could not be traced and around 10% of patients were missing body weight. This finding underscores the challenge of data collection, storage and retrieval that many ART sites are currently experiencing.

Baseline CD4 cell count

The immunological status at baseline in this study (median CD4 count of 131 cells/µl, IQR: 75-216) showed consistency with other studies as in general most patients entered ART care with advanced to severe immune suppression. Moore *et al.*(2007), Laurent *et al.* (2002) reported a median baseline CD4 count of 127 and 108 cells respectively. The Khayelitsha cohort found an even more profound immune suppression with median of 43 cells/µl. A combination of patient and provider factors may be at play. Awareness, motivation, level of stigma and discrimination are important patient factors in accessing care. On the other hand, using a cut off for treatment eligibility of 200 cells/µl may constitute a barrier to an optimal treatment initiation time. As a matter of fact, this finding should be considered as normal in terms of compliance with the national guideline. However, when disaggregated by sex, it would appear that males were more likely to have lower median CD4 cell count (107 cells/µl) as compared to females (148 cells/µl) (F=14.4, p-value<0.0001). This finding is similar to that of a recent publication from Collazos *et al* (2008) who found at a borderline statistical significance that the women's average CD4 cell count was higher than men's. They further argued that there was a general tendency of women having lower viral load and higher CD4 cell counts when they initiated ART as compared to their male counterparts. It can be speculated that some difference might reside in better health seeking behaviour amongst females and availability of PMTCT services that provide a canvassing ground for HIV positive women.

Follow up parameters
Weight

Serial measurements of weight at baseline and follow up periods provided the basis for comparison. Missing values at random at different follow up periods limit the analysis of trend. We compared mean weight obtained in the entire cohort using the available dataset at each encounter to mean weight obtained among patients with weight measured at all encounters. In the entire cohort the weight gains from baseline were 5.7, 7.2, 8.1 and 7.7 Kg respectively at 6, 12, 18 and 24 months. In the smaller

population with weight measurements at all visits the gains at 6 and 12 months were 4.6 and 5.6 Kg respectively. Whichever analysis we used, these findings would appear to suggest similar weight gains observed in other studies. At 6 months, the BMS analysis (2006) showed weight gains at different sites between 3.8 to 6.2 Kg. The MSF (2003) cohort indicated a gain of 5 Kg at 6 months and 9 kg at 12 months. The assumption is that a good clinical response on ART will result in weight gain that clinicians need to monitor regularly.

Functional status

The progression of functional status from bedridden through ambulatory to working status (productive life) provided additional information on clinical responses to ART. Whereas the percentage in bedridden status decreased (22.9% to 0%), the working status increased (6.8% to 68.2%) indicative of health gains achieved for PLWHA receiving ART . This is called the "Lazarus effect" by many PEPFAR programme managers. Though encouraging, this result (68.2%) is lower than the 85% fit to work reported by Libamba *et al.*(2006). The longer study period and the larger sample size in their study might account for the difference.

CD4 cell count

CD4 cell count is the best proxy of ART effectiveness in resource poor settings. We have analysed in two ways to obtain the most accurate reflection. Using the available dataset at each encounter, we had a median cell count increase of 158 and 206 cells/µL at 6 and 12 months, respectively. The gains for clients who had CD4 counts done at both 6 and 12 months were very similar - 136 and 217 cells/µL, respectively. Although these results differ from some published studies (Laurent *et al.,* 2002; Gallant, 2003) that reported a lower increase of about 85 cells at 6 months, they are consistent with those of the MSF cohort (2004) in Khayelitsha which found a similar increase of 133 and 221 at 6 and 12 months, respectively. It is argued that in general, most patients on potent regimens and with good adherence will achieve a successful CD4 count response in the course of time. By 24 months close to 90% of patients on ART had a CD4 cell count above 200 cells/µl.

These findings accord with our earlier observations which showed significant gain in weight and improvement in functional status over time.

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There is a major limitation in these findings in that the impact of adherence level on all these CD4 cell count responses were not evaluated.

Adherence

Adherence is critical to the success of any ART programme. Our results are based on self-reported adherence and a once-off measurement enquiring on a 28-day medication supply. Most patients (76.7%) had an adherence rated as good by WHO standards and this dataset suggested a highly statistically significant association between adherence level and outcome. Those who died were twice more likely to have fair or poor self-reported adherence. (OR: 2.4, 95% CI: 1.17-5.28, p-value=0.008). The lack of validation with other adherence measurement method and viral load assay testing and a correlation study to CD4 cell count response are major limitations in interpreting these findings.

Treatment outcome

The cumulative treatment outcome indicated retention in care of 69% (those alive and on ART at the analysis time). The observed attrition rate of 31% is mainly driven by a relatively high mortality on ART of 23.5% (This mortality represents 75.8% of the total attrition). Although this mortality is comparable to that found by Ferradini *et al.* who reported 19%, it would seem to be relatively higher than most studies have reported. The ART-LINC cohort indicated a mortality of 4% while Libamba *et al.* (2006) had 8% in their study. It is possible that some of the studies that reported lower mortality had a higher loss to follow up as many patients would die at home without being reported as such. Active defaulter tracing and closer follow up could explain a relatively high reported death on ART.

The cumulative retention in care of 69% (mean duration 16.5 month) observed in this study was above the gloomy 60% reported recently by Rosen (2007). In his systematic review of 32 publications in 13 African countries, he found that "since the inception of large-scale ART access early in this decade, ART programs in Africa have retained about 60% of their patients at the end of 2 years". Compared to the 80% reported in the west for the same duration, Africa has still a lot to do in improving its model of care.

Mortality on HAART is higher in males than in females. Our results showed that 29.9% of males died as compared to 20.6% of females. The odds of dying was 1.87 times greater among males as compared to females. This was supported by the KM survival analysis which indicated at 24 months better survival amongst females as compared to males with a high level of statistical significance when stratified by CD4 cell count group (cum survival of 0.71 vs. 0.55, log rank, p-value=0.029) and the Cox regression model which showed male gender associated with shorter survival (OR: 2.30, 95% CI: 1.19-4.43, p-value=0.01). According to Collazos *et al.* (2007), for the past 2 decades there are conflicting findings on the difference between men and women in their response to HIV infection and treatment.

In general, with only death events accounted for, the Kaplan-Meier probability of survival was 0.75 at 24 months. This is below the 0.81 reported by Ferradini, 2006, for the same duration. Cumulative survival appears lower in Nyangana cohort and factors such as rural population, unemployment, food security, advanced/severe disease at treatment initiation and the TB burden might account for this.

In addition, as per the Table 14, the Cox regression analysis showed that patients with lower body weight and functional status of ambulatory or bedridden were less likely to survive. This is similar to Moore *et al.* (2007) whose recent study outlined that low CD4 cell count, low body weight, TB and anaemia were major risk factors for death after ART commencement.

More than 60% died within the first 3 months and close to 80% within the first 6 months of initiating ART. This is a common feature reported in several studies in African cohorts as cited by Laurent *et al* (ref). They argued that death and loss to follow up tend to happen in the first 6 months of ART commencement. Factors such as cut off CD4 cell count for treatment initiation, patients presenting at ART clinic with advanced to severe disease, multiple co-morbidity amongst most patients and earlier immune reconstitution inflammatory syndrome are cited as possible explanation for this prevailing situation (Laurent *et al.*, 2006).

The main causes of death in our cohort were TB with 37.9% and gastroenteritis with 18.2% of cases). The proportion of unknown causes of death is relatively high

(13.6%). Most likely related to the fact that more than 25% were reported to have died at home making it difficult to accurately account for their cause of death. Nonetheless, TB is the leading cause of death of PLWHA world wide. Our findings are in agreement with this reality. On the other hand, it is not surprising that gastroenteritis comes second as in this rural setting, limited access to safe drinking water, poor sanitation and poor food hygiene contribute to water borne diseases in PLWHA.

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Chapter 5. Conclusions and recommendations

5.1. Conclusion

The Namibian country driven process of scaling up ART programme in view of achieving universal access to ART for those who need it is well underway and the Nyangana District ART coverage of 46% is indicative of those efforts. However, this access to ART is characterised by poor male involvement as demonstrated by the low percentage of men enrolled in ART care. Not only is their accessibility to treatment limited but men also present with unfavourable baseline profile (advanced disease, lower CD4 cell count) resulting in poor treatment outcome (higher mortality, shorter cumulative survival). In a multivariate analysis, mortality was associated with male gender, low baseline weight and poor baseline functional status. The clinical response to ART observed through weight gain and improved functional status as well as the immunological response observed through CD4 cell count gain, comparable to findings in other similar settings, were indicators of a successful ART treatment programme. High quality ART services can be implemented in a rural setting in Namibia despite several challenges ranging from socio-economic dynamics to data management issues at the ART site.

5.2. Recommendations

Based on the findings in this study, the followings are some of our recommendations:

- Consider replicating the study in other faith-based ART sites in a multi-center analysis to allow comparability between these sites and consider national cohort analysis
- Considerable efforts need be applied to increase male participation. Formulate behavioural change communication strategies and design incentives that will go to the root of why men do not come or ultimately come late to the ART clinic
- Consider review of the optimal cut off CD4 cell count for treatment initiation to allow earlier initiation that is likely to reduce the mortality rate on HAART. Alternatively, an improved pre-ART monitoring and care might also result in

timely treatment initiation as patients followed up regularly can be started as the declining CD4 cell approaches the cut off point.

- Further analysis on this dataset can be done to explore other factors associated with mortality on HAART in order to devise strategies to improve survival of PLWHA initiating HAART in Nyangana

- Strengthen data quality to minimise missing values and allow use of simple clinical parameters such weight, functional status and WHO stage to monitor patient progress on ART

- Increase use of viral load testing opportunities to ensure monitoring of therapy, validation of adherence and timely therapy switch when required

- Improve adherence monitoring activities

- Improve TB/HIV collaborative activities in order to decrease TB-related morbidity and mortality among PLWHA attending ART care

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Annexure A

Data abstraction tool

The following were extracted from patients records (individual files and various registers)

Record No. _____

1. Date of birth_____
2. Age at HAART initiation (years) _____
3. Sex: M = 1   F=2
4. Date of HAART initiation _____
5. Quarter initiated (from August 2004): Q1=1, Q2=2, Q3=3, Q4=4, Q5=5, Q6=6, Q7=7, Q8=8
6. Pregnancy status: N/A=0   Yes=1   No=2
7. Marital status:
    - Single=1
    - Married=2
    - cohabiting=3
    - Divorced=4
    - Widow(er)=5
8. Employment: Employed=1   Unemployed=2
9. Weight (Kg)_____
10. Weight at 6, 12, 18, 24 months:_____
11. Height (m)_____
12. TB status: Yes=1   No=0
13. Baseline WHO Clinical Stage : Stage 1=1, stage 2=2, Stage 3=3, Stage 4= 4
14. WHO clinical stage at 6, 12, 18, 24 months
15. Baseline functional status:
    - Working=1
    - Ambulatory=2
    - Bedridden=3
16. Functional status at 6, 12, 18, 24 months
17. HAART regimen prescribed at start up:
    - D4T/3TC/EFV = 1

- D4T/3TC/NVP = 2

- AZT/3TC/NVP= 3

18. Therapy substitution: Yes=1   No=0

19. Therapy switch: Yes=1   No=0

20. Adherence level:

- Good=G

- Fair=F

- Poor=P

21. Baseline CD4 cell count (cells/µl) _____

22. CD4 cell count at 6, 12, 18, 24 months_____

23. Duration on treatment by April 2007 (month)_____

24. Outcome by April 2007:

- Alive=1

- Died=2

- Lost to follow up=3

- Transferred out=4

25. If died, duration on treatment by the time of death event_____

26. If died, cause of death

- TB=1

- GE=2

- Pneumonia=3

- Anemia=4

- Meningitis=5

- Hepatitis=6

- Others=7

- Unknown=8

27. if died, place of death: Hospital=1, Home=2