Profile and Clinical Outcomes of HIV-infected persons enrolling in an HIV Service in Khayelitsha during 2002

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Khayelitsha Photo source: Michael von Aichbergeri

[1] From: http://www.nangu-thina.de/thandabantu/sld003.htm (Accessed 25th Dec, 2004)

Declaration

I, Ali Al-Kfeiri, hereby declare that the work on this dissertation is based on my original research and has not, in whole or in part, been submitted towards another degree, at this university or elsewhere. The university is empowered to reproduce either the whole or any portion of the contents for the purposes of research.

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Abstract

Introduction

Most people infected with HIV live in Africa where access to health care is limited. Antiretroviral Therapy (ART) is not yet the standard of care for those with advanced disease. Recent studies of the outcomes of HIV/AIDS programmes are mostly focused on evaluating ART programmes in terms of the cost-effectiveness and feasibility of providing ART in resource-limited settings. The integrated HIV/AIDS programme in Khayelitsha (where patients on ART and not on ART are followed) provides a unique opportunity to explore overall programme outcomes irrespective of subsequent access to antiretrovirals.

Aim

The aim was to describe the profile and clinical outcomes of all persons attending an HIV-service in a resource–limited setting, in Khayelitsha, Cape Town.

Design

A cohort of persons infected with HIV in Khayelitsha was followed up prospectively from the time of enrolment in 2002 until 30th of June, 2004. The existing database of patients was validated using records of opportunistic infections, laboratory markers such as CD4 count, and other outcomes such as death or loss to follow up.

Results

A total of 534 HIV-infected patients were studied. The median age was 31 years and 392 were women (73%). The baseline demographic and clinical characteristics revealed the following: there was no significant difference in the median baseline weight between

women (60.0kg) and men (58.8kg), (p=0.114); there was a significant difference in the median baseline CD4 count between women (241 cells/μl) and men (154 cells/μl), (p=0.015); 15.4% of all patients had an AIDS-defining illness (WHO HIV clinical stage IV) and 30.9% had a history of prior tuberculosis (TB) at the time of enrolment. The median CD4 cell count at first visit was highest for patients referred from the Programme for the Prevention of Mother to Child Transmission (394 cell/μl).

Approximately 50% of the cohort were lost to follow-up and 21% started ARV therapy during the period studied. The LTF group was analyzed and the median baseline CD4 cell count was 261 cell/μl compared to 185.5 cell/μl for those not LTF (p=0.039). The median duration of care was 16.2 months for those not receiving ART and there was no significant difference for different CD4 count categories (p=0.234). Age in years, male sex and previous history of TB were significantly associated with LTF (p-value < 0.001).

The cumulative estimate of survival was 90% in the first year and 87% at 18th months for those not yet on ART. There was no significant difference when comparing different categories of CD4 count (p=0.87) in the survival estimate.

Seventy eight percent of the cohort remained free of TB by the end of the second year. Restricting the analysis to those not receiving ART and with CD4 count <200 cells/μl, 54% contracted TB by the second year.

One hundred and fourteen (21.3%) of the total cohort started ART during enrolment. Fifty percent of those with a CD4 count <50 cells/μl started ART by the second year and 45% of those with a CD4 count between 50 and 200 cells/μl (product-limit estimate). The product-limit estimate of being lost to follow-up after starting ART was 3% by the first year. The product-limit estimate of survival was 87% at the 12th month with significant improvement in both CD4 count and viral load.

Conclusion

The Khayelitsha HIV programme has been extensively reported in terms of ART outcomes. This is the first attempt to review overall clinical outcomes for all adults enrolled in care.

The rate of loss to follow-up is higher than expected and severely comprises the ability of the programme to report on non-ART outcomes. An examination of sources of referral and CD4 counts does however go some way to explaining the loss to follow-up.

The time to starting ART was long and could have been shorter. The outcomes for those patients starting ART in this clinic are consistent with those of the overall programme.

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Abbreviations

AIDS	Acquired immune deficiency syndrome
ARV	Antiretroviral therapy
HAART	Highly active antiretroviral therapy
HIV	Human immunodeficiency virus
MTB	Mycobacterium tuberculosis
MTCT	Mother to child transmission
MSF	Médicine Sans Frontières (Khayelitsha HIV project)
OI's	Opportunistic infections
TB	Tuberculosis
WHO	World Health Organization

CHAPTER 1

1.1 LITERATURE REVIEW

1.1.1 AIDS and the immune system

The immune system is a complex network of cells and organs that works together to defend the body against foreign organisms. This system is highly developed and produces millions of different antibodies and cells, which help to target specific organisms effectively. In the early 1980's people in the United States (particularly homosexual men and haemophiliacs) acquired infections in alarming numbers, rarely seen in healthy adults. It was soon recognised that infection with a virus, Human Immunodeficiency Virus (HIV), resulted in the depletion of an important component of the immune system, the CD4+ T cells. The loss of these cells left the body vulnerable to infections that would normally be controlled by a healthy immune system (Stine 1993).

AIDS was described as a collection of symptoms that make up a recognisable pattern and have a similar cause - the acquisition of infection with HIV, transmitted through the exchange of bodily fluids from someone infected with HIV. The bodily fluids that contain sufficient amounts of HIV to be able to transmit infection are blood, semen, vaginal secretions and breast milk (Stine 1993).

The impact of HIV on the immune system is the important feature of AIDS. HIV itself does not directly kill people but it rather weakens the immune system and people infected with HIV are vulnerable to diseases that they would normally resist. These diseases are called opportunistic infections (OI's) because they take advantage of a weakened immune

system to spread and cause disease. The range of opportunistic infections differs depending on the prevalent infections in an area. HIV not only makes both existing diseases more common and more severe (e.g. tuberculosis) but also makes rare diseases more common (e.g., *pneumocystis carinii* pneumonia, Kaposi's sarcoma).

1.1.2 Epidemiology and burden of HIV

1.1.2.1 *The global HIV/AIDS epidemic*

HIV/AIDS is the leading cause of mortality among adults aged 15 to 59 years in the developing world and it is in the top 10 leading causes of all deaths reported by the World Health Organization in 2003 (World Health Organization 2003). Ischemic heart disease (IHD) and tuberculosis (TB) ranked second and third, respectively, for this age group. For adults of age 60 years and older, IHD, cerebrovascular disease (CVD), TB and colon and rectum cancers are the main causes of death (World Health Organization 2003).

It is estimated that 40 million people were living with HIV/AIDS, 5 million new infections with HIV and 3 million deaths from HIV in 2003 (UNAIDS 2004). Sub-Saharan Africa has the highest number of adults and children living with HIV/AIDS compared to the other regions in the world (UNAIDS 2004), (figure 1).

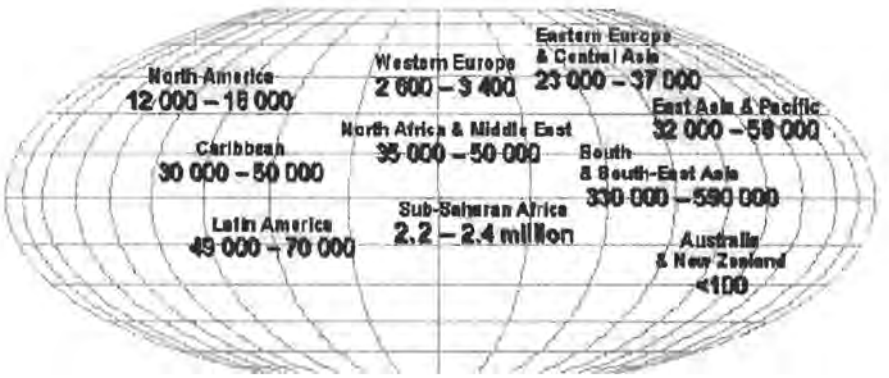


Figure 1: Adults and children estimated to be living with HIV/AIDS as of end 2003[i].

In Sub-Saharan Africa, the estimated number of adults and children living with HIV/AIDS at the end of 2003 was 28.2 million, (World Health Organization 2004). However, not all African countries exhibit the same patterns of HIV prevalence and there are very large differences in Sub-Saharan African countries (samoah-Odei, Garcia Calleja, & Boerma 2004).

1.1.2.2 *HIV/AIDS in South Africa*

The estimated number of adults and children living with HIV/AIDS in South Africa by the end of 2003 was 5.3 million, of which adults aged 15 – 49 years comprised 5.1 million and children aged 15 years and younger numbered 230 000. The number of women in the age group 15 to 49 years living with HIV/AIDS was 2.9 million (UNAIDS 2003).

[i] Adapted from UNAIDS, AIDS Epidemic updates 2004.

In South Africa, as many other countries, national sentinel HIV sero-prevalence surveys of antenatal clinic (ANC) attendees have been conducted since 1990. HIV prevalence among pregnant women in South Africa has increased since 1990. In 2003, the prevalence was 27.9% compared to 26.5% in 2002. This increasing pattern is evident yearly since 1990 (figure 2) (Department of Health 2003a).

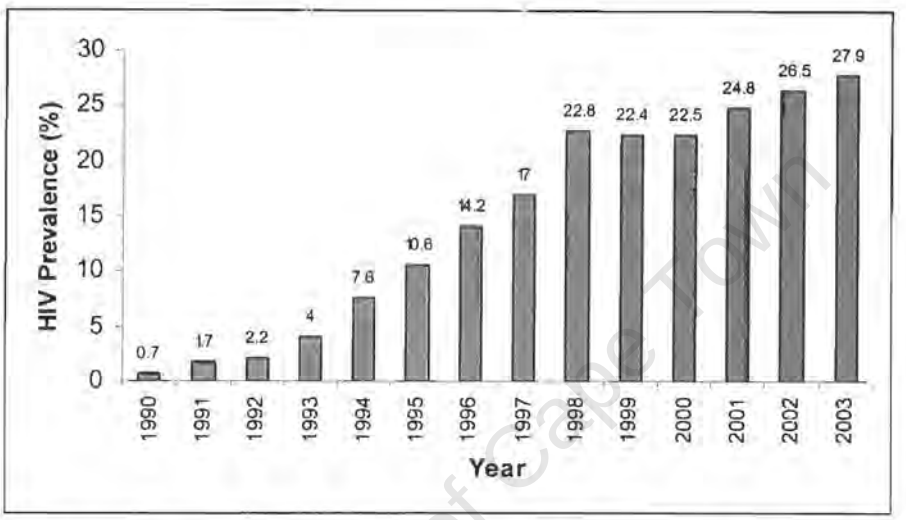


Figure 2: prevalence of HIV among antenatal care attendees in South Africa, 1990 – 2003.

These findings show that the HIV prevalence rates remain high and that between provinces variations are observed. A prevalence rate of 37.5% was observed for KwaZulu-Natal followed by Mpumalanga (32.6%), Free State (30.1%), Gauteng (29.6%) and Eastern Cape (27.1%). The other provinces showed prevalence rates below 20% with the Western Cape having the lowest prevalence (13.1%). HIV prevalence by age group showed that the age group 25 to 29 has the highest rate (35.4%) and that the lowest prevalence rate (15.8%) was recorded among teenagers (and particularly women under 20 years) (Department of Health 2003a).

While the antenatal surveys have been useful in determining trends overtime, they are less reliable for generating population–level estimates (Fylkesnes et al. 1998;Kigadye et al. 1993) as only pregnant women who use public sector health-care facilities were included. This can produce different types of bias because it excludes not only women attending private health-care institutions, but also women who are not pregnant and all men and children. One of the latest studies using the general South African population to determine HIV prevalence was done by Connolly (Connolly et al. 2004) . It was one of few national community-based HIV surveys conducted in South Africa. A sample of persons over 2 years of age from both sexes and of all racial groups was included in the study using pre-designed geographical maps of households around South Africa. HIV prevalence in the general population was estimated to be 11.4 % (12.8% in females and 9.5% in males) and varied significantly by province from 6.6% in the Eastern Cape to 14.9% in the Free State. The prevalence in pregnant women was 24% which is similar to estimates from the latest antenatal surveys (Department of Health 2002;Department of Health 2003a).

1.1.2.3 *Impact of HIV/AIDS in South Africa*

A study by (Bradshaw et al. 2003) has reported on the estimated burden of HIV/AIDS. It asserted that HIV/AIDS accounted for 30% of deaths in 2002 and the proportion of HIV-related deaths in women was higher than deaths due to injury in men. Young adults of both sexes were most affected. In terms of years of life lost (YLL), 38% of YLL was due to HIV/AIDS, disproportionately higher for women (47%) than for men (33%).

1.1.2.4 *HIV/AIDS in Khayelitsha*

1.1.2.4.1 *HIV/AIDS epidemic in Khayelitsha*

One of the most affected areas at national and provincial level is Khayelitsha in the Western Cape Province. Khayelitsha is a poor township 30 kilometers from the centre of Cape Town, South Africa, (figure 3). Khayelitsha is one of the fastest growing townships in Africa and has 500,000 inhabitants of whom 50% are unemployed and more than 70% live in informal housing (figure 4).

At the beginning of 1999, the antenatal prevalence of HIV was 15.0%, increasing to 19.3% in 2000, 24.7% in 2002 and to 27.2% in 2003 (Department of Health 2003b;Médecins Sans Frontières (MSF) & Infectious Disease Epidemiology Unit 2004). These rates reflect the national prevalence rather than those of the Western Cape as shown in Table 1.

Table 1: HIV prevalence in South Africa, Western Cape Province and Khayelitsha district [1]

Year	National	Western Cape	Khayelitsha
2000	24.5%	8.7%	19.3%
2001	24.8%	8.6	23.2%
2002	26.5%	12.4%	24.7%
2003	27.9%	13.1%	27.2%

Despite the fact that the Western Cape Province had the lowest antenatal HIV prevalence rate nationally, homicide and HIV/AIDS are amongst the top ten causes of premature deaths in Cape Town and sub-districts in 2001(Groenewald et al. 2003). In Khayelitsha, premature deaths due to homicide accounted for 22.3% followed by HIV/AIDS (17.0%) and TB (13.3%).

[1] Adapted from Médecins Sans Frontières (MSF): Khayelitsha Activity Report, Cape Town; 2003

1.1.2.4.2 *Brief description of Khayelitsha and ARV programme*

In January 1999, the Health Department of the Provincial Administration of the Western Cape (PAWC) introduced a programme for the Prevention of Mother to Child Transmission (PMTCT). This resulted in the identification of many women who were infected with HIV. In response, PAWC concluded an agreement with the international medical NGO, Médecins Sans Frontières (MSF) in April 2000, to open clinics for patients with HIV-related problems within three community health centers in Khayelitsha. Three clinics at different sites started providing comprehensive care for persons infected with HIV. The clinics provide appropriate counselling, support, prophylaxis, treatment, screening and referral for conditions related to HIV/AIDS. They aim to provide comprehensive care for HIV infected patients in the primary health care setting.

MSF started providing in Highly Active Antiretroviral Therapy (HAART) in May 2001. The aim of this pilot project was to test the effectiveness, feasibility, acceptability and cost-effectiveness of providing HAART in a primary health setting. MSF requested the technical assistance of the School of Public Health and Family Medicine at the University of Cape Town to support and evaluate this programme.

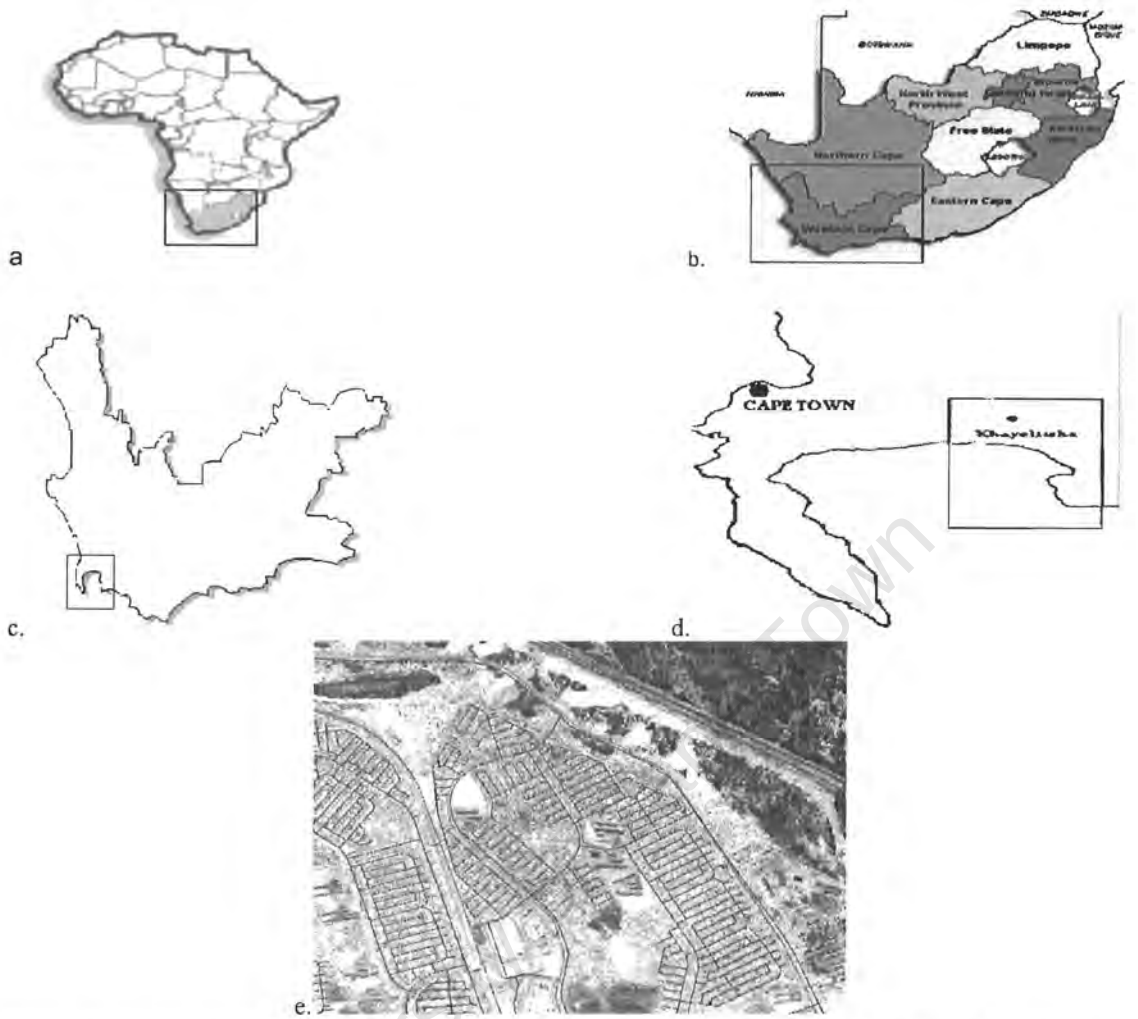


Figure 3: Diagram illustrates the location of Khayelitsha ; *a.* Map of Africa, *b.* Map of South Africa, *c.* Map of Western Cape province, *d.* Map of Khayelitsha, *e.* Aerial photo of Khayelitsha.

Figure 4: Pictures from the community of Khayelitsha.

1.1.3 Clinical epidemiology of HIV/AIDS and HIV services

1.1.3.1 *Survival, causes of death and incidence of opportunistic infections (OI's)*

Studies of clinical outcomes of routine dedicated HIV services in developing countries are few. A study by (Okongo et al. 1998) explored the causes of death in a rural population in Uganda. It included all deaths rather than a biased sample of autopsy data only. In addition, all clinic staffs were blind to the HIV serostatus of the participants. The causes of death in HIV-infected persons included wasting syndrome (31%), chronic diarrhoea (22%), cryptococcal meningitis (13%), and chest infections (non-TB) (11%). Eighty seven percent of deaths were in patients classified in WHO stage IV (AIDS).

The epidemiology of opportunistic infections varies in developed and developing countries. In a retrospective study done in London (Petruckevitch et al. 1998), the initial AIDS defining conditions in 627 patients attending HIV/AIDS units were *Pneumocystis carinii* pneumonia (25%), tuberculosis (16%), Kaposi's sarcoma (15%), oesophageal candidiasis (10%) and other conditions (12%). Most persons with AIDS in developed countries do not die from infectious diseases but rather from lymphomas (Franceschi, Dal, & La 1999). On the other hand, in developing countries AIDS defining conditions have a significant impact on the prognosis of HIV infection. In one study conducted to define the natural history and disease progression of HIV infection in Haiti, a developing country, (Deschamps et al. 2000), the AIDS defining conditions that had the highest impact on survival were tuberculosis, wasting syndrome, cryptospordiasis, cyclosporiasis, candida oesophagitis, toxoplasmosis, and cryptococcal meningitis.

HIV has different impacts on the progression and mortality and morbidity of many other diseases. For example, patients with haemophilia have shown that the incidence of end-stage liver disease and hepatocellular carcinoma are increased in HIV/hepatitis C virus co-infected individuals compared with non-infected individuals (Eyster et al. 1993;Telfer et al. 1994). Also, several histological epidemiological studies have suggested that hepatic fibrosis, the main cause of morbidity and mortality from hepatitis C virus infection(HCV), is increased two-fold in HIV/HCV co-infected individuals (Benhamou et al. 1999;Puoti et al. 2001).

Little is known about the progression and natural history of HIV in developing resource-limited countries. A number of studies have been conducted in developed and developing countries to determine the survival after seroconversion and after AIDS. In a population based cohort study (Morgan et al. 2002), comparing the differences in survival between a poor setting country like rural Uganda in Africa with industrialized countries, the results showed that the median survival from seroconversion was 9.8 years in Uganda compared to a survival time of around 10 years in industrialized countries. The study concludes that although the median survival after infection was similar, the time from an AIDS defining illness to death was shorter (9.2 months). However, survival with AIDS tends to be shorter in Africa (Grant, Djomand, & De Cock 1997).

Studies in two cohorts of HIV-1-infected adults, mostly women, in Uganda (Morgan et al. 1997) and Côte d'Ivoire(Salamon et al. 2002), showed that the chance of remaining free of symptoms 3 years after seroconversion ranged from 40% to 79%. Weak health

services and the existing health status of most African populations contribute to the rapid development of AIDS and there is no difference in the progression of HIV infection by sex (Danel et al. 2002).

1.1.3.2 *CD4 changes and HIV progression*

The progression and natural history of HIV infection are known to be more rapid in Africa and Asia than in other developed countries (Kitayaporn et al. 1996;Nunn et al. 1997). The explanations for this rapid progression includes lack of access to health care, co-infection with other pathogens and malnutrition (Camp et al. 1998;Del Amo et al. 1998;Lucas, Odida, & Wabinga 1991). CD4 count and level of HIV RNA (viral load) are known markers and predictive of clinical progression to AIDS in developing countries (Anastos et al. 1999;Vlahov et al. 1998). The progression of these markers is not consistent. In one study in India (a developing country) (Mehendale et al. 2002) , the annual increase in HIV viral load was 8274 RNA copies/ml/year and the annual decline in CD4 cell count was 120 cells/year. The study reported that the median increase in viral load in Indian seroconvertors was greater than that reported in untreated HIV seroconvertors in the United States. Hence, the study suggested, the rapid increase in viral load within the first 2 years may change considerations when applying treatment guidelines for ART and prophylaxis. The progression may change when ARV therapy is provided in resource–limited settings, with reported improvements from baseline levels of CD4 counts. In one study done in South Africa (Coetzee et al. 2004), the reported CD4 count progression after 6 months of ART, compared to pre-treatment levels, increased by a median of 134 cells/μl. After 24 months on treatment, the median increase in CD4

count compared to baseline was 288 cells/μl and the median absolute CD4 count at this duration on treatment was 323 cells/ μl. This study concluded that ART could be provided in resource–limited settings with good patient retention and clinical outcomes.

1.1.3.3 *HIV and TB*

The advent of the HIV epidemic has increased the burden of TB significantly and TB is the leading cause of mortality in HIV infected persons. Tuberculosis disease increases mortality in HIV-infected patients (Leroy et al. 1997;Whalen et al. 1995) and patients co-infected with HIV and tuberculosis have high rates of reactivation of latent tuberculosis infection (LTBI) (Moss et al. 2000;Selwyn et al. 1989). In some countries, more than 70% of the TB patients are HIV-infected (Raviglione et al. 1997) and this has had a dramatic effect on the TB epidemic in Sub-Saharan Africa and requires effective HIV prevention as a priority for TB programmes (Bleed, Dye, & Raviglione 2000).

HIV is the strongest factor capable of promoting progression of Mycobacterium tuberculosis (MTB) infection to active tuberculosis (Rieder et al. 1989) both in people with recently acquired and with latent MTB infections (Maher, Floyd, & Raviglione 2002). The lifetime risk for active TB in an HIV-negative person is 5 to 10% while the annual risk in HIV-infected persons is 5 to 15% (von Reyn 1999).

Research shows that even in areas where there is a good TB control program, when the sero-prevalence of HIV is greater than 20%, the annual percentage increase in TB will be high at over 10% (Cantwell & Binkin 1996). On the other hand, TB in HIV disease is

associated with decreased survival. TB specific mortality is four-fold higher among HIV-infected patients than amongst the uninfected (17.8 and 4.4 deaths per 100 per year for HIV-infected and uninfected patients respectively) (Connolly et al. 1999). In addition the TB epidemic in persons infected with HIV increases the infectious pool and the risk of TB transmission in the community, whether or not HIV-infected (Maher, Floyd, & Raviglione 2002).

In resource-poor countries in Sub-Saharan Africa, 32% of patients with TB are HIV-infected. The prevalence of both HIV and TB patients is above 10%. The burden of co-infection is concentrated in Sub-Saharan African countries where the two infections highly prevalent (Girardi et al. 2000b). The estimated tuberculosis incidence rate was 191/100 000 in 1990 compared to 257 in 1997 in Africa. In industrialized countries[i] the incidence rate was 23 per 100 000 in 1990 and it had dropped to 16 by 1997.

A study was conducted of the changes in biological markers of HIV infection before and after the development of TB disease in a cohort of HIV-positive Ethiopians (Wolday et al. 2003). In this longitudinal study 804 adult factory workers (95 HIV-positive, 709 HIV-negative), were followed for a median of 3.8 years at 6 months intervals. The HIV-infected participants who developed TB disease had low CD4 counts (median 201cell/μl, range 45 – 419), and high viral load (median 4.97 log copies/ml, range 3.70 – 5.58). However, there is a higher incidence of TB in all stages of HIV. In one study, 25% of patients with TB had a CD4 cell count above 500 cell/μl at time of diagnosis. The same

[i] Include Western European countries, Japan, Australia, New Zealand, the United States and Canada.

study shows that the incidence of TB among HIV-infected participants was higher than HIV-negative participants (45.1 versus 6.8 per 1000 persons years).

1.1.3.4 *TB and Antiretroviral Therapy (ART)*

In the era of ART the clinical features of AIDS defining conditions may change in addition to the incidence of opportunistic infections and mortality. ART and to a far less extent other prophylactic drugs will change the natural history and progression of HIV.

In developing countries, TB occurs more frequently than in industrialized countries and it accounts for more than one third of mortality among HIV-infected patients in Sub-Saharan Africa (De Cock et al. 1992;Greenberg et al. 1995). Lack of resources in Africa has limited access to ART, but studies on effectiveness of such treatment shows significant impact of ART on TB. In a cohort study (Badri, Wilson, & Wood 2002), conducted in Cape Town (South Africa), the investigators compared the risk of tuberculosis in two cohorts, one receiving HAART and the other not. The HAART cohort accrued from 12 clinical trials carried out between 1995 and 2001 in Cape Town. The non-HAART cohort consisted of patients who attended clinics between 1992 and 2000 in Cape Town. The baseline clinical characteristics did not include viral load, as this was not always available. Other predictors including CD4, WHO clinical stage, and socioeconomic status where included in the analysis. The results of the study showed a significant association between HAART and lower incidence of tuberculosis (2.4 per 100 patient-years in HAART cohort versus. 9.7 per 100 patient-years in non-HAART). The results also showed that the greatest number of TB cases averted by HAART was in patients with WHO clinical stage 3 or 4 and those with a CD4 count of less than 200

cell/μl. The study showed an 81% (95% CI 62-91) reduction in the risk of TB associated with use of HAART. This is similar to studies in the US (Jones et al. 2000) and Italy (Girardi et al. 2000a).

1.1.3.5 *HIV and Antiretroviral Therapy (ART)*

The benefits of ART in reducing mortality have also been shown in resource-poor settings. A study in Khayelitsha (Coetzee, Hildebrand, Boulle, & et al 2004), showed that cumulative survival on antiretroviral treatment was 86.3% at 24 months, similar to other studies in African settings (Laurent et al. 2002;Weidle et al. 2002). Survival without ART reported in another study in Cape Town for those with CD4 count less than 50 cells/μl was less than 12 months (Post, Wood, & Maartens 1996). The survival outcomes were similar to that reported in Canada and USA(Chan et al. 2002) for patients with very low CD4 cell counts at the time of initiation of ART.

1.2 Motivation of the study

There are few studies that deal with outcomes of populations seeking routine HIV care in the era of ART in Africa.

1.3 Aim of the study

The aim of the study was to describe the profile and clinical outcomes of HIV-infected patients who enroll at an HIV service in a resource-limited setting in Khayelitsha, Cape Town.

1.2.1 Specific objectives

1. To describe the profile of patients enrolled at the HIV service including:
    - Demographic variables
    - Stage of disease
    - Source of referral
2. To determine the clinical outcomes of HIV-infected patients who are not on ART therapy in order to determine
    - The proportion of patients who are placed on ART,
    - The proportion of patients who died.
    - The proportion of patients lost to follow up.
3. To determine the incidence of tuberculosis infections amongst HIV-infected patients who are not on ART.
4. To examine risk factors, such as demographic variables, CD4 cell count, HIV stage or a previous history of TB, associated with the incidence of TB among HIV-infected patients who are not on ART.
5. To briefly describe outcomes for those receiving ART.

CHAPTER 2

2.1 SUBJECTS AND METHODS

2.1.1 Definition of terms

HIV: Refers to HIV-1 unless otherwise indicated.

History of TB: Any episode of TB before enrollment at the service.

HIV clinical stage: Refers to the HIV clinical staging proposed by World Health Organization (World Health Organization 1990)

2.1.2 Study design

The study design used was a follow up of a cohort of HIV-infected patients using prospectively collected data that was validated.

2.1.3 Study population and sampling

2.1.3.1 *Study population*

The study population was all HIV-infected patients who enrolled at Site B HIV service in Khayelitsha during 2002.

2.1.3.2 *Study setting*

The subjects were patients from Khayelitsha Site B HIV service. Site B-HIV clinic is one of three clinics providing free counselling, treatment and follow up of HIV-infected persons. This study was part of a larger project currently ongoing in Khayelitsha.

2.1.3.3 *Sampling*

All adult patients attending the service at Site B for the first time from the 1st January 2002 until the 31st December 2002 were included in the study.

2.1.3.4 *Sample size*

As there are many outcomes, for the purposes of sample size, the following three calculations were performed with a significance level of 0.95 and a power of 0.90.

- Comparing loss to follow-up between men and women, assuming 30%

  and 15% loss to follow-up respectively, the calculated sample size required was 396 (132 men and 234 women)

- Comparing the proportion of patients with a new tuberculosis diagnosis

  in the first year of follow-up in patients enrolling in clinical stage II with patients enrolling in clinical stage IV and assuming equal numbers in each stage the calculated sample size was 348.

- Determining the proportion of patients enrolling in care in stage IV. Using a precision of 0.1 – the calculated sample size is 233

The total number of adults enrolled in care during 2002 at the Site B clinic was 534, suggesting that the above sample sizes were achieved with the proposed sampling strategy.

2.1.4 Data collection

All information was extracted from the electronic database. In order to verify and validate data, clinical records were used. The following information were collected; age and gender, attendance at clinic, adherence to treatment, weight and height, diagnoses of

infections and AIDS defining illnesses, prophylaxis and treatments, and CD4 cell counts and HIV RNA levels, sputum smears and culture results for TB and information from chest radiographs.

(Appendix A includes Data Record Sheet with the information require to be validated)

2.1.5 Pilot study

This study was piloted in order to ensure that the data were correctly defined and captured. About 30 records from database were verified with the clinical records at Site B clinic. Difficulties in extracting and entering data were identified and corrected.

2.1.6 Data management and statistical analysis

The data were checked for errors and corrected before and after entry into the database. Clinical data had already been entered once into a database, and this process was validated.

After cleaning the data, graphical explorations and listings were done to check for errors and to elicit patterns and relationships. For purposes of this study and its specific objectives, the analysis was divided into two sections, descriptive and analytical. In the descriptive section, the main statistical methods used were proportions and percentages, cross tabulations and graphical displays. In addition, the t-test for two samples on the equality of means was used.

For the analytical section, a range of classical and modeling approaches were used in determining outcomes including: Survival analysis and proportional hazards regression for the mortality and loss to follow-up outcomes as well as the time to the first event for TB and certain opportunistic infections. Patients were categorized into strata according to CD4 cell count of <50, > or = 50 and <200, and > or =200). A *p value* of less than 0.05 was used in all analyses as a measure of statistical significance. Loss to follow-up was right-censored in this analysis.

Analyses was performed using STATA™ 8.0 Statistics/Data Analysis software package (Copyright 1984-2003, Stat Corporation, 4905 Lakeway Drive, College Station, Texas 77845 USA).

2.1.7 Ethical and legal considerations

This study was part of larger MSF/UCT research project currently being conducted in Khayelitsha to evaluate the HIV and ART services. Approval and consent from patients has been obtained for the project.

Ethics approval for this project was obtained from the Research Ethics Committee of the Health Sciences Faculty at the University of Cape Town.

All data was extracted from the database used to monitor the programme in Khayelitsha. The names of patients were not included. Clinical records were accessed to validate data. The confidentiality of these records was maintained at all times.

2.1.8 Reporting of results

All results will be reported to all major stakeholders, the local government and provincial services, MSF and the School of Public Health at UCT.

CHAPTER 3

3.1 RESULTS

3.1.1 Section 1: Descriptive analysis of the study

This section includes a description of the baseline characteristics of the cohort at the time of enrolment in 2002. In addition, sources of referral and the main outcomes are also presented.

3.1.1.1 *Demographic and baseline clinical characteristics of the cohort*

The main baseline characteristics are presented in table 2.

Table 2: Baseline demographic and clinical characteristics of a cohort of HIV-infected persons attending an HIV clinic in Khayelitsha, 2002

	(n=534)		
Characteristic	N (%)	Median (IQR)	*P-value*
Age(years)			
All	534 (100)	31.25 (27.1 – 36.8)	
Females	392 (73.4)	29.9 (26.3 – 35.5)	
Males	142 (26.6)	34.8 (29.8 – 41)	≤0.001[i]
Baseline Weight (kg)			
All	508 (95.1)	60 (52.5 – 71.6)	
Females	374 (70.0)	60 (52.4 – 70.9)	
Males	134 (25.1)	58.8 (52.7 – 66.7)	0.114[ii]
Baseline CD4+ T-lymphocyte (cells/μl)			
Total CD4+	474 (88.8)	221.5 (76 – 394)	
CD4+ < 200	222 (41.6)	70.5 (25 – 126)	
CD4+ ≥ 200	252 (47.2)	376 (287 – 529)	
CD4 count by Sex			
Females	352 (89.8)	240.5 (80 – 432.5)	
Males	122 (85.9)	154 (55 – 289)	0.015[iii]
Prior TB			
Yes	165 (30.9)		
No	369 (69.1)		
AIDS- defining illness (Stage IV)	82 (15.4)		

[i] Chi-squared Non-parametric K-sample test on the equality of medians(Chi-squared statistic is calculated with, and without a continuity correction).

[ii] Two-sample t test with equal variances.

[iii] Non parametric test on the equality of medians.

The size of the study cohort who registered in 2002 was 534 subjects. Women comprised 392 (73.4%) of the total cohort. The median age for women was 29.9 years and for men 34.8 years ($p \leq 0.001$) with the inter-quartile range (IQR) being 26.3 to 35.5 for women and 29.8 to 41 for men.

The median and IQR for baseline weight for all subjects in the cohort (*first recorded weight irrespective of being at first visit or later on*) was 60kg with IQR (52.5 – 71.6). The total number of subjects with their baseline weight recorded was 508 (95.1%) and this did not differ significantly between women and men (p=0.114).

First CD4 count (*first CD4 count irrespective of the first visit date*) was available for 474 patients or 88.8% of the cohort with a median of 222 cells/μl and IQR (76 – 394 cells/μl). The availability of the first CD4 count was slightly higher for women than for men, 352 (89.8%) and 122 (85.9%) respectively. First CD4 count was significantly different for women and men (p=0.015) and the median CD4 count for women and men was 240.5 cells/μl (IQR, 80 – 432.5 cells/μl) and 154.0 cells/μl (IQR, 55 – 289 cells/μl) respectively.

Forty-two percent of the cohort had baseline CD4 counts below 200 cells/μl with a median of 70.5 and IQR of 25–126 cells/μl for the same category. The first CD4 count was ≥200 cells/μl for 252 patients (47.2% of the total cohort) with a median of 376 and IQR of 287 – 529 cells/μl.

One hundred and sixty five patients (30.9%) had a history of prior tuberculosis (TB) at the time of enrollment and 81 (15.4%) presented with an AIDS-defining conditions (*HIV-stage IV*).

3.1.1.2 *Sources of referral*

Table 3 and figures 5 and 6 present the different sources of referral for the cohort with the median and IQR of the CD4 count at first visit for each source. Self-referral comprised 20.2% of the total sources of referrals followed by mother-to-child transmission prevention programmes (MTCT) and Khayelitsha clinics (18.7%) each. Non-Governmental Organizations and home-based care comprised only 1.3% of the total sources of referral. The median CD4 count presented at first visit was highest for the MTCT group and the self-referral group, 394 cells/μl (IQR, 239–566) and 243.5 cells/μl (IQR, 110–451) respectively. The individuals referred from hospitals and NGO's presented with the lowest CD4 counts at the first visit, the median and IQR was 73 (16 – 236) and 47 (25 – 105) cells/μl respectively with a total of 32 subjects (6%) from hospitals and 7 (1.3%) from NGO's. TB clinics in Khayelitsha referred 67 (12.5%) of the HIV-infected cohort and the median CD4 count was 110 cells/μl (IQR, 54.5 – 259). Of the 48 recorded baseline CD4 counts for those referred from TB clinics, 32 (66.7%) were less than 200 cells/μl.

Table 3: Sources of referral and the median CD4+ count at the first visit for persons attended HIV clinic in Khayelitsha, 2002

Sources of referral	*(n=534)*	
	Number of persons	CD4+
	n (%)	n Median (IQR)
MTCT (*Mother To Child Transmission programs*)	100 (18.7)	79 394 (239-566)
Self referral	108 (20.2)	78 243.5 (110-451)
Unknown	68 (12.7)	30 230.5 (79-347)
Khayelitsha clinics	100 (18.7)	74 224 (83-387)
Private clinicians	32 (6)	24 136 (52.5-274)
Non-Khayelitsha clinics	20 (3.7)	18 115 (37-301)
TB clinics	67 (12.5)	48 110 (54.5-259)
Hospitals (*Tertiary & Secondary Hospitals)*	32 (6)	31 73 (16-236)
NGO's (*Non Governmental Organizations and Home-based care*)	7 (1.3)	6 47 (25-105)
Total N (%)	534 (100)	n 388

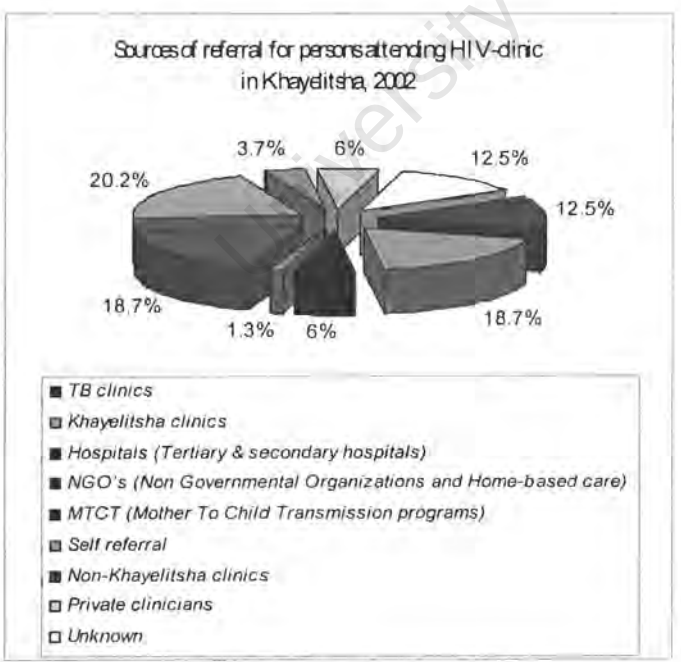


Figure 5: Sources of referral for persons attending HIV-clinic in Khayelitsha, 2002.

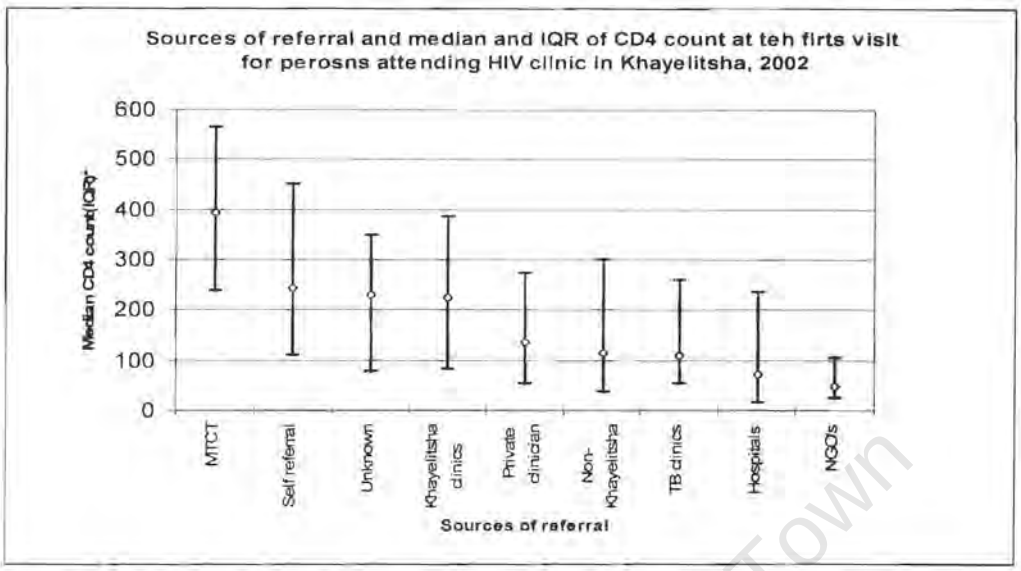


Figure 6: Sources of referral with median and IQR of the first CD4 count for persons attending HIV clinic, Khayelitsha, 2002.

3.1.1.3 *Outcomes of the cohort*

The main outcomes of the cohort analyzed are summarized in table 4. Two hundred and sixty eight (50.2%) of the cohort were lost to follow-up (LTF) whereas the number still in care on ARVs was 114 (21.3%) and the number still in care without ARV was 108 (20.2%). The other outcomes included transferred out, died of HIV, died of non-HIV causes and died of unknown reasons.

Table 4: Outcomes for HIV-infected persons attending an HIV-clinic at Khayelitsha, 2002

	(n=534)
Outcome	N (%)
Loss To Follow up(LTF)	268 (50.2)
Transferred out (*no more follow up at Khayelitsha clinic*)	2 (0.37)
Died HIV (*The cause of death recorded as HIV*)	39 (7.3)
Died (Non-HIV)	1 (0.19)
Died (Unknown)	2 (0.37)
Still in care on ARV treatment	114 (21.3)
Still in care not on ARV treatment	108 (20.2)
Total	534 (100)

There was a progression in the clinical stage during follow-up (table 5) with a higher proportion of patients being in stage IV and a lower proportion in stage I the last time recorded compared to the first. Table 6 presents the CD4 count stratified by stage at first visits. The median CD4 count for those in stage I was 380 cells/μl with IQR (263 – 504) and for HIV stage IV, 50 and IQR (19 – 128) cells/μl. The median CD4 dropped as patients progressed through from stage I to stage IV as shown in table 6.

Table 5: HIV clinical stage at first and last visits of the persons attended HIV-clinic, Khayelitsha, 2002

		(n=534)
Stage	At first visit N (%)	At last visit N (%)
I	90 (16.9)	53 (9.9)
II	128 (24)	101 (19)
III	182 (34.1)	177 (33.1)
IV	82 (15.4)	141 (26.4)
Total	482 (90.4)	472 (88.3)

Table 6: Summary statistics of CD4 count by stage at first visit of the HIV- infected cohort attending an HIV-clinic at Khayelitsha, 2002.

	Summary of CD4 count by stage at first visit	
stage at first visit	N (%)	Median (IQR)
I	84 (15.7%)	380 (263-504)
II	122 (22.8%)	322 (195-478)
III	164 (30.7%)	157 (84-290)
IV	70 (13.1%)	50 (19-128)
Total	440 (82.4%)*	

* Thirty four subjects did not included because they don't have specific stage

3.1.1.4 *Descriptions of lost to follow up (LTF) group*

Fifty percent of the cohort were lost to follow-up. This group is described to show some of its characteristics and compared to those not lost to follow-up.

The source of referral for both LTF and others group is presented in Table 7. Self-referral is the highest source of referral for the LTF group while Khayelitsha clinics are the highest for others. Source of referral is the same for MTCT programme for both groups and the same when comparing for NGO's.

Table 7: Sources of referral of LTF group and others

Source of referral	LTF n(%)	Others n(%)
Self referral	61 (23.37)	47 (18.01)
MTCT (Mother To Child Transmission programme)	50 (19.16)	50 (19.16)
Khayelitsha clinics	43 (16.48)	57 (21.83)
Unknown	34 (13.03)	17 (6.51)
TB clinics	23 (8.81)	44 (16.86)
Private clinicians	21 (8.05)	11 (4.21)
Hospitals (Tertiary & Secondary Hospitals)	17 (6.51)	20 (7.67)
Non-Khayelitsha clinics	10 (3.83)	10 (3.83)
NGO's (Non Governmental Organizations and Home-based care)	2 (0.76)	5 (1.92)

The median CD4 cell count at first visit (*irrespective of visit date*), was 261 cells/μl (IQR, 93–444.5) in those LTF compared to 185.5 cells/μl (IQR, 73 – 347) in those not LTF (Table 8).

Comparing the number of persons in the different CD4 count categories (Table 9) at first visit, 18% of subjects in both groups had a CD4 count under 50 cells/μl. For those placed on ART, the last recorded CD4 count was less than 50 cells/μl in 20% of those LTF as compared to 11.2% for those not lost to follow up. The distribution of the first and last CD4 count for both groups is presented in Figures 7 and 8. The distribution of the last CD4 cell count shows that there are more subjects in the categories <50 and > 200 cells/μl for those LTF.

The median duration from first visit until loss to follow up was 2.1 months with the IQR (0.4 – 7.1). The number of females and males was not different (p= 0.262). There was a

significant difference when comparing the HIV staging at last visit for both groups, LTF and not LTF ($p<0.001$), (Table 8).

Table 8: Description of the main characteristics of the lost to follow up (LTF) group compared to those not LTF.

Characteristic	LTF group		Other		
	(n) mean	Median (IQR)	(n) mean	Median (IQR)	p-value*
First CD4 count	(216) 306.2	261.5 (93 - 444.5)	(258) 253.4	183.5 (73-347)	0.039
Last CD4 count	(216) 303.1	259.5 (86-433.5)	(258) 286.9	262 (130-378)	0.504
Duration before LTF in months†	(268) 4.8	2.1 (0.4 7.1)	-	-	
Sex	N (%)		(n%)		
Females	191 (71.3)		201 (71.3)		
Males	77 (28.7)		65 (24.4)		0.262
HIV stage at first visit					
I	49 (22.5)		40 (15.6)		
II	57 (26.2)		69 (26.9)		
III	66 (30.3)		112 (43.8)		
IV	46 (21.1)		35 (13.7)		0.547
HIV stage at last visit					
I	41 (19.2)		12 (4.7)		
II	53 (24.8)		48 (18.6)		
III	64 (30)		113 (43.8)		
IV	56 (26.8)		85 (32.9)		0.000

* Two-sample t test with equal variances(LTF group and others group).
† Duration not displayed for others group because they are still on care.

Table 9: Percentage of lost to follow up (LTF) and other groups in each CD4* count category at first and last CD4 test.

Categories of first CD4 count						p-value†
Group	<50	<200	<500	<1000	>1000	
LTF group(n=215)	18.6%	22.8%	40.0%	16.3%	2.3%	
Other groups(n=257)	17.9%	33.9%	36.58%	10.1%	1.5%	0.039
Categories of last CD4 count						
Group	<50	<200	<500	<1000	>1000	
LTF group(n=215)	19.5%	21.7%	41.4%	14.9%	2.33%	
Other groups(n=258)	11.2%	28.7%	46.1%	12.0%	1.9%	0.504

* CD4 count (cells/μl)
† Two-sample *t* test with equal variances (CD4 in LTF group equal CD4 in others group)

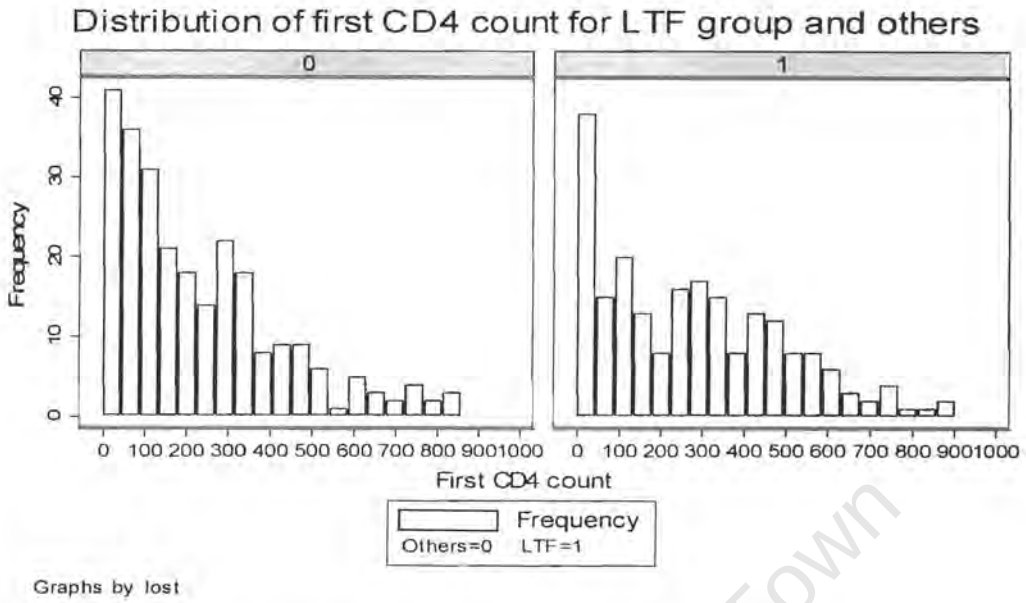


Figure 7: Distribution of first CD4 count for LTF group and others in the cohort

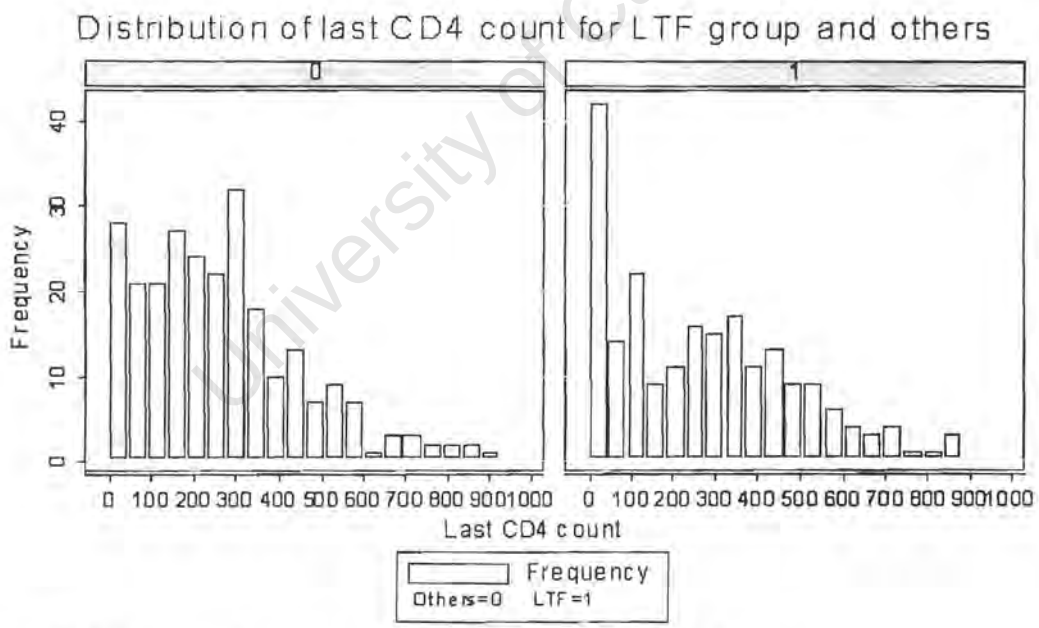


Figure 8: Distribution of last CD4 count for LTF group and others in the cohort.

The median number of visits was 3 (IQR 2-5) for those lost to follow-up compared to a median of 12.5 visits (IQR 8–19) for those not lost to follow-up, (Table 10, Figure 9).

Table 10: Number of visits before loss to follow-up for LTF group and others group. (n=534)

Group	N (%)	Median (IQR)	p-value*
LTF	268 (50.2)	3 (2-5)	
Others	266 (49.8)	12.5 (8-19)	0.000

* Two-sample t test with equal variances

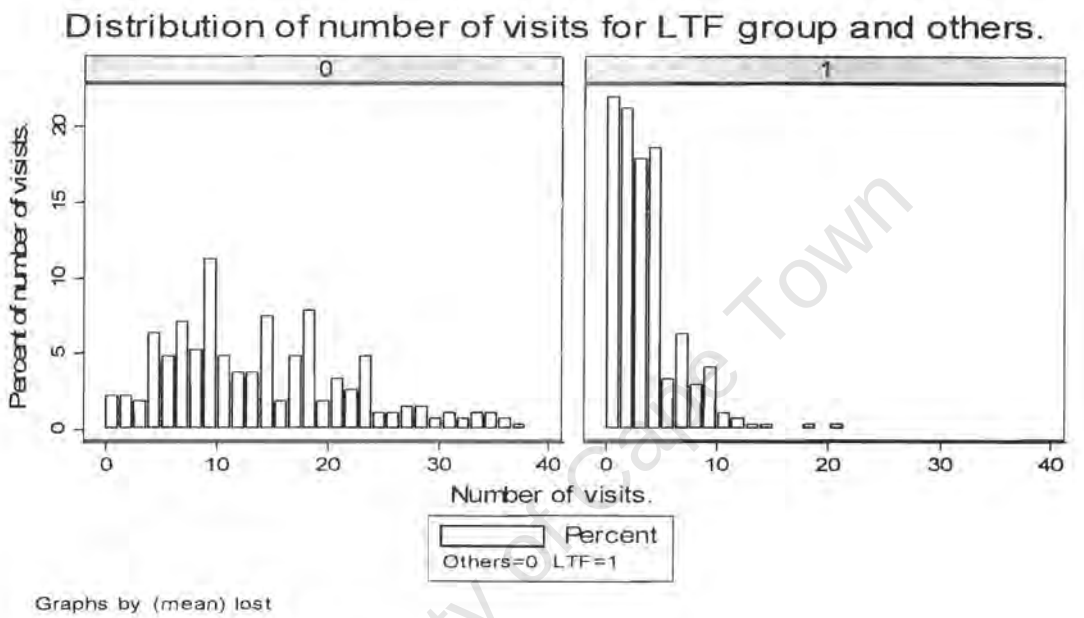


Figure 9: Distribution of number of visits for LTF group and others.

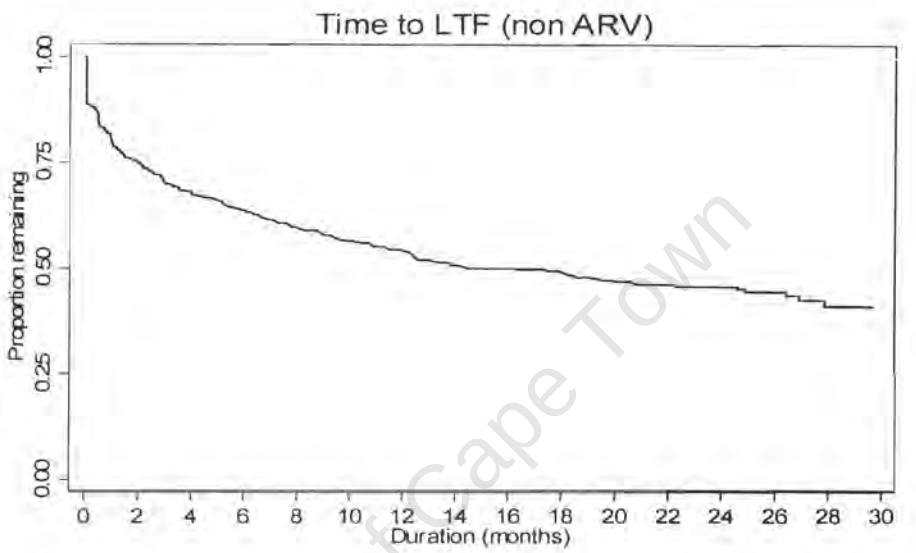
3.1.2 Section II: Survival analysis for the cohort excluding person-time on ARV therapy

In this section, time to LTF, time to death from HIV and time to start ART for all patients (excluding person time when on ART), are analyzed.

3.1.2.1 *Time to LTF in the cohort (non-ARV)*

About 50% of the cohort was LTF at the time of the analysis of this data. The time to LTF for persons not on ARV was analyzed and yielded a median product-limit estimate

of remaining in care of 16.2 months and 74% (95% CI 70 – 77%) of the cohort remained in care for at least 2 months before LTF (Figure 10).



Persons remaining	391	311	237	190	153	106	54	10
LTF	133	19	13	13	4	2	2	0
Percentage remaining	74.8	69.7	56.5	50.9	48.9	46.2	44.5	41
95% confidence interval	70 - 78.3	58.4 - 67.6	52 - 60.7	46.3 - 55.3	44.2 - 53.3	41.5 - 50.1	39.6 - 49.3	35.0 - 46.9

Figure 10: Time to LTF for non-ARV persons in the cohort.

When comparing for different CD4 count categories the product limit estimate of time to LTF showed that those with CD4 counts <50 cells/μl were at higher risk of LTF, although this wasn't significant (p=0.234)[i] and there was not a significant trend in the survivor functions for these categories (p=0.37)[ii], (Figure 11).

[i] Log-rank test for equality of survivor functions.
[ii] Test for trend of survivor functions.

When comparing the time to LTF by source of referral (TB clinics versus other sources of referral), there was a significant difference (p=0.036)[1] . Persons referred from TB clinics were more likely to remain in care than those referred from other sources, (Figure 12).

There was an significant association between male sex, age and previous history of TB and LTF. Table 11 presents hazard ratios and p-values for these variables included in the final Cox regression model.

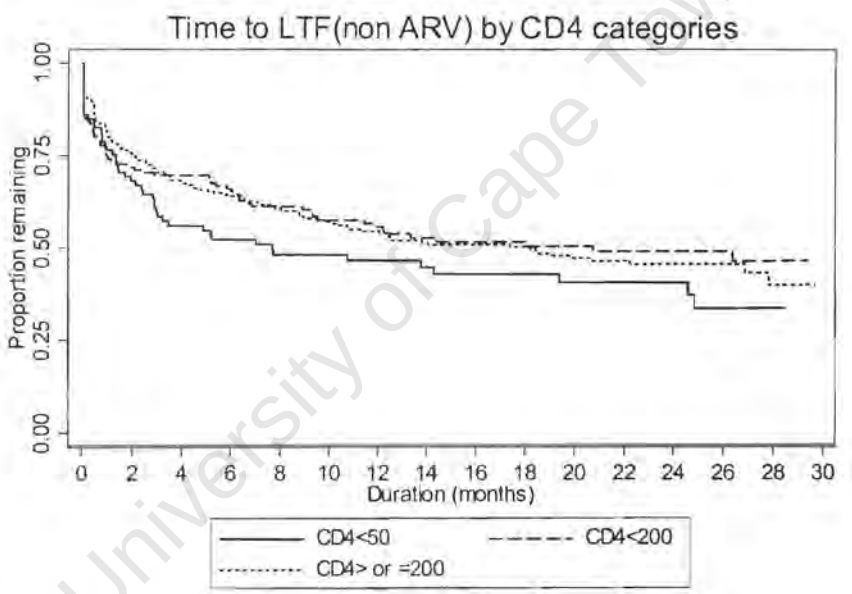


Figure 11: Time to LTF in (non ARV group) by baseline CD4 count categories.

[1] Log-rank test for equality of survivor functions.

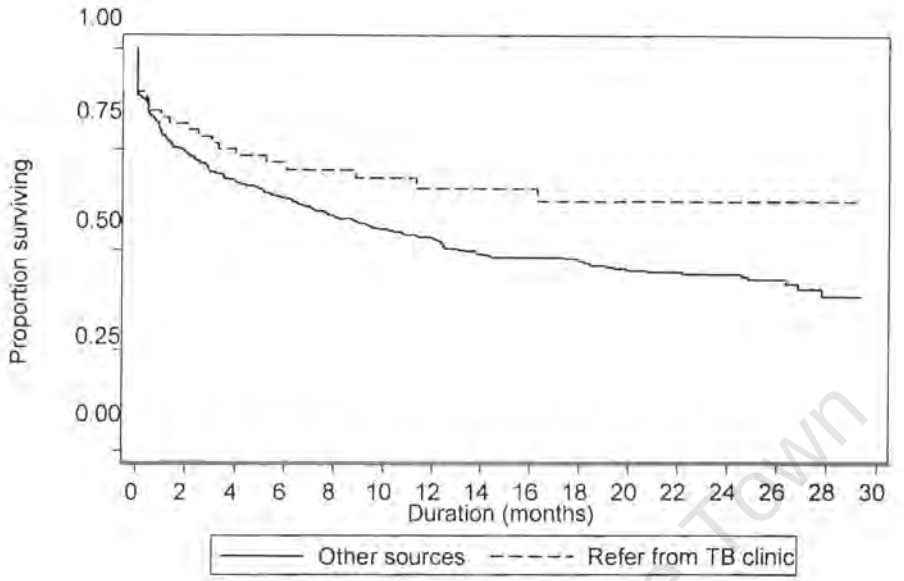


Figure 12: Time to LTF in (non-ARV group) by source of referral.

Table 11: Baseline characteristics associated with LTF in non-ARV group in the cohort

Characteristic*	Hazard Ratio (HR)	p-value	95% CI
Age in years	0.97	0.000	0.96 - 0.98
Male sex	1.37	0.008	1.1 - 1.8
Previous history of TB	0.64	0.031	0.48 - 0.85

* All baseline characteristics included in Cox regression model are categorical variables except for age (continuous).

Increase in age by one year reduces the risk of LTF by almost 3% ($p<0.001$) and being male increases the risk of LTF by 37% ($p=0.008$). TB disease before enrolment in HIV care reduced the hazards ratio ($p=0.031$).

3.1.2.2 *Time to Death of HIV in the cohort (non-ARV person time)*

The survival estimate at one year was about 90% and after 18 months. There was no significant difference in the survival estimates when comparing first CD4 counts ($p=0.87$,

test for trend p=0.89)[i], (Figure 14). The survival estimates were similar for all patients with stratified by first CD cell count after 2 months (98%, 99%, and 97%) and after 2 years (89%, 83%, and 88%) duration (Figure 5).

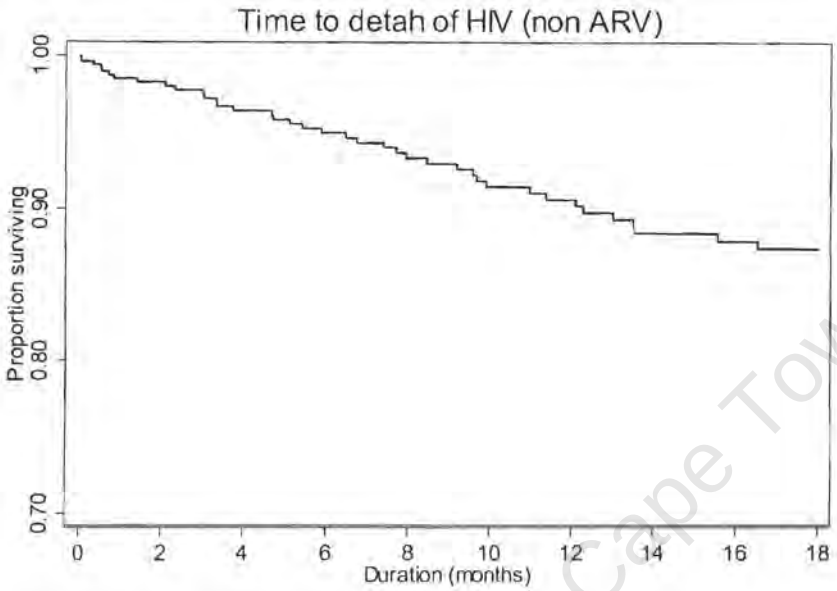


Figure 13: Time to death from HIV in the cohort (non ARV).

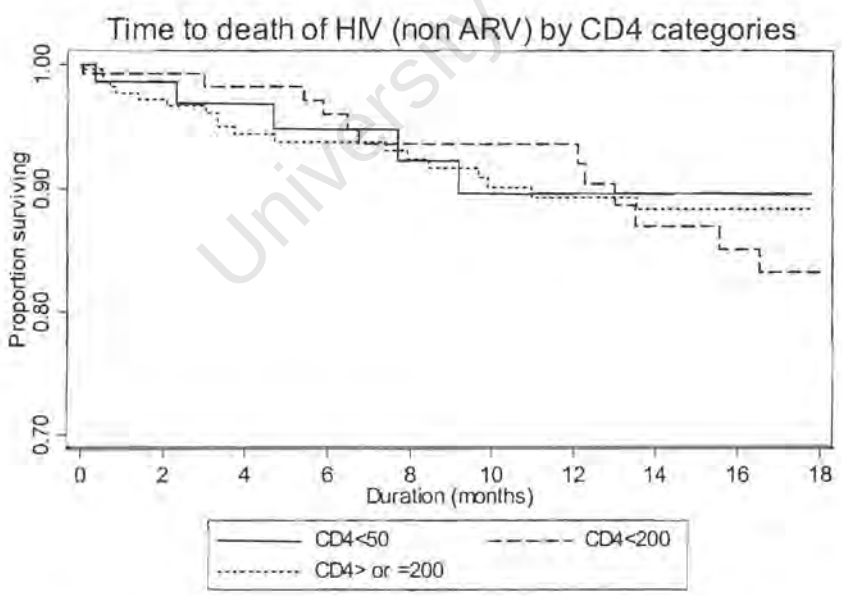


Figure 14: Survival estimates in the non-ARV by different CD4 levels.

[i] Log-rank test for equality of survivor functions

When analyzing the association between baseline characteristics and outcome "Time to death", only a previous history of TB was significant (p=0.028).

3.1.2.3 *Time to start ART in the cohort*

The duration of time before starting ART was analyzed (Figure 15). Approximately 80% (95% CI, 75.8 – 84.8%) of the cohort remained without ART at one year and 60% (95% CI 52 – 65.7%) by the second year.

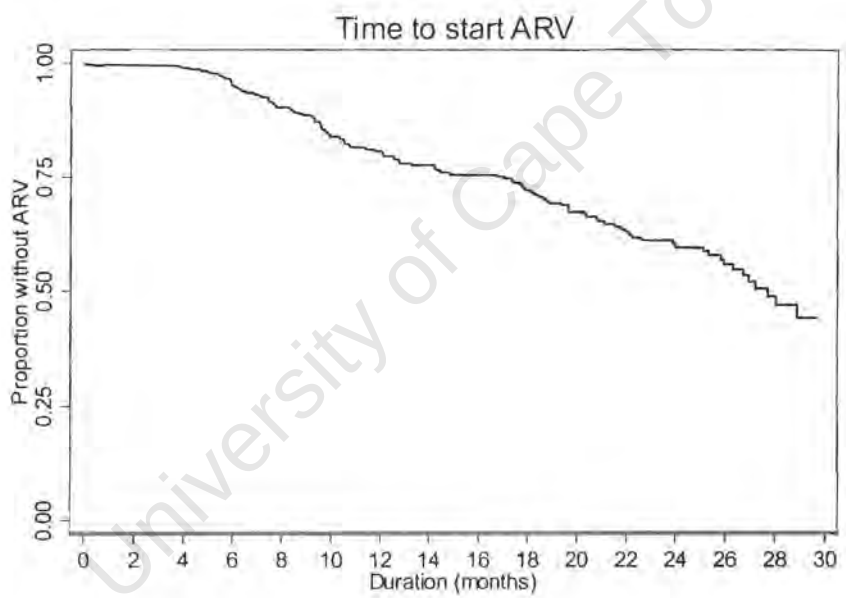


Figure 15: Time to start ARV in the cohort.

The time from enrolment to starting ART was a minimum of 4 months. Three-quarters of those with an initial CD4 count < 50 cells/µl and who remained in care, had started ART by one year, and all of them had started ART by two years. Three-quarters of those who initially enrolled in care with a CD4 count between 50 and 200 cells/µl had started ART within 2 years (figure 16).

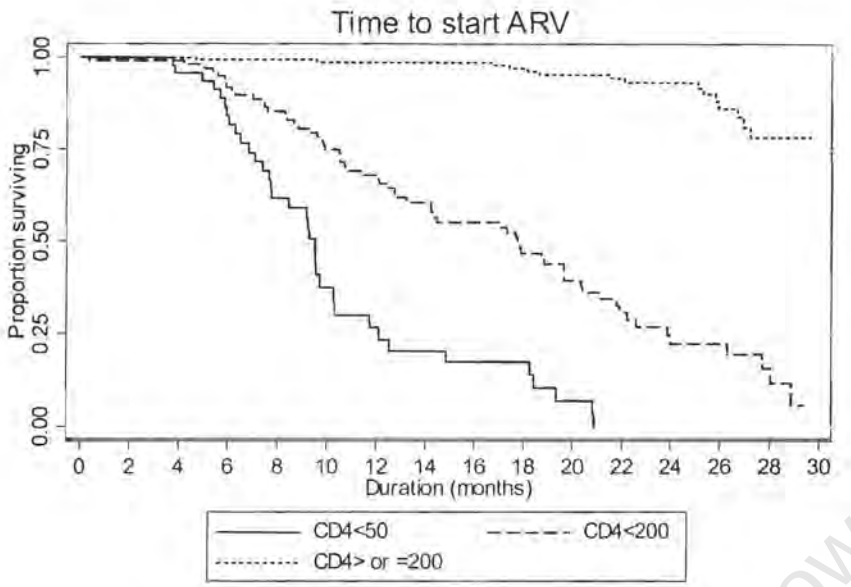


Figure 16: Time to start ARV in the cohort by CD4 categories.

3.1.2.4 *Time to LTF or death from HIV in the cohort (non-ARV patient-time)*

The outcomes LTF and death due to HIV were combined and analyzed using the survival curves. The median time to LTF or death in the cohort was 11.4 months (Figure 17).

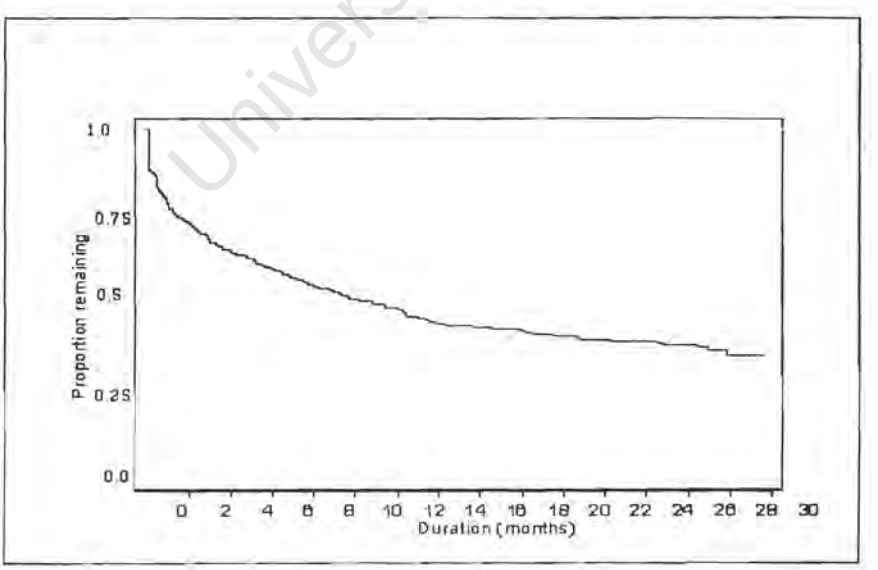


Figure 17: Time to LTF or death of HIV in the cohort (non-ARV).

Each one-year increase in age protected against the outcome by 3% (p<0.001) and males were at 48% greater risk of LTF or death from HIV than females (p=0.003).

3.1.3 Section III: Time to TB in the cohort

The time to TB was analyzed in the cohort, which revealed that 87.8% remain without contracting TB in the first year and 78% in the second year (Figure 18). When restricting the analysis to those not receiving ART with a first CD4 count <200 cells/μl, 18% contracted TB cumulatively by the first year and 46% by the second year (Figure 19).

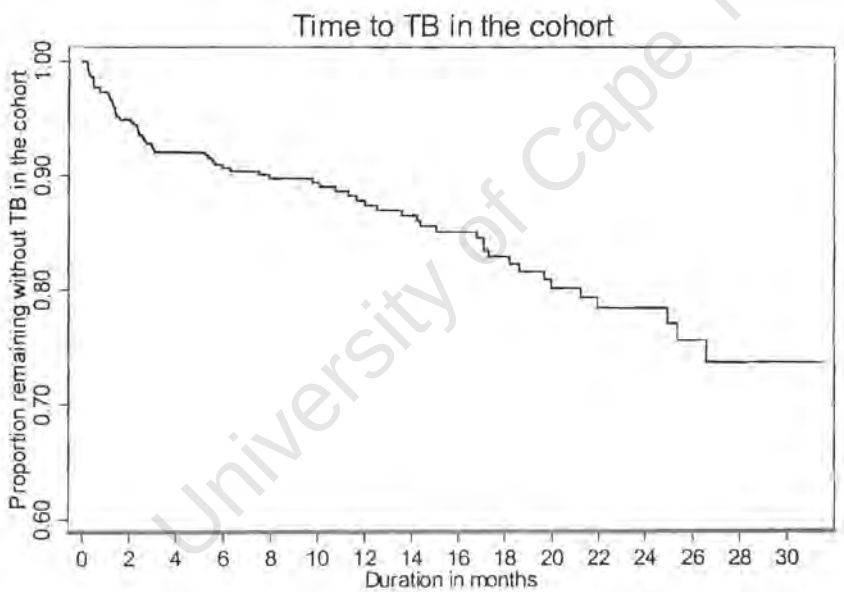


Figure 18: Time to TB in cohort.

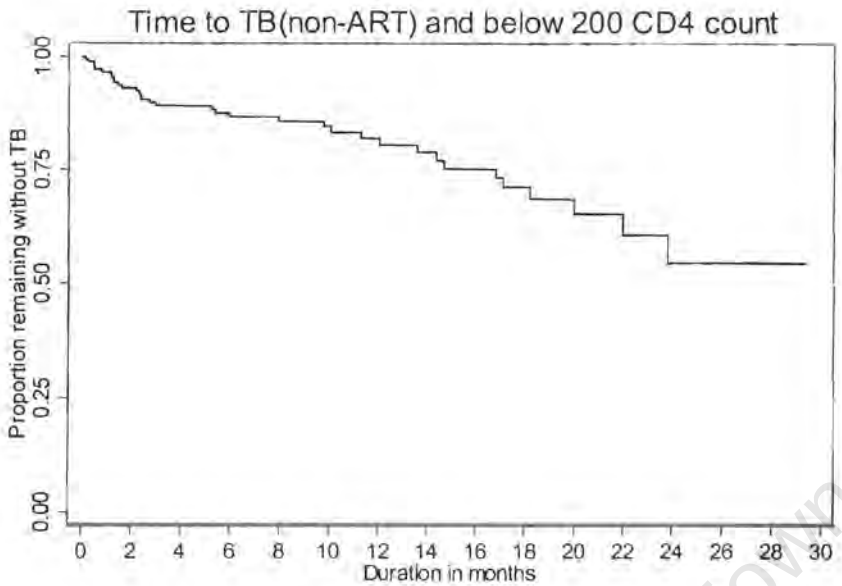


Figure 19: Time to TB in the cohort restricted to (non-ART) and below 200 CD4 count.

3.1.4 Section IV: Analysis of ARV group

One hundred and fourteen (21.3%) of the total cohort started ARV therapy. Time to LTF and death due to HIV was analysed to describe the effectiveness of ART within this cohort. The analysis describes the duration to outcomes such as HIV related death, and certain laboratory outcomes such as CD4 count and viral load.

The survival estimate of remaining in care (excluding deaths) after starting ART was 97% (95% CI, 83–95%) at 12 months (Figure 20). The product-limit estimate of survival (free of death due to HIV) was 87 % (95% CI, 54–71%) at 12 months (Figure 21).

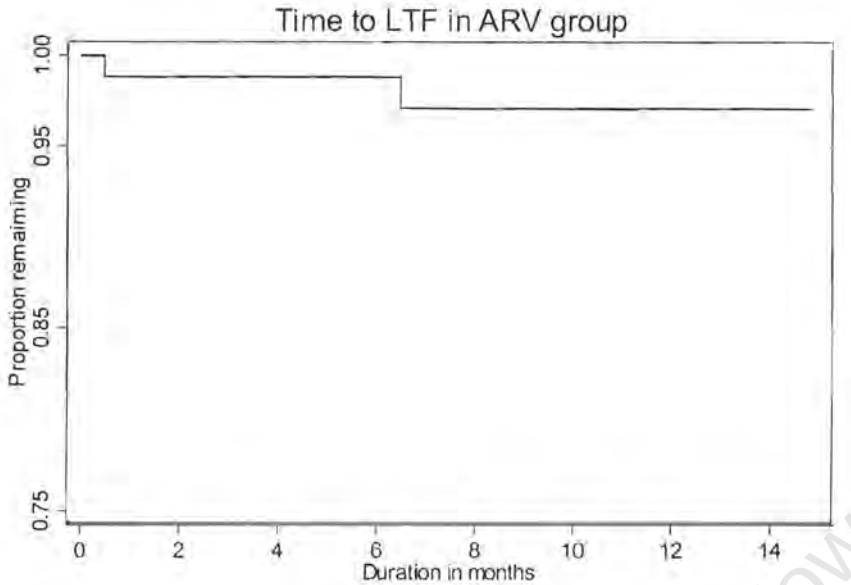


Figure 20: Time to LTF in ARV group.

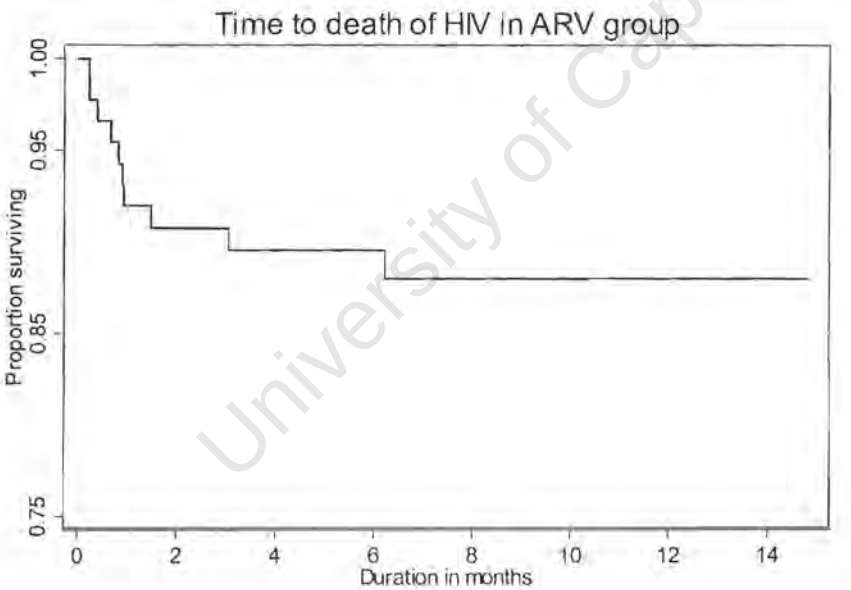
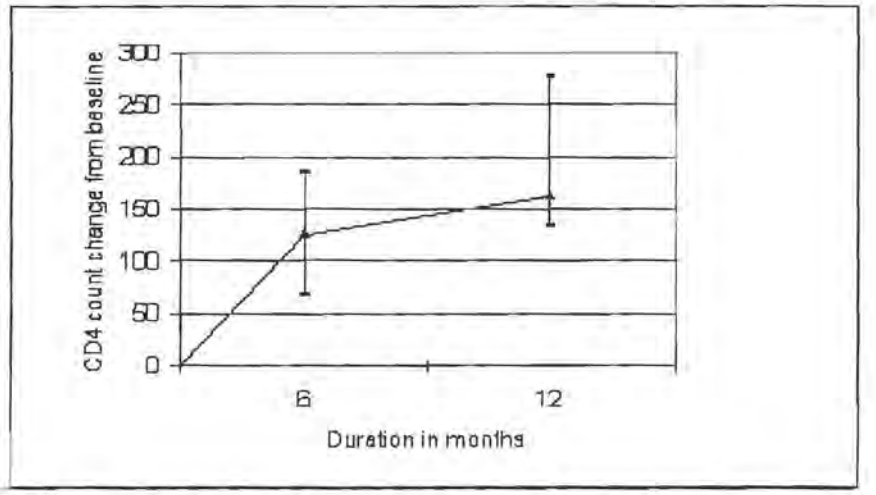


Figure 21: Time to death of HIV among (ARV group).

The changes in CD4 count and viral load from the baseline compared with at 6 and 12 months after starting ART are presented in Figure 22.



Number with CD4 count	47	27
Median change from baseline	127	163
Interquartile range (IQR)	68 - 184	132 - 277
Number with Viral load results	45	26
Percentage <400 copies/ml	87.1	92.9

Figure 22: Laboratory outcomes by duration of treatment (the first year only)

CHAPTER 4

4.1 DISCUSSION

Five hundred and thirty four patients enrolled at the HIV service at site B in 2002 or 45 patients each month. Women comprise a higher proportion than men. Women also tend to be younger in keeping with the epidemiology of HIV in South Africa (Simbayi, Shisana, & Human Sciences 2002) . Approximately forty percent of the cohort presented with CD4 counts less than 200 cells/μl. Those with advanced disease were more likely to be referred from other clinical services such as TB and hospitals. Women present with higher CD4 counts, which could in part be due to the larger number of women undergoing voluntary counselling and testing (VCT) as part of MTCT when they are not otherwise ill. The fact that those referred from MTCT have higher CD4 counts confirms this.

The correlation between the CD4 count and HIV clinical stage, (Table 6), was comparable to a study done in South Africa (Post & Maartens 2001) before ART was available.

The WHO identifies MTCT and TB as major entry-points for ARV therapy. With TB patients comprising 30.9% of the cohort at the time of enrolment, and as they generally present with lower CD4 counts, it is clear that this is an important potential ART recruitment strategy.

The lower risk of loss to follow-up for TB patients may relate to better knowledge of HIV as a result of attendance at a health facility for 6 to 8 months, or to the relationship developed with the health services during that period. It could also be related to the fact that TB patients are sicker, and therefore more motivated to remain in care.

The extremely high rate of loss to follow-up is a major limitation in describing outcomes pre-ART initiation. This study attempted to explore, as far as possible, the characteristics of patients lost to follow-up, comparing them with the cohort in general. Patients who are not eligible for ARVs are less ill, and are less likely to remain in care. The higher proportion of those lost to follow-up with very low and very high CD4 counts suggests that many of these patients are either not attending as they are clinically well, or that they may have died and their vital status is not known to the clinic.

At the time of the analysis, there was less capacity to provide ART than the demand, and the procedures for starting ARVs were more stringent than they are now, resulting in a long duration before ART was initiated. The average time from enrolment to starting ART was longer than is optimal for patients with very advanced disease such as for those with CD4 counts <50 cells/μl. It is encouraging nevertheless, that those with the lowest CD4 counts were prioritized, and that the majority of those remaining in care and who were eligible for ART were eventually started on ART.

The fact that 78% of the cohort remained free of TB by the second year is limited by the inclusion of persons receiving ART and patients with different CD4 count categories.

However, the results are encouraging in these settings with limited infrastructure. The factors that may have contributed to this include the widespread use of co-trimoxazole prophylaxis, and the fact that patients may have been diagnosed and treated for other opportunistic infections (OI's) as suggested by findings of other African studies (Badri et al. 1999;Nunn et al. 1992).

The very low rate of loss to follow-up after starting ART reflects a selection bias (those starting ART demonstrated that they were more likely to remain in care), as well as a positive impact of the adherence-promoting interventions. The clinical outcomes for this group clearly demonstrate excellent retention and survival, and laboratory outcomes are comparable with those described elsewhere for the entire Khayelitsha cohort (Coetzee, Hildebrand, Boulle, & et al 2004)

4.2 Conclusion and recommendations

The rate of loss to follow-up is higher than expected and severely comprises the ability of the programme to report on non-ART outcomes. An examination of sources of referral and CD4 counts does however go some way to explaining the loss to follow-up. The time to starting ART could have been quicker in this period, but the prioritization was overall appropriate. The outcomes for those patients starting ARVs in this clinic are consistent with those of the overall programme.

Recommendations include:

- An attempt should be made to reduce loss to follow-up as an outcome in general HIV care (where ART is not provided or before ART is provided).
- With high proportions of patients enrolling at services for first time with CD4 cell counts below 200 cells/μl, a faster process to enroll patients on ART needs to be developed as soon as possible.
- As TB clinics are likely to be an important entry points to ART, given the numbers referred from there and the low CD4 counts of patients referred, every attempt should be made to provide VCT at these points and to ensure adequate referral for HIV care and where indicated, ART.

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Appendices

A:

Data Audit Check List

Audit #

Date

Folder B

Routine

- [ ] Referred from, prior TB, prior Rx
- [ ] Dates, Visit numbers, and visit sequence
- [ ] Staging, weight outlyers
- [ ] Results - checking for AE's at same time
- [ ] OI's - Entered and correctly coded
- [ ] Rx - regimen and individual medicines
- [ ] Referrals, presence and duration of hospitalisation

Specific

- [ ] Tb diagnosis method recorded in comments - AFB, culture, emperic,hist
- [ ] Reason for S4 diagnosis entered in comments - eg. pos thrush

Survey - every 10th folder

- [ ] Check dates in notes, and OI's, staging, vs. tally sheets
  - [ ] Visits on tally sheets
  - [ ] Visits in notes
- [ ] Make a note for clinician to jot down scheduled dates from pink card

OI's not captured on tallysheet

Admin

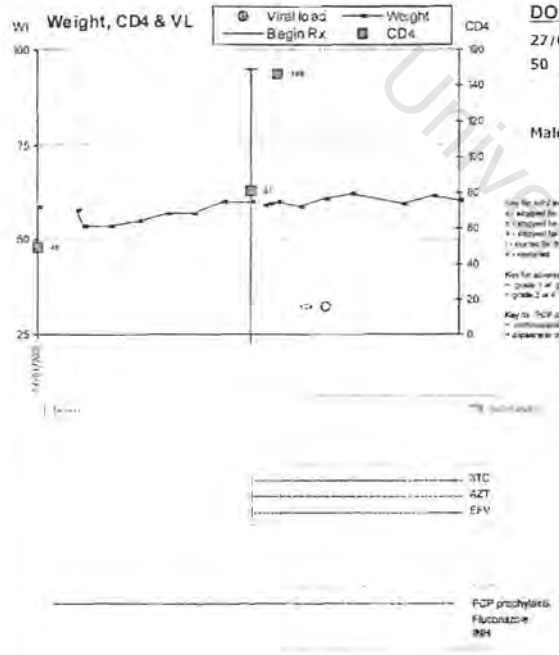
- [ ] Review form corrected in red
- [ ] Entered into computer, including audit date, and notes
- [ ] Checked timepoints for investigations
- [ ] Summary printed for clinician, with instructions on outstanding data
- [ ] Summary printed for patient and folder

Clinic
Site B

Audit Report B

Phone

Treatment and outcomes over time



DOB
27/04/1954
50 years old.

Male

Clinic History

Refered from: Private clinician
Diagnosed: 2002
Previous ART? Naive
Prior TB: Yes

Visit Summary

Visit	Date	Stage	Duration (mnths)	
First Visit	1	14/01/2003	3	Clinic ARV Stopped
First ARV Rx Visit	10	01/09/2003	3	7.6
Visit Stopping Rx				
Last Visit		13/04/2004	3	15 7.4

CD4 count, viral load and weight

Date	CD4	VL	Wt
14/01/2003	49		59
01/09/2003	81 , Base		60 , Base
29/09/2003	146		60
20/11/2003		124 3 mo	61 , 3 mo
16/03/2004			62 , 6 mo

Referrals / hospitalisation

Comments

Baseline VL and 6m missing
CD4 6m

Printed: 28-Apr-04

Case	B	B	B	B	B	B	B	B	B	B	B
Date	**14/01/2003**	**29/01/2003**	**25/02/2003**	**04/03/2003**	**01/04/2003**	**02/05/2003**	**03/06/2003**	**01/07/2003**	**01/08/2003**	**01/09/2003**	**08/09/2003**
Provider											
next visit	29/01/2003	25/02/2003	04/03/2003	01/04/2003						08/09/2003	
Height											
CD4	49									81	
HIV RNA											
TLC	224									1720	
Refer to Hospdays											
Entrydate											
Regimen											
TB, pulmonary	New	New	Ongoing	Ongoing							
3TC										Begin	Continue
AZT										Begin	Continue
EFV										Begin	Continue

Case	B	B	B	B	B	B	B	B	B
Date	15/09/2003	22/09/2003	29/09/2003	24/10/2003	20/11/2003	18/12/2003	12/02/2004	16/03/2004	13/04/2004
Provider									Nurse
next visit	22/09/2003		28/10/2003	20/11/2003	18/12/2003	12/02/2003	16/03/2004		10/05/2004
Height									
CD4			146						
HIV RNA					124				
TLC			1440		139				
Refer to Hospdays									
TB, pulmonary									
3TC	Continue	Continue	Continue	Continue	Continue	Continue	Continue	Continue	Continue
AZT	Continue	Continue	Continue	Continue	Continue	Continue	Continue	Continue	Continue
EFV	Continue	Continue	Continue	Continue	Continue	Continue	Continue	Continue	Continue