A STUDY TO EXPLORE THE IMPACT OF SOCIO-DEMOGRAPHIC FACTORS ON THE RESPONSE TO ANTIRETROVIRAL THERAPY IN GAUTENG DEPARTMENT OF HEALTH

BY

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DECLARATION

I Dr/Mr/Ms/Mrs ..... do hereby solemnly declare that this work is as a result of my efforts and has never been presented by any body or appeared any where for any qualification, certificate or publication.

Signature: .....

Date: .....

DEDICATION

This dissertation is dedicated to my husband Osborne Majuru and the three boys, without forgetting my mom Esther Mangwende, she has always been there for me and my family. This will not have been possible without your patience and support.

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ABSTRACT

Objectives

The study aims to describe the socio-demographic characteristics, clinical outcomes of the patients in the Gauteng public sector roll-out programme and establish the association between these. There are contradictory results from international studies on these associations, in the absence of SA results.

Methods

This is a retrospective cohort, exploratory, secondary data, record review study and a comparison between two sites. Routinely collected socio-demographic data and clinical data were used to establish the impact of socio-demographic factors on response to HAART. This was collected for patients who enrolled from April 2004 to August 2004. Chris Hani Baragwanaath (CHB) had 494 records, Helen Joseph (HJ) had159 records collected. Exposure variables (age, sex, marital status, education level, residential area, employment, baseline viral load and baseline cd4 count). Outcome variables were (CD4 and Viral load at 3 months, 6 months and 12 months).

Data Analysis

T tests were used for comparing means; logistic regression was used to find the effect of ordered exposure variables and binary outcome. Chi square and fishers exact were used to find frequencies and association between the categorical variables. Regression was used to find the association between the continuous exposure variables and the continuous outcome variables. In a multivariate model, to assess the effect of the exposure variables to the outcome variables Multivariate regression was used.

Statistical significance was assessed at the 5% significance level, giving 95% confidence interval.

Results

The majority of the patients (653) were female, African, unemployed and were literate. At CHB, at the end of the first year, three quarters were still on treatment however; just under a fifth (19%) had died. The majority responded well to treatment and had a mean baseline CD4 count of 58.9cells/mm3 (CHB) and 78.4cells/mm3 (HJ) and mean CD4 count of 245 (CHB) and 268 (HJ) after 12 months. increasing age, and being widowed, lowers the immunological response. Employment, education, sex and had no impact on response.

Conclusion

- There is positive virological and immunological response to HAART in Gauteng ARV roll-out programme despite the low socio economic status of the majority of the patients.
- Provision of free antiretroviral drugs and access to the disability grant has assisted in mitigating the effects of HIV/ AIDS on the socio-economically disadvantaged.
- The elderly and the widowed might need close monitoring as their response appears to be lower than the others.
- The group with no schooling is not well represented in this sample; the question is whether the HIV/AIDS prevention messages and treatment is accessible for this group. This needs further research.

Key words: socio demographic, ART, CHB, HJ South Africa, HIV

TABLES and GRAPHS

GRAPHS

Definition of terms

AIDS	-Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
ARV	-Antiretroviral
HAART	-Highly Active Anti-retroviral therapy
HIV-1	-Human immunodeficiency virus type 1
HIV-RNA	-Human immunodeficiency virus Ribonucleic Acid
NNRTI	-Non Nucleoside Reverse Transcriptase inhibitor
NRTI	-Nucleoside Reverse Transcriptase Inhibitor
PI	-Protease Inhibitor
AZT	-Zidovudine
3TC	-Lamivudine
CHB	Chris Hani Baragwanaath
HJ	Helen Joseph

A study to explore the impact of socio-demographic factors on the response to antiretroviral therapy in Gauteng Department of Health

CHAPTER 1 INTRODUCTION

1.1 Background

Sub-Saharan Africa bears a disproportionate burden of the HIV/AIDS epidemic, which in North America and Europe has since become a manageable health problem after the advent of triple antiretroviral therapy as pointed out by Flanigan and others.[1] In 2006, more than 63% of all the people living with HIV were in Africa, Southern Africa being the epicenter of the global HIV epidemic.[2] There has been a noticeable increase in access to antiretroviral therapy in developing countries. According to the WHO Director Southern Africa, the number of HIV-positive Africans accessing AIDS Drug treatment has grown from less than 300 000 in 2003 to more than 1 million by June 2006. In Sub-Saharan Africa however only 23 percent of those in need of antiretroviral are receiving them.[3] Scale-up efforts have been strong in some countries in East and Southern Africa, South Africa being one of them.[2]

As per UNAIDS (2004) report, South Africa continues to have the highest number of people living with HIV in the world.[4] It is estimated that by the middle of 2006 about 5.4 million people in the South African population were infected with HIV.[5] It is one of the countries in Sub-Saharan Africa that embraced the WHO 3 by 5 initiative. A number of public health centers countrywide are already providing free antiretroviral drugs to the qualifying HIV/AIDS patients. This is anticipated to be one of the largest roll out programs in the world.[6] By the end of August 2004, four sites in Johannesburg Metro had enrolled a total of 2301 patients into the ARV roll-out programme.[7] According to the Gauteng Department of Health (April 2005), within the first year of roll out, the Gauteng provincial government had successfully opened 23 service points and had about 12 208 patients on antiretroviral therapy. By the middle of 2006, it was estimated that 230 000 HIV-infected individuals were

receiving antiretroviral therapy in South Africa.[5] According to the Deputy President of South Africa by September, 213 282 people countrywide had benefited from the government roll-out programme and another 11 000 were joining the program every month.[8]

Prior to public sector roll-out programme, those who could afford ARV treatment sourced their treatment privately or through company initiatives or non-governmental organizations like Medecins Sans Frontieres (MSF) and clinical trials. Due to high costs some of the patients were not taking adequate doses and combinations.

The public sector roll-out program is open to any South African who is HIV positive, has a CD4 count of less than 200cells/mm^3 and meets the criteria spelt out in the National ARV Plan,[9] whether treatment naïve or not. In this context challenges brought about by being not naive, socio-demographic features and questionable adherence are anticipated to interfere with response to HAART.

The **not-naïve** group will present with a multitude of challenges which will range from treatment failure due to non adherence or drug resistance due to inadequate combinations and doses. Response to HAART in this group is expected not to be the same as in the **naïve** group. Compared with ART-experienced patients, ART-naïve patients were less likely to experience treatment failure.[10]

In the South African roll-out programme, all ARV drugs and laboratory tests are available for free. In addition all those who are HIV-positive, unemployed and have a CD4 count of less than 200cells/mm^3 are entitled to a government disability grant of about R700 per month. This grant is meant to allow patients to have decent nutrition and be able to meet simple day to day needs like transport costs during their time of illness and therefore help them recover quickly. Patients are therefore expected to be diligent in taking their treatment.

The South African ARV roll-out programme is using the following drugs:

Nucleoside Reverse Transcriptase Inhibitors: Zidovudine (AZT), Lamuvidine (3TC), Stavudine (ZERIT), Didanosine (VIDEX), Non-Nucleoside Reverse Transcriptases (NNRTIs): Efavirenz (EFV), Nevirapine (NVP) and Protease Inhibitors (PIs): Kaletra.

Description of the Study Location

This study was carried out at two hospitals in the City of Johannesburg, Gauteng Province. Gauteng is the smallest of all South African provinces.[11] The province is subdivided into 12 administrative municipalities, the City of Johannesburg Metropolitan Municipality being one of them.[11] The City of Johannesburg was sub-divided into 11 health and administrative regions, (region 1-11) but this is being changed into 7 regions as of November 2006, region (A- G) *(See Map 1 page 6)*

Socio-demographic and economic status of the population

The Gauteng province has an estimated population of about 8.8million.[12] Gauteng is the economic habour of South Africa and is growing rapidly.[11] The largest number of unemployed adults in Johannesburg is found in region D and G (Soweto, Orange farm).[13] These are areas of immense poverty, compounded by low education levels and there are large areas of informal settlements.[14] A large proportion of Johannesburg residents live in Soweto. This is estimated to be about a third of the City of Johannesburg's population.[15] Many parts in Soweto rank among the poorest in Johannesburg although individual suburbs in Soweto tend to have a mixture of wealthier and poorer residents.[15]

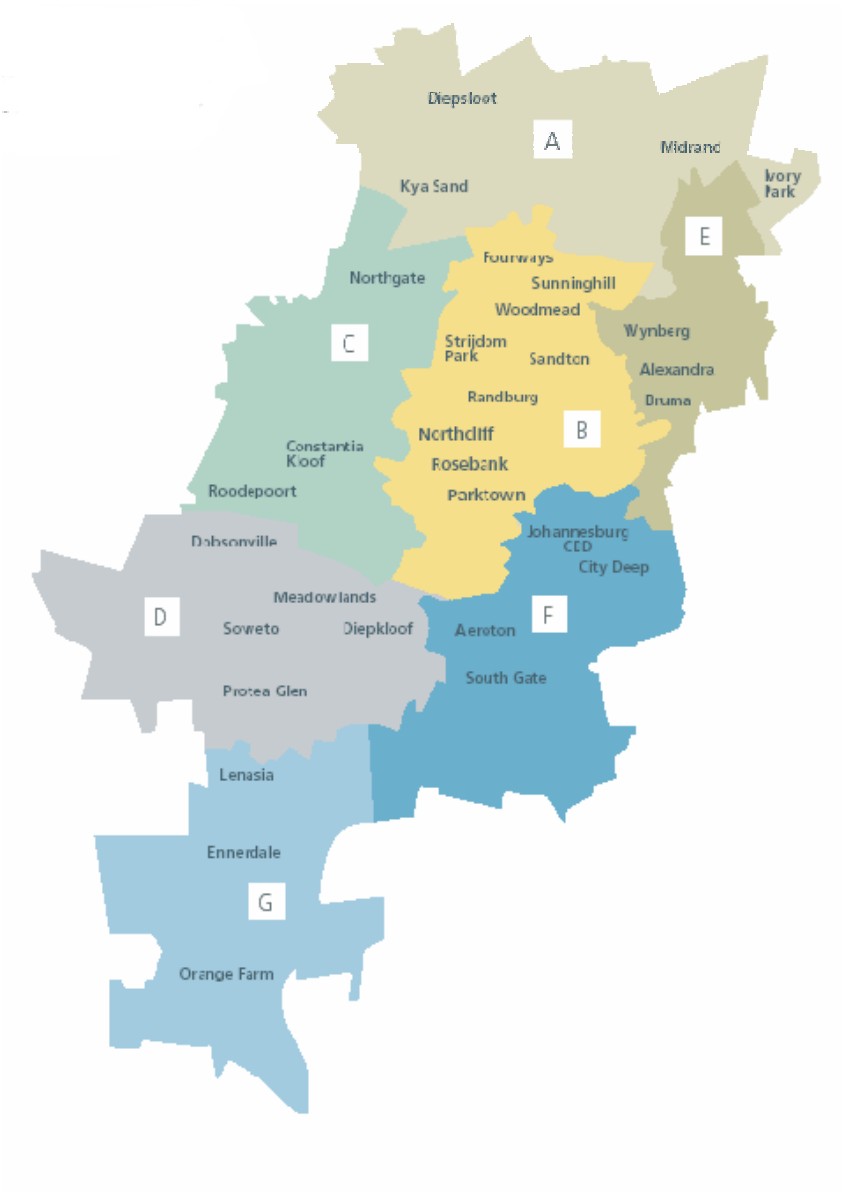
It is estimated that 8.4% of Johannesburg residents aged 20 and over have received no schooling, 11.2% have some schooling, 34% have some high school education, 28% have finished high school and 12.6% have tertiary education.[12] The education profile of the City of

Johannesburg will be used as a reference against which those on HAART at the two sites are assessed.

The ARV sites

The two hospitals involved in this study were Chris Hani Baragwanaath Hospital (CHB) and Helen Joseph (HJ). CHB a public hospital is one of the 40 Gauteng provincial hospitals. It is located in Soweto in region D. CHB is the largest hospital in the world with about 3200 beds.[16] Nearly 2000 patients are seen at this hospital daily.[16] It could be running one of the biggest ARV roll-out sites in the country. It caters not only for Soweto residents but for the residents in regions F, G, as well as people from other municipalities and provinces. HJ is also a provincial hospital but smaller than CHB located in region B. This is a 500 bedded hospital.

Map 1: City of Johannesburg Metropolitan Municipality[17]



1.2 Statement of the problem and justification for the study

Despite the advent of effective combination of antiretroviral therapy (ART) for the treatment of HIV infection many doubt the feasibility of ART treatment programmes in resource-poor settings.[18] The socio-demographic features of those who are HIV positive in the developed world are different from those who are HIV-positive in developing countries. The poor are the most affected by HIV in the developing world as it is a heterosexual epidemic in this context. The sex /gender distribution of the infection is also different for the two contexts. There are more infected females in the developing countries than in developed countries. Women in sub-Saharan Africa bear a disproportionate burden of the disease. Across sub-Saharan Africa women are more likely to be infected than men and they are the ones more likely caring for the infected.[2] In this region for every 10 men living with HIV there are about 14 women who are infected with the virus.[2] The age profile of those infected also differs by sex. It was reported that 15–49-year old adults are the most affected.[19] Due to lack of knowledge and resources most patients in the third world present in the late stages of the disease, with very low CD4 counts, high viral loads and an array of opportunistic infections. "Those presenting for care with very low CD4 cell counts may make large demands on clinical resources, particularly over the first few months".[20] The availability of cheaper generic antiretroviral drugs complimented by the massive treatment thrust of the WHO 3 by 5 initiative has brought a lot of hope for the infected and affected in Sub-Saharan Africa. The benefits of antiretroviral drugs are being appreciated in the region now despite other controversial theories and mistrust.

This study is set to assess the impact of socio-demographic factors on response to HAART in the developing world at large public health facilities outside controlled research settings. This is in an endeavour to assess population effectiveness of the programme despite low

socio-economic status of the population. Population effectiveness is an important public health measure of the impact of treatments.[21]

The standard antiretroviral treatment prescribed for a treatment naïve patient, also known as Highly Active Antiretroviral Therapy (HAART), consists of a combination of at least three drugs; two NRTIs with an NNRTI or a protease inhibitor. These combinations are known to provide potent suppression of HIV-1 RNA in treatment naïve patients.[22]

The hallmark of triple combination HAART has been profound suppression of viral load to undetectable levels (<400 copies/ml) with increases in CD4 cell count.[1] Current therapeutic guidelines recommend achieving an undetectable viral load, preferably <50copies per/ml and at least less than 400copies/ml.[23] However once this is achieved this does not guarantee sustainability, cases of viral load rebound to levels above undetectable levels are seen after initial viral suppression.[23**]

Positive responses to antiretroviral are expected to be increasing CD4 counts and lowered viral loads. In real practice this has not always been the case. Discordant virological and immunological responses have been observed.[10**, 24] Immunological and virological failures have been observed to occur independently during HAART.[10**] To realize sustained full response and reduced resistance, adequate doses and strict adherence to therapy are important prerequisites. In the developed world there has been noticeable decrease in the AIDS morbidity and mortality due to access to drugs.

** the original article quoted in journal 10 and 23 could not be traced.

A lot of questions still remain unanswered regarding the effect of other factors peculiar to the region, such as socio-demographic characteristics, late presentation and opportunistic infections. These factors might have an impact on the sustainability of a therapeutic response to HAART which leads to the aim of this study.

The aim of this study is to explore the relationship between a range of socio-demographic factors and response to HAART. The links between these are explored in the literature review.

CHAPTER 2 LITERATURE REVIEW

2.1. General

Many studies and trials to confirm the effectiveness and responses to HAART Highly Active antiretroviral therapy were carried out in North America and Europe. The main HIV subtype in these areas is B as compared to type C in Africa. A few studies carried out in Africa do indicate good therapeutic response to HAART in the short-term. Responses to antiretroviral therapy in Africa are in line with those obtained in industrialized countries.[25] A study by Cassol and others, reported that among TB and Kaposi Sarcoma patients in South Africa started on NRTI/NNRTI based HAART, 93.8% and 80% respectively had undetectable HIV-1 levels at 90 days.[26] In a study done in Uganda it was shown that although many HIV infected people treated with ARVs in Kampala had advanced HIV disease, the majority of these patients experienced viral suppression and clinical benefit.[27]

The treatment regimen, virus subtype and adherence are not the only factors influencing response to HAART. There are other factors peculiar to the African region that might influence individual response to treatment, such as socio-demographic characteristics, nutrition, opportunistic infections and availability of care.

2.2. Effect of age on response to HAART

It appears age, may be an important determinant of response to HAART. Studies were done in the developed countries to assess the effect of age on response to HAART. No literature on African studies looking at age as a factor could be found. In a study done in the United Kingdom to investigate factors influencing increases in CD4 cell count in HIV-positive, treatment naïve patients starting HAART, mean CD4 increases were evaluated at 3, 6, 12 and 24 months. It was reported that age was not associated with increases in CD4 cell

counts.[28] In another study in Australia, age was found to determine the level of immune response to HAART.[29] The study population was comprised of males only. Younger age was independently associated with greater increases in CD4 cell counts, and higher absolute CD4 cell counts at 48 months. The EuroSida Study carried out across Europe and Israel confirmed this phenomenon.[30] In a study of children done in the UK and Ireland, (The Collaborative HIV Paediatric Study), better immunological response was seen in younger children.[31] However there was poor virological response in the younger children.

In the USA an increased number of older HIV positive patients are being seen in practice and this trend is likely to become pronounced as the HIV-infected population ages as a consequence of effective treatment.[32] Old age and being treatment naïve were identified as a predictor of a sustained virological response during HAART [10**], whilst younger age was shown to be a predictor of virological failure.[10]

2.3. Effect of ethnicity/race on response

There is very little literature available describing the role of ethnicity in the response to HAART. There is an assumption that disease progression is more rapid in Africans than in non African people. In a UK study by smith and others found an association between white ethnicity and greater increases in CD4 count.[28] Sixty three percent (63%) of the study population in this UK study was of white ethnicity. In contrast in another study by Frater and others no differences were found in the initial response to HAART between European (White) and African (Black/Asian).[33] However in Frater's Study there was a difference in the sustainability of the virological response. There was evidence of increasing viral load after 9 months of treatment in the African group. From the literature there is no definite evidence to confirm the effect of race on response to HAART.

2.4. Effect of sex on response

Sex might be a significant factor determining response to HAART.

The cause for gender difference in response to HAART is thought to be multi-factorial.[21] The female hormonal make up and their more likely poor socio-economic status can influence response to HAART.[21] In a UK study by Smith and others there was no association between sex and response to treatment.[28] In another study carried out at Royal Free Hospital in the United Kingdom, women achieved virological responses at a faster rate than men but other clinical outcomes were not assessed.[34] A later study suggested a possible benefit in women compared with men.[35] A study on a EuroSIDA cohort showed no gender difference in response to HAART.[36] Most of these studies were done in countries where males constitute a higher proportion of the patients. Therefore from the literature sex might have an impact on response to HAART. Studies done in Africa including South Africa have shown a higher proportion of females on antiretroviral therapy than males.[37, 38, 39, 40] There is no evidence in the literature to show if there is any difference in response between the two groups.

2.5. Effect of baseline CD4 count on response

There is contradictory information on the impact of baseline CD4 cell count and viral load on response to treatment. The extent of the pre-existing level of immunodeficiency was found to influence response to HAART. There was better immunological response in those who had the lowest baseline CD4 count.[21, 31] Higher pre-HAART viral load and lower pre-HAART CD4 and CD8 cell counts were associated with greater increases in CD4 cell counts during the first 3 months of HAART.[28] In contrast an Australian study reported that poor immunological responders who did not reach 500cells/ul at 48 months showed lower nadir CD4 count than good responders.[29] Studies carried out in the Khayelitsha programme by Medicins San Frontiers and University of Cape town in South Africa, have shown that

patients with CD4 counts <50cells/mm^3 at baseline have a significantly lower probability of survival than those with levels above.[41] The same was reported in Cote d'voire.[42]

Some studies have shown that patients with a higher pre-HAART CD4 count are at an increased risk of immunological failure.[10]

In conclusion there appears to be contradictory evidence from a range of studies on the association between HAART and socio-demographic factors. Further this has not been specifically explored for the Gauteng area of South Africa. These observations lead to the aim and objectives of this study.

Chapter 3 Objectives

3.1 Aim:

- Ascertain the role of various socio-demographic factors on positive response to HAART in Gauteng, making use of two sites.

3.2 Specific Objectives

1. To describe the socio-demographic characteristics of the patients in the Gauteng public sector ARV roll-out programme at two sites.
2. Describe the clinical outcomes within the first 12 months
3. To establish the association between socio-demographic factors and response to HAART at each site
4. To establish the association between baseline CD4 count, viral load and response to HAART.
5. To identify groups prone to side effects.
6. To describe the occurrence of opportunistic infections in patients on HAART in the Gauteng roll-out programme.
7. To compare response to HAART by treatment center.
8. To use the findings to inform the Gauteng Department of Health ARV roll-out programme.

Definitions

Naïve: Any patient who was recruited into the government roll-out programme and was receiving antiretroviral therapy for the first time in their lifetime.

Non-Naïve, not-naïve, treatment exposed: These are patients who had received some form of antiretroviral therapy before joining the government roll-out programme. This could have been PMTCT, mono therapy, dual therapy or HAART.

CHAPTER 4 METHODOLOGY

4.1. Study Design

This is a retrospective cohort, exploratory, secondary data, record review study and a comparison between two sites.

Routinely collected socio-demographic data and clinical data were used to establish the impact of socio-demographic factors on response to HAART.

4.2. Study Population:

These two ARV sites were chosen because of their ARV management experience and the need to select sites at the outset of this study where a significant number of patients were on treatment for over a year. The study population were adult patients aged 18 years and above, enrolled on the antiretroviral roll-out programme between April 2004 and August 2004 at these two sites in the City of Johannesburg.

According to the Gauteng Department of Health, CHB had 873 patients on treatment by August 2004 and HJ had 650 patients on the register. These two sites commenced the roll-out programme at the official beginning date i.e. the 1st of April 2004. All the patients were receiving free antiretroviral therapy, laboratory testing and comprehensive HIV management. Both treatment **naïve** and **not naïve** patients were included in the study.

All patients went through a process of initiation into the roll-out programme before commencing therapy. This involved counseling on ARVs, disclosure, having treatment supporter and treatment adherence. There is a follow up system for patients who default. This has helped in getting information on deaths that occur at home. The follow up system is

hampered by those on treatment changing addresses and contact numbers without updating hospital records.

4.3. Sample size and sampling

Available data from adult patients enrolled between April 2004 and August 2004 and treated for a year at the two sites was reviewed. The government roll-out programme officially started on the 1st April 2004.

The study sample therefore comprises the patients that were enrolled at the beginning of the programme. Data was collected from 494 patient files at CHB out of a list of about 687 patients. The CHB pharmacy dispensing list was used to identify this sample.

Data for 159 patients was extracted from the computerized Helen Joseph data sets.

There could be several reasons why my figures do not tally with the Department of Health's figures. The most important ones being:

(i) The exclusion of those under the age of 18 years.

(ii) Inability to locate files at CHB, especially for patients who use more than one name.

(iii) Duplicate files for patients**.**

Despite not getting access to some records both data sets are considered to be representative of those on ARVs at these sites.

4.4. Data Collection

A. General

CHB hospital has an informed consent process applicable to patients attending the HIV clinic, seeking permission for unlinked data use for research purposes. The informed consent form was in the files for most of the patients but often not signed. CHB does not

have computerized data sets, therefore all the information was collected manually from patient files. I had access to 498 files at CHB .Some of the files had some of the information required for this study missing. As a result the total number analyzed at every stage of analysis is not constant.

HJ as a multi-study centre and has consent forms for the different studies but there were no consent forms for the government roll-out program. Therefore unlinked computerized data was extracted from the HJ data sets for this study. The data set had 161 patients enrolled during this defined period.

B. Data extracted from records and data sets

1. Exposure Variables

Age was calculated from the date of birth and roll-out date. Sex, race, marital status, education status, residential area, employment status were collected where available. HJ data sets did not have data on marital status and education status. Baseline CD4 count and Baseline viral load were collected as clinical exposure variables.

Data Management: For the baseline CD4 and viral load results in the **naïve** patients, the latest result before the roll-out date/start date was collected as long as it was done in 2004. For the **not naive** patients the latest result before the roll-out date was collected as long as it was done in 2004, because for most of these patients, the result before initiation of treatment was not available.

2. Outcome variables

(i). Viral load and CD4 count

Viral load and CD4 count at 3, 6 and 12 months time points were collected where available.

Data Management: For some patients the tests were not done at exactly the expected time point. Some were done a bit earlier some were done later. The results for the 3rd month

were taken from the latest results available between 8-16 weeks, for the 6th month the latest results taken between 20- 28 weeks, for the 9th month the latest taken between 32-40 weeks and for the 12th month the latest taken between 44-52 weeks. Calculating these periods was based on the on the start date for the **naïve** and on the roll-out date for the **not naïve.**

The start date was when the patient was started on ARVs. The roll-out date was when the patient joined the government roll-out programme, these dates are the same for the **naïve** patients and they differ for the **not naïve** patients.

The viral load was log 10 transformed for easy analysis.

3. Measuring Response

a) Immunological response

Immunological response was calculated as changes in CD4 count from baseline to 3, 6, and 12 months time points, by simply subtracting the baseline values from the 3 month, 6month and 12 month values.

(i) The mean and median CD4 count increases were derived and used as response.

(ii) Achieving a CD4 count of >=200 in was also considered as positive immunological response.

b) Virological response**.**

Positive response was assessed in two ways.

1 Analysis for the undetectable viral load was considered at <=400 (2.6log 10) copies/ml as a cut off and

2 The <=50 (1.7 log 10) copies /ml and <=500 (2.7log 10) copies\ml undetectable levels were also used in this analysis for comparison with other studies.

At a certain period the NHLS used the 400copies/ml as undetectable levels and currently the <50 is being used.

4. Clinical information collected

The naivety status of the patient was confirmed. Any AIDS defining conditions before and during treatment were recorded. Occurrence of TB before and during treatment was also of interest was also recorded.

C. Challenges

- Challenges included pulling out files from the file room, going through each and every one of the 498 files at CHB collecting the required data before capturing it into Epi info questionnaires.
- Interference with the busy clinic in order to complete data collection.
- Inability to enforce the signing of the informed consent, even if it was already attached to most of the notes.
- There was a problem of incomplete records. At each level of analysis there is missing data not necessarily due to death or loss to follow up but due to data not being collected and the timing of laboratory tests (i.e. the test falling out of the time point range. This creates potential bias in assessing both exposure and outcome variables.
- Manipulating the DATA sets from HJ to suit my analysis was not an easy task.

4.5. Data Analysis

As the aim of the study was to assess the association between the socio-demographic factors of those on HAART and treatment outcomes (virological response and immunological response) at two ARV roll-out sites the following data analysis plan was used:.

1. Data for each site is considered separately and then a comparison is made between the two sites.
2. The socio-demographic status and clinical outcomes for the patients on HAART are described first. The clinical outcomes are described for the **combined** (**naïve** and **not naïve**) and for the **naïve** separately.
3. Thereafter the association between the socio-demographic variables and treatment outcomes are assessed

- ✓ Epi Info was used for data entry.
- ✓ Stata 9 was the main statistical package used for analysis.
- ✓ T tests were used for comparing means, Chi square and fishers exact were used to find frequencies and association between the categorical variables
- ✓ Logistic regression was used to find the effect of ordered or continuous exposure variables and binary outcome.
- ✓ Regression was used to find the association between the defined continuous exposure variables and the continuous outcome variables.
- ✓ In a multivariate model, to assess the effect of the exposure variables to the outcome variables Multivariate regression was used.
- ✓ Statistical significance was assessed at the 5% significance level, giving 95% confidence interval sufficient for an exploratory study of this nature.

The results of each site are presented and discussed followed by a comparison between the two sites.

4.6. Ethical Considerations

An ethical application supported by letters of permission from the Gauteng Health Department was submitted to the University of Witwatersrand Ethics Committee for ethical approval. CHB had an informed consent allowing the Department of Health to use the routinely collected data without personal identifiers for surveillance and research purposes. There was very little evidence of the signed informed consent although there is one in place. See attached copy of the consent. HJ as multi-study centre has a number of informed consent forms but the one for government roll out had not yet been approved by the ethics committee. Therefore unlinked data was extracted from the HJ data sets for this study.

CHAPTER 5 RESULTS

5.1 Introduction

The results will be presented following the order of the objectives. Firstly the results for CHB will be described, and then followed by the results for HJ. The final section of this chapter compares the two sites. The findings are then discussed in the following Chapter.

5.2 Chris Hani Baragawanaath (CHB)

The hospital is described in Chapter 1 and 4.

5.2.1. Socio demographic factors

The results on socio-demographic factors are summarized *in Table 5.1, Graphs 5.1 and 5.2.*

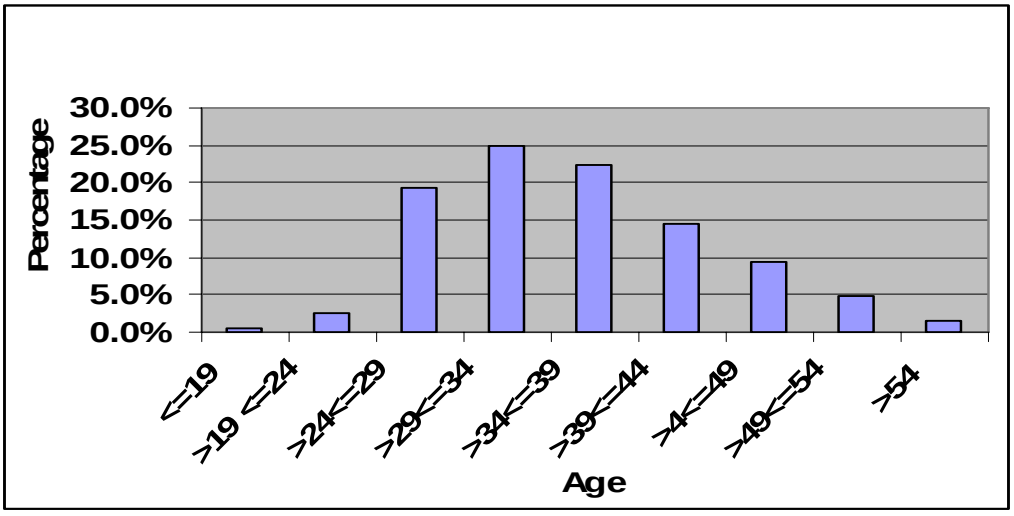
A. Sex and Age

Females constituted 60.9 % (n=298) of the patients. The mean age of the patients at CHB was 35.9 years. Females had a lower mean age than males, 34.5 and 38.1 years respectively (p=0.000). The detailed age analysis showed that the majority of men and women were in the age group 30-39 years although women predominated in the 20-29 age category and men in the 40-49 age groups. Overall, 6.1% of all the patients were more than 50 years old. *(See Table 5.1; Graphs 5.1 and 5.2)*

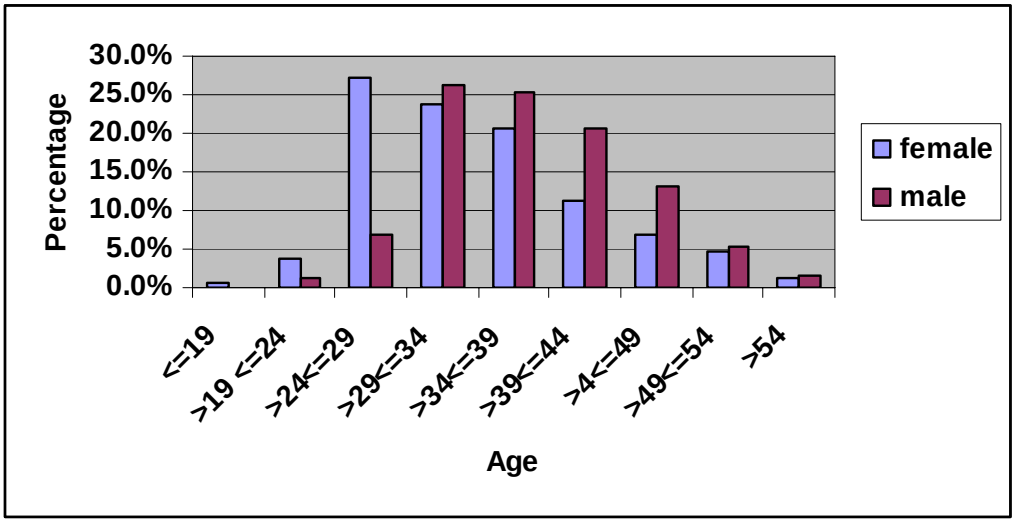
Table 5.1: **Summary: socio-demographic factors (CHB)**

Sex	
Female	(n=298) 61%
Male	(n=191) 39%
Age (in years)	(n=493)
Mean *(standard deviation)*	34.9 *(7.81)*
Education status	
No education	(n=4) 1.0 %
Grade 0-5	(n=35) 8.8%
Grade 6-7	(n=44) 11.1%
Grade 8-12	(n=296) 74.8%
Higher education	(n=17) 4.3%
Employment	(n=480)
Employed/self employed	18.1%
Unemployed on grant	51.9%
Unemployed not on grant	30%
Marital status	
Married	(n=68) 13.9%
Single	(n=376) 77.1%
Divorced or seperated	(n=22) 4.5%
Widowed	(n=22).4.5%

Graph 5.1: **Categorised Age (CHB)**



Graph 5.2: **Categorised Age by Sex (CHB)**



B. Race

The majority of the patients (97%) were African with a very small percentage of Coloreds and Indians.

C. Education

The education profile of the patients showed that over three quarters (79%) of the patients had achieved at least grade 8. The proportion of those on ARVs who had tertiary education was 4.3% and those with no schooling were 1%. *(See Table 5.1)*

There were a higher proportion of females compared to males with at least grade 8 (85%vs.67%) (p=0.000).

D. Employment

Of the 480 records analyzed, only 18.1% of the patients were employed/self-employed, 51.9% were unemployed but accessing a disability grant and the other 30 % were neither employed nor received a grant. *(See Table 5.1)*

The sex breakdown by employment showed that a very similar percentage of men and women were employed (17.9% of females were employed as compared to 18.7% males). When assessing those receiving grants, there were slightly more females on grants than males (55.2% and 46.7%) respectively (p=0.149).

E. Marital status

Three quarters (77.1 %) of the patients were single, 13.9% were married. The balance (divorced, separated and widowed) constituted the other 9% in equal proportions. A higher proportion of males were married (22%) when compared to females (9%) (p=0.001).

F. Residential Area

More than three quarters (77%) of the patients lived in Soweto; the location of Chris Hanoi Baragwanath, A further (8%) came from an adjacent region, Region G within the City of Johannesburg (to the south). In total, (9.6%) of the patients came from outside of the City of Johannesburg. Refer to Map 1 page 6.

5.2.2 Clinical outcomes

A. General

More than half (67.1%) were treatment **naïve** and the remainder were **not naive**.

Type of treatment

There were three, three drug combinations available as first line treatment for the naïve patients. More than three quarters (89.1%) of the **naïve** patients were on D4T, 3TC, EFV, followed by (9.7%) on AZT, 3TC, EFV and the rest were on D4T,3TC,NVP.

The **not naïve** who constituted a third of the sample had more than five combinations of treatment available which included DDI and Kaletra which are not in the first line for the **naïve**. More than a quarter (40%) were on AZT, 3TC, EFV, a quarter (25.7%) were on D4T, 3TC, EFV, (18.8%) were on D4T, DDI, EFV and the rest were on other combinations.

Treatment change and Side effects

In the **combined group** more than (20%) had their treatment changed during the year. This proportion was high due to a sizeable number of the **not naïve** patients starting on a new regimen different from the one they had before the roll-out. Treatment was not changed for 90% of the **naïve** patients. In the **naïve** the treatment change was mostly after 6 months of treatment, i.e. for about two thirds. The reasons for changing treatment in the **naïve** in order of proportions were; side effects (56.7%), treatment failure (33.3%), unknown, 6.7% and pregnancy (3.3%). In the **combined group,** the reasons for changing treatment in order of proportions, were, treatment failure (47.2%), side effects (24.5%), change to roll out drugs (21.7%), unknown (4.7%) and pregnancy (1.9%). Only(6%) suffered side effects that warranted change of treatment. The proportions were similar in the **combined** group and **naïve.**

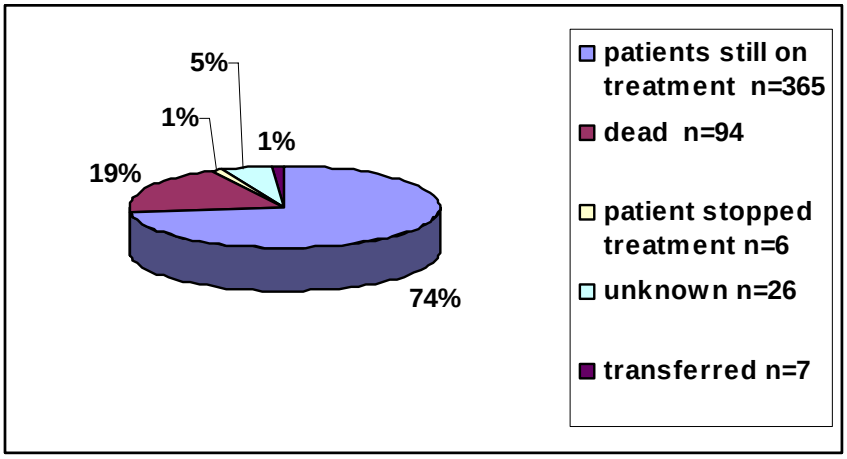
General outcomes at 12 months

Patients still on treatment

At twelve months almost three quarters of the patients (74%) enrolled during the first four months of the roll-out programme were still on treatment.

About (7%) had stopped treatment, transferred or their whereabouts was unknown. *(See Graph 5.3)*

Graph 5.3: **General outcomes at 12 months(CHB)**



Dead

Nearly one fifth of the enrolled patients i.e. (19%) had died by the end of the first twelve months. Confirmation of deaths was obtained from hospital notes and reports from next of kin during follow up. The **naïve** had a higher proportion of deaths (22.8 %) than the **not naïve** (11%).

Of all those who died, (61.7%) died in the first three months of the roll-out programme. Nearly three quarters (70.7%) of the dead had a baseline CD4 count <=50cells/mm^3. More than half of the dead (53.2%) had TB prior to roll-out. Over three quarters (77.5%) of the dead came from region D. Among those who were still on treatment at 12 months, less than half (42%) had a baseline CD4count <=50 cells/mm^3.

Defaulters and Transfers

Less than a tenth (6%) of the patients defaulted treatment in the first year of roll-out.

A very small percentage (1%) was formally transferred to other roll-out centers.

Opportunistic Infections: Occurrence of TB

Tuberculosis

Almost half (49.8%) of the patients had been treated for TB prior to roll-out programme. In the **naïve** 47% had TB before HAART was commenced. Less than a tenth (6.7%) of the **naïve** patients had TB after HAART was commenced. The proportions were similar in the **combined group** and the **naïve.**

B. Immunological Response

CD4 Count: As expected, the mean CD4 count for the **combined** group increased from 85.1cells/mm^3 at baseline to 261cells/mm^3 at 12 months. However, this masks the variation between the **naïve** and the **not naïve** group in starting CD4 counts as well as treatment progression.

The CD4 count of those who were treatment **naive** had a mean at baseline of 58.9cells/mm^3. At 12 months the mean CD4 count of those who were treatment **naïve** was 245cells/mm^3 as compared to 261cells/mm^3 for the **combined** group. *(See table 5.2)*

At the outset, three quarters of the treatment **naïve**, (77%) of the patients had a CD4 count of less than to 100cells/mm^3, with (58%) starting with a CD4 count of less than or equal to 50cells/mm^3. At the outset, in the **combined** group (66.7%) had a CD4 count of less than 100cells/mm^3, with (48.3%) having a CD4 count of less than 50cells/mm^3. Over the first three months after starting treatment, the treatment **naïve** responded quickly with an almost three fold (2.7 times) increase in mean CD4 counts during this initial period. In the **naïve** the

median baseline CD4 count was higher in those >=50 years age group (81 cells/mm^3 vs. 57cells/mm^3) as compared to those <50 years (p=0.062).

Positive immunological response

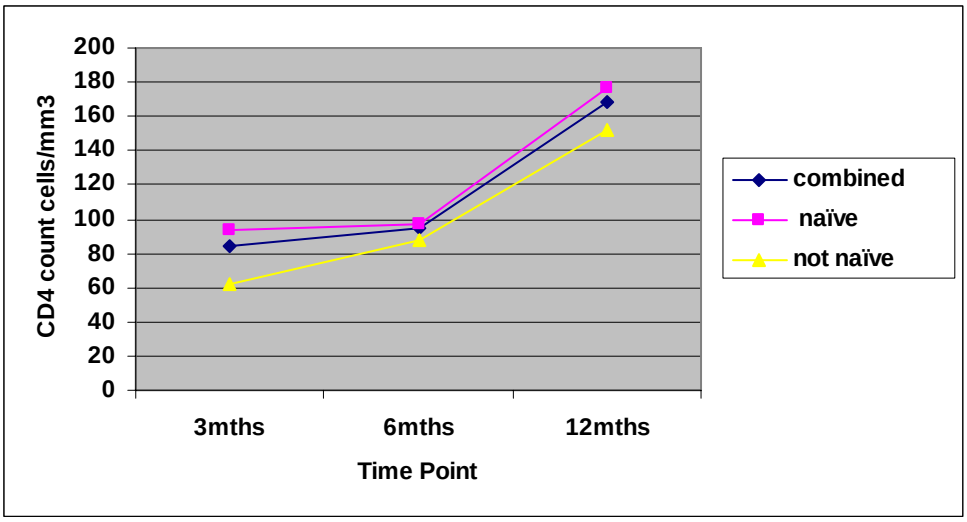
The mean/median CD4 count increase was higher in the **naïve** than in the **combined** group at all time points during the first 12 months. The median increase at 12months was 177.1cells/mm^3 for the **naïve** as compared with 169cells/mm^3 for the **combined** group. (*See Table 5.2 and Graph 5.4 below)*

Table 5.2: **Immunological and Virological outcomes(CHB)**

OUTCOME	NAIVE	NOT-NAIVE	COMBINED	pvalue
Mean Baseline CD4 count(cells/mm3)(*sd)*	(n=330) 58.9 (*57.6)*	(n=148) 143.6 *(119.5)*	(n=478) 85.1*(90.7)*	0.000***
Mean CD4 count at 12 months(*sd)*	(n=200) 245 (*134.8)*	(n=89) *297 (173.8)*	(n=289) 261 *(149.6)*	0.006***[*]
Mean CD4 count increase at 12 months*(sd)*	(n=200) 177.1 *(123.5)*	(n=85) 152.2 *(145.6)*	169 *(130.7)*	0.141
CD4 count >= 200 cells/mm3 at 12 months	(n=113) 56.5%	(n=53) 66.3%	59.5%	0.117
Baseline Viral load (log 10copies/ml)(*sd)*	(n=321) 5.43 *(0.6)*	(n=142) 3.99 *(1.36)*	(n=463) 4.99 *(1.12)*	0.000***
Viral load at 12 months(log 10)*(sd)*	(n=194) 1.85 *(0.92)*	(n=88) 2.23 *(1.17)*	(n=282) 1.97 *(1.01)*	0.003***
Viral load <=400(2.6 log10) at 12 months	(n=167) 86.1%	(n=60) 68.2%	79.9%	0.000***
Dead	(n=76) 22.8%	(n=18) 11%	19%	0.004***
Died <=3months	(n=47) 61.8%	(n=11) 61.1%	61.7%	0.702

*** Statistically significant

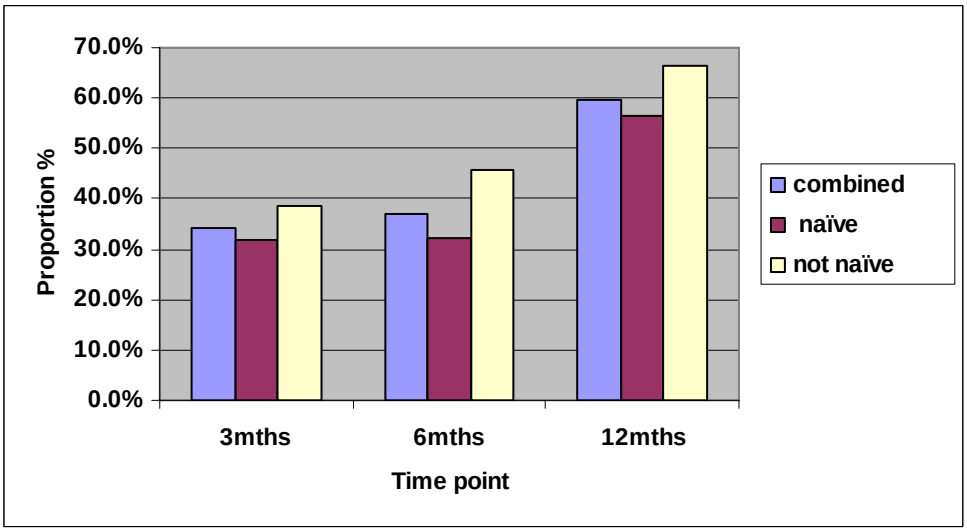
Graph 5.4: **Immunological response(mean CD4 count increase) (CHB***)*



CD4 count>=200cells/mm^3

(i) At 3 months 32 % of the **naïve** patients had a CD4 count of greater than 200 cells/mm3 and. At 6 months 32.2% of the **naïve** patients had a CD4 count of >=200cells and as compared to 36.9% in the **combined** group. By 12 months 56.5% of the **naïve** patients had a CD4 count of >=200 cells and the proportion was 59.5% for the **combined** group. (*See Graph 5.5*)

Graph 5.5: **CD4 count>=200cells/mm^3 (CHB***)*



C. Virological Response.

(See Table 5.2 and Graph 5.6).

The viral load was transformed to the log 10 at data entry.

The mean viral load for the **combined** group decreased from a baseline of 4.99 log 10 copies/ml to 1.97 log 10 copies /ml at 12 months

Positive Virological Response

Viral load <= 400 copies/ml (CHB*)*

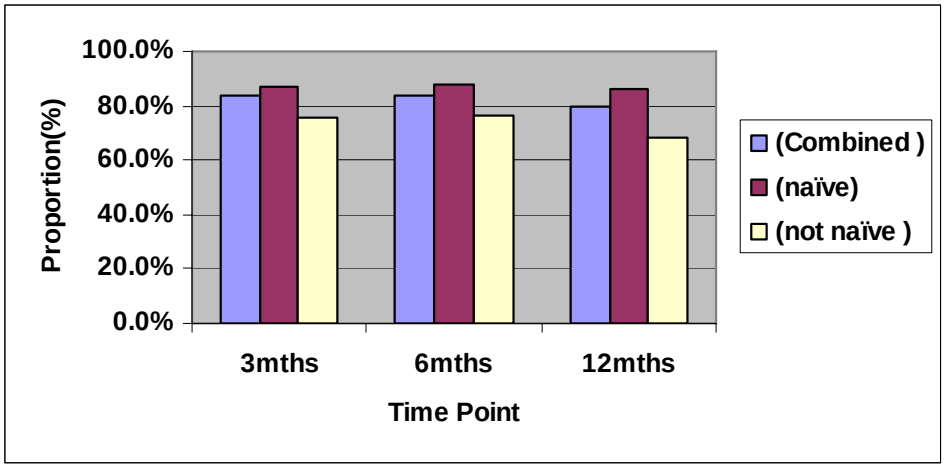
(i) As from 3 months at least 85 % of the **naïve** patients had positive response i.e. viral load <=400copies/ml,

(ii) In the **combined** group this was about 80% at 3 months dropping to less than 80% at 12months. Similar proportions of positive virological response results were shown when only those with complete viral load results at all time points were analyzed.

(iii) In the **not naïve** positive response was just above (75%) at 3 months and 6 months, falling to 68% at 12 months.

The **combined group** had just about half (57.3%) of the patients <= 1.7 log10 (50copies) at 12 months compared to the **naïve** who had nearly three quarters (73.2%) of the patients <=to 1.7 log 10 (50) copies/ml

Graph 5.6: **Virological response viral load <= 400 copies/ml (CHB***)*



5.2.3. Association between socio-demographic factors and response at 12 months. (*See tables 5.3 and 5.4)*

A range of socio-demographic factors described in section 5.2.1 were assessed for their statistical relationship to immunological and virological response. In univariate analysis most of these socio-demographic factors have no effect on immunological response. Age and marital status were found to have an effect on response. Race and residential area were not analyzed because of the small numbers in the in the subgroups.

- ✓ *Age effect:* There is a negative correlation between age and immunological response. There is reduced immunological response with increase in age (p=0.001). In categorized age, the <50years group have better immunological response than the >=50 years group (p=0.047). This association was found to be significant at 12 months of treatment. At 12 months on HAART it was found that there is better virological response with increasing age.
- ✓ (ii) *Marital Status effect*: the widowed had reduced immunological response as compared to the (single, the divorced/separated and the married).

***Stastically significant.

Table 5.3: **Regression of socio-demographic variables and increase in CD4 count at 12 months. (CHB)**

Variable	Coefficient, Confidence, intervals ,pvalues		
	coefficient	95% CI	pvalue
Sex: female	ref		
Sex: male	-11.9	-43.3 - 19.5	0.456
age	-3.49	-5.45 – (-1.53)	0.001***
Education: grade 7 and below	ref		
Education grade 8 and above	21.44	-19.14 – 62.02	0.299
Employed	ref		
Unemployed on grant	24.6	-16.8 - 66	0.243
Unemployed not on grant	30.1	-15.7 - 75.9	0.197
Marital status: married	ref		
Marital status: divorced	37	-38.57 - 112.5	0.336
Marital status: single	-26.4	-69.8 - 17	0.232
Marital status: widowed	-108	-183.7 - (-32.5)	0.05***

Table 5.4: **Logistic regression of socio-demographic variables and viral load <=400 copies/ml at 12 months. (CHB)**

	Odds ratio and Confidence intervals		
	OR	95% CI	pvalue
Sex: male	1.4	.7 - 2.5	0.338
Age	1.04	1 - 1.08	0.046***
			0.366
Education: (Grade 8 – tertiary)	0.62	0.257 – 1.486	0.282
Unemployed on grant	0.8	0.4 - 1.8	0.611
unemployed not on grant	1.4	0.5 - 3.5	0.496
Marital status: single	2.7	0.8 - 9.25	0.106
Marital status: divorced	1.2	0.25 - 5.54	0.828
Marital status: widowed	0.72	0.19 - 2.72	0.627

5.2.4 Association between Baseline CD4 Count, Baseline Viral Load and Response at 12 months (*See Table 5.5)*

Table 5.5: **Regression of Baseline CD4 count, Baseline viral load and response at 12 months (CHB)**

Baseline CD4, Baseline Viral load and increase in CD4 count at 12 month			
	Coefficient	95% CI	pvalue
Baseline CD4 count	-0.17	-0.35 – (-0.001)	0.048***
Baseline viral load	14.9	1.2 - 28.5	0.033***
Baseline CD4, Baseline Viral load and viral load <=400 copies/ml at 12 months			
	Coefficient	95% CI	pvalue
Baseline CD4 count	0.00003	-.0005 - 0.0005	0.916
Baseline viral load	0.02	-.02 - 0.06	0.39

- ✓ Baseline CD4 count effect: Baseline CD4 count has an effect on immunological response. Every unit increase in baseline CD4 count is associated with reduced immunological response. It has no effect on virological response.
- ✓ Baseline Viral Load Effect: It has an effect on immunological response. The higher the baseline viral load the higher the CD4 increase. It has no effect on virological response.

Multi-variate analysis at 12 months

Immunological response

In a multivariate model using regression, adjusting for, age, age_50, marital status, baseline viral load, baseline CD4 count and sex at 12 months. Age was the only factor which had an effect on immunological response.

Virological Response

After adjusting for age, age_50 marital status, baseline viral load, baseline CD4 count and sex there was no difference in virological response between groups at 12 months.

5.2.5. Groups prone to side effects

There is no pattern in the occurrence of side effects. No particular group is particularly affected by side effects.

5.3 Helen Joseph (HJ)

Helen Joseph as a hospital is fully described in Chapter1 and 4.

5.3.1. Socio demographic factors (*See Table 5.6)*

Table 5 .6: **Summary: Sex, age, employment, (HJ).**

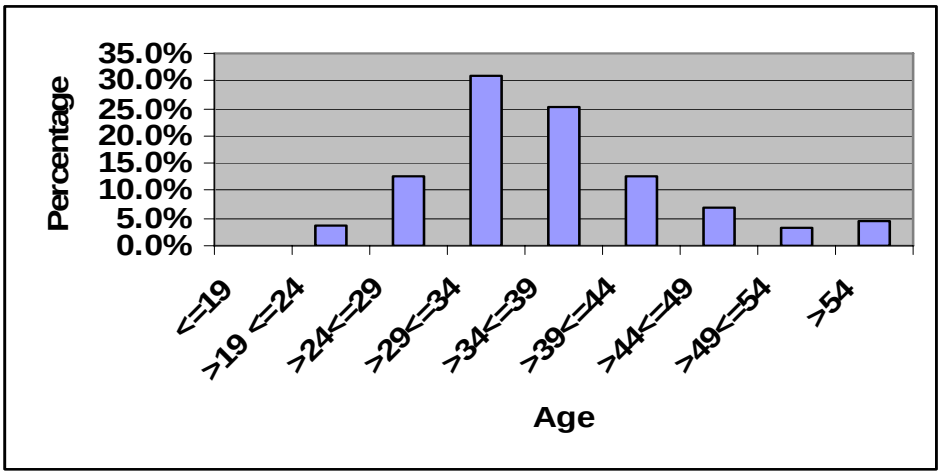
Sex	
Female	(n=96) 60.4%
Male	(n=63) 39.6%
Age	n=158
Mean *(sd)*	36.3 *(8.2)*
Employment status	
employed/self employed	(n=44) 36.1%
unemployed on grant	(n=7) 5.7%
unemployed not on grant	(n=71) 58%

A. Sex and Age

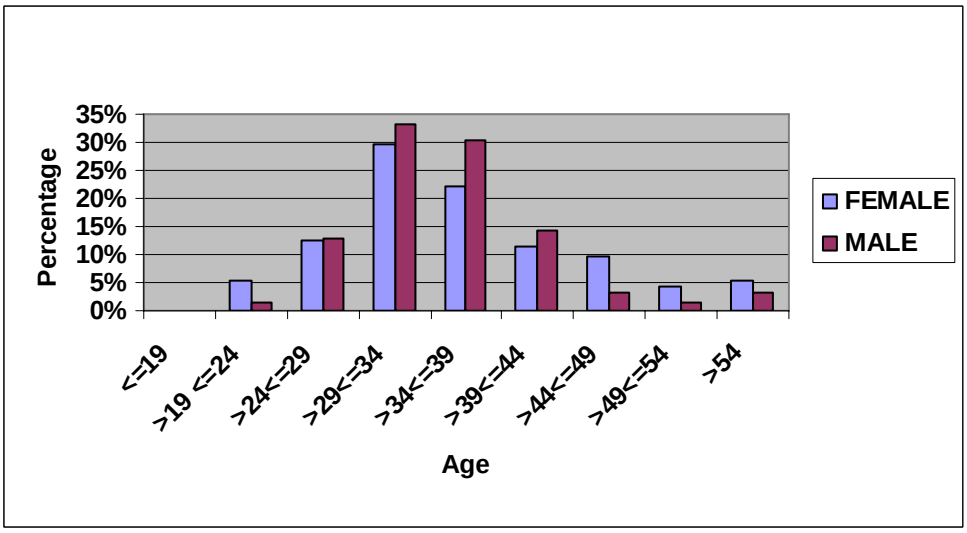
The majority of the patients were female (60.4%). The mean age in the sample was 36.3 years. Females had a slightly higher mean than males 36.8 years and 35.7years (p=0.432) respectively. The median age was 35 years for the group and for both sexes.

The peak age for both sexes was between 30 and 39 years. Less than a tenth of the patients were >=50 years. The female proportion was higher than the males in the 45 years and above age group. (*See Graphs 5.7 and 5.8).*

Graph 5.7: **Categorised Age (HJ)**



Graph 5 8: **Categorised Age by sex (HJ)**



B. Employment Status

More than a third (36.1%) was employed/self-employed. Just above half (58%) were unemployed and not on grant. A very small percentage of patients were on grant. Employment status by sex showed that a similar percentage of females and males were employed (35.5% vs. 37%). (*See Table 5.6)*

C. Race

The majority of the patients were African (95.4%).

D. Place of Residence

Just about a third (36.8%) of the patients came from region B, followed by about 17.6% and 16.5% from region D and F respectively. Almost a similar proportion (14.9%) came from outside the City of Johannesburg. The remainder came from the other regions of Johannesburg and the province.

5.3.2 Clinical Outcomes (HJ)

A. General

There was no information on PMTCT on the data set, therefore the not naïve were only those who were on any antiretroviral therapy before joining the roll-out programme. Very few patients had viral loads results recorded. None (0%) of the HJ patients have all their results recorded. 0% had all their viral load results recorded. only 4% had all their CD4 Counts available. The rest had one or two results available. More than three quarters of the patients (81.4%) were treatment **naïve**.

Type of treatment

More than three quarters (84%) of the **naïve** patients were on D4T, 3TC, EFV and about 10% on NVP, 3TC, D4T. Almost half (44.8%) of the **not naïve** patients were on D4T, 3TC, EFV followed by 24.1% on a PI or DDI containing combination. There was more than one type of PI available for these patients.

Opportunistic Infections: Occurrence of TB

Less than a tenth (7.7%) of the patients had TB prior to roll-out. The proportions were similar in both the **naïve** and **not naïve** (7.89% vs. 7.4%). Less than one percent (0.71%) was treated for TB after roll-out and they were all naïve.

General outcomes at 12 months

Defaulters, transfers, dead, and patients still on treatment.

The data set did not have enough information to describe this group.

There were 3 confirmed deaths within the first year of treatment i.e. (1.9%) of the sample. Another (5%) had no other results after roll-out. There could be defaulters, transfers and other deaths in this group.

B. Immunological Response

CD4 count: The mean CD4 count for the **combined** group increased from 109.2 cells/mm^3 at baseline to 295.3 cells/mm^3 at 12 months. The mean for the **naïve** was much lower than for the **combined** group 78.4 cells/mm^3 at baseline to 268.2 cells/mm^3at 12 months.

Just above a third (39.6%) of the **naïve** patients had a baseline CD4 count <= 50 cells/mm^3 as compared to (33.3%) in the **combined** group. Two thirds (64.2%) of the **naïve** patients had a baseline CD4 count <=100 cells/mm^3 as compared to (56.1%) in the **combined** group.

The median baseline in the >=50year old group was higher than in the <50 years 82 cells/mm^3 vs.62 cells/mm^3 (p=0.820).

Positive immunological response

This was measured as described for CHB.

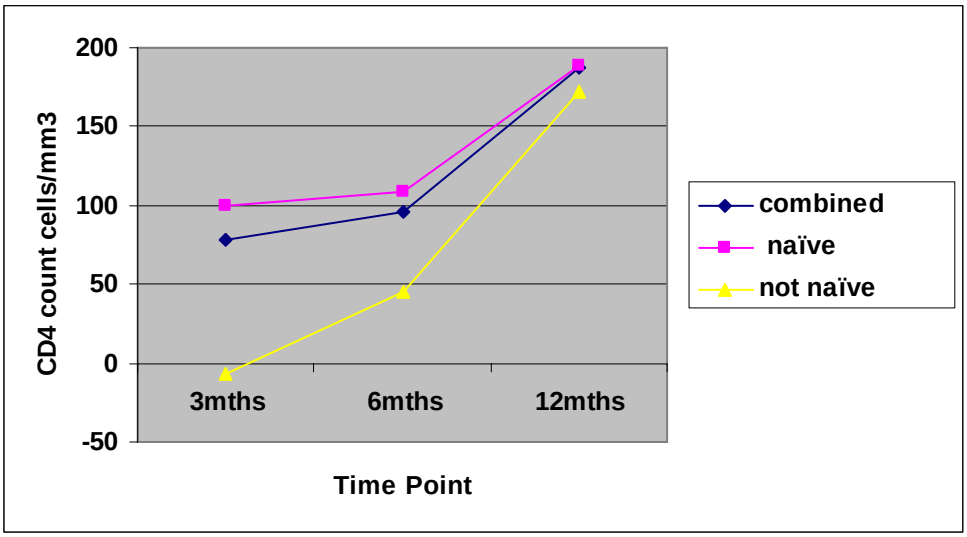
The mean CD4 count increase was higher in the **naïve** than in the **combined** group at all time points. The mean increase at 12 months for the **naive** was 188.8cell/mm^3 vs. 187.3cells/mm^3 for the **combined** group. (*See Table 5.7 and Graph 5.9).*

Table 5.7: **Immunological response and Virological response (HJ)**

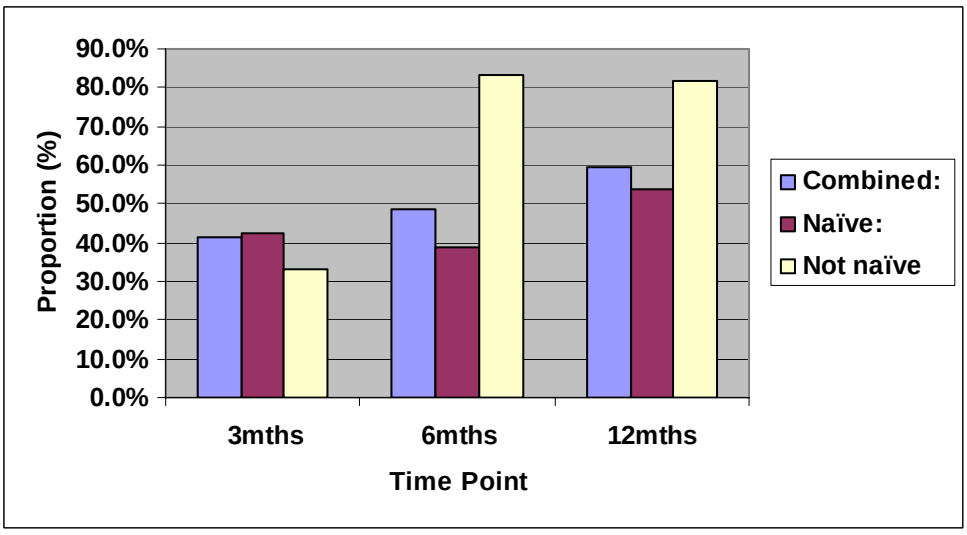
OUTCOME	NAIVE	NOT-NAIVE	COMBINED	pvalue
Mean Baseline CD4 count(cells/mm3)*(sd)*	(n=106) 78.4 *(58.5)*	(n=24) *232 (173.9)*	(n=) 109.2	0.000***
Mean CD4 count at 12 months *(sd)*	(n=52) 268.2 *(138)*	(n=11) 389.5 *(222)*	(n=63) 295.3 *(160.9)*	0.0218***
Mean CD4 count increase at 12 months(*sd)*	(n=43) 188.8 *(128.3)*	(n=11) 171.7 *(173,5)*	(n=55) 181.7 *(136.5)*	0.715
CD4 count >=200 cells/mm3 at 12 months	(n=52) 53.8%	(n=11) 81.8%	(n=64) 59.4%	0.087
Baseline Viral load (log 10 copies/ml)*(sd)*	(n=10) 4.97*(4.35)*	(n=12) 4.23*(4.77)*	(n=23) 4.78*(4.98)*	0.046
Viral load at 12 months(log 10)*(sd)*	(n=42) 3.60*(4.35)*	(n=9) 3.60*(4.05)*	(n=52) 3.60*(4.32)*	0.992
Viral load <=400(2.6 log10) at 12 months	(n=42) 95.2%	(n=9) 88.9%	(n=52) 94.2%	0.449

(i) 53.8% of the **naïve** had a CD4 count >=200 copies/mm^3 as compared to 59.4% for the **combined** group at 12 months (*see Graph.5.10)*

Graph 5.9: **Mean CD4 count increase (HJ)**



Graph 5.10: **CD4 count >=200cells/mm^3 (HJ)**



C. Virological response

(See Table 5.7 and Graph 5.11)

Viral load results were not available for most of the patients and for some if they were available they were not in the defined time frame. There were very small numbers for analysis and this masks the differences or similarities between **naïve** and **not naïve**.

The **naïve** started at a higher viral load mean than the not naïve (4.97 log 10 copies /ml vs.4.23 log 10copies /ml). At 12 months the two groups had similar viral load means 3.60 log 10 copies /ml). A similar pattern is reflected in their medians.

Positive virological Response

Viral <= 2.6 log 10 (400) copies /ml,

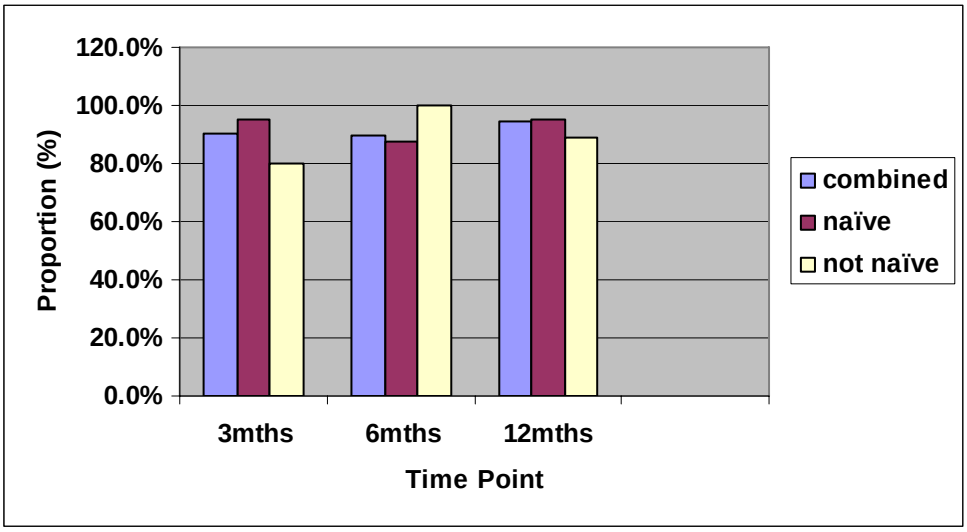
Positive response was assessed as for CHB

As from 3months 95 % of the **naïve** patients had mean viral load below or equal to 400 copies dropping to less than 90% at 6months and increasing to about 95% at 12 months,

The **naïve** had a higher proportion at 12 months below this cut off level than the **combined group**. The **naïve** had more than 95% <= to 2.6 log10 (400) copies/ml compared to the **combined group** which had 90%.

Using the 1.7 log10 (50) copies/ml, the **naïve** and the **combined group** had similar proportions of patients below or equal to 1.7 log10 (50) copies/ml at 12 months (40.5% vs. 40.4%)

Graph 5.11: **Virological response Viral Load <=400 copies (HJ***)*



5.3.3. Association between socio-demographic factors and response at 12 months

The HJ socio-demographic factors described above were also assessed for their association with immunological and virological response.

There was no association between all these factors and immunological response at 12months. Association with virological response was not undertaken because of insufficient observations. *(See Table 5.8) below*

Table 5.8: **Regression of socio-demographics and increase in CD4 xount at 12 months (HJ***)*

Variables	coefficient and Confidence intervals		
	coefficient	95% Cl	pvalue
Sex: Female	ref		
Sex: male	17.5	-57.5 - 92.4	0.641
age	0.18	-3.9 - 4.1	0.953
Employment: Employed	ref		
Employment: Unemployed on grant	-31.3	-210 - 147.5	0.726
Employment: unemployed not on grant	-52.5	-143.9 - 38.9	0.253

5.3.4. Association between Baseline CD4 Count, Baseline Viral Load and Response at 12months

There were insufficient observations for assessing association between baseline viral load and virological response.

Baseline CD4 count had an effect on immunological response. *(See Table 5.9).*

- ✓ *Baseline CD4 count effect*: the effect was the same as for CHB. For every unit increase in baseline CD4count there is a decrease in response. This was only seen at 6 months.

Table 5.9: **Regression of Baseline CD4 count, Baseline viral load and response at 12 months (HJ)**

Baseline CD4, Baseline Viral load and Immunological response at 12 months			
	Coefficient	95% CI	pvalue
Baseline CD4 count	-0.0060	-.4 - 0.34	0.974
Baseline viral load	-.0007	-.0030 - 0.0002	0.516
Baseline CD4, Baseline Viral load and Virological response at 12 months			
	Coefficient	95% CI	pvalue
Baseline CD4 count	0.00003	-.0005 - 0.0005	0.916
Baseline viral load	0.02	-.02 - 0.06	0.39

5.4. Comparisons between CHB and HJ

5.4.1 Socio-demographic factors

The differences and the similarities between these two groups are masked by the small number of patients in the **HJ** sample. Some analyses are not possible for the **HJ** data especially where viral load is needed.

A. Sex and Age

The female to male proportion was the same for the two samples (60% vs. 40%). The mean age for **HJ** was slightly higher than for **CHB** (36.3 vs.34.9 years) but statistically not significant (p= 0.579). The females in **HJ** had a higher mean age than the males as compared to **CHB** but this was not significant (p=0.433).

B. Race

The race proportions were similar for the two samples more than 95%of the patients were African.

C. Employment

HJ had a higher percentage of employed patients as compared to **CHB**, (36.1% vs.18.1%) (p=<0.001).At **HJ** only a small percentage (5.7%) was unemployed and on grant as compared to 51.9% at **CHB.**

D. Residential Area

HJ had about (15%) of its patients coming from outside the City of Johannesburg as compared to about (10%) for CHB.

5.4.2. Clinical Outcomes

A. CD4 count and immunological response

The mean baseline was lower at CHB and this was significant (p=0.013). CHB had higher proportion of patients with baseline CD4 count <=50cells/mm^3 (58.6 %) as compared to (39.6%) at HJ this was statistically significant (p=0.003). In the **naïve** the mean CD4 count increase was higher for HJ than CHB at all time points but this was not statistically significant p>0.05 at all time points.

B. Viral Loads

HJ had very few patients with viral load results which made it difficult to make meaningful comparisons between the two samples.

At 12 months in the **naïve** patients, HJ, (95%) had viral load <=2.6 log10 (400) copies/ml as compared to (86%) at CHB.

Chapter 6 Discussion

The results of the study are explained and compared with other studies.

There is no one way of monitoring and evaluating antiretroviral therapy. CD4 counts and viral load levels give an indication of response to therapy but at times they respond independently, once treatment has been commenced and thus they don't always give the same story.

6.1.1 General

There was minimum variability between the two study sites. They were located in different regions. The other significant differences between the two samples were the proportions of those employed, naive and the mean baseline CD4 count. These were all lower in the CHB sample. The rest of the comparable socio-demographic factors and clinical factors were similar. These differences did not have an impact on the immunological response. The immunological response was similar in the two samples at all time points. HJ had very few viral load results and these might not adequately represent the sample. HJ data on side effects was not adequate and was omitted from the analysis.

6.1.2 Type of treatment

The majority of the patients were on WHO recommended regimens for the resource limited settings i.e. NNRTI-containing HAART regimen. In terms of the regimens the 2-NRTI backbone should consist of zidovudine or stavudine plus lamivudine. The primary NNRTI to be used includes efavirenz or nevirapine.[43] All the **naïve** patients were on combinations of treatment containing the drugs mentioned above. More than 80% of the **naïve** were on D4T, 3TC, EFV combination.

6.2. Socio-demographic factors

6.2.1. Age and Sex

The mean age of patients on HAART at CHB and HJ were 34.9 years and 36.3 years respectively and this difference was not statistically significant (p=0.579), (the median for both samples was 35 years). The mean was similar to what was found in other African studies involving patients on HAART with the mean median from (34-38.8) years.[37, 38, 39, 27] The proportion of female patients on HAART was just above 60% in this study. This does not differ from other studies in South Africa and other African countries this ranged from (60-70%).[37, 38, 39, 40.] This reflects the distribution of the HIV epidemic in Africa. Age and sex distribution of the patients in the study reflect the HIV prevalence distribution by age and sex obtained in a number of studies in South Africa.[44, 45, 46] The >50 years age group constitute less than 10 % of the patients on roll-out.

Although the females had higher mean CD4 increase at all time points after initiation of HAART this was not statistically significant. (p=0.456) for CHB and (p=0.642) for HJ at 12 months.

Sex had no effect on virological response (p=0.338) at 12 months at CHB.

Age had an effect on immunological response. Age is negatively correlated to immunological response, as age increases immunological response is reduced, at CHB (p=0.001) at 12 months. This concurs with findings in a study done in the USA, among homosexual men but this was at 6 months.[47] Other studies confirmed the same finding.[48], [32] Age also has an impact on virological response as those who achieved undetectable viral load at 12 months (i.e.<=400copies/ml) were older than those with detectable viral loads (p=0.046) for CHB. Older age was associated with good virological response in other studies done in the developed countries, although different values were used as undetectable levels.[49, 50, 32, 51]

6.2.2. Race

Race comparisons were not possible because almost all patients were African above (95%) for both sites. The proportions that were still on therapy at 12 months i.e. (73 %) and the proportions that achieved undetectable viral loads at 6 months and 12 months i.e. (> 85%) for both sites are evident enough to show Africans do well on therapy. Their socio-economic status is likely to deter them from adhering to therapy thus resulting in reduced response. It is likely that findings would have been different if patients were sourcing their own antiretroviral drugs.

6.2.3. Marital Status at CHB

The majority of the patients were single (77%). Males had a higher proportion of the married than the females (21.8% vs.8.6%). There could be two explanations for this.

- ✓ Married women are not coming for HAART.
- ✓ The other explanation may be that the AIDS scenario in Gauteng might be different from the commonly accepted theory that the married women are more vulnerable.

The widowed who constituted 4.5% of the patients showed lower immunological response as compared to the married (p=0.05) at 12 months. One explanation could be lack of a social support system compounded by ill health and increased responsibilities in the family structure when the spouse dies.

6.2.4. Socio-economic status: Education, Employment and Residential area

Interestingly the majority of the patients in the CHB sample are educated. More than three quarters (79.1%) had attained Grade 8 and above level of education. In some studies done to find the correlation between socio-economic status and HIV in Africans in South Africa there was no discernible trend.[44] However HIV prevalence was significantly lower in those with tertiary as compared to those with no schooling or some schooling.[44.] This may explain

the low proportion of patients with tertiary education in the study i.e. (4.3%). Another explanation for such a small proportion in the roll-out programme is that, this group can afford private health care thus they are being treated elsewhere.

In contrast to popular belief that women are less educated, in this study there are more females in the high school and tertiary education groups (86% females as compared to 67% males) p=0.000.

This raises a few questions.

- ✓ Are we not missing those with little or without schooling in this life saving intervention? This group is poorly represented in this sample?
- ✓ Is the message regarding access to ARV getting across to this group especially females?

Education had no effect on both immunological and virological response to HAART, (p=0.299 and p=0.282) respectively at CHB.

The majority of the patients were not employed i.e. (81 % for CBH and 63% for HJ.) Employment had no impact on both immunological and virological responses (p=0.197 and p=0.496) respectively. However employment had a significant impact on baseline CD4 count. Baseline CD4 count was lower for those unemployed as compared to the employed (p=0.022). Those who were already receiving a grant had a slightly higher baseline CD4 count than those who were not on grant. These differences disappear after HAART is commenced.

The regions in which the two sites were located were socio-economically different. This is clearly reflected in the proportions of those employed (HJ 36% vs. CHB 18% p=<0.0001). The differences in baseline CD4 count between the two sites also reflect this socio-economic inequality. A very low CD4 count is a sign of AIDS illness. AIDS current or

previous was associated with current or recent poverty.[52] The majority of patients on this study came from areas with a high number of informal settlements of Soweto and Orange Farm and according to the Nelson Mandela Study, persons in these settlements have by far the highest HIV prevalence (25.8%) compared with the national value of (16.9%).[44]

None of these socio-economic differences reflects on the immunological and virological responses to treatment at either site. This is a clear indication that the availability of continuous free comprehensive HIV care eradicates the baseline inequalities. The fact that all patients were receiving free comprehensive treatment, the real socio economic status which inhibits access to therapy and promotes non-adherence to treatment is eradicated or masked. In addition to free treatment, access to disability grants improves the socio-economic status of the patients. These grants play an important role in mitigating the impact of HIV/AIDS.[53] They reduce inequality and decrease the prevalence, depth and severity of poverty in affected households.[53]

6.3 Clinical outcomes

6.3.1. General

Clinical outcomes like the occurrence of death, opportunistic infections and malignancies are important indicators of disease progression and response to treatment.

Mean CD4 increase and proportions of undetectable viral load are some of the important indicators needed for monitoring and evaluation of the programme.[18]

6.3.2. CD4 count: Baseline and response

It is physiologically known that relative to males, females have a higher CD4 count, whether HIV positive or negative. This has been found to have no functional significance.[54] The female mean CD4 count at all time points after the start of HAART were higher than for the males in both **combined** and **naïve** analysis but this was statistically not significant. There was no gender difference in virological and immunological responses to therapy. This was similar to findings in a EuroSIDA study.[36]

The naïve >=50 year age group had a baseline CD4 count higher than the <50 years age group (81cells/ mm^3. vs. 57 cells/mm^3). This concurs with earlier studies done in developed countries, older naïve patients i.e. those >= 50years tend to have a higher baseline median CD4 count than those less than 50 years although this age group is known to have reduced CD4 cell recovery.[48,49]

In the study (CHB data), a higher proportion of patients who died were in the group with a baseline CD4 count of <=50cells/mm^3 as compared to those who had a baseline CD4 count >50cells/ mm^3 (p=0.001). Studies done earlier showed that the **naïve** patients with a baseline CD4 count less than 50 cells/ mm^3, were associated with an increased progression of clinical disease.[55, 41]

There was no association between those who had TB prior to roll-out and the CD4 count <=50 cells/mm^3, neither was it associated with the occurrence of TB after commencing HAART.

This study showed that both sites, just less than (60%) of the patients achieved a CD4 count of >=200 cells/mm^3 at 12 months. This is lower than what another site in a South African rural setting revealed. This site in the Eastern Cape had (75%) of the patients achieving a CD4 count >=200cells/mm^3.[56] The cause for such a difference could be the differences in baseline CD4 counts between the two sites.

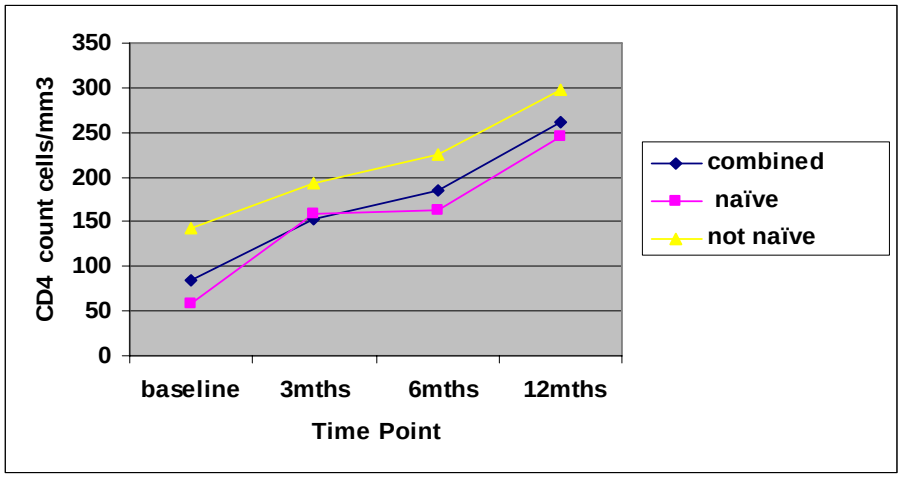
Almost all the **naïve** patients in the CHB study have a baseline CD4 count of less than 200cells/mm^3. In this sample no patients with WHO stage III and IV disease who had a CD4 count of greater than 200cells/mm^3 were enrolled. A study done in Cape Town showed that individuals with stage III and IV disease regardless of their CD4 count had more AIDS events and deaths than those with stage I and II disease and a CD4 count less than 200 cells/ul.[57] Is this group not being missed in the programme?

The median CD4 count increases were comparable to other studies.[47, 43, 50, 27] In a study done in the USA the median increase inCD4 count of 160 cells/ml was recorded for the **naïve** patients at 12 months this is similar to our findings.[43] Better short term and long term responses were seen in the **naïve** patients than the **not naïve.**[47] This concurs with findings in this study, the **naïve** had better response than the **not naïve** at all time points. At 12 months the mean CD4 count increase (CHB data) was 177.7cells/mm^3 for the **naïve** and 152.2cells/mm^3 for the **not naive**. The short term (about 3 months) increase in the **naïve** (American European study) of 82cells/mm^3 was comparable to findings in this study, CHB (93.3cells/mm^3) and HJ (100cells/mm^3) at three months.[47]

In this study, there was reduced immunological response with increase in baseline CD4count p=0.048.(*See Table 5.5)*. In the USA the strongest responses in CD4 counts occurred among those who began with the lowest CD4counts.[21]

There is a steep improvement in the first phase up to week 12; the second phase beginning after week 12 has minimal increase in CD4 count which is then followed by a slightly steep rise in the third phase. The graph is therefore triphasic. (*See Graph 6)*The CD4 count rise in the **naïve** typically exhibits a biphasic pattern; the second phase begins after week 12.[58] The difference between this study graph and the typical graph could be due to the much lower baseline CD4 count in this study.

Graph 6: Mean CD4 count



6.3.2 Viral load response

In this study more than (85%) of patients at both sites had undetectable viral load (<=400copies/ml) at 6 and 12 months. The proportion of patients with undetectable viral load at 6 months and 12 months is comparable and in other cases better than what has been found in other African countries.[18, 43, 27] This is similar to what has been found in the developed world even under some research settings.[59] In a collaborative analysis of

European and North American patients on antiretroviral therapy, (83%) of the patients in 2002-2003 had achieved an HIV-RNA (viral load) of 500 copies /ml by 6 months or less.[59] In this study, virological response results compare favourably and even show better results than other South African ARV sites.[60, 56] At 12 months the proportion of undetectable viral load (>85%) was still high as compared to results from Lusikisiki, which had (78%) undetectable rate in hospital settings.[56] One study confirmed that availability of free medication had a significant impact on the mean proportion of subjects who had positive virological response.[18] The provision of free antiretroviral therapy has been found to increase the proportions by between (29%-31%) at 6 months and 12 months.[18]

There might be variations between sites in South Africa, depending on the proportions of the **naïve** and **not naïve** patients. Treatment **naive** patients are more likely to reach undetectable levels (<400 copies/ml) than the **not naïve**.[27, 47]
The proportion was lower and progressively going down over the first year for the **not naïve** which raises the question of treatment failure. There are two main reasons to explain this failure,

- ✓ Is there emerging resistance already?
- ✓ Is it a question of adherence?

Patients are expected to achieve undetectable viral load and maintain it after 6 months of HAART treatment.[23] This appears to be true in the CHB data as there is an obvious increase from baseline to 3 months then to 6 months. From 6 months to 12 months this proportion appears to remain the same or slightly lower than at 6 months.
Baseline viral load was found to predict virological success at 12 weeks and 24 weeks.[61] In this study, baseline viral load had no effect on virological response at 12 months, (p=0.389). Unfortunately data was only available from one site, CHB.

6.3.3. Opportunistic Infections: Occurrence of TB

TB is the leading cause of mortality in the HIV infected and the TB epidemic is being driven by HIV.[62] TB in a patient on ARVs poses a lot of challenges including adherence due to the increased pill burden.[37] In two studies done in Africa (5%) of patients had to change treatment or withdraw from the study as a result of tuberculosis.[43**] In the CHB study more than half of the **naïve** patients who died had TB prior to roll-out although this was not statistically significant when compared to those who did not have TB (p=0.276).

6.3.4. Side Effects

The proportion of patients experiencing side effects at CHB was low (6%) but this could be an underestimation as those who experienced side effects which did not require change of treatment were not included in the data set. The commonly reported and confirmed side effects were peripheral neuropathy, lactic acidosis, anemia and lipodystrophy. Two studies in Malawi also recorded low levels of side effects.[39, 40] One of the Malawian studies recorded adverse events as low a 3.7%.[39] However in other African studies adverse events occurred in 14.3%-80.2%.[43] Some of these were in research settings.

6.3.5. Treatment change

The major reason for changing treatment was treatment failure. There are two explanations for this.

(i) Emerging drug resistance especially in the **not naïve** patients.

(ii) Patients not adhering to treatment.

Resistance to both NNRTIs and NRTIs has been documented in Africa.[27, 43] These are the drugs used as first line treatment.

6.3.6. Deaths and retention of patients

In this study (61.7%) of deaths occurred in the first 3 months of treatment. A Malawian study in a rural setting showed that a similar proportion of deaths (61%) occurred in the first three months of treatment.[39] In a Malawian study (12.6 %) died during the first year of HAART.[39] This is lower than what was found in this study which had (18.9%) deaths in the first 12 months. At 12 months nearly three quarters (74 %) of the patients in this study (CHB) were still on treatment. This is similar to findings in other African countries, (79.8%)[43] and (73%) in Malawi were still on treatment at 12 months.

In this study HIV/AIDS was not the only cause of death in these patients. It is difficult to ascertain the cause of death in those who die at home. Road traffic accidents, chronic conditions e.g. diabetes, cardiopulmonary disorders contributed to these deaths.

CHAPTER 7 CONCLUSION and RECOMMENDATIONS

7.1 CONCLUSION

1. The results from this study show that there is positive virological and immunological response to HAART in Gauteng ARV roll-out programme despite the low socio economic status of the majority of the patients.

There is positive response on this large scale program which is comparable to what has been found in the developed world under research settings.

2. The provision of free antiretroviral drugs and access to the disability grant has assisted in mitigating the effects of HIV/ AIDS on the socio-economically disadvantaged.

3. Provision of HAART is taking the resource limited countries a step further in controlling the TB pandemic as the number of TB cases fall in the HAART treated patients.

4. Age may affect immunological response. Age is the only socio-demographic factor which has a significant impact on immunological response to therapy. The elderly in this programme will need special attention

5. The widowed are a vulnerable group they did not respond as well as the single, married or the divorced patients. There could be other psychosocial factors affecting the response of the older people and widows that need further research

6. The group with no schooling is not represented in this sample, the question is whether the HIV/AIDS prevention and treatment message is accessible for this group.

7.2 RECOMMENDATIONS

1. There is a lot of clinical data for research purposes at CHB HIV Clinic This data cannot be accessed easily without going back to individual patient files.

Investing in proper data capturing methods will make an important contribution to research for Monitoring and Evaluation purposes for the benefit of the Gauteng Health Department. HJ already has a computerised HIV data set, it is necessary to have comparable data sets for the whole province. This will make comparisons and combined analysis possible and easier.

2. Further continuous research is needed as the ARV programme progresses to assess the sustainability of the outcomes confirmed by this study at 12months.

3. Treatment failures have been observed, although still at low levels, further research is required to monitor closely adherence and the emergence of resistance.

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