August 2007

Large Scale Implementation of Antiretroviral Therapy: Early Results from Faith-based Clinics in South Africa.

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Abstract

International funding and a multi-sectored response have resulted in a rapid expansion of antiretroviral therapy in resource-poor countries. In sub-Saharan Africa faith-based organisations have played a large role in expanding access to ART. This is the first combined report of ART outcomes from the programmes of the Catholic Relief Services (CRS), International Youth Development (IYD) and the Southern African Catholic Bishops' Conference (SACBC) in South Africa. Data was collected from January 2003 to October 2006 from sites providing ART services in rural, peri-urban and mining communities throughout South Africa. Standardised data collection forms were used to collate demographic, clinical and laboratory data from all individuals accessing CRS, IYD and SACBC ART services. A total of 14,464 patient records from 28 sites distributed through 7 provinces of South Africa were available for analysis. Females made up 68 percent of the cohort. Males presented with more advanced disease, 40 percent of males presented with CD4 counts less than 100 cells/ml compared with 33 percent of females. The median CD4 cell count at entry was 159 cells/µl which increased by an approximate 150 cells after 12 months of ART. The median viral load at baseline was 4.22 $\log_{10}$ copies/ml with a subsequent 2 $\log_{10}$ decline within 6 months of starting on ART. Eighty percent of individuals on treatment achieved viral loads suppressed to less than 400 copies/ml. This faith-based network of clinics throughout the country has provided ART to approximately 7 percent of those presently on therapy in South Africa. Despite a rapid scale up, virologic and immunological responses to ART are comparable to those reported from other programmes in the region. Faith-based organisations can efficiently provide ART services in a wide variety of poorly serviced areas of South African settings and significantly compliment the national ART programme.

1. Introduction

International efforts to increase access to ART in resource-poor settings have been led by the World Health and UNAIDS[1]. By December 2005, unprecedented funding from the Global Fund to Fight AIDS, Tuberculosis and Malaria[2] and the President's Emergency Plan for AIDS Relief had supported 641,000 individuals in 65 countries of Latin America, Africa, Asia and Eastern Europe[3].

The HIV epidemic has grown to 5.5 million infected[1] and borne a heavy toll in South Africa with a resultant life expectancy in 2004 estimated to be 48.5 years for males and 52.7 years for females and an infant mortality rate of 56 per 1000 live births (Dorrington, Bradshaw, Johnson & Budlender, 2004). In 2010 there will be an estimated 2 million maternal orphans under the age of 18 years of which 1.5 million will be AIDS orphans. Without antiretroviral therapy (ART) the estimated annual number of AIDS related deaths will increase to 495,000 by 2010[4].

There are over 600,000 individuals in immediate need of ART with an estimated accumulated total of 1.9 million deaths related to AIDS up to 2006[1]. The scale of the numbers requiring care necessitates a multi-sectorial response to HIV care and treatment. To date in South Africa the outcomes of ARV treatment programmes have been published from the NGO, Government and private sectors (Bekker, Orrell, Reader, Cohen, Matoki, Martell, Abdulla & Wood, 2003; Coetzee, Hildebrand, Boulle, Martens, Louis, Labatala, Reuter, Ntwane & Goemare, 2004; Badri, Bekker, Orrell, Pitt, Cilliers & Wood, 2004; Bekker, Myer, Orrell & Wood, 2006; Charalambous, Grant, Day, Pemba, Chaisson, Kruger, Martin, Wood, Brink & Churchyard, 2007). By May 2006 a total of 200,000 individuals were estimated to be receiving ART in South Africa of which 110,000 were receiving treatment in the public sector and 90,000 in the non-government and private sectors[5].

The faith-based organisations, Catholic Relief Services, International Youth Development and the Southern African Catholic Bishops' Conference, initiated an HIV care and treatment programme in January 2003. With support from the Department of Health and PEPFAR this has become one of the largest ARV treatment programmes in sub-Saharan Africa with over 15,000 patients recruited by August 2006. The demographic characteristics at recruitment and treatment outcomes of this large South African programme are presented.

2. Methods

2.1. Treatment Sites

The Catholic Relief Services HIV care and treatment clinics are widely distributed throughout South Africa. There are 28 reporting sites in seven provinces; Eastern Cape, Gauteng, Kwa-Zulu Natal, Limpopo, Mpumalanga, North West, and Free State provinces (Figure 1). There is considerable diversity of the sites which include a 200 bed hospital serving the Western district of metropolitan Durban, 7 rural primary health care clinics, 9 clinics with in-patient hospice facilities and 5 with residential facilities for abandoned HIV-positive orphans. Population groups served include children and adults from indigent rural, peri-urban squatter settlements, and mining communities. Each typical site employs a doctor, one or two nurses, counsellors and adherence monitors. Treatment protocols closely follow World Health[6] and South African Department of Health National ART Guidelines[7].

Figure 1: Treatment sites Catholic Relief Services and Southern African Catholic Bishops' Conference

2.2. Patient Monitoring

After pre- and post-test counselling HIV-seropositive individuals routinely have initial baseline blood taken for CD4-cell count, full blood count and HI-viral load performed at an accredited laboratory (Toga Laboratories, Edenvale, Gauteng or the National Health Laboratory Services of Kwa-Zulu Natal). Individuals meeting the Department of Health ART criteria for therapy (AIDS or a CD4 cell count >200 cells/ml) are commenced on standard scheduled ART with stavudine, lamivudine and efavirenz in the absence of specific contraindications for the use of these medications. Adherence education is provided both prior to and during ART. Routine monitoring with CD4 cell count, full blood count and viral load is performed 6 monthly during ART.

2.3. Data Collection

Each site maintains standardised data reporting forms which are entered locally into Microsoft Excel® electronic spread sheets. Demographic parameters include date of birth or age and gender. Clinical parameters include HIV clinical stage, functional status, pregnancy status, weight and prior ART exposure. Follow up data include CD4 cell counts and viral load estimations at initiation of ART and thereafter at 2 months, 3 months, 6 months, 12 months, 18 months and 24 months. After stripping of personal identifiers all the site data is collated centrally into a Microsoft Access® database for further statistical analysis using Statistica™ version7

3. Results

A total of 14,464 records of patients enrolled into the programme between January 2003 and June 2006 were made available for analysis. The size of each site varies considerably, with four clinics having more than a thousand clients each and together contributing over 40 percent of total programme numbers. In contrast there are four small clinics reporting less than 100 clients and 20 clinics with between 100 and 1000

clients. The number of patient records received from each of the individual reporting sites is shown in Table 1.

Table 1: Number of patients per site

Site name	Patients enrolled
Blessed Gerard	286
Centocow	446
Emmanual Haven	497
Good Shepherd Middelburg	184
Great Kei Komga 1	341
Great Kei Moiplaas	79
Hamburg	263
Hamburg Lists	307
Hamburg Nora	25
Hamburg Umta Wewlanga	20
Hamburg Wesley	17
Holy Cross	183
Kurisani- Holy Family	395
Kurisani- St Joseph's Clinic	296
Masibamisane	570
Mtubatuba	1410
Nazareth House	471
Newcastle	516
Orange Farm	193
Sinosizo	970
Sizanani	630
Sophumelela	1754
St Annes	196
St Francis	967
St Francis-Reigerpark	129
St Mary's	1477
Tapologo	1242
Winterveldt	600

3.1. Patient Enrolment

Patient enrolment per calendar month is shown in Figure 2. Patient enrolment commenced with relatively small numbers in January 2003 and remained at low levels through to January 2004 when 215 patients were on the programme. Numbers increased to 1478 by October 2004 and from November 2004 there was a steep linear growth in programme numbers to over 12,000 clients by January 2006. The subsequent slower growth in numbers during 2006 may represent delayed entry of data into the database. This trend will be made clear when 2006-7 data becomes available.

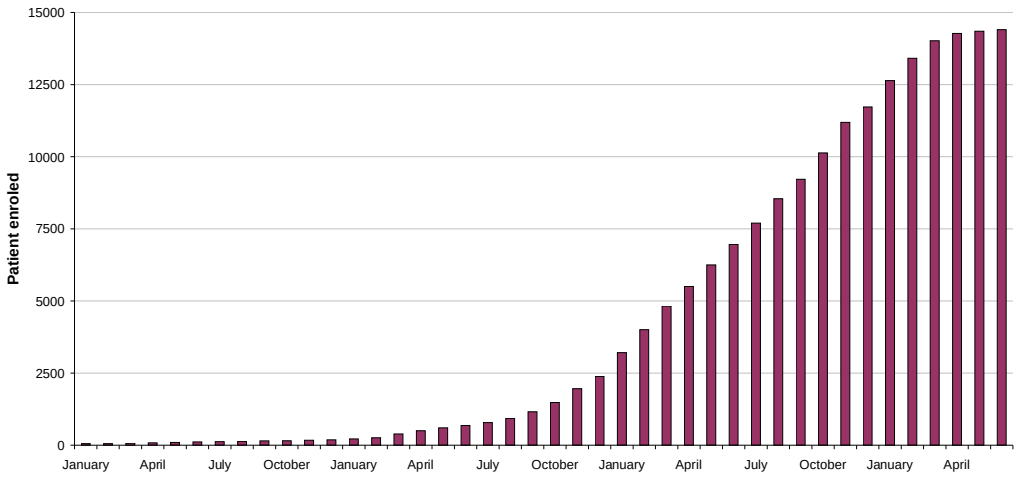

Figure 2: Patient enrolment from January 2004 till April 2007

3.2. Age at Entry to the Programme

The distribution of ages of patients entering the programme is shown in Figure 3, which shows a clear bimodal distribution compatible with two distinct modes of HIV acquisition. The 0-14 years probably represents survivors of maternal to child HIV transmission from 1992 onwards and the 14-80 years is compatible with sexually transmitted infection.

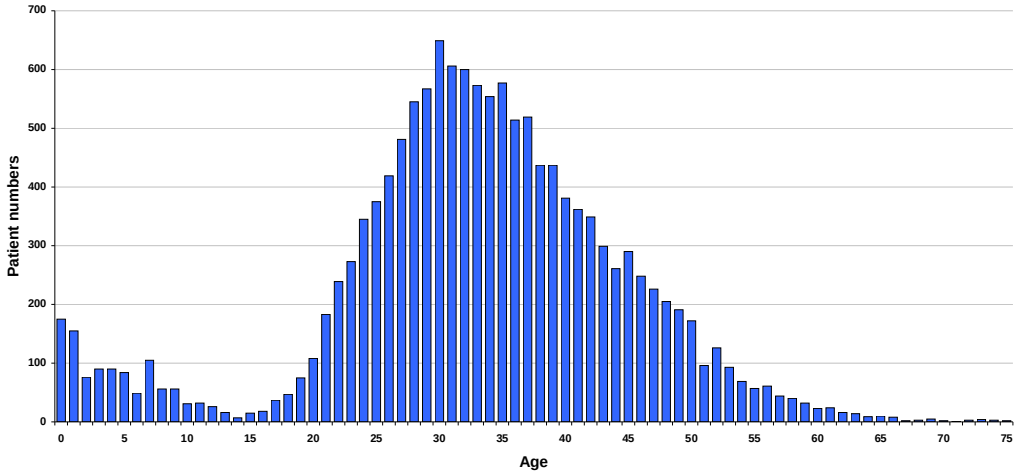

Figure 3: Age at entry to the programme

3.3. Gender at Entry to the Programme

The gender make up of the cohort is shown in Figure 4. Females represent 68 percent and males 32 percent of the recruited cohort. The lower recruitment in males compared to females may represent in part, lower health seeking behaviour amongst males. The 0-14 age cohort has similar numbers of both males and females, a finding which is consistent with this population representing survivors of maternal to child transmission. In contrast the adult gender distribution is very asymmetric. The recruitment is not just lower in males than females but there is a markedly skewed age distribution, with a peak in female presentations at 30 years of age and with a much higher initial female preponderance in the 15-25 years. The age of presentation in males is older with a peak between 30 and 40 years of age. The higher recruitment among younger females may represent a true higher prevalence due to earlier sexual debut in females compared to males. Females constituted the majority of recruitments between the ages of 15 and 20 years and this is an indication that young female adolescents are an important target group for HIV prevention education programmes. Above the age of 45 years there is an equal representation of both genders.

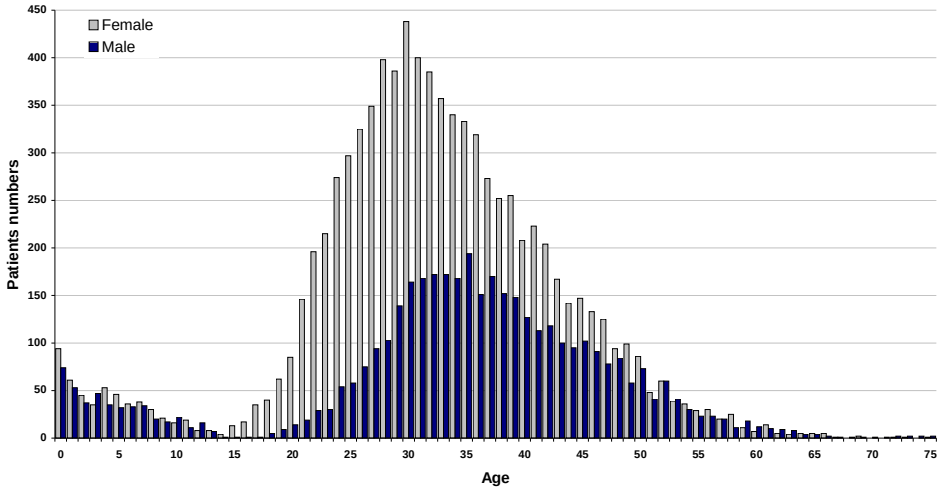

Figure 4: Gender at entry to the programme

3.4. CD4 cell count at entry to the programme

The median CD4 cell count of patients accessing the programme was 159 cells per ml. Although a median CD4 cell count of 159 appears low it is much higher than that of patients accessing treatment programmes elsewhere in Africa. A greater proportion of individuals presenting at higher CD4 cell counts is a probable measure of the quality of counselling and testing programme and may be improved with greater access to CD4 cell counts and an increased willingness to be aware of HIV status when benefits of early care are perceived to outweigh stigma.

The number and distribution of CD4 count strata of all patients who entered the programme is shown in Figure 5. Patients accessing the programme predominantly had low CD4 cell counts with 56 percent of individuals presenting with a CD4 cell count less than 200 cells/ml. Approximately 30 percent present with a CD4 cell count greater than 300 cells/ul and 16 percent with CD4 cell counts greater than 500 cells/ml. Well over half the population would therefore qualify for antiretroviral therapy on the basis of low CD4 cell count alone. Figure 6 shows the proportion of males and females contributing to each CD4 cell count strata. The numbers of individuals of both genders increases markedly in the lower CD4 cell strata.

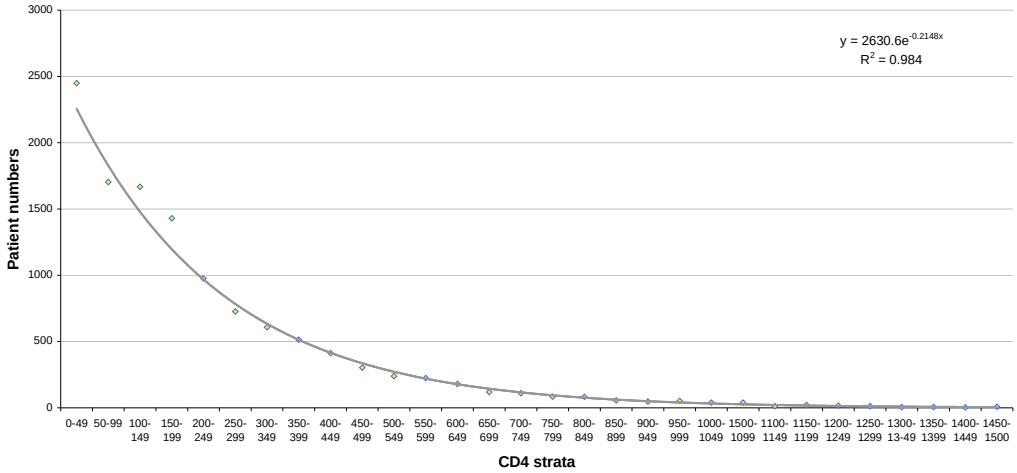

Figure 5: CD4 cell count at entry to the programme

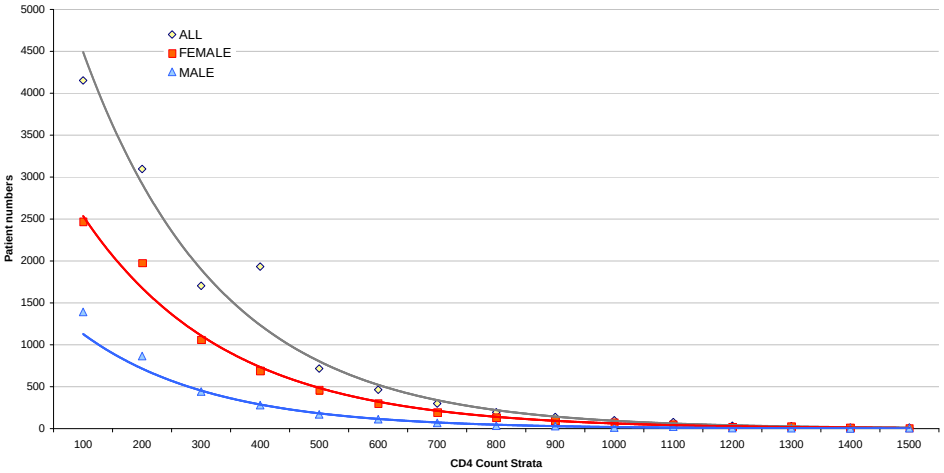

Figure 6: Proportion of males and females and CD4 cell count

The proportion of each gender presented in each of the CD4 strata is shown in Figure 7. Forty percent of males had CD4 cell counts less than 100 cells/ml at their initial visit and a further 25 percent were between 100 and 200 cells/ml. The corresponding values for females were 33 percent and 26 percent respectively. It appears that females are accessing the care programme at an earlier stage in their HIV illness than males.

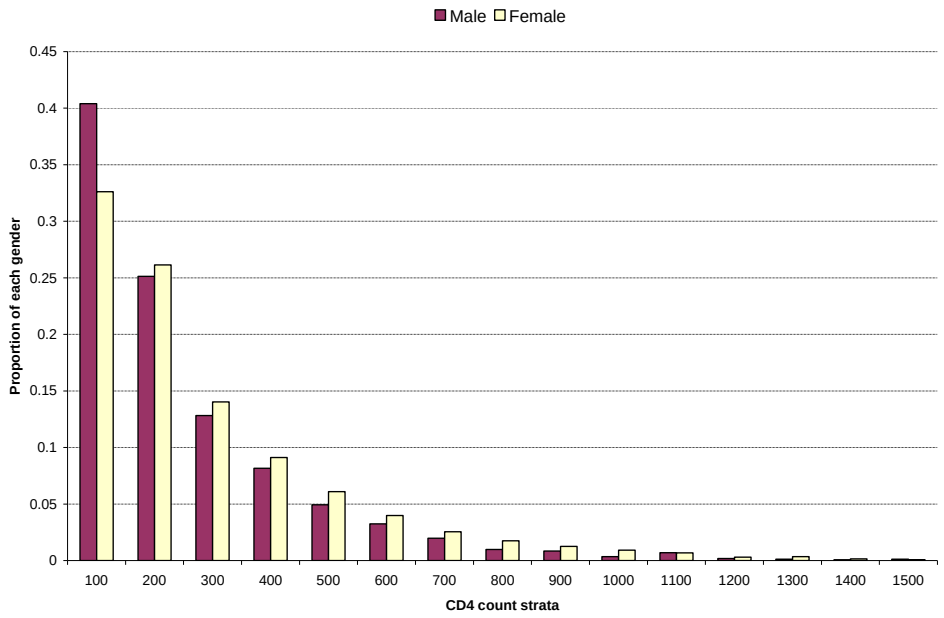

Figure 7: Proportion of males and females and CD4 count strata

3.5. On Treatment Numbers

There were very few patients receiving antiretroviral therapy prior to January 2004 with an increase in numbers to over 1000 on ART by November 2004 and a subsequent rapid recruitment to a total of 8214 patients. The cumulative numbers on ART are shown in Figure 8.

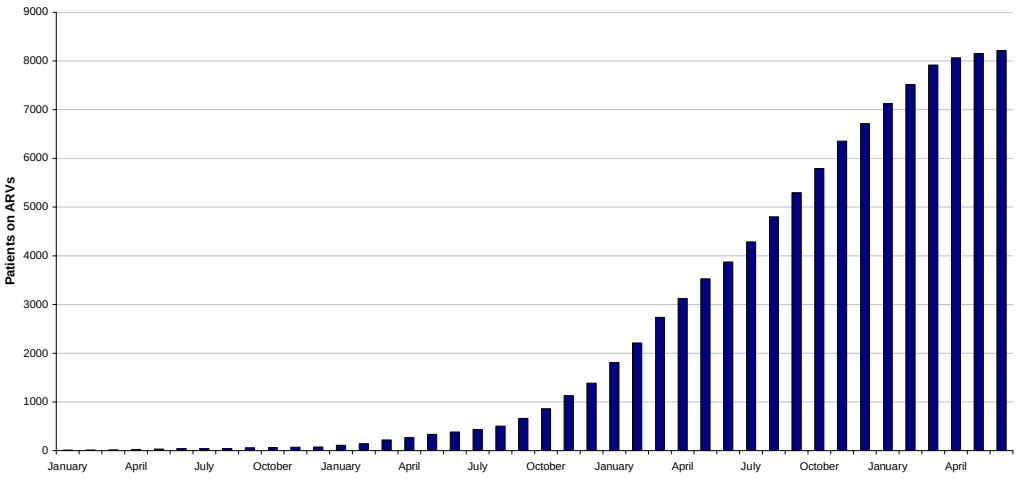

Figure 8: Patients on ARV

3.6. On Treatment Numbers as Proportion of Enrolled

The proportion of patients entering the programme that start on antiretroviral therapy has increased from 23 percent in January 2003, to 52 percent in January 2004 and has since January 2005 remained at an approximate 57 percent (see Figure 9).

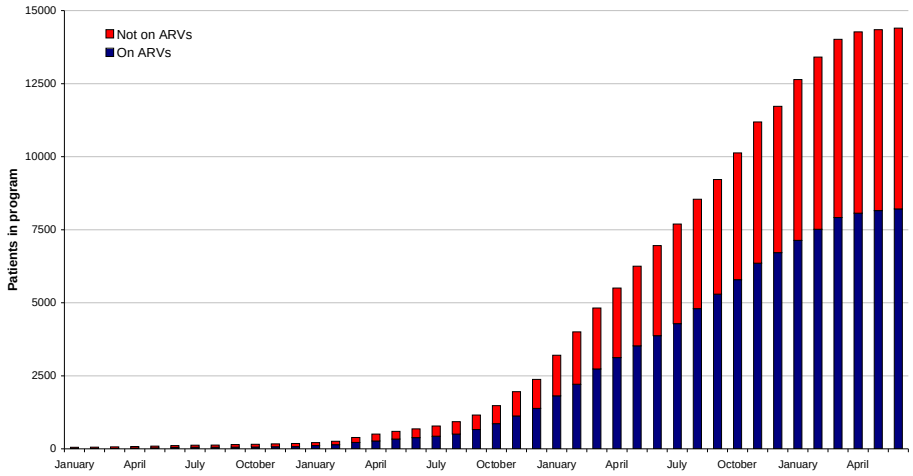

Figure 9: Patients in the programme

3.7. CD4 Distribution at ART Initiation

CD4 count at ART initiation is largely dependent on the application of existing ART treatment guidelines. The median CD4 cell count at ART commencement was 117 cells/ml with 78 percent of patients initiating ART at an initial CD4 count of less than 200 cells/ml. The distribution of patients in each CD4 cell strata at ART commencement is shown in Figure 10.

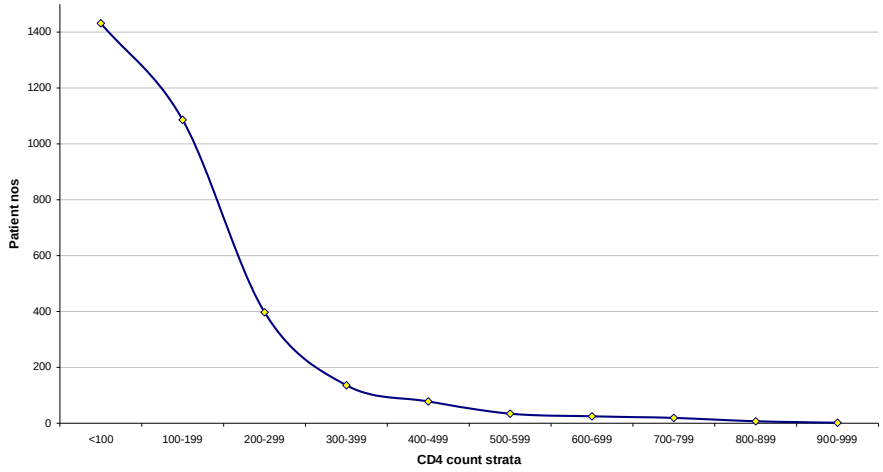

Figure 10: Distribution of patients in CD4 count strata

3.8. Viral Load Distribution

Baseline viral load estimations were available for 3497 individuals and the distribution of values is shown in Figure 11. Of these the most frequent value (mode) of the $\log_{10}$ viral load at time of ART commencement was 5.0 $\log_{10}$ which is equivalent to 100,000 copies/ml. However 12 percent of patients (n=425) started ART with a viral load less than 50 copies/ml. These individuals are shown as the “rising tail” at the right hand end of the graph in Figure 11. This is a very unusual distribution of viral load which does not appear to be part of the majority distribution. This could be a real phenomenon or could result from either a failure of the laboratory assay, or misclassification of patients as drug-naïve at a time when they had already commenced ARV treatment.

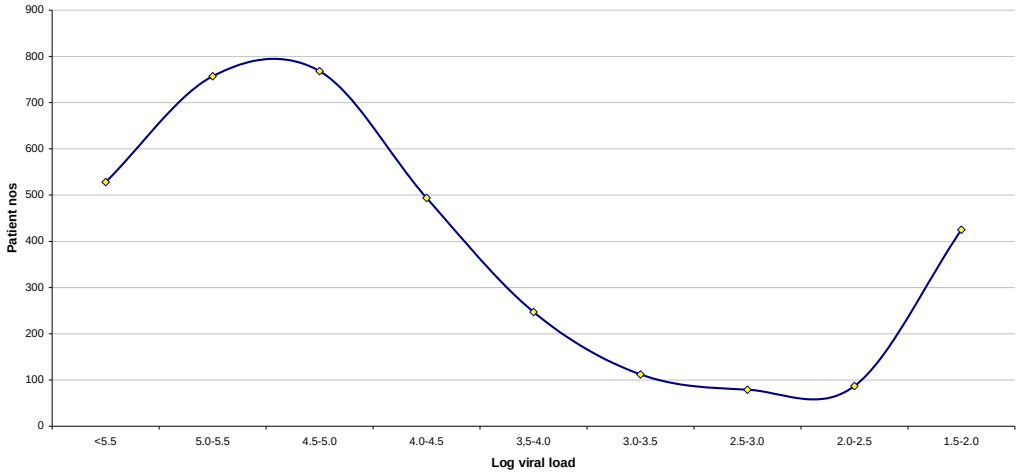

Figure 11: Viral load distribution

3.9. ART Regimens

The initial ART regimens utilised within the programme are shown in Figure 12. The majority (88%) of individuals were commenced on triple ART regimens. The mono and dual regimens recorded may represent the use of non-triple regimens for maternal to child prevention. Stavudine was used as the initial thymidine nucleoside reverse-transcriptase inhibitor (NRTI) in 96 percent of patients with the more expensive thymidine NRTI AZT (zidovudine) used in only 4 percent of cases. The most frequently prescribed non-nucleoside reverse-transcriptase inhibitor (NNRTI) was efavirenz which was initiated in 88 percent of individuals. Nevirapine a much cheaper NNRTI was prescribed in only 2 percent of regimens.

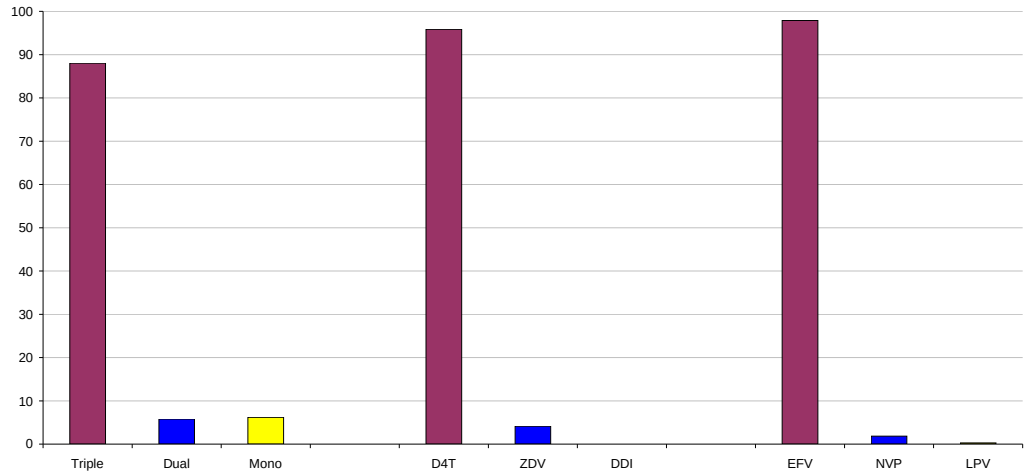

Figure 12: Distribution of ART regimes utilised

3.10. CD4 Cell Response

Of the 3239 patients starting ART, CD4 cell count results were available for 407, 765, 1383, 833, 208 and 66 patients at 2, 3, 6, 12, 18 and 24 month time points respectively. The change in median CD4 cell count of the evaluated patients at each time point is shown in Figure 13. The median CD4 cell count at baseline was 117 cells/ml, which increased linearly at a rate of approximately 10 cells per month up to 278 cells/ml at 18 months. The median CD4 cell count at 24 months is based on only 66 laboratory estimations and will be more accurately evaluated in the 2007 result analysis.

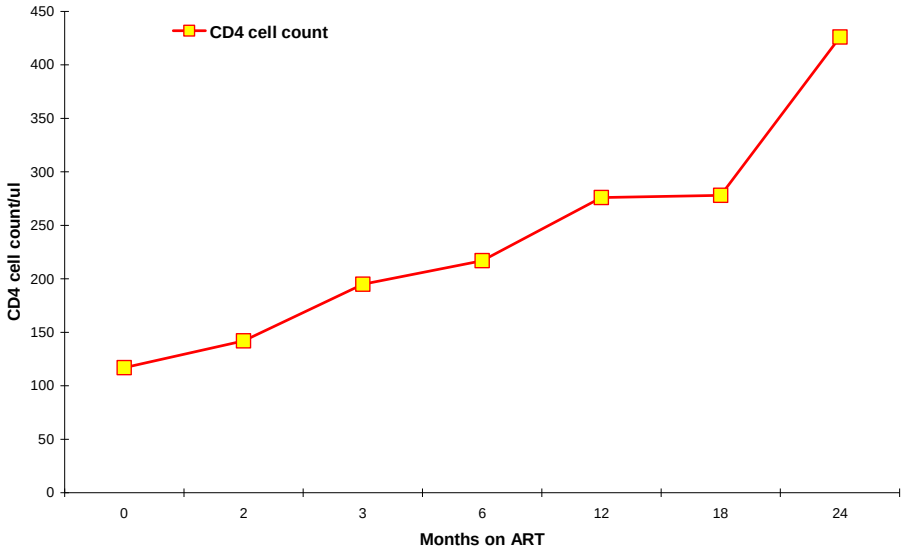

Figure 13: Change in CD4 cell count over time

3.11. Virological Response

The HI viral load at commencement of ART was 4.22 $\log_{10}$ copies/ml which reduced rapidly to 2,53 $\log_{10}$ copies after 2 months of treatment, followed by a slower but continued decline to less than 2.1 $\log_{10}$ copies after 12 months. The decline in $\log_{10}$ viral load together with the proportion of patients < 400 copies/ml at each time point are shown in Figure 14. More than 80 percent of patients evaluated at each time point were virally suppressed to levels less than 400 copies per ml. This proportion of suppressed patients would fulfil the ART programme effectiveness target as outlined in the 2007-2011 HIV and AIDS Strategic Plan for South Africa.

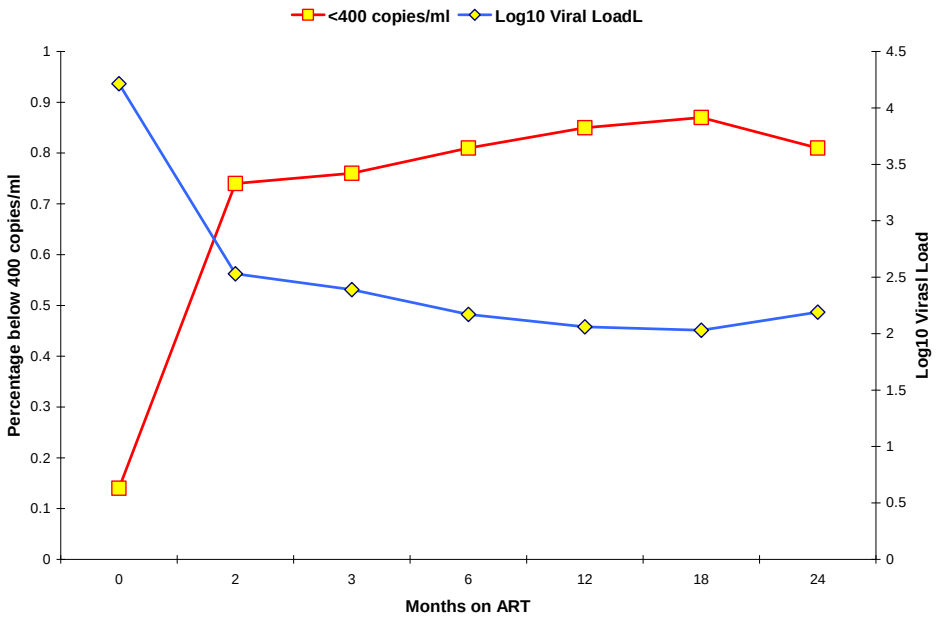

Figure 14: Decline in log_{10} viral load and proportion of patients < 400 copies/ml over time

4. Discussion

The programme is one of the largest in the world and has achieved a massive increase in number of patients in both HIV care and commencement of ART between January 2003 and September 2006. This programme presently provides approximately 7 percent of the ART access within South Africa.

The age and gender distribution of individuals at entry to this programme indicate two distinct groups of individuals accessing HIV care; those under 15 years of age in whom both genders are approximately equally represented which are probably survivors of maternal to child transmission (MTCT) and a second group over the age of 15 years with a markedly higher female preponderance at younger ages, that represents a population with recent sexually acquired HIV-infection. As the cohort of survivors of MTCT from the early 1990's continue aging, they, will increasingly present to ART programmes during adolescence. As a result of delayed implementation of effective prevention of MTCT strategies programmes will need to address the needs of a variety of HIV-infected adolescents who are either, long-term survivors of MTCT, those who initiated ART in childhood or those who have recently

acquired HIV-infection. Treatment and retention of this increasingly diverse group of adolescents will provide a future challenge for ART programmes.

Adult males accessed health services less frequently and with more advanced HIV infection, as manifested by lower CD4 cell counts, than females. The relative lack of males in care represents a lost opportunity for transmission prevention and to decrease HIV-associated morbidity and mortality. Programme modifications to encourage recruitment of adult males into care need to be developed.

This programme demonstrates that co-ordination of a large ART programme across a wide geographic distribution of rural and peri-urban sites throughout South Africa can be implemented within an existing health-care network of a faith-based organisation. The programme has managed to supply ART to approximately 7 percent of those presently receiving ART in South Africa. The preliminary results of this programme compare favourably with the early reported outcomes from pilot programmes within both the public and industrialised health sectors.[6-10]

Monitoring and evaluation of the programme has required a standardisation of medical, pharmacy and laboratory data collection, together with allocation of scarce personnel resources at each clinic site to collect and forward this data for centralised analysis. As the programme continues to develop longer term outcomes such as survival and programme retention of patients will be required to be captured. There is therefore an urgent need to develop “user friendly” programme evaluation tools in parallel with the rapid scale-up of ART services.

Notes

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