.

4.1.4 Enrolment trends

The fluctuation over time in the number of patients enrolled is closely related to developments and scale-up events at clinic level. Changes in the programme structure and environment tend to have a direct effect on the numbers of patients initiated.

For example:

- Creating capacity for ART service delivery:

In the first two years of the programme the enrolment of new patients at the clinic was limited to two days a week, because of the availability of staff and physical space. It is documented that the chronic shortage of health care workers is a major bottleneck to health provision and scaling up treatment. (17) (22) The average number of patients started in 2004 was 19 patients per month and in 2005, 22. In 2006 the number of patients enrolled monthly increased to an average of 35 patients reaching a maximum of 60 patients in one month of the year. The increase in numbers in 2006 follow on the employment of full time doctors at TC Newman CDC ART clinic and the ability of the team to put patients on treatment for 5 days a week.

- Physical space was a critical constraint in the expansion of the programme.
The sharp increase in total number of patients on treatment since 2006 put a lot of pressure on the need for more physical infrastructure. In 2007 the clinic was relocated and patients were seen at three different rooms in three different corners of the facility. The lack of physical space was one of the main reasons for the drop in the number of patients started on treatment in the second part of 2007. Infrastructure as a key barrier to implementation of ART was identified and it was agreed that new infrastructure were needed, but it would take 3 years for the infrastructure to catch up with the patient needs. Physical space as barrier to implementation of ART access was also identified by Bekker. (9)
- Decentralization of ART services:
With the help of non-governmental organisation, ART services were decentralised to Primary Health Care clinics in the Drakenstein sub-district. The decentralisation of ARV services started at the end of 2007 and had an impact on the enrolment at TC Newman CDC as seen by the decline in the number of patients enrolled in 2008. In 2008 only 21 patients were on average started on treatment per month, but 4 new ART service points were available in the Drakenstein sub district. Decentralization and task shifting has been shown to work in a number of settings (16) (23) (24)
- Reduction of the frequency of visits for stable patients
In 2009 a new strategy at the clinic focussed on identifying stable patients and reducing follow-up visits to the clinic to once every 2 or 3 months. Clinic staff had more time to initiate patients and since 2009 (average of 28) there was a steady growth to an average of 31 per month.

4.2 Objective 2: Evaluating outcomes: The Strugglers

Harries documented that good ART clinic practise must include reliable ascertainment of outcomes of death, loss to follow-up and the formal recording of transfer outs from one ART facility to another. (25)

It was possible to identify treatment outcomes at the clinic through regular scrutiny of the paper-based files and register, but it was labour intensive, done only quarterly and by the time the treatment outcome report became available, it already needed updating. Introducing the electronic registered made it possible to have a daily treatment outcome report after all

the patients visits were entered. The sustainability and timeliness of the electronic register greatly enhanced the ability of the clinic to trace patients who are either late for appointments or who have been recorded as lost to follow-up.

4.2.1 Retention in care

The scale-up of ART has been one of the success stories of sub-Saharan Africa, however tempering the success is a growing concern about patient retention

We defined attrition from ART programs to include patients who died or were lost to follow-up and retention were defined as the opposite of attrition (i.e. 1- attrition) Using the definition 63.5 % of the patients started on ART in 2004 (73-84 month on treatment) are retained in care. The retention in care for the 6 cohort groups averaged 68.8% and with a variation of (63.5%- 73.5%)

This compare well with analysed done by Fox on 33 sources describing 39 cohorts and 226 307 patients on ART in sub-Saharan Africa. It was found that the overall retention by 24 months averaging 70%-77% and overall retention by 36 months averaging 65%-72%.(26)

Measuring retention in care is critical for determining the effectiveness of programmes and can be used as a proxy for the quality of care. (5) Tassie also reported that the countries with highest burden of patients, South Africa, Kenya, Nigeria, India, Zambia did not report on retention as indicator.

By June 2011, 6 and a half years since the start of clinic, 6.9% patients had died after enrolment into the ART programme, 51.5% of patients were still on ART, 16.7% Transferred/Moved Out and 24,7% of patients were reported as Lost to Follow-up. These findings at the TC Newman clinic document that retaining patients in care for lifelong treatment is difficult.

4.2.2 Mortality rate

The overall low mortality rate of 6.9% in the programme was encouraging. Of all the patient who died after enrolment, 49.4% of patients died in the first 6 months after treatment initiation and another 17,2% died between 6 and 12 months on treatment. These findings compare well with other programmes, Bekker reported a 7% mortality rate in Guguletu with 63% of deaths occurring in the first 90 days of ART.(9) and Lawn reported that 8% to 26% of patients entering ART programmes die in the first year in African settings. (27)

The low mortality rate at TC Newman needs to be interpreted with caution, because the high Lost to Follow-up rate can mask a higher mortality rate.

Analysing gender as a variable against outcomes it was founded that 9.7% of males died and 5.2 % of females died. This finding is consistent with other studies documenting men having a higher mortality risk. (28)

The reasons for patients dying on treatment at the clinic need further investigation and to reduce the death rate intervention need to focus on reducing early on treatment mortality.

4.2.3 Lost to follow-up rate.

Of the patients not staying in the program 54% were reported as Lost to follow up, 35% reported as transferred out and 11% died. We do not have a good understanding of reasons for patients not returning to care at the clinic. A systematic review and meta-analysis of studies that traced patients who were Lost to follow up in ART programmes in resource-limited settings showed that the outcome of over a third of patients remained unknown. (29) and among those traced 20% to 60% had died. Common reasons included the transfer to another ART site, financial problems, improvement or deteriorating health and stigma. (29)

Of the patients reported as Lost to follow-up 44.9% become lost to follow-up within 0-6 months. The results confirm the results of previous studies that once a patient have initiated ART and survived the initial few months of treatment the risk of lost to follow up and death is low. (30)

To understanding the Lost to Follow up group it is recommended that, reasons for lost, and outcomes after Lost to Follow-up, get documented at TC Newman CDC. For this patient tracing procedures need to be in place. (31)

Harries, Zachariah, Lawn and Rosen presented and discuss key interventions they believe might help with improving patient retention.(25) Some of the strategies (the need for simple and standardized monitoring systems to track what is happening, reliable ascertainment of true outcomes of patients lost to follow-up, implementation of measures to reduce early mortality in patients both before and during ART, the use of simple, non-toxic ART regimes and the decentralization of ART care to health centres and the community) were implemented at the TC Newman CDC. Operational research at facility level is needed to evaluate the outcome of these quality improvement strategies.

4.2.4 Transferred/Moved out

Because of the expansion and decentralization of ART services an increasing number of patients were transferred between treatment centres. Good communication and sharing of patient information between treatment centres are needed. Implementing the electronic register at more clinics will help to identify patients that have moved between clinics.

4.3 Objective 3: Evaluating patients on treatment: The Stayers

4.3.1 Regimen durability

Six years after the programme was started at TC Newman CDC, 87.3% of the patients on treatment were still on Regime 1 and 12.7% on Regime 2. Even with the increase in time the % of patients on treatment on Regime 1 stayed high compared to the number on Regime 2. Change from Regime 1 to Regime 2 was due to treatment failure. Boulle reported on similar settings to TC Newman that at 2 years, 3.7% of adults were on Regime 2, rising to 17.9% at 4 years. (32)

4.3.2 Virological outcome

Routine viral loads were done to monitor efficacy of ART. Of the patients remaining in care, 85.5% of the last viral load reported was 'Lower than Detectable Levels'. The proportion of patients with "Lower than detectable Levels" compares favourably with those reported in other studies. (6) (33) (34)

The stable patients on treatment form the bulk of the patients visiting the clinic daily. They are an ever growing group and because of the nature of ARV treatment will never be discharged out of the ARV services. There is a need to develop sustainable processes and platforms at clinic and community level that will deliver high volume ART safely to stable patients in the context of limited resources.

The good virological and regime durability documented in this study is a motivation for the decentralization and mainstreaming of ART services to stable patients. This is in line with recommendations from the Development of Antiretroviral Therapy in Africa (DART) trial that shows that treatment outcomes are as good with simple clinical monitoring compared with clinical and laboratory monitoring. (35)

5 Conclusion

Good quality data on enrolment (starters), retention in care (strugglers) and virological outcomes is available at TC Newman CDC and can be used to benefit patients directly and indirectly. Access to ART expanded rapidly at the clinic and the number of patients enrolled (starters) is closely related to developments and scale-up events at the clinic.

Retention in care rate over the 6 years (63,5%-73.5%) equal those in other published treatment cohorts. The high 'loss to follow-up' rate is of concern and needs further investigation. (strugglers)

Good virological outcomes over time were documented for the patients in care (stayers).

6 Recommendations:

6.1 Data capturing and analysing

The implementation of the electronic data register at TC Newman CDC opened opportunities for better data quality and the use of the electronic data register is recommended. In the face of the rapid increase of patient numbers, a balance between the needs for services provision and collection of good quality data is needed. A study looking at the impact of implementing the e-register on service provision and to validate data quality in the e-register is needed.

6.2 Starters

Despite progress made with the enrolment on to ART, a lot of people are still in need of ART. Clear enrolment targets are needed and strategies enhancing the enrolment need to be implemented and studied. Sub-groups, like men, are more difficult to enrol and justify investigation.

6.3 Strugglers

It is recommended that retention in care be used as an indication of the quality of care. A better understanding of reasons for not returning to care at the clinic is needed and needs further investigation. The reasons for patients dying on treatment and for early mortality need investigation.

6.4 Stayers

The stable patients on treatment are an ever growing group of patients and form the bulk of the patients visiting the clinic. It is recommended that facilities define the minimum package of services needed to ensure safe ART to this group of patients.

References

1. World Health Organisation and UNAIDS. *Treating 3 Million by 2005: Making It happen*. Geneva, Switzerland: WHO; 2003 <http://www.who.int/3by5/Publications/en/3by5strategy-making-it-happen.pdf> (accessed June 2009)
2. WHO, UNAIDS, UNICEF. *Towards Universal Access. Scaling up Priority HIV/AIDS interventions in the Health Sector, Progress Report*. Geneva, Switzerland: WHO; 2009, <http://www.who.int/hiv/pub/tuapr-2009-en.pdf> (accessed June 2010)
3. World Health Organization. *Scaling up antiretroviral therapy in resource-limited settings: Guidelines for a public health approach; executive summary*. Geneva: World Health Organization, 2002 www.who.int/medicinedocs/library.fcgi?e=d-Oedmeb (accessed June 2009)
4. Harris AD, Nyangula DS, Hargreaves NJ, Kaluwa O, Salaniponi FM. Preventing antiretroviral anarchy in sub-saharan Africa. *Lancet* 2001; 358: 410-414
5. Tassi J-M, Szumilin E, Calmy A, Goemaere E. Highly active Antiretroviral therapy in resource-poor settings: the experience of Medecins Sans Frontieres. *AIDS* 2003; 17: 1995-1997
6. Coetzee D, Hildebrand K, Boulle A, Maartens G, Louis F. Outcomes after two years of providing Antiretroviral treatment in Khayelitsha, South Africa: *AIDS* 2004, 18: 887-895
7. Ivers LC, Kendrick D, Doucette K. Efficacy of antiretroviral therapy programs in resource-poor settings: a meta-analysis of the published literature. *Clin Infect Dis* 2005; 41:217-24.
8. Akileswaran C, Lurie MN, Flanigan TP, Mayer K: Lessons learned from use of Highly Active Antiretroviral Therapy in Africa. *Clin Infect Dis* 2005;41:376-85
9. Bekker L-G, Myer L, Orrel C, Lawn S, Wood R: Rapid scale-up of a community-based HIV treatment service: programme performance over 3 consecutive years in Guguletu, South Africa. *SAMJ* 2006, 96(4):315-20
10. Bekker LG, Orrell C, Reader L, Matoti K, Cohen K, Martell R, Abdullah F, Wood R.. Antiretroviral therapy in a community clinic-early lessons from a pilot project: *SAMJ* 2003, 93(6):458-62
11. Orrell C, Harling G, Lawn S. Conservation of first line antiretroviral treatment regimen where therapeutic options limited. *Antivir Ther* 2007; 12: 83-88
12. Rosen S, Fox MP, Gill CJ. Patient retention in antiretroviral therapy programs in sub-Saharan Africa: a systematic review. *PloS Med* 2007, 4(10):e298
13. Actuarial Society of South Africa. ASSA2003 AIDS and the demographic model. Available at <http://www.assa.org.za/aidsmodel.asp> (accessed June 2009)

14. The Western Cape Antiretroviral programme. Monitoring report Cape Town: provincial Government of the Western Cape Available from <http://web.uct.ac.za/depts/epi/artroll/files/Artmonitoringreport-wc-062006.pdf> (accessed June 2009)
15. National Department of Health. *Antiretroviral Treatment Guidelines*, 1st ed. Pretoria: 2004
16. Provincial Government of the Western Cape. *Antiretroviral Treatment Protocol Version 2*. Cape Town: 2004
17. Bedelu M, Ford N, Hilderbrand K, Reuter H: Implementing Antiretroviral Therapy in Rural Communities: The Lusikisiki Model of Decentralized HIV/AIDS Care. *JID* 2007;169(suppl3):S464-S468
18. Cornell M, Technau K, et al. Monitoring the South African National Antiretroviral treatment programme, 2003-2007: The IEDEA Southern Africa collaboration: *SAMJ* 2009, 99(9):653-9
19. Forster M, Baily C, Brinkhof MW, Graber C, Boulle A, Spohr M, Balestre E, May M, Keiser O Jahn A, Egger M. Electronic medical record systems, data quality and loss to follow-up: survey of antiretroviral therapy programmes in resource-limited settings: *Bulletin of the World Health Organization* 86:939-47
20. Kranzer K, Lewis J, Ford N, Zeinecker J, Orrel C, Lawn S, Bekker L-G, Wood R: Treatment interruption in a primary antiretroviral therapy programme in South Africa: cohort analysis of trends and risk factors; *JAIDS* 2010 ,55 (3): e17-e23
21. Cornell M, Meyer L, Kaplan R, Bekker LG, Wood R. The impact of gender and income on survival and retention in a South African antiretroviral therapy programme. *Trop Med Int Health* Jul 2009, 14 (7):722-31
22. Van Damme W, Kober K, Laga M. The real challenges for scaling up ART in sub-Saharan Africa, *AIDS* 2006, 20:653-6
23. Philips M, Zachariah R, Venis S. Task shifting for antiretroviral treatment delivery in sub-Saharan Africa: not a panacea. *Lancet* 2008, 371,682-4
24. Jaffer S, Amuron B, Foster S. Rates of virological failure in patients treated in a home-based versus a facility-based HIV care model in Jinja, southeast Uganda: a cluster-randomised equivalence trial. *Lancet* 2009,374:2080-9
25. Harris AD, Zachariah R, Lawn SD, Rosen S. The Strategies to improve patient retention on antiretroviral therapy in sub-Saharan Africa: *Trop Med Int Health* 2010, 15:70-5
26. Fox MP, Rosen S: Patient retention in antiretroviral therapy programs up to three years on treatment in sub-Saharan Africa, 2007-2009: Systematic review: *Trop Med Int Health* 2010, 15(suppl1):s1-s15

27. Lawn SD, Harris AD, Anglaret X, Myer L, Wood R: Early mortality among adults accessing antiretroviral treatment programmes in sub-Saharan Africa. *AIDS* 2008, 22:1897-908
28. Milles EJ, Nachenga JB, Bangsberg DR. Adherence to HAART: a systematic review of developed and developing nation patient-report barriers and facilitators. *PloS Med* 2006, 3(11):e438
29. Brinkhof MWG, Pajudes-Rodriguez M, Egger. Mortality of patients lost to follow-up in Antiretroviral treatment programmes in resource-limited settings: Systematic review and meta-analysis. *PloS ONE* 2009, 4 (6):e5790
30. Lawn SD, Myer L, Harling G, Orrell C, Bekker LG, Wood R. Determinants of mortality and nondeath losses from an antiretroviral treatment service in South Africa: Implications for program evaluation. *Clinical Infectious Disease* 2006, 43:770-6
31. Rosen S, Fox M, Gill CJ: Patient Retention in Antiretroviral Therapy programs in Sub-Saharan Africa: A Systematic Review.. *PloS Medicine* 2007, 4(10): e298
32. Boulle A, Bock P, Osler M, Cohen K, Channing L, Hilderbrand K, Mothibi E, Zweigenthal V, Slingers N, Cloete K, Abdullah Fareed. Antiretroviral therapy and early mortality in South Africa, *Bulletin World health Organization* 2008, 86 (9):678-9
33. Boulle A, Orrell C, Kaplan R, van Cutsem G, McNally M, Hilderbrand K, Myer L, Egger M, Coetzee D, Maartens G, Wood R: Substitution due to antiretroviral toxicity or contraindication in the first 3 years of antiretroviral therapy in a large South African cohort. *Antiviral Therapy* 2007, 12:753-60
34. K Fielding, S Charalambous, A Stenson, L Pemba, D Martin, R Wood, G Churchyard, A Grant: Risk factors for poor virological outcome at 12 months in a workplace-based antiretroviral therapy programme in South Africa: A cohort study: *BMC Infectious Diseases* 2008, 8:93 doi:10.1186/1471-2334-8-93
35. DART Trail Team: Routine versus clinically laboratory monitoring of HIV antiretroviral therapy in Africa (DART): a randomised non-inferiority trial, *Lancet* 2010, 375, (9709):123-31