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University College Cork, Ireland

Comparing antiretroviral treatment outcomes between a community-based and hospital-based programs for HIV patients in a resource limited-setting: A retrospective cohort study from Uganda[1]

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DECLARATION FORM

University College Cork, Ireland

Department of Epidemiology and Public Health

Title of Thesis:

Comparing Antiretroviral Treatment Outcomes Between Community Based and Hospital Based Programs for HIV Patients in a Resource Limited Setting: A Retrospective Cohort Study from Uganda

Name of Student: Samuel Waliggo
Student Number: 111220042
Module code: EH6050

I declare that the content of this assignment is all my own work. Where the work of others has been used to augment my assignment it has been referenced accordingly.

Signed: _____ Date: 15th October 2012

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DEDICATION

This thesis is dedicated in loyalty to Dr. Brigid Corrigan, Wesley and Jackie Forde, Nalubowa Margret (Mum). If riches could be measured by love and esteem in which someone is held, you're then the richest people the world can count on and the pivot of my success.

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AHF	AIDS Health Care Foundation
AIDS	Acquired Immune deficiency Syndrome
ART	Antiretroviral Therapy
ARVS	Antiretroviral drugs[2]
BCC	Behaviour change communication programs
BMI	Body Mass Index
CBC	Community Based Care
CBO	Community Based Organisation
CD4 T cells	CD 4 T Lymphocyte Cells
CI	95% Confidential Interval
CWs	Community Workers
ECs	Expert Clients
GOU	Government of Uganda
HAART	Highly Active Antiretroviral Therapy
HBC	Home Based Care
HCT	HIV Counselling and Testing services,
HIV DR EWI	HIV drug Resistance Early Earning Indicators
HIV RNA	Human Immune Deficiency Virus
HRQL	Health-Related Quality of Life questionnaire
IPs	Implementing partners
IQR	Inter-Quartile Range
Kitovu Mobile	Kitovu Mobile AIDS Organization
LTFUP	Lost to follow-up
MDGs	Millennium Development Goals
MMM	Medical Missionary of Merry
MOH Uganda	Ugandan Ministry of Health
MRRH	Masaka Regional Referral Hospital
MTCT	Mother-to-child HIV Transmission
OIs	Opportunistic Infections
OpenMRS	Open Medical Record System
PEPFAR	US President's Emergency Plan for AIDS relief
PLHA	People Living with HIV and AIDS
PMTCT	Prevention of Mother to Child Transmission
PNFP	Private Not For Profit
RHSP	Rakai Health Science Project
SSA	Sub-Saharan Africa
TASO	The AIDS Support Organization
TB	Tuberculosis
UAC	Uganda AIDS Commission
UNCST	Uganda National Council for Science and Technology
USAID	United States Agency for International Development
WHO	World Health Organisation

[2] **AZT**: Zidovudine, **ABC**: Abacavir **D4T**: Stavudine, **3TC**: Lamivudive, **EFV:** Efavirenz, **FTC**: Emitricitabine, **TDF**: Tenofovir Disoproxil Fumarate, **DDI**: Didanosine, **LPV/r**: Lopinavir/ rotonavir, **NVP**: Nevirapine

ABSTRACT

Background: Globally about 34 million people are living with the human immune deficiency virus (HIV), the cause of immunodeficiency syndrome (AIDS). Among individuals who are infected, 95% live in developing countries and Sub Saharan Africa remains the most severely affected. Currently 5 million of the estimated 9.5 million people needing antiretroviral therapy (ART) are still without access to treatment. Despite this global short fall, an effort to achieve universal access to ART in Sub-Saharan African countries is the goal for many Governments' National HIV Strategic Plans. Uganda in particular is strengthening the integration of community-based HIV programs into the existing national health system in order to accelerate access to ART in the country. This goal for "universal access to ART" must be balanced with the ability of these programs to monitor patients' treatment outcomes. However, even in long standing reputable community programs, for instance, the Kitovu Mobile AIDS Organisation in Uganda, it has not been well researched and documented whether community-based care confers benefits on survival and retention that are better or similar to those reported in established Government hospital settings.

The research: This study aimed 1) to investigate whether community-based HIV care and support influences antiretroviral treatment outcomes compared to hospital-based care in a resource-limited setting, and 2) to assess possible risk factors related to mortality among patients who received ART from the community and hospital programs.

Methods: A retrospective cohort study design was used to compare the overall treatment outcomes of 293 People Living with HIV and AIDS (PLHA) started on ART in a community-based program in Kitovu Mobile AIDS organisation with 293 PLHA in a hospital-based ART program in Masaka Regional Referral hospital at Uganda Cares HIV clinic in the Masaka district, between the years 2007 and 2011. Cox proportional hazard model was used to assess the possible risk factors associated with mortality for ART in both treatment programs.

Results: For all patients started on ART in the community based and hospital-based programs, treatment outcomes in all categories, with the exception of patients transferred out, were significantly better among patients who received community-based care ($p<0.001$). Those who were alive and continuing on ART were 85.0% and 72.7% ($p< 0.001$); death was 8.9% and 15.4% ($p=0.02$); and loss to follow up was 2.7% and 9.2% respectively ($p=0.001$). Mortality incidence rate was 3.83 per 100 person years in the community program compared to 7.19 per 100 person years in the hospital program with an incidence rate ratio of 0.53 (95%CI, 0.32 - 0.88, $p= 0.01$). The probability of survival among patients was also higher among patients in the community-based program (Log rank test: $p=0.01$). The risk factors related to mortality of patients on ART in the multivariate Cox proportional hazard model include: the type of facility (hospital) (HR=1.89; 95%CI, 1.11- 3.22, $p=0.02$), tuberculosis (TB) co-infection (HR=2.92; 95%CI, 1.69 - 5.04, $p<0.001$), advanced WHO clinical stage 3 and 4 at baseline (HR=2.62; 95%CI, 1.25-5.47, $p=0.01$) and adherence to ART $\leq$ 95% (HR=2.97; 95%CI, 1.85-4.79, $p<0.001$).

Conclusion: Overall ART treatment outcomes, survival and retention are better and feasible in the community programs. Community care is associated with considerably lower patients' attrition and mortality rates. Therefore, strengthening community care and collaboration with the existing health care system could potentially impact on positive patients' treatment outcomes in resource limited countries such as Uganda.

CHAPTER 1: INTRODUCTION AND BACKGROUND

Introduction: This chapter is the platform for this thesis. It highlights that HIV/AIDS is a global public health concern and shows strategies that have been adopted by different countries to scale up Antiretroviral therapy (ART) with a particular focus on Uganda. The chapter presents the problem statement as the challenges faced in monitoring patients' ART treatment outcomes. The justification for carrying out this type of study in Uganda is also presented.

1.1 GLOBAL EPIDEMIOLOGY OF HIV AND AIDS

HIV/AIDS continues to be a major global health problem [1]. It was estimated in 2010 that 34 million people were living with HIV globally, including 3.4 million children less than 15 years. In the same year over 2.7 million new infections occurred among adults and about 390 000 among children, most of whom acquired HIV infection from their mothers during pregnancy, birth or breastfeeding [2].

Among individuals affected, 95% live in developing countries of which Sub-Saharan Africa (SSA) remains the most severely affected region, accounting for two thirds of the people living with HIV worldwide [3]. For instance, in 2010, the World Health Organisation (WHO) estimated that 1.9 million people became infected in the region. However, this was 27% fewer than the annual number of people who became newly infected between 1996 and 1998, when the incidence of HIV in SSA peaked overall. Recent studies indicate that the epidemic has begun to stabilize or decline in many countries in this region, although not all countries fit the overall trends [2].

Numerous studies indicate that without efforts to scale up Antiretroviral Therapy (ART), the majority of those infected would die in the next ten years, leaving behind shattered families and crippled prospects for development [4]. However, with the introduction of ART, the annual number of people dying from AIDS- related causes worldwide is steadily decreasing from a peak of 2.2 million in 2005 to estimated 1.8 million in 2010. In addition, studies have also demonstrated that among patients infected with HIV, Tuberculosis (TB) is the most common opportunistic infection (OI). Over 50% of HIV patients have UN recognised active tuberculosis [5]. The serious co-morbidity of tuberculosis and HIV accelerates HIV disease progression so that tuberculosis is now the major cause of mortality among people living with HIV in SSA where access to early ART is still limited [6]. Evidence indicates increasing progress in scaling up of National HIV and TB collaborative interventions. This effort is towards universal access to HIV testing, treatment and care as well as intensified TB case finding and provision of isoniazid preventive therapy among people living with HIV. However overall coverage of these interventions remains low in SSA countries [2].

1.1.1 Global, regional and Uganda's progress of antiretroviral therapy (ART)

The international momentum that was generated by the "3 by 5 initiative" at the United Nations General Assembly in 2003, declared HIV and AIDS as a global public health emergency. Since then efforts to scale up access to ART for people living with HIV in low- and middle-income countries is the ultimate goal for Governments [7]. Countries adopted a public health approach to treatment guidelines that are characterized by simplified and standardized clinical decision-making, drug regimens and recommended

systems to monitor the outcomes of people receiving treatment. With such approach resource-limited countries have been able to make ART available to an increasing number of those medically eligible from an estimated 400,000 people to over 4 million people by the end of 2008. There has been documented evidence of improving treatment health outcomes and patient retention. Global political commitment and considerable financial support from partners such as the Global Fund, President's Emergency Plan for AIDS Relief (PEPFAR) and other bilateral, national and non-Governmental institutions have resulted in this massive increase in the number of people receiving HIV treatment. This has in turn led to the promotion of a comprehensive and an integrated approach to the achievement of health-related Millennium Development Goals (MDGs) [8].

The greatest expansion in the number of people receiving treatment is in SSA, where approximately 3 million people were receiving antiretroviral therapy by the end of 2008 compared to an approximate 2 million people who were on treatment by the end of 2007 [9]. Nevertheless, current global access to treatment services falls far short of the need. More than 5 million of the estimated 9.5 million people needing antiretroviral therapy are still without access to treatment [9]. Further, as the number of people enrolled in treatment programs continues to grow with increasing access to HIV Counselling and Testing (HCT) services, several challenges are emerging. People are being diagnosed at late stages of disease progression, resulting in delayed access to treatment and high rates of mortality in the early months after ART initiation. This is because of the inadequate human resource, laboratory monitoring facilities, and patients' self-stigma [9]. It follows therefore that, expanded access to HCT must be followed by the early scaling up of ART, continued high-quality services and improved patient monitoring systems. This would increase retention and patient treatment outcomes, since the cost of second-line drug regimens continue to be high in those who fail on the first line treatment regimen.

In Uganda the fight against HIV/AIDS has been at the forefront since the HIV virus was first identified in the 1980s. Innovative HIV care approaches, political and financial commitment by both Government and international funding agencies had Uganda actively participate in the scale up of prevention, HIV testing, care, prevention and management of the epidemic [10]. In an era of HIV and AIDS, Uganda is considered a success story [11, 12]. In 2005 the Ugandan Ministry of Health (MOH) in partnership with a private not for profit (PNFP) institution Uganda Cares and with support from the AIDS Health Care Foundation (AHF) pioneered the provision of free HIV medicines in the central districts of the country. Since then the MOH has steadily rolled out ART in both private and public health facilities based on the World Health Organization (WHO) recommended public health approach. The number of facilities providing ART services has increased from just around five research facilities in 1993 in urban areas of Uganda to currently 419 health facilities spread throughout the country, the majority of which are public hospitals and health centers. In the recent years the MOH has intensified efforts to unify and improve patients reporting and monitoring systems in all of these HIV facilities [13].

Community based care programs, such as the Kitovu Mobile AIDS Organization (Kitovu Mobile), The AIDS Support Organization (TASO) and Nsambya Home Based Care (HBC) have been part of the effort since the beginning of the epidemic in Uganda. They have played a crucial role in behaviour change and in Uganda's success story [14]. The methodology of care in these community-based programs is to assess, treat, and follow-up clients living in hard to reach areas in the communities. These collaborative actions have resulted in the significant reduction of HIV prevalence from the peak of 18% in 1992 to the

current 6.4% in adults between 15-49 years. Latest figures show that an estimated 1.2 million people of 32 million Ugandans are infected with HIV, 248,222 of which have access to ART [36]. Recent data show however that the epidemic has also shifted its concentration from affecting the 24-25 year's age group to one affecting the 30-34 years age group [15].

With the expansion of ART across the country, the Ministry of Health's responsibility in close collaboration with implementing partners (IPs), health facilities, district health teams and local Governments, is to coordinate and provide technical guidance of ART services in all facilities accredited to provide ART in the country. Because of the massive need for ART coverage that is not matched with available resources, the MOH framework for ART services delivery prioritised provision of services to the sickest. These are the individuals in advanced stages of HIV disease with a high risk of death. In line with this the guideline for ART eligibility criteria for adults and children has also evolved overtime according to WHO recommendations from initiating treatment in PLHA with CD4 T cell of $\leq$ 250 to currently those with CD4 T cell of $\leq$350 cell/ul or alternatively WHO stage 3/4 disease among adults and any HIV+ child less than 12 months [16]. This evolution in treatment guidelines is because data from WHO program monitoring systems indicate that initiation of treatment earlier during the course of the disease may herald more favourable treatment outcomes among HIV+ patients on ART.

1.2 STATEMENT OF THE PROBLEM

Cohort monitoring has become critical for successful program management and generating evidence on the treatment outcomes of ART and patient retention [9]. Although efforts have been made in this direction, the existence of highly heterogeneous monitoring systems and the use of non-standardized definitions across programs create additional hurdles for accurately measuring the success of programs. Attrition from an ART program is classified in three underlying causes: stopping treatment, death and lost to follow-up. A systematic review of cohorts in SSA estimates that less than 5% of attrition in cohort studies fall under treatment cessation [17]. Death is the main outcome used to estimate survival of people who start treatment. A meta-analysis of 17 studies from SSA tracking outcomes of 6420 people lost to follow up found that 34% were not traceable due to poor registration problems, 29% had died and 37% were still alive [18]. The number of people receiving ART who transfer from one clinic to another is increasing with scaling up and the decentralisation of services in communities. A study in Malawi tracing 805 people found that 737(92%) of them could not be found in their clinic and yet were continuing to receive ART [19]. Nevertheless, as people remain on treatment, albeit at different clinics, the transfer seems to remain mostly an issue of monitoring and proper recording rather than attrition.

Recent evidence indicates that the quality of the data collected at the clinical level can also vary substantially among programs. In Malawi, researchers performing supervision and data control in 89 facilities estimated that routine reports undercounted the number of people receiving antiretroviral therapy by 5% and the number of people receiving first-line antiretroviral drug regimens by 12% [20]. In Mali, the opposite was found: a data quality control study undertaken for the Global Fund estimated that routine reports over counted the number of people receiving antiretroviral therapy by 7% [21].

The effectiveness of HIV/AIDS management not only depends on the efficacy of ARVs against the virus but also critically on the program mechanisms for monitoring and follow-up of registered clients on

treatment outcomes. Like any other SSA country, Uganda generally faces a dire shortage of human resources and the patient burden on the existing health services is extremely high [22, 23]. Most health facilities face a severe staff shortage that has consequences for HIV/AIDS care management. Estimates from MOH show that only 40% of facilities in Uganda are able to compile quarterly ART reports on time and face enormous challenges to monitor expected ART outcomes as recommended by the Ugandan MOH [13]. These unnoticed poor treatment outcomes in any HIV program are associated with many adverse consequences to both individuals and communities including; treatment failure due to non-adherence resulting in drug resistance, transmission of HIV resistant strains, progression of HIV disease, increased cost of care and poor quality of life, and yet many patients have limited access to health care due significant poverty levels.

To improve patients' monitoring on ART, WHO introduced standardized outcome indicators that include; Alive and active on ART, Dead, lost to follow up (LTFUP), Stopped on ART and Transfer out. These were then were adopted in Uganda and customized by the MOH for all HIV programs for quarterly analysis [24].

This study is aimed at finding out if community-based HIV care and support influences core treatment outcomes. To facilitate answering the research question, the study will seek to compare the treatment outcomes of patients registered in a community-based care program (Kitovu Mobile) with those of patients in a facility-based HIV care program (MRRH-Uganda cares HIV clinic).

1.3 STUDY AIM

To investigate whether community-based HIV care and support influences antiretroviral treatment outcomes compared to hospital-based care in a resource-limited setting. The results of the study will identify and address gaps in the patient monitoring system and will help to influence HIV operational policy making in Uganda.

1.3.1 OBJECTIVES

1.3.1.1 Primary objective

i. To compare the overall ART treatment outcomes for patients enrolled in the community-based care program and hospital ART program between the years of 2007-2011.

ii. To compare survival and retention rates of PLHA on ART registered in the community-based care program (Kitovu Mobile) with those in the hospital-based program (MRRH, Uganda Cares HIV clinic) between 2007-2011

1.3.1.2 Secondary objective

i. To assess the possible risk factors related to death among patients who received community care and those who received hospital care.

1.4 STUDY VARIABLES

1.4.1 Predictive variables

Age, Sex, Weight and occupation,

Level of adherence to ARVS and type of ART regimen

WHO Clinical stage (1, 2, 3, and 4)

Baseline CD4 T cell count.

Tuberculosis co-infection

Time from HIV diagnosis to initiation into ART (Date of ART start-Date of HIV test)

Eligibility duration (Date of ART start-Date considered eligible for ART)

1.4.2 Outcome variables

1.4.2.1 Primary outcomes

Overall, ART treatment outcomes

Survival and retention on ART

1.4.2.2 Secondary outcome

Possible risk factors to mortality

1.5 RESEARCH QUESTIONS

i. Is there a difference in the overall treatment outcomes among patients who started ART in the community and hospital care programs between the years of 2007-2011?

ii. Is there a difference in survival and retention rates of PLHA on ART registered in a community-based ART program compared to those in a hospital ART program between the years 2007-2011?

iii. What are the possible risk factors related to death among PLHA on ART in community and hospital programs?

1.6 STUDY HYPOTHESES

1.6.1 Null Hypotheses (Ho)

i. There is no difference in the overall ART treatment outcomes (Alive on ART, death, LTFUP and transfer out) among PLHA accessing ART treatment in the community and those in the hospital program.

ii. There is no difference in the primary and secondary ART treatment outcomes of PLHA on ART registered in a community-based program, the Kitovu Mobile and those in a hospital-based ART program-the Uganda Cares HIV Clinic in MRRH.

1.6.2 Alternative Hypotheses *(H_A)*

i. Overall, ART treatment outcomes are likely to be better among PLHA accessing ART in community program compared to those and in a hospital program.

ii. PLHA accessing ART from a community-based ART program are likely to have better primary treatment outcomes compared to those registered in a hospital-based program.

iii. Low patient attrition related to death among patients on ART is likely in a community-based care program rather than in a hospital-based ART programs.

1.7 JUSTIFICATION OF THE STUDY

Increasing access to ART in the country through Government and Private not for profit (PNFP) institutions is the goal for the Uganda National HIV strategic plan 2008/12 [25]. To achieve such an objective, Government is strengthening the integration of community-based HIV programs into the existing national health system [26]. However, even in a long-standing reputable program like Kitovu Mobile it has not been well researched and documented whether community-based care confers benefits on survival and retention that are better or similar to those reported in established Government hospital settings. Scaling up of treatment must be balanced with the ability of newer community-based programs to monitor and report treatment outcomes for all registered patients in care. This equity and quality of care will result in a decreased risk to development of HIV Drug Resistant strains and will in turn reduce the cost of care.

This study will be the first in Uganda to assess and compare the status of ART treatment outcomes community-based program (the Kitovu Mobile) and facility-based HIV program (the Uganda Cares MRRH) in the Masaka district of Uganda. It is expected that study findings and conclusions will generate evidence on survival, retention and attrition of patients registered in both care programs. The results of which will;

i. Be used to identify and address gaps in the patients' monitoring system and formulate hypothesis for further research protocols.

ii. Feed into the national HIV policy bi-annual development as universal access to quality care and treatment in the communities the top Millennium Development Goals (MDGs).

CHAPTER 2: LITERATURE REVIEW

Introduction: This literature review examines a number of scientific papers and studies that have been carried out mostly in Sub Saharan Africa with the highest HIV burden. It shows the history and the success stories in HIV care and prevention in Uganda. It also examines the balance in patients' monitoring systems with the rapidly expanding HIV programs and the World Health Organisation's goal towards universal access to ART. The overall aim of this review is to assess the current performance on the expected standardised ART treatment outcomes in ART Programs and to identify gaps in the reviewed publications.

2.1 UGANDA'S SUCCESS STORY IN THE HIV PREVENTION

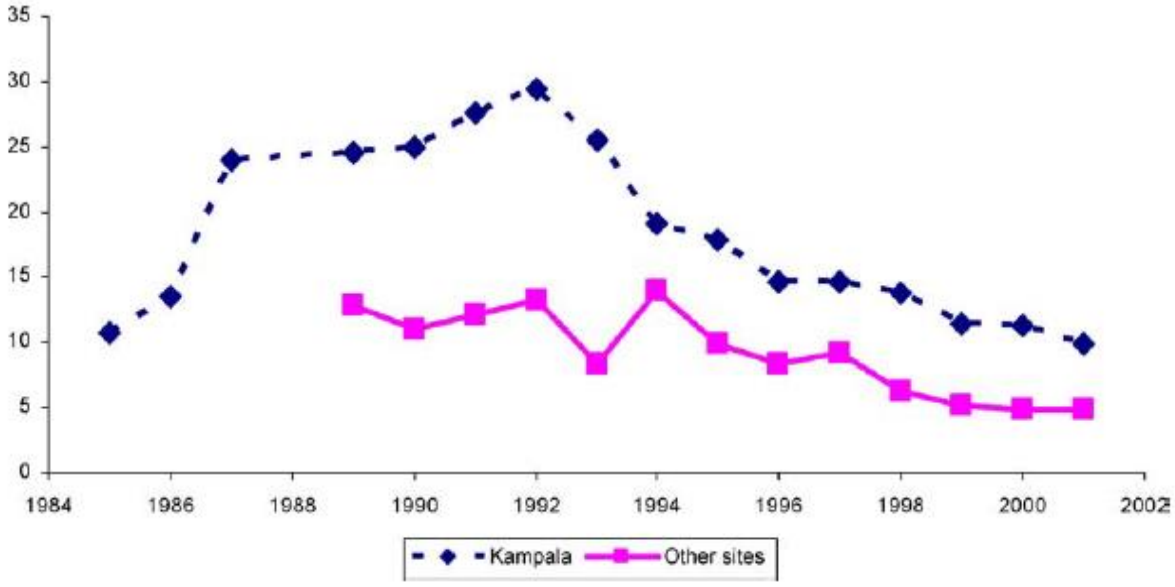
Uganda pioneered a politically led, multisectoral and open national response to the HIV epidemic in SSA as far back as the mid-1980s.The HIV epidemic has now been generalised for more than two decades. Since the HIV virus was first identified, Uganda has played an exemplary role in HIV/AIDS prevention and control interventions, research and training to the rest of the world [12]. Innovative HIV care approaches, political and financial commitment by both Government and international funding agencies made the country actively participate in the management of the epidemic [10, 27]. These collaborative actions with Implementing Partners (IPs) have resulted in a significant reduction of adult HIV prevalence from a peak of 18% in 1992 to the current 6.4% in adults between the ages of 15-49 years and to 0.7% in children less than 5 years. Latest figures show that an estimated 1.2 million people of the 32 million Ugandans are infected with HIV. In a behavioural survey carried out in 2009 to assess the modes of HIV transmission in the country, 81% of HIV transmission among adults occurred through heterosexual contact and 18% through mother-to-child transmission (MTCT) in children [25]. Prevention has been the cornerstone to Uganda's success and it has been integrated into all Government programs. Additionally, the political commitment and leadership for prevention campaigns has been documented as best practice in Africa [11].

2.1.1 Declining prevalence and incidence of HIV and AIDS trends in Uganda

In Uganda, the national HIV prevalence estimates are derived from sentinel surveillance among pregnant women in selected sites. Sero prevalence among pregnant women is believed to be reflective of the overall HIV incidence [15, 28]. However, the major limitation to this type of data in estimating the HIV prevalence is that it does not include men and non-pregnant women. Therefore, it is difficult to make assumptions about infection rates in the general adult population. Nevertheless, evidence from such data and several sero prevalence surveys studies have indicated that HIV prevalence in Uganda has continued to decline over time.

Figure 2.1 below, is an example showing adjusted HIV prevalence among pregnant women from surveillance data. It can be seen that the HIV prevalence reached its peak in 1992 at around 25-30% and since then it has declined to less than 10% from 2001 onwards. According to MOH Uganda, prevalence among pregnant women has declined consistently since the early 1990s at all of the country's sentinel sites until 1995 or 1996, and since then it has remained low.

Figure 2.1: Unadjusted median HIV prevalence among pregnant women in Uganda



Source: HIV/AIDS Surveillance report, STD/AIDS Control program, Ministry of Health, Uganda, June 2012

This dramatic decline in prevalence over the past decade is unique worldwide in the past decade, especially among younger age cohorts [29]. For instance, in Masaka Regional Referral Hospital, the HIV incidence fell from 7.6% per thousand per year in 1990 to 3.2% per thousand per year by 1998. As with HIV prevalence, the decline was more pronounced among younger women [12].

Although it is now known that increase in HIV knowledge, risk perception, and risk avoidance options can ultimately influence reduction in HIV incidence, there seems to be a complex set of epidemiological, socio-cultural, political, and other elements that affected the course of the epidemic in Uganda [30]. Some probable factors responsible for the decreased HIV prevalence in Uganda include;

- decentralized planning and implementation for behaviour change communication (BCC), programs reaching both general populations and key target groups [31],
- interventions that addressed women and gender, youth, stigma and discrimination,
- religious leaders and faith-based organizations have been active on the front lines of the response to the epidemic and,
- decreased incidence as a result of decrease in multiple sexual partnerships and networks.

However, many of these elements appear to have been less significant in other African countries such as Zimbabwe, South Africa, Botswana, Malawi. In these countries the HIV prevalence is as high as 15% and above, yet they have experienced the HIV epidemic for nearly as long as Uganda—and have also had at least as severe epidemics as like Uganda as is shown in the Table 2.1 below.

Table 2.1: HIV/AIDS Data for Selected African Countries

	Estimated number of people living with HIV				AIDS death
	HIV+ adults and children 2005	HIV+ Adults (15+) 2005	Adult (15-49) HIV rate (%) 2005	Adult (15-49) HIV rate (%) 2003	Deaths in adult and children 2005
Sub-Saharan Africa	**24,500,000**	**22,400,000**	**6.1**	**6.2**	**2,000,000**
Angola	320,000	280,000	3.7	3.7	30,000
Botswana	270,000	260,000	24.1	24.0	18,000
Congo DR	1,000,000	890,000	3.2	3.2	90,000
Losotho	270,000	250,000	23.2	23.7	23,000
Kenya	1,300,000	1,200,000	6.1	6.8	140,000
Madagascar	49,000	47,000	0.5	0.5	2,9000
Malawi	940,000	850,000	14.1	14.2	78,000
Mauritius	41,000	4,100	0.6	0.2	100
Mozambique	1,800,000	1,600,000	16.1	16.0	140,000
Namibia	230,000	210,000	19.6	19.5	17,000
Rwanda	190,000	160,000	3.1	3.8	21,000
South Africa	5,500,000	5,300,0000	18.8	18.6	320,000
Swaziland	220,000	210,000	33.4	32.4	16,000
Tanzania	1,400,000	1,300,000	6.5	6.6	140,000
Uganda	**1,000,000**	**900,000**	**6.7**	**6.8**	**91,000**
Zambia	1,100,000	1,000,000	17.0	16.9	98,000
Zimbabwe	1,700,000	1,500,000	20.1	22.1	180,000
Global	**38, 600,000**	**36,300,000**	**1.0**	**1.0**	**2,800,000**

Source: UNAIDS (2006)

In Table 2.2 below, when the HIV prevalence was categorised by age in the Uganda National HIV/AIDS sero-behavioural survey in 2004; it was observed that prevalence increased and reached its peak at about 30-34 years for women and 35-44 years for men. Prevalence was generally higher for women than men at ages 15-49 years, but men are slightly higher in the 40-44 years and ages 50-59 years age ranges.

Table 2.2: HIV Prevalence in Uganda by Age, 2004/05

Age category	Women 15-49		Men 15-49		Total	
Age category	Percentage HIV positive	Number tested	Percentage HIV positive	Number tested	Percentage HIV positive	Total tested
15-19	2.6	2,062	0.3	1,932	1.5	3,994
20-24	6.3	1,803	2.4	1,184	4.7	2,987
25-29	8.7	1,679	5.9	1,123	7.6	2,802
30-34	12.1	1,374	8.1	1,139	10.3	2,513
35-39	9.9	1,029	9.2	868	9.6	1,897
40-44	8.4	823	9.3	745	8.8	1,568
45-49	8.2	621	6.9	524	7.6	1,125
50-54	5.4	513	6.9	452	6.1	965
55-59	4.9	322	5.8	332	5.4	654
Total 15-49	7.5	9,391	5.0	7,515	6.4	16,906
Total 15-59	7.3	10,227	5.2	8,298	6.3	18,525

Source: MOH, (2006): HIV/AIDS Sero-Behavioural Survey 2004-2005 [32]

It has been noted with concern that in the recent years the epidemic has shifted its concentration from the 24-25 years age group to 30-34 years age group. The HIV prevalence among older people of age between 50-59 years is 5.8%. Married couples contribute almost 42% of the new infections. This is because of engagement in sex with multiple partners outside marriage. This is more likely to reverse the success in HIV prevention in care and treatment as the number of new infections is much higher than those in need of ART in the country [15].

2.2 INTERGRATING HOME BASED CARE MODEL INTO THE UGANDAN HEALTH SYSTEM

In Uganda the MOH has developed a comprehensive continuum of care for people living with HIV &AIDS. This includes interventions described as clinical services, nursing care, counselling, social support, palliative care and community-based care (CBC) sometimes referred to as Home Base Care (HBC). CBC is now regarded as a visible mechanism for expansion of HIV services in the communities because it has important benefits for everyone along the continuum [26]. The developed HBC policy guideline ensures harmonised and standardised service delivery that aims at integrating and strengthening CBC into the Uganda's existing health care system. Within the health sector, supporting and expanding the provision of CBC and strengthening referral systems to other health facilities are key objectives of the Ugandan National AIDS Strategic Plan (2007/8-2012/12) and the health sector AIDS Control Program.

Although there is increased availability of AIDS control program services, notably ART, HIV counselling and Testing (HCT) sites and Prevention of Mother to Child Transmission (PMTCT); HIV/AIDS service coverage is still constrained. There is:

- insufficient access to entry points,
- insufficient adherence to medication,
- widely prevalent stigma,
- strong resistance to sero-status disclosure or sharing of treatment information with household members and,
- low utilisation and availability of HIV/AIDS prevention services.

For instance, in a national sero behaviour survey conducted in 2005 many people did not know their HIV sero status. Only 10-12% of men and women between the ages of 15-49 years had been tested and received HIV results. However, at the same time about 70% of the population expressed the desire to be tested [15]. Therefore, with the new efforts to increase HCT services coverage, more HIV positive clients are expected who will need care, treatment and prevention services. Provision of quality HIV/AIDS services beyond the health facility and particularly communities is expected to bridge the gap of restricted access to quality health care. This is because majority of newly diagnosed HIV patients are living in adverse conditions of poverty in hard to reach areas. Therefore, if chronic HIV/ART care is persistently restricted in Government hospital settings which are commonly found in urban centres, many patients will succumb to poor treatment outcomes like death and lost to follow-up (LTFUP) when they start on treatment [26]

The HIV disease has created a severe and unsustainable burden on the already scarce health sector resources as funds are tapered from other sectors to HIV prevention, care and treatment services. This demand for services has led to over burdened health facility services in Uganda [15]. It is estimated that there is only one doctor for every 22,000 patients in Uganda, accounting to an 80% overall deficient [32]. Thus, with the current situation of low staffing, poor patients and staff morale and other hospital constraints, the CBC approach is increasingly recognised and formally integrated into the continuum of HIV/AIDS as a means of accelerating universal access to early ART treatment and care to individuals diagnosed with HIV [26].

2.3 THE ERA OF ANTIRETOVIRAL THERAPY (ART) IN UGANDA

The increased availability of ART for HIV/AIDS in low-income countries has changed the clinical management of PLHA and has dramatically increased rates of survival [33, 34]. Despite the fact that antiretroviral ARVs were known to be effective in improving the quality and quantity of life, Uganda did not use them initially as a standard treatment because of the costs involved that were very high. However, with the steady decline in prices of anti-retroviral drugs, the MOH Uganda in collaboration with WHO/UNAIDS and other health development partners established a comprehensive care program for the HIV infected persons [10]. There is now increasing access to antiretroviral drugs. National antiretroviral treatment and care guidelines for adults and children have been developed principally to lead the health workers in management of HIV patients and the correct of use antiretroviral drugs [35, 36, 16].

For the last seven years, Uganda has been steadily rolling out ART in health facilities based on the WHO recommended public health approach [27]. Currently over 248,222 PLHA have access to ART in 400 public and private clinics nationwide [36]. The provision of ART services is mainly supported by global health initiatives especially the US President's Emergency Plan for AIDS relief (PEPFAR) and Global Fund as well as domestic Government resources. It has been noted that during the past couple of years, the Government of Uganda's (GOU) contribution to ART service delivery has significantly increased to about US $ 30 million in 2010 [10].

Due to the enormous need for ART that is not yet matched by the available services, the MOH framework for ART service delivery has been prioritising provision of services to the sickest individuals who are at highest risk of death. Thus, the first guidelines for ART service delivery in Uganda recommended ART eligibility criteria for adults of CD-4 T-cell count < 200 cells/ul, or WHO clinical stage 3 and 4 [35]. However, the MOH Uganda eligibility criterion for ART has been evolving over time according to the need for treatment and WHO recommendations. These guidelines were revised in 2008 to include all adult HIV- infected individuals with < 250 CD- 4 T cell/ul or WHO clinical stage 3 and 4 disease [36]. In 2010 the national guidelines were again revised to be in line with the latest WHO guidance of ART care, i.e. initiating ART in all individuals with CD- 4 T cell count of 350 cells/ul or WHO 3 and 4 disease [16]. In addition, all HIV infected children less than 24 months of age are considered eligible for ART under all these guidelines and since 2008. This was because evidence from routine patient monitoring system in the country indicated a trend towards more favourable treatment outcomes among patients initiated on treatment earlier in the course of the disease. These guidelines also recommend routine Cotrimoxazole prophylaxis for all HIV-infected individuals registered for chronic HIV care regardless of whether or not they are receiving ART. This is because several studies indicated a

reduction in mortality among HIV positive patients due to opportunistic infections (OIs) in particular Pneumocystis Jiroveci Pneumonia (PCP), Toxoplasmosis, Malaria and diarrhoeal diseases [37].

Owing to various constraints in the health sector as mentioned above, the proportional of HIV infected individuals eligible for ART but not yet receiving treatment remains high. For instance, out of the estimated 1.2 million HIV-infected individuals in the country, less than half (41%) are enrolled in chronic HIV/AIDS care and 46% of adults and children eligible for ART in the country are enrolled on ART. This calls for an integrated HIV and ART program coverage including early diagnosis, treatment and follow-up [13].

2.4 MONITORING OF ANTIRETROVIRAL THERAPY (ART) TREATMENT OUTCOMES

In order to track the progress and outcomes of the program, the MOH maintains a patient monitoring system, and has been working collaboratively with IPs to standardise ART patient information systems in facilities. Under this system, longitudinal patient records are supposed to be maintained in health facilities on paper forms or electronic registries or both. The records are maintained in treatment cohorts comprising of groups of individuals that started treatment at the same time, to facilitate cohort analysis of treatment outcomes. The system also has a reporting system whereby all health facilities are supposed to provide quarterly cross-sectional reports of the number of individuals in chronic HIV/AIDS care and ART, including new clients enrolled during the quarter [27].

The reporting system also requires quarterly reporting of ART outcomes for cohorts making their anniversary during the quarter. In cohort reports, the proportional of clients who are; still active on ART on first and second-line regimens, dead, LTFUP, have stopped treatment, and that have transferred in and out of the facility after 6, 12, 24, 36, 48, 72, 84 months are reported every quarter. The MOH maintains a data base of these outcomes, and compiles and disseminates quarterly reports to all IPs and other stakeholders. However, despite all these efforts, the reporting system on ART standardised outcomes is still incomplete with many facilities either not reporting or reporting late. Furthermore, very few facilities provide reports of treatment outcomes for long periods of treatment (over five years). These short comings have been the focus of efforts to improve patient monitoring in the past couple years [27].

2.4.1 Survival, retention, lost to follow and medium CD4 T cell count of PLHA on ART

Survival data on ART is used to assess the success of treatment programs, as well as providing inputs during the estimation of program indicators including estimation of the number of HIV infected individuals including those individuals in need of ART among others. Currently, the data reported through the routine system does not provide adequate information on temporal trends of treatment outcomes. Because treatment guidelines have evolved over time to include enrolment of HIV infected individuals earlier in the course of the disease, before severe immune-suppression, the treatment outcomes appear to have improved over time. The nationwide assessment conducted in Uganda by MOH on treatment outcomes for different cohorts in a sample of facilities indicated an apparent temporal improvement in the survival outcomes overtime especially in the recent cohorts making 6 and 12 months. This appears to correlate with the recent changes in the ART eligibility criteria for individuals to enrol on treatment earlier during the course of the disease [27].

In Uganda provision of ART in public and private health system has increased tremendously during the past seven years [13, 27], but still limited research has been done to find out if community care has any influence on survival of patients on treatment compared to hospital care. In Malawi, a prospective cohort study was conducted by Zachariah, R et al [33] to verify if community involvement influenced ART treatment outcomes in a resource limited area of the district. Standardised ART outcomes were measured in terms of being alive and continuing ART, death, lost to follow up (defaulters) and stopped ART. These were compared with areas with and without community involvement. In this study a total of 1634 individuals who had been registered and placed on ART at the facility between April 2003 and December 2004 were assessed. More than half (55%) (895) individuals were offered community support, while 45 % (739) received ART from health facilities with no such support and the key findings on the status of treatment outcome are shown in the table 3 below.

Table 2.3: ART outcomes in areas with and without community involvement in HIV/AIDS activities in Malawi district

Treatment outcome variable	Areas without community involvement n (%)	Areas without community involvement n (%)	P-value (X^2 test)
Placed on ART(N=1634)	**895(55%)]**	**739(45%)**	**-**
Alive and ART	895(95.6)	560(76.0)	<0.001
Died	31(3.5)	115(15.5)	<0.001
Lost to follow up	1(0.1)	39(5.2)	<0.001
Stopped	7(0.8)	25(3.3)	<0.001

Source: R. Zachariah et al, 2006

In Table 2.3, when ART outcomes among individuals who received community support and those with no such support were compared. For all patients placed on ART with and without community support, those who were surviving and continuing ART were 95.6% and 76.0%, respectively ($P < 0.001$); death was 3.5 and 15.5% ($P < 0.001$); loss to follow-up was 0.1 and 5.2% ($P < 0.001$); and stopped ART was 0.8 and 3.3% ($P < 0.001$). The relative risks (with 95% CI) for alive and on ART [1.26 (1.21-1.32)], death [0.22 (0.15-0.33)], loss to follow-up [0.02 (0.0-0.12)] and stopped ART [0.23 (0.08-0.54)] were all significantly better in those offered community support ($P < 0.001$). In this study community support was associated with a considerably higher survival and lower death rates [33].

Nevertheless, it should be noted that to enable comparison of one group with the other, one has to seriously consider that the two groups should be as similar as possible to avoid confounding. In this study reported by Zachariah et al., it seems unlikely that the two community groups were similar in many issues and this could potentially confound the relationships between the exposure and the outcome. In addition, the incidence rates would probably have been the best estimates to compare differences rather than proportional. This is because the total length of follow up of individual cases, which then

adds to produce the total person-time, is unlikely to be the same in this type of the study since participant were followed for different periods since ART initiation.

In another prospective cohort study by Kipp, W et al [3] whose primary aim was to compare ART treatment outcomes and mortality in a community-based HIV program with a well-established hospital in the rural districts of Kabarole western Uganda. This study revealed that successful treatment outcomes after two years in both the community and hospital cohort were high. For instance, all cause mortality, and median CD4 cell count increase was similarly in both cohorts. However, community-based patients had good adherence to treatment and were more likely to achieve viral suppression. Almost all patients in community-based program (CBP) reported significant increase in their overall quality of life, as measured by a standardized health-related quality of life (HRQL) questionnaire.

It is now known that many countries are expanding HIV treatment towards universal access; however, retention of patients in care is a major challenge and varies across health facilities. In Ethiopia, Assefa Y et al [38] conducted out a retrospective longitudinal study to determine the levels of patient retention in care, CD4 count and switching to second-line ART regimen. This study took place in 30 hospitals and 25 health centres selected as sentinel sites for monitoring the outcomes of ART program in the country. The ART outcomes were determined at baseline, after 6, 12 and 24 months on ART as shown in table 4 below.

Table 2.4: Outcomes of patients on ART in 55 health facilities in Ethiopia between September 2006 and August 2008

Duration of ART	Patients in the cohort	Transfer in during the cohort	Transfer out during the cohort	Active cohort	Second-line ART during the cohort	Died during the cohort	Lost to follow up during the cohort	Alive on ART at the end of the cohort
6 months	38,061	1,709	2,304(6%)	37,466	12 (0.33%)	1,897(5%)	5,676 (15%)	29,893 (80%)
12 months	27,668	1,904	2,511(9%)	27,061	158 (0.58%)	1,716 (6%)	5,266(19%)	20,079(74%)
24 months	7,519	814	882(12%)	7,451	159(2.13%)	619 (8%)	1,763 (24%)	5,069(68%)

Source: Assefa, Y et al (2011)

Table 2.4, shows that of the total number of patients who started ART in each cohort, health facilities were able to retain 80%, 74% and 68% of their patients after 6, 12 and 24 months on ART, respectively. Mortality and lost to follow up (LTFU) on treatment after; 6 months was (5% and 15%), 12 months (6% and 19%) and at 24 months (8% and 24%) respectively. Comparing this high mortality and LTUP during the first 12 months of treatment with studies done in Zambia and Uganda appeared similar [34, 39]. The contribution of LTFU to patients' attrition from facilities increases steadily with treatment duration. In Uganda among cohorts of patients that started treatment in 2005, of the 14% attrition at 6 months of follow up, LTFU contributed 6%, which is 42% of overall attrition. This had increased to 50% of overall attrition, i.e. (21% of the 42% patient attrition) at 60 months of follow up [27].

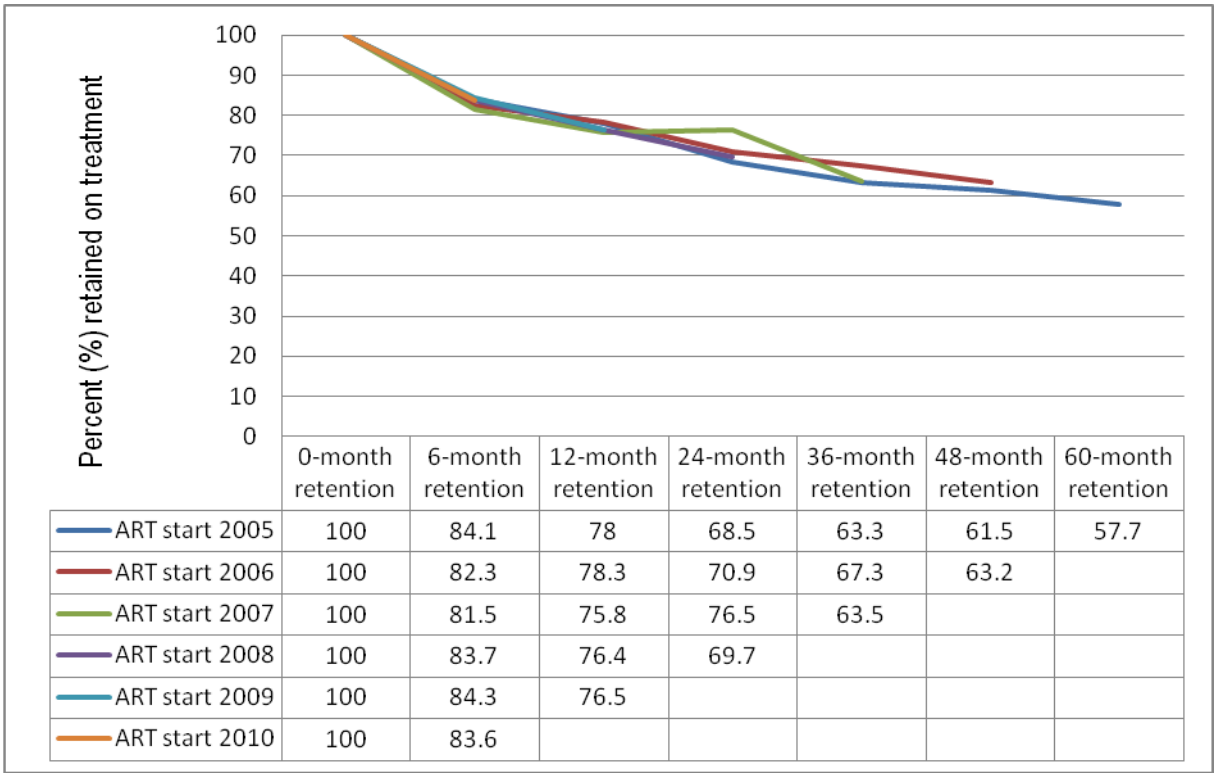
Similarly, in this study by Assefa, Y et al [38], more than 79% of patients with available CD4-cell counts had a baseline CD4-cell counts less than 200 cells per micro-liter of blood. The median CD4-cell counts based on patients who were retained after 24 months on ART increased from 125 (inter-quartile) (IQ), 68-189) at baseline to 242 (IQ, 161-343), 269 (IQ, 185-380) and 316 (IQ, 226-445) cells per micro-liter after 6, 12, and 24 months on ART, respectively. This indicates that medium CD4 count increases with the duration on ART. The transition to second-line regimens in all the health facilities remained very low. This is an indication that if health facilities could optimise adherence and close monitoring of patients especially in the early months of treatment, long term clinical, immunological and virologic benefits can be achieved.

In Uganda, MOH through the AIDS control program continues the vigilance to monitor performance of both private and public HIV programs as a measure to improve quality of care. In 2011 a national assessment of the trends over time in antiretroviral therapy outcomes was carried out in 277 HIV health facilities [27]. These were evaluated and compared at different time periods of treatment in patients who started ART in 2005-2010 using retrospective cohort analysis of routinely collected patient monitoring data as demonstrated below.

2.4.2 Trends in retention of clients on treatment after various intervals in Uganda

WHO recommends that at least 80% of clients initiated on ART should be retained in care [40], however as expected, data from ART programs indicate that the proportion of clients still on treatment falls steadily with the duration of follow up on all treatment cohorts (Figure 2.2).

Figure 2.2: Retention of clients on treatment at 6, 12, 24, 3648 and 60 months cohort that started treatment in 2005-2010



	0-month retention	6-month retention	12-month retention	24-month retention	36-month retention	48-month retention	60-month retention
ART start 2005	100	84.1	78	68.5	63.3	61.5	57.7
ART start 2006	100	82.3	78.3	70.9	67.3	63.2	
ART start 2007	100	81.5	75.8	76.5	63.5		
ART start 2008	100	83.7	76.4	69.7			
ART start 2009	100	84.3	76.5				
ART start 2010	100	83.6					

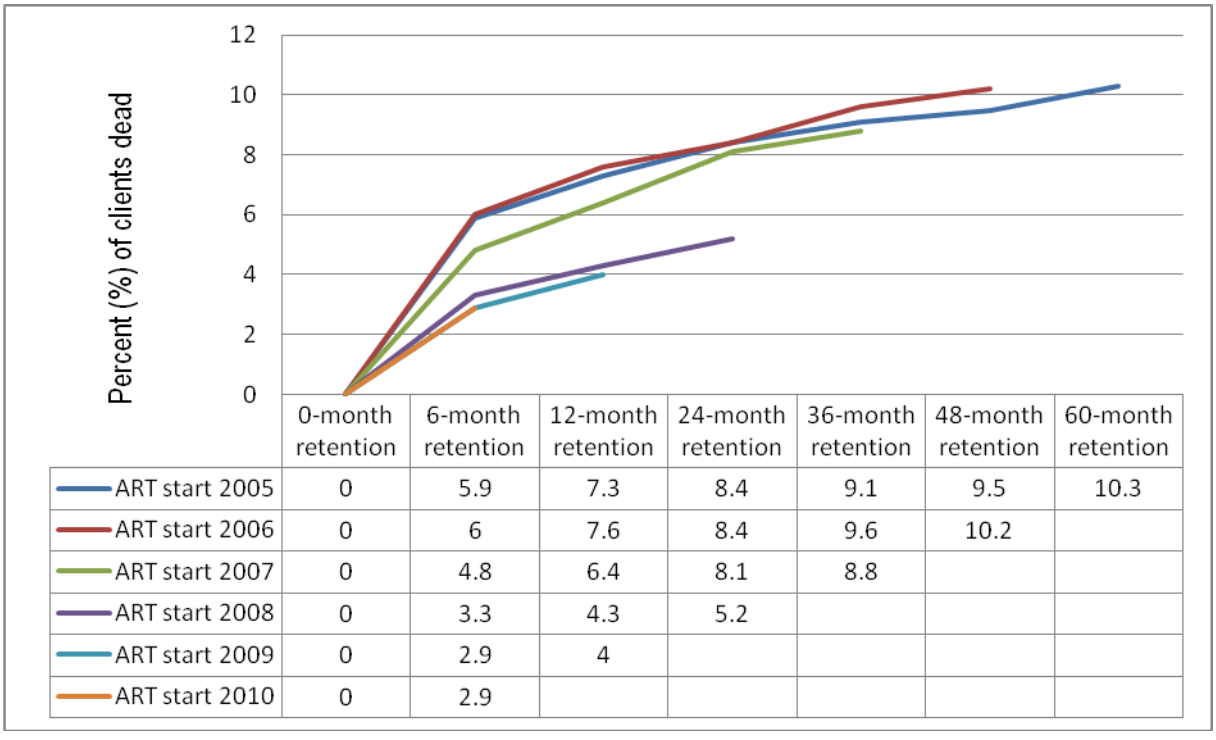
Source: MOH, STD/AIDS Control program, (2011)

As indicated in Figure 2.2, it is noted that among patients who started treatment in 2005, 84% were still on treatment at 6 months of treatment, but this had fallen to 58% by 60 months, however there is no difference in the proportion of patients retained in a particular cohort in successive years. For instance the proportional of individuals that were still on treatment at 6 months was 84% among clients that started ART in 2010, 2009, 2008 and 2005 and at 12 months about three quarters of clients were still retained on treatment among clients that started treatment in 2008, 2009 and 2007 [27].

2.4.3 Mortality at various follow up Intervals in Uganda

From Figure 2.3 below, it can be seen that unlike retention on treatment, there is a consistent decrease in trend of mortality over time among patients on ART at 6, 12 and 24 months of treatment in successive years since 2005. In this national assessment in Uganda [27], the 6 month mortality decreased by half from 6% among individuals that started treatment in 2005 to 3% in cohorts that started treatment during 2010 and 2009. The 24 months mortality fell from 8.4 % among cohorts that started treatment in 2005 to 5.2% among the cohorts that started treatment in 2008. As expected, among individuals in the same cohort, cumulative mortality increased with the duration on treatment, for example in the cohort that started treatment in 2005, about 6% of patients had died at 6 months of follow up, but this increased to 10.3% by 60 months. The relative contribution of mortality to patient attrition decreases with treatment duration.

Figure 2.3: Proportion of clients that died at 6, 12, 24, 36, 48 and 60 months among cohorts that started treatment 2005-2010



	0-month retention	6-month retention	12-month retention	24-month retention	36-month retention	48-month retention	60-month retention
ART start 2005	0	5.9	7.3	8.4	9.1	9.5	10.3
ART start 2006	0	6	7.6	8.4	9.6	10.2	
ART start 2007	0	4.8	6.4	8.1	8.8		
ART start 2008	0	3.3	4.3	5.2			
ART start 2009	0	2.9	4				
ART start 2010	0	2.9					

Source: MOH, STD/AIDS Control program, (2011)

2.4.4 Trends in median CD-4 T- Cell count at baseline and follow up

The national ART treatment guidelines recommend that ART initiation should be based on CD-4 T cell count and that CD4 cell enumeration should also be conducted at follow up interval of 6 months to monitor clinical progress [36, 13]. However, several service outlets still lack the capacity for routine CD4 T cell counts of their ART clients. In Uganda only about 50% of cohorts of patients started on ART get a CD4 count test and less than 30% of clients receive follow up CD-4 enumeration at 6, 12, 24, 36, 48 and 60 months of follow up among these cohorts [27]. Despite these limitations in performing CD4 count test in most of the HIV facilities in Uganda, the MOH patient monitoring system used in facilities tracks medium CD4 count at baseline and at follow up among patients with data on this parameter [41, 42] Aggregated quarterly reports from HIV facilities in the country show that there has been a small increase in the baseline medium CD4 count among individuals starting ART. For instance, the medium CD4 count among individuals that started ART in 2010 was 161 cell/ul compared to 106 cell/ul in 2005. The follow up medium CD4 count in all treatment cohorts of patients that started ART in 2005-2010 also steadily increased with the duration of treatment. For instance the medium follow-up CD4 count among individuals that completed 5 years of treatment, was 553 cell/ul compared to the baseline CD4 count of 106 cell/ul [27].This increase in both the baseline and follow up CD4 counts is probably a reflection of a trend towards initiation of ART earlier during the course of the disease in relation to the new WHO treatment guidelines [16].

2.5 ADHERENCE TO ANTIRETROVIRAL THERAPY

Poverty and limited health services in rural African communities present a barrier to ART adherence, yet better treatment outcomes can only be attained with maximum adherence to the prescribed medication. Such challenges necessitate innovative options to strengthen community partnership with health facilities to adequately monitor progress of registered patients. This is because the early mortality among patients on ART is associated with high baseline viral load (HIV RNA) levels, WHO stage 3 or 4 at the beginning of treatment, low body mass index, severe anaemia, and low CD4 cell count [43]. Recent studies have demonstrated that even in areas where resources are limited, good adherence to ART is critical for survival of HIV infected patients. For example, in a pooled meta-analysis of North America and African studies, survival, retention and increase in patients' CD4 count were better in Africa with adherence of 77% (95% CI 68%–85%) versus 55% (95% CI 49%–62%) versus in North America [44].

Several studies have shown that non adherence to HIV medicines is a major public health concern. It leads to virological, immunological and clinical failure. This is associated with increased risk of transmission of HIV drug resistant virus and cost of care [45]. The ministry of health Uganda recommends adequate adherence counselling when preparing a patient for ART initiation. This is because the status of adherence to ART is one of the standard measures for HIV drug resistance and early warning indicators (HIV DR EWI) in facilities providing ART [40]. ART adherence requires that adherence be assessed on an objective method such as pill adherence as shown in the table below.

Table 2.5: Ministry of health coding for ART adherence

% adherence=(no.of pills taken)/(Total no.of pills expected to have been taken)×100		Missed doses per months	
Adherence	**Percentage**	**1 x daily dosing**	**2X daily dosing**
G[Good]	≥ 95%	<2 doses	≤ 3 doses
F[Fair]	85-94%	2-4 doses	4-8 doses
P[Poor]	≤ 85%	>5 doses	≥ 9 doses

Source: MOH [Uganda] HIV/ART card

However, in the National Indicator Survey (2008), many HIV facilities in Uganda did not routinely document the method and level by which adherence was assessed. For instance, of the 76 facilities that were assessed on HIV EWI, only 57 facilities had data on ART adherence among 3,415 clients. Of these, 87.3% had attained ART adherence of at least 95% during the 12 months [40].

Table 2.6: Distribution of facilities with enrolled clients that had ART adherence of at ≥95% in 2008

Category of facilities that met the target	Number of facilities	Percentage (%)
Type of facility		
1. Regional referral hospitals	6	66.7
2. General hospitals	14	78.6
3. Health centers and private clinics	12	66.7
4. Special ART clinics, NGO including community based organisation	6	83.3
Type of medical record system		
• Paper based	25	72.0
• Electronic	13	76.9

WHO, MOH [Uganda], 2009

From Table 2.6, the proportion of facilities that met the WHO adherence target (95%) varied among the sub-types of facilities. Specialised ART clinics, NGOs including community-based programs were more likely to have a high proportion of patients meeting the required adherence threshold compared to hospital HIV programs. It was also noted that performance on the indicator did not vary by whether the facility used paper based or electronic medical record system for patients monitoring.

Poor adherence to ART is significantly associated with the risk of death. In a retrospective cohort study by Abaasa M, A et al [46] that involved 897 patients initiated on ART at the TASO clinic Kampala,

Uganda between 2004 and 2006. With 7,856 adherence assessments done, a total of 701 (78.2%) patients were found to have a mean adherence to ART of $\geq$ 95%. The crude death rate was 12.2 deaths per 100 patient years, with 42.5 deaths per 100 patient-years among poor adherence compared with 6.1 deaths per 100 patients- years for adherent patients. Given such complexity, mentoring clinical teams, providing community support to monitor of patients is crucial to maximise attainment of good treatment outcomes in the resource limited setting.

2.6 GAPS IDENTIFIED IN LITERATURE

Most studies discussed in literature used proportions to compare difference between exposure and treatment outcomes rather than the incidence rates. Use of such measures eliminated for example the total persons time of follow-up of individuals. Therefore, the measured estimate could be an overestimation as a result that is confounded by other factors.

Expanding HIV/ART programs in low-income settings requires increased human resource and capacity to monitor progress of patients on treatment. This review highlights that SSA faces the greatest health work force challenges as it has only had 3% of the world's health workers, with 11% of the world's population and 24% of the global burden of disease [47, 48]. There is a positive correlation between health work force density, service coverage and ART treatment outcomes including other health outcomes such as maternal mortality and child mortality especially in the resource limited setting [9, 49]. The findings from this study will inform current literature especially for Uganda about the effectiveness and performance of community-based and hospital ART programs in relation to patients' monitoring and follow-up care system.

It will also identify ways in which systems can be modified to include the needs of the community which is currently the new model Government is adopting to scale up HIV services in the communities. This is because achieving universal access and equity to quality HIV care requires efforts to strengthen health systems to facilitate delivery of services to all those in need, including marginalised populations.

If the Government of Uganda is planning to expand community-based HIV services, it is important that evidence is produced that the already existing programs show real advantage to the registered patients compared to hospital-based facilities. Therefore, this study is expected to feed into that concept and strategy.

CHAPTER 3: METHODOLOGY

Introduction: The aim of this chapter is to highlight the methodology of this study: sampling, data collection, and analysis used in this study design. It also highlights the methods of care and follow up of ART patients used in the selected study areas: i.e. the community based and hospital-based ART programs.

3.1 STUDY SETTING AND POPULATION

The greater Masaka distinct is situated 37km south of the equator with an average altitude of between 1066m and 1524m above the sea level. It is bordered by the districts of Ssembabule in the northwest, Mpigi in the north, Rakai in the west and Kalangala in the east. The total area of the district is about 6,413.3 sq. km of which 3,214 sq. km is land and the rest is water and wetlands. The district has a total population of 767,759 people (50.8%F, 49.2% M) of which 71% of the population are engaged in subsistence agriculture as their main occupation. The majority of the population (50%) is below 15 years, 46% between 15 and 64 years and only 4% is over 65years. There is a high population growth of about 1.7% per annum. The district is among the regions that have faced the socio-economic impacts of HIV and AIDS in south western region of Uganda [50]. However with the enormous interventions and support from various IPs that include Uganda Cares HIV Clinic Masaka Regional Referral Hospital (MRRH), Kitovu Mobile HBC program, TASO Masaka, Viira Maria Hospital, Kitovu Hospital, Medical Research Council (MRC), Rakai Health Science Project (RHSP) and health centers, the HIV prevalence has significantly reduced in the region with wide scale up of antiretroviral therapy to PLHA living in both urban and rural communities.

3.1.1 Kitovu Mobile AIDS Organization (Kitovu Mobile)

This is a commuity based care program under the registered trustees of Masaka Catholic Diocese. It was started in 1987 by the Medical Missionaries of Mary (MMM) from Ireland in response to the early HIV and AIDS crisis in Rakai district, where the first AIDS cases in Uganda were identified. The organisation employs a holistic approach to addressing needs of both the infected and affected people within their communities especially in the "hard to reach areas" where access to medical care is limited. The operational area is predominantly rural and poor, with HIV prevalence 7-12%. The HBC program- the core intervention program of the organisation operates in 111 patients care centers spread in 27 sub counties of the targeted districts [51]. Currently, a total of 6146 HIV postive patients are registered in the program of which 1200 (828 F, 372 M) clients are active on ART [41]. The success and effectiveness of the Organization depends critically on a very strong community support network and involvement. A total of 750 (238F, 512M) Community Volunteers work with the clinical teams and particpate in the implementation of the program's activitites. In order to increase accessibility and monitoring of ART adherence, the organization has proactively involved PLHA in the management of ART. There are 145 (80F, 65M) Expert Clients (ECs)[3]whose role is to provide adherence counselling,

[3] *'Expert Clients' are PLHA who have been stabilized on ART, trained in the management of HIV and AIDS care and support, particularly about the action of ARVs and their correct usage and are an integral part of the clinical team as a liaison between the clinic and the community [46].*

home visit, share experiences with fellow clients and to report any patients experiencing drug related side effects to the clinical teams. Whereas the intervention began in Rakai district, they have since spread to other districts that include the greater Masaka region, and Ssembabule district.
The main goal of Kitovu Mobile is "to alleviate the medical, psychosocial and economic consequences of HIV & AIDS in the target districts". The key thematic areas of the organization are: prevention, care and support and community capacity building. These are implemented through three main programs as follows: HBC for PLHA; Orphans and Family Support; and Counselling and Training Program.

The HBC program specifically sought to;

- Provide counselling and HIV testing services.
- Treatment of opportunistic infections (OIs).
- Provide palliative care including chemotherapy.
- Management of clients on ART.
- Management of Tuberculosis.
- Conduct health education, HIV/AIDS awareness.
- Provide social and material support and engagement in gender main streaming.

3.1.1.2 Approach of patient's registration, care and follow up

In Kitovu Mobile, individuals who have undergone HCT in the target communities and are found HIV positive are registered and enrolled for HIV chronic care or are referred to the other HIV facilities depending to the distance to the nearby health centers or client's choice. The registered HBC clients meet once each month at the 111 designated patients care centers in the 27 sub counties. Each day, 3 follow up HBC teams (Doctors and Nurses), 1 ART team and 1 palliative care team move out to meet the patients at their centers according to their scheduled appointments. Patients who are bedridden and those who cannot reach centers for several reasons are reported and home visited by either community workers (CWs) or the clinical teams. Assessment for ART eligibility, preparation, initiation and follow-up including management of ARV related side effects is done by the ART clinical team until the patients stabilize on treatment and are then subsequently followed up by the HBC follow up teams on the monthly basis in the communities. Each patient has a file containing a standardized MOH HIV/ART card which puts summary and keeps track of individual patient chronic HIV and ART care details. Follow up for all patients on ART over years is done in the ART registers according to their treatment cohort. The commonly recorded variables on the these tools include;

- Patient demographic data, ART start date and cohort,
- Baseline and follow up characteristics,
  - Weight, WHO clinical stage, Function status
  - Type of ARV regimens, potential side effects and substitutions
  - Review and follow dates,
  - TB status, Opportunistic infection,
  - Laboratory investigations for example CD4 count

- Adherence level to treatment,
- Contrimoxazole prophylaxis and
- Expected treatment outcome status: Alive on ART, dead, transfer out, and lost to follow-up.

The trained ECs, under coordination by the ART program provide education talks to fellow clients on various topics relating to ARV treatment education, adherence, HIV and AIDS awareness and BCC, TB screening and socio-economic activities for those whose quality of life has improved. For improved service delivery, the Organization collaborates with different local partners that includes: RHSP, MRC, Uganda cares for laboratory CD4 monitoring; district hospitals (Kitovu Hospital, MRRH) for referral and management of complicated cases and MOH Uganda for supply of all the ARV medicines, clinical mentoring and support in ART monitoring and reporting system [52].

3.1.2 The Uganda Cares HIV clinic, Masaka Regional Referral Hospital

The UGANDA CARES initiative is a partnership of the MOH Uganda, AHF, Global Immunity and Uganda Business Coalition on HIV/AIDS. The name was derived from the World AIDS Day theme for the year 2001: “I CARE, DO YOU?” It was thus worked out as an anticipatory and positive answer to the question that the theme posed, thus the name “UGANDA CARES” and the first Uganda Cares clinic was opened in February 2002 in Masaka Regional Referral Hospital (MRRH). For the first time at this clinic, ART was provided outside of Kampala, the capital city and at no cost to those who needed the lifesaving medicines. The project was identified by the World Health Organization and UNAIDS in 2003 as a best practice model for ART delivery in Africa. The clinic is guided by the core values of AHF mission "*to provide quality HIV/AIDS care to those in need, regardless of the ability to pay”* [53]

Currently Uganda Cares provides quality HIV/AIDS care in partnership with Government health facilities in Masaka, Soroti, Rakai, Lyantonde, Kalisizo, Gombe and Nkozi hospitals, Kakuuto, Maddu, Mulanda, and Nagongerera Health Centres IVs. The institution also operates HIV clinics in the two largest national markets (St. Balikudembe and Nakawa Market) in Kampala, the capital city of Uganda. This is in close collaboration with key partners noted above as well as TASO Masaka, Kitovu Mobile, Medical Research Council (MRC), AID Child, the main HIV programs in the district [54]. By using such a model that involves partnership with static and outreach clinics, non-Governmental organisations (NGOs), CBOs as well as families and friends who refer loved ones, Uganda Cares has created a network of HIV care and treatment, psychosocial support and other basic HIV/AIDS services, instrumental in providing the kind of support that enables clients on ART to receive comprehensive care.

The main services offered by Uganda care HIV clinic in MRRH include;

- Medical consultations, training and capacity building.
- Antiretroviral Therapy
- Treatment of OIs
- Infrastructure development
- Laboratory monitoring including CD4 T Cell monitoring.
- Psychosocial counselling
- HIV/AIDS prevention services
  - Massive HCT services
  - Condom education and distribution

- Referral and linkage into care and treatment

3.1.2.1 Approach of patient's registration, care and follow up

The Uganda Cares clinic MRRH is the largest provider of HCT and ART services in the rural-urban areas of Masaka region. Clients who have tested HIV positive from the clinic and the general wards of Masaka hospital are counseled and registered for HIV chronic care by nurses. Assessment for ART eligibility and initiation is done at the clinic daily through immunological criteria (CD4 T cell count) and WHO clinical staging by the medical doctors and clinical officers according MOH clinical guidelines. The facility has 4 ART AID and 45 ECs who help to prepare clients for ART and also provide adherence counseling daily to clients. Follow-up is done monthly for drug refills, management of OIs and any ARVS related side effects. The clinicians organize case conferences monthly to discuss the appropriate management clients failing on first line regimens and need to be switched to second line ART regimen. All patients' medical records are kept using the MOH monitoring tools as is the case with Kitovu Mobile above and then entered in the open Medical Record System (Open MRS) by the dedicated data personnel. The facility procures its ARVs with support from AHF to supplement those received from the MOH Uganda to avoid any stock outs for the large number of clients on treatment. In order to ensure good referral mechanism, the facility collaborates with above stakeholders mainly the CBOs (Kitovu mobile and TASO) for continued follow up of clients facing transport challenge to maximize adherence to treatment.

3.1.3 ART eligibility, initiation and treatment regimens

ART eligibility and initiation in the two programs is according to WHO and the National Antiretroviral Treatment guidelines for Adults, adolescents and children [16]. The guidelines recommend that ART initiation should be based on level of HIV immune suppression as assessed by WHO HIV stage and CD-4 T cell count. In Uganda adults and adolescents with documented HIV infection are initiated on ART if;

- CD4 T cell count of $\leq$ 250 cell/ul or
- CD4 T cell count between 250 - 350 cell/ul in those;
  - who are co-infected with tuberculosis (TB) or with WHO stage 3
  - women who are pregnant
- WHO stage IV disease irrespective of CD4 T cell count or
- WHO stage I or II with CD4 T cell count if <250

Table 3.1: The recommended first and second line regimen in Uganda for adults and adolescents

1st line regimen	2nd line regimen	Comments
Preferred* AZT+3TC+NVP or EFV	ABC + DDI + LPV/r **or** TDF+ 3TC* or FTC + LPV/r	~ Relatively inexpensive regimen ~ AZT less toxic than d4T ~ AZT cause anaemia ~ If patient anaemic, start with TDF
Alternative 1 TDF+3TC or FTC Plus NVP or EFV	AZT + DDI + LPV/r **or** ABC + DDI + LPV/r **or** AZT + 3TC* LPV/r	~ Use of TDF, FTC and EFV has low toxicity, once daily administration, and effective against hepatitis. ~ When affordable, this combination is the preferred first line regimen. ~ Patients who have peripheral neuropathy and anaemia may be considered for this first line regimen.
Alternative 2 D4T + 3TC + NVP or EFV	ABC + DDI + LPV/r **or** TDF + 3TC or FTC + LPV/r	~ Generic co-formulated d4T+3TC+NVP is cheap but has been phased out in the recent guidelines to D4T associated toxicity. ~ Only d4T 30mg is recommended irrespective of weight.
AZT:Zidovudine 3TC:Lamivudive D4T: Stavudine	TDF: Tenofovir FTC: Emitricitabine NVP: Nevirapine	ABC: Abacavir, DDI: Didanosine LPV/r: Lopinavir/Rotonavir EFV: Efavirenz

Source: MOH Uganda [16]

3.2.4 MONITORING AND FOLLOW UP OF TREATMENT OUTCOMES IN THE STUDY AREA

Treatment outcomes in the two facilities are monitored by cohort analysis, which is carried out retrospectively every quarter by going through patient medical (master) cards and the ART patient register or patients data based in facilities with electronic patients monitoring systems. Outcomes are standardised and Include alive on ART, dead, lost to follow-up, stopped and transfer out (Table 3.2)

Table 3.2: Standardised monthly treatment outcomes for patients on antiretroviral treatment (ART)

1. Alive and on ART	Patient who is alive and has collected his her own 30-day supply of drugs
2. Died	Patient who has died for any reason while on ART
3. Lost to follow up (defaulted)	Patient who was placed on ART and not seen at all during a period of 3 months thereafter irrespective of the number of days the last missed appointment.
4. Stopped	Refers to complete cessation of the entire ART regiment either because of side effects or because of other reasons within the 12 month follow up period.
5. Transfer out	Patient who has transferred out permanently to another treatment unit.

Source: WHO, MOH Uganda [40]

3.2.4.1 Quarterly ARV cohort analysis

All patients who start on ARV therapy during one full quarter for example 1 January to 30 March form the fixed cohort for this period. Treatment outcomes, function status, TB assessment and drug adherence rates for the last month of that quarter are documented in the ART register from the patient's medical card soon after the quarter has finished. Every three months, the outcome data in this particular cohort are analysed (Appendix 3). In this way, new events occurring in patients in that cohort are monitored over time, as outcome data will change as patients die, default, transfer-out or stop treatment. The patients who start ARV treatment between 1 April and 30 June form the next cohort of patients, and they are followed-up in a similar way every three months by looking through the treatment cards or ARV patient register. These cohorts then increase in number as more patients over time are started on ARV therapy, and each cohort is analysed as a separate entity.

3.2.4.2 Cumulative ARV quarterly analysis

When the first two cohorts of patients have started on ARV therapy for example between 1 January and 30 June, it is important to know at a particular moment in time the total number of patients on therapy and the number alive, dead, defaulted and transferred-out. This constitutes the cumulative quarterly analysis, or, in other words, an analysis of all patients who have ever started on treatment. The data are obtained from a combined treatment outcome analysis of the April to June cohort and the July to September cohort. A form for this combined analysis is completed every quarter, and represents a cumulative record of the previous updated quarterly ARV cohort analysis forms.

3.3 METHODS AND STUDY DESIGN

A retrospective cohort study design was used to analyse the treatment outcomes of the 586 PLHA who had initiated on ART in Kitovu Mobile and Uganda cares HIV clinic-MRRH, Masaka district between the period of Feb 2007 - Dec 2011. This study aimed to assess if exposure to community-based care for example in the Kitovu Mobile influences ART treatment outcomes among PLHA compared to PLHA that have not had that form of care but were receiving hospital care in the Uganda cares HIV clinic in MRRH.

3.3.1 Sample size

By the end 2011, the total number of 1120 (781 F, 339M) adult HIV positive patients were active on ART in Kitovu Mobile [41] and 5500 in Uganda Cares Clinic, MRRS [Open MRS patient data base]. Given an approximate patient retention rates on ART at 36 months of 80% and 70% in Kitovu Mobile and Uganda Cares Clinic respectively. With a sample size of 293 in each program, we shall be 80% confident of achieving a statistically significant result at 5% level. Therefore, the total sample size (N) required for the study= 586 PLHA on ART (PS power and sample size program Version 3.0.43).

3.3.1.1 Sampling technique: Proportionate stratified random sampling

The study employed proportionate stratified random sampling technique to identify the sample size from the sampling population of patients registered on ART between 2007-2011 in Kitovu Mobile and Uganda Care clinic. Patients' data in the two programs was already stratified according to ART cohort. This data

was further stratified according to gender to ensure that both women and men are represented proportionally within the sample in each cohort that formed the study sample size. This technique ensures higher statistical precision compared to simple random sampling because the variability within the subgroups (cohorts) is lower compared to the variations when dealing with the entire population.

Table 3.3: Sample size (N_1=293) required from the community program (Kitovu Mobile)

Steps in proportionate stratified random sampling	6 months Jun-Dec 2011	12 months Jan - Dec 2010	24 months Jan - Dec 2009	36 months Jan - Dec 2008	48 months Feb - Dec 2007	Total (M)
1. Identifying the number of sampling units in the sampling population for cohorts (K)	150	192	200	173	196	**911**
2. Determining the proportional of each stratum in the *study population (P)* = *elements in each stratum (K)* / *total population size(M)*	150/911 = 0.165	192/911 = 0.211	200/911 = 0.219	173/911 = 0.189	196/911 = 0.215	
3. Determining the number of elements to be selected in each cohort= *P x sample size (N1)*	0.165*293 =48.2	0.211*293 =61.8	0.219*293 =64.3	0.189*293 =55.6	0.215*293 =63.0	**293**
Number of patients records to be assessed in Kitovu Mobile	**48**	**62**	**64**	**56**	**63**	**293**
Male	12	19	19	17	19	86
Female	36	43	45	39	44	207
4. Simple Random Sampling (SRS) was used to select the required number of patients' records by picking the 3th record in each stratum. Note: Proportional of male and females in Kitovu Mobile is 30% and 70% respectively.						

Source: Kumar R, (2011) and Kitovu Mobile, 2011

Table 3.4: Sample size (N_2=293) required from the hospital program (Uganda Cares ART clinic, MRRH)

Steps in proportionate stratified random sampling	6 months Jan-Jun 2011	12 months Jan-Dec 2010	24 months Jan-Dec 2009	36 months Jan- Dec 2008	48 months Feb-Dec 2007	Total (M)
1. Identifying the number of sampling units in the sampling population for cohorts (K)	265	910	1163	951	747	**4036**
2. Determining the proportional of each stratum in the *study population (P)* = *elements in each stratum (K)* / *total population size(M)*	265/4036 = 0.066	910/4036 = 0.225	1163/4036 = 0.288	951/4036 = 0.236	747/4036 = 0.185	

3.	Determining the number of elements to be selected in each cohort= *P x sample size (N1)*	0.066*293 =19.2	0.225*293 =66.1	0.288*293 =84.5	0.236*293 =69.0	0.185*293 =54.2	
	Sample size of the records to be assessed in Uganda Cares ART clinic	**19**	**66**	**85**	**69**	**54**	**293**
	Male	04	13	16	13	10	56
	Female	15	53	69	56	44	237
4.	Simple Random Sampling (SRS) was used to select the required number of patients' records by picking the 14th record in each stratum. Note: Proportional of male and females in Uganda cares ART clinic is 38% and 62% respectively.						

Source: Kumar R, (2011), and OpenMRS patients' data base

3.3.2 Inclusion criteria

Patients' clinical records that will be assessed for ART treatment outcomes will be comprised of;

- Patients registered for HIV care in either Kitovu Mobile or Uganda Cares HIV clinic MRRH but not both and should have been initiated on ART between 2007-2011,
- Adult HIV+ patients aged 15 to 65 years,
- and not having been started on ART at another site (Transfer in).
- All patients should be ART naive prior to initiation.

3.3.3 Exclusion criteria

The following categories of patients' records were excluded from the study;

- Mothers who become pregnant during a particular cohort of the study
- Patients not taking contrimoxazole (known hypersensitivity to Contrimoxazole)
- Patients taking ART for period less than 6 months and children

3.3.4 Data collection, feasibility and logistics

Data collection was carried out in Kitovu Mobile community-based program and Uganda Cares HIV clinic-MRRH. All study variables and ART treatment outcomes developed on the individual patient data entry tool [Appendix 2], were coded and entered directly into the epiData software. After all the entries were done, data was then exported to the STATA 12 software for cleaning and analysis. The sources of data were the facility HIV/ART patients' monitoring tools. These included;

- ART cohort registers, patients' medical records (HIV/ART patient card)
- Comprehensive HIV care including quarterly cohort analysis facility reports
- Patients' Medical database- OpenMRS in the hospital program.

All the necessary logistics for the study including; ethical approval cost, transport, stationary, facilitation to data personnel in the programs during data collection, were covered by the Irish Council for International Students (ICOS) after submission of the approved proposal.

3.3.4.1 Primary treatment outcomes for the study

- Overall treatment outcomes
- Survival and retention on ART

3.3.4.2 Secondary outcome

- Risk factors related to mortality.

These treatment outcomes were determined at baseline and at follow-up after 6, 12, 24, 36, and 48 months of ART. This is because patient survival and mortality change with increase duration on treatment.

3.3.5 Statistical methods and analysis

Data was coded, cleaned and analysed using STATA release 12 (StataCorp, USA), standardised treatment outcomes between Kitovu Mobile and Uganda Cares HIV clinic- MRRH were compared using the Pearson Chi square test (X^2 test) for all variables. Incidence rates of mortality between community and hospital were calculated using STATA_12 statistics functions. Death was the main treatment outcome used for survival analysis and the rest of the outcomes (Alive and active on ART, LTFUP and Transfer out) were considered censored. Measurement of survival time for each outcome is described in Chapter 4 (Section 4.3). The Kaplan-Meier plots and log rank tests were used to assess and illustrate survival functions stratified by the type of facility, adherence, baseline; CD4-cell count, WHO HIV clinical stage and TB co-infection. Cox proportional hazard model was used to assess the possible risk factors associated to mortality among patients on ART. All P-values were double-sided and the levels of significance was set at P=0.05 or less and 95% Confidential Intervals (CI) used throughout. Multivariate analysis was used to adjust for potential confounding variables that include; the social economic status, age of participants, duration before ART.

3.4 QUALITY ASSURANCE AND QUALITY CONTROL OF DATA

Proportionate stratified random sampling was used to identify individual patient's records from the different cohorts of study population to avoid selection and information bias. All patients' medical records, follow-up registers and databases were accessed and handled with utmost confidentiality and anonymity to avoid any potential risk of data linkage. Only patients unique ID numbers but not names were recorded on the data collection forms and all data will be protected by password and only accessible by the study investigators. The researcher adhered to good clinical practice guidelines based on UNCST guidelines. The data from the ART registers and openMRS database in the two programs was verified from the source documents (Individual HIV/ART care cards).

3.5 ETHICS

The study was approved by the Clinical Research Ethics Committee, Cork, University College Cork (UCC), in Ireland and the Uganda National Council for Science and Technology (UNCST), Kampala Uganda. In this study, there was no primary data collected from the study population. Therefore, at the facility level the researcher only sought general consent and permission from the head of each facility in to access patients' medical records.

CHAPTER 4: DATA ANALYSIS AND RESULTS

Introduction: The findings presented in this chapter are in line with the study objectives. All the findings compare the community-based ART program with the hospital-based ART program respectively throughout in the following order; patients' demographic and clinical baseline characteristics, survival and retention on ART, and a Cox proportional hazard model assessing the possible risk factors related to mortality among patients on ART.

4.1 DEMOGRAPHIC AND BASELINE CLINICAL CHARACTERISTIC OF HIV PATIENTS IN THE STUDY AREA

Table 4.1: Baseline social demographic and clinical characteristics of the study population

Demographics	Community Based Program Kitovu Mobile	Hospital Uganda Cares ART Clinic-MRRH	P. value
Number in the Study [N=586]	293 (50.0%)	293 (50.3%)	
Gender: Female	206 (70.3%)	238 (81.2%)	0.002
Male	87 (29.7%)	55 (18.7%)	
Age: Mean [SD]	36.9 (9.3)	34.4 (9.1)	0.99
Marital Status:			
Single	67 (22.9%)	55 (18.8%)	
Married or Cohabiting	90 (30.7%)	137(46.8%)	<0.001
Widow(er)	82 (27.9%)	28 (9.6%)	
Divorced or Separated	36 (12.3%)	60 (20.5%)	
Not documented	18 (6.1%)	13 (4.4%)	
Occupation			
Unemployed	2 (0.7%)	19 (6.5%)	<0.001
Paid Job	48 (16.4%)	95 (32.4%)	
Peasant Farmer	243 (82.9%)	179 (61.1%)	
Weight (kg): Mean [SD]	51.3 (9.12)	52.3 (8.93)	0.08
Overall baseline CD4 cell count (cell/ul): Median [IQR]	***n (282)* 168.5[95-218]**	***n (289)* 134 [052-198]**	**0.0002**
6 months cohort	*n (45)* 231[185-316]	*n (18)* 216.6 [127-289]	0.33
12 months cohort	*n (61)* 195 [83-233]	*n (66)* 145 [046-205]	0.04
24 months cohort	*n (63)* 160 [51-220]	*n (86)* 157 [068-207]	0.78
36 months cohort	*n (54)* 151[116-188]	*n (67)* 134 [038-183]	0.06
48 months cohort	*n (59)* 135[075-184]	*n (52)* 96.5 [037-166]	0.09
WHO HIV clinical Stage			
Stage 1	15 (5.1%)	11 (3.8%)	
Stage 2	73 (24.9%)	122 (62.6%)	<0.001
Stage 3	184 (62.8%)	126 (43.0%)	
Stage 4	21 (7.17%)	34 (11.6%)	
Contrimoxazole prophylaxis			
Yes	291 (99.3%)	285 (97.3%)	0.06
No	2 (0.68%)	8 (2.73%)	
Tuberculosis co-infection			
Yes	37 (12.6%)	61 (20.8%)	0.008
No	256 (87.4%)	232 (79.2%)	
Function status			
Bedridden [B]	2 (0.7%)	4 (1.4%)	0.52
Ambulant [A]	82 (27.9%)	73 (24.9%)	
Working [W]	209 (71.3%)	216 (73.7%)	

Initial ARV regimen			
AZT-3TC-NVP	198 (67.6%)	197 (67.2%)	
AZT-3TC-EFV	9 (3.1%)	24 (8.2%)	<0.001
TDF-3TC-NVP	9 (3.1%)	24 (8.2%)	
TDF-3TC-EFV	38 (12.9%)	7 (2.4%)	
D4T-3TC-NVP	39 (13.3%)	41 (13.9%)	

A total of 586 patients met the inclusion criteria for the study; 50% (293) received ART from community-based program and 50% (293) from the hospital program. Patients in the community program were identified from the MOH ART register and those from the hospital program were identified from the hospital OpenMRS electronic data base. All demographic and treatment outcomes were assessed from individual medical files. Patients' socio demographic and clinical characteristics were described and compared between the two treatment programs as shown in **Table 4.1.** The mean (± SD) age was 36.9 years (± 9.34) and 34.4 years (± 9.05) (p=0.99) for patients in the community and hospital program respectively. The majority of patients 243 (82.9%) in the community program were peasant farmers and overall, there were significant differences in patient's occupation status between programs (p<0.001) The proportion of patients with baseline CD4 T cell count done at the start of ART were 282 (96.2%) in the community compared to 289 (98.6%) patients in the hospital program. Patients in the community group had higher median CD4 T cell count [IQR] 169 [95-218] cells/ul than those in the hospital group 134[52-198) (p=0.0002). This difference in the medium CD4 T cell count between the two facilities was observed in all the ART treatment cohorts. At the start of ART, 205 (69.9%) and 160 (54.6%) patients were in the advanced WHO clinical stages 3 and 4. 88 (30.0%) and 133 (45.4%) were started on treatment while still in the less advanced stages of HIV infection (Stage 1 and 2) in the community and hospital respectively, probably due to low baseline CD4 counts (p<0.001). All clients in both facilities were started on first line triple ARVs regimens. Almost similar proportions of patients 198(67.6%) in community versus 197(62.7%)] in the hospital were initiated on AZT-3TC-NVP based regimen as recommended by WHO and MOH Uganda National ART guidelines. However, the difference in the distribution of other regimens in the two facilities was significant (p<0.001). Tuberculosis being one of the major opportunistic infection in HIV patients was assessed before and during ART, 61 (20.8%) patients in hospital had HIV and TB co infection compared to 37 (12.6%) patients with similar co infections in the community care program (p=0.008). There were no significant differences in the baseline function status of patients between the two facilities (p=0.52). As recommended by WHO, the majority of patients 291(99.3%) in the community and 285 (97.3%) in the hospital program (p=0.06), were taking contrimoxazole prophylaxis to prevent occurrence of bacterial opportunistic infections.

4.2 ANTIRETROVIRAL TREATMENT (ART) OUTCOMES IN PATIENT WHO RECEIVED COMMUNITY CARE COMPARED TO THOSE WHO RECEIVED HOSPITAL CARE (FEB 2007- DEC 2011)

Table 4.2 below compares ART treatment outcomes among individuals who received ART community care in Kitovu mobile with those who were accessing treatment in Masaka Regional Referral Hospital-Uganda cares ART clinic. For all patients who were put on ART during the study period in community and hospital program, those who were alive and continuing on ART were 249 (85.0%) and 213 (72.7%) respectively (p<0.001); dead 26 (8.9%) and 45 (15.4%) (p=0.02); Lost to follow up 8 (2.7%) and 27 (9.2%) (p=0.001). Treatment outcomes in all categories with the exception of those patients who were

transferred out of the facility 10 (3.1%) and 8 (2.7 %) (p=0.63) were significantly better among patient who received ART from the community program (p<0001).

Table 4. 2: Antiretroviral treatment (ART) outcomes for HIV positive adults' patients according to whether under community or hospital care in Masaka district, Uganda (N=586)

ART treatment outcome	Receiving community-based program: Kitovu Mobile [n (%)]	Receiving hospital: Uganda cares ART clinic-MRRH [n (%)]	P. value
Placed on ART (N=586)	293 (50.0)	293 (50.0)	-
Alive and active on ART	249 (85.0)	213 (72.7)	<0.001
Dead	26 (8.9)	45 (15.4)	0.02
Lost to follow up	8 (2.7)	27 (9.2)	0.001
Transferred out	10 (3.1)	8 (2.7)	0.63

Overall Pearson chi2 X^2: p<0.001

4.3 PRIMARY OUTCOME: SURVIVAL ON ART IN COMMUNITY AND HOSPITAL PROGRAM

As noted in the figure 4.2, 'death' was significantly associated with patient attrition in both the community and hospital ART program. Therefore, in this study the effect of death on patients' survival was the main treatment outcome of interest. During survival analysis patients who were still alive active on ART, LTFUP and transfer out to other facilities were considered censored. The survival time in months and years contributed by each patient unto ART in each facility was calculated from the "patient ART start date" to the date each outcome occurred for patients who were dead, LTFUP and transferred out. While as for patients who were still alive and active on ART, their survival time was calculated from the "ART start date" to the "date they were censored" from the study. Study censoring date was the date last patient who made 48 months during the study period was followed up (12th December 2011). For patients LTFUP, the date they were last seen in the clinic was the date considered censored in this study. However, all the dates they were declared LTFUP after 3 months of their last appointment were all recorded.

Table: 4.3: Mortality incidence rate for patients exposed to community ART care compared to those in the hospital

	TYPE OF FACILITY		
	Exposed: Community based care (N_1=293)	Unexposed: Hospital based care (N_2=293)	Total N=586
Failures (Deaths)	26	45	71
Time at risk in years	677.6	626.0	1303.6
Average time years	2.3	2.1	4.4
Incidence rate	3.83 per 100 person years	7.19 per 100 person years	5.45 per 100 person years
Incidence rate ratio	**0.53 (95% CI, 0.32-0.88, p=0.01)**		

Although there was staggered entry of patients into ART in each cohort during the study, the average time of follow up in years was almost similar in the two treatment programs. That is to say 2.3 and 2.1 years in the community and hospital respectively. Therefore, calculating the incidence rates for the death that impacted on patient's survival was thought to be the best estimate to compare this outcome of interest among the two programs rather than reporting proportions. Table 4.3, shows that the mortality incidence rate was lower among patients who received community ART care (3.83 per 100 person years) compared to those in the hospital (7.19 per 100 person years). This resulted into an incidence rate ratio of 0.53 (95%CI, 0.32 - 0.88). This means that patients who were exposed to community care had their risk of mortality on ART reduced to almost half compared to those under hospital care. These results were consistent in statistical significance (p=0.01) with findings shown Table 4.2, that treatment outcomes were better in the community compared to the hospital ART programs.

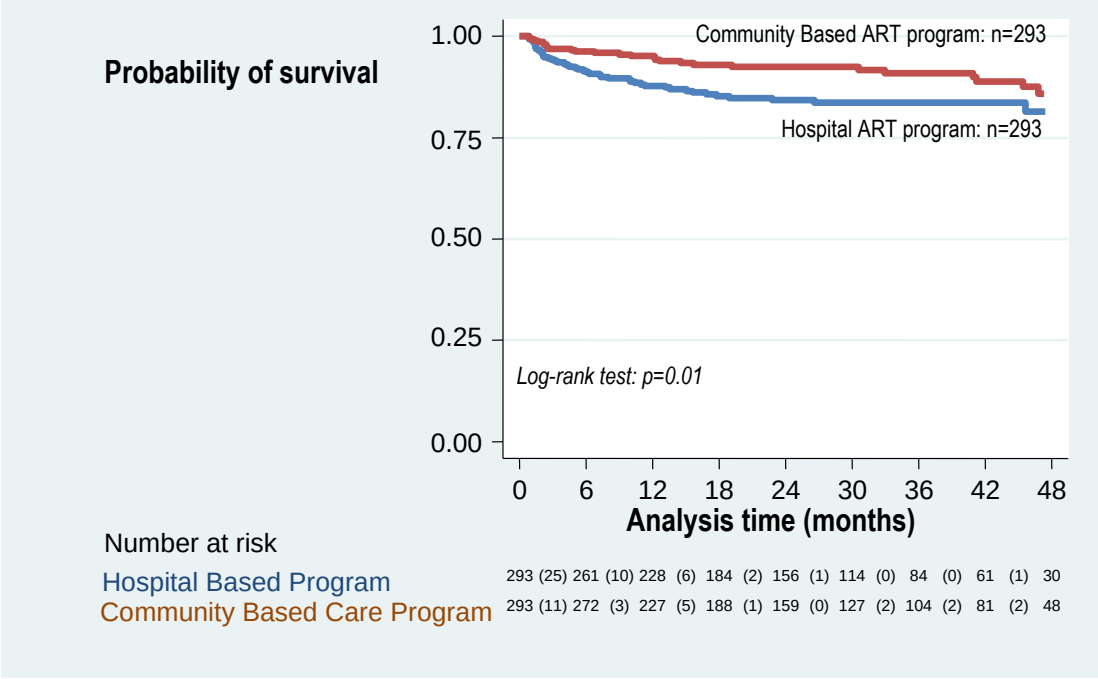
Table 4.4: Life table comparing list of survivor function and cumulative hazard (death) over specific time points

Time in months	Patients beg Total	Failures (Dead)	Survival function (%)	[95% CI]
Community based care program				
6	262	11	96.2	93.3 - 97.9
12	229	3	95.1	91.9 - 97.1
24	156	6	92.4	88.4 - 95.1
36	137	0	92.4	88.4 - 95.1
48	31	6	86.9	78.5 - 90.1
Hospital based program				
6	273	25	91.5	87.6 - 94.1
12	228	10	87.8	83.3 - 91.1
24	168	8	84.2	79.2 - 88.1
36	150	0	84.2	79.2 - 88.1
48	49	2	85.9	74.6- 86.7

Note: Survivor function is calculated over full data and evaluated at indicated times; it is not calculated from aggregates shown at left.

Table 4.4 and Figure 4.1 below, compares survival on ART in the community and hospital programs at 6, 12, 24, 36, and 48 months on treatment. Overall probability of survival of patients on treatment was higher in the community program compared to patients accessing treatment in the hospital (log-rank test: p=0.01). However, at 48 months the probability of survival is almost similar in both programs (86.9%; 95%CI, 78.5-90.1) and (85.9%; 74.6-86.7) respectively. In this study, it appears that mortality on ART tends to be high in the first 6 and 12 months. If the patients survived this period, mortality on ART apparently reduced as demonstrated in the Kaplan Meier curve (Figure 4.1).

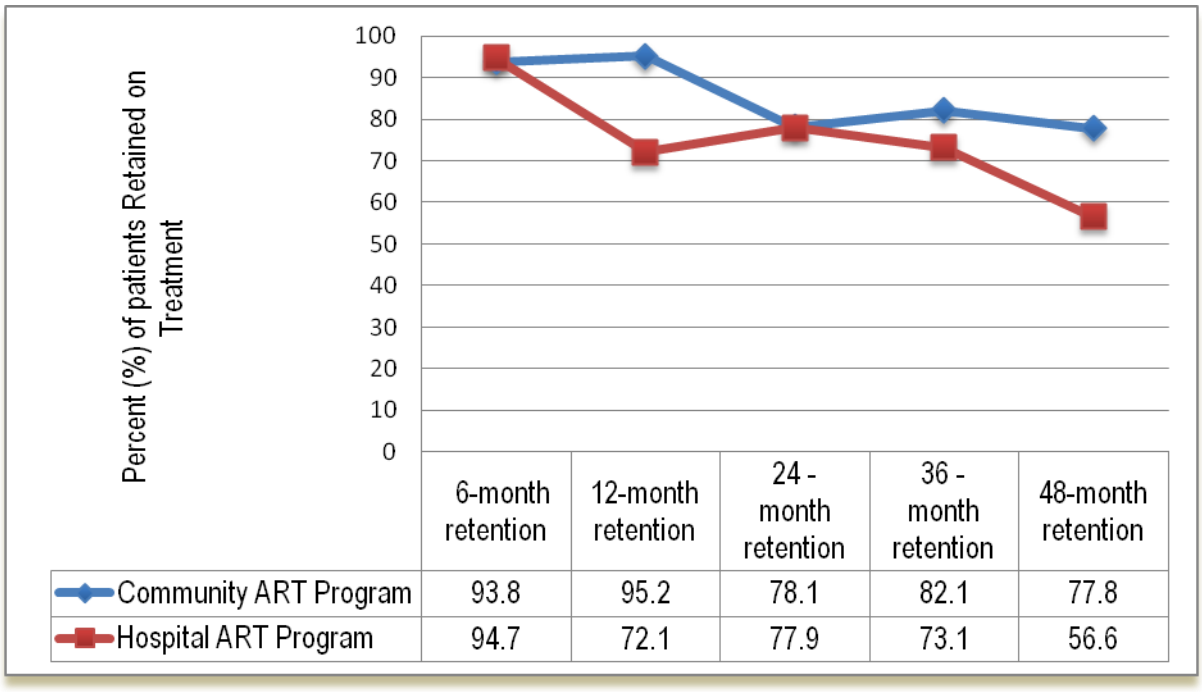
Figure 4.1: Kaplan Meier curve survival estimates in patients receiving community and hospital ART care between Feb 2007- Dec 2011



() Failures (deaths) at different time intervals

4.3.1 RETENTION ON ART

Figure 4.2: Trends in retention of clients on treatment at various intervals in the community and hospital ART programs.



	6-month retention	12-month retention	24 - month retention	36 - month retention	48-month retention
Community ART Program	93.8	95.2	78.1	82.1	77.8
Hospital ART Program	94.7	72.1	77.9	73.1	56.6

Figure 4.2, Shows the retention of patients on treatment after various follow up periods for patients recruited between 2007 to December 2011. The proportion of patients still alive and active on treatment fell steadily with time in all treatment cohorts. This correlates with the probability of survival in each

treatment program. Retention on treatment was still better in all treatment cohorts in the community ART program compared to the hospital. For instance, among clients who reached 48 months during the study period (ART start 2007), 77.8% were still on treatment in the community program compared to 56.6% in the hospital ART clinic. Of the total losses in the hospital [(80 (27.3%)], death contributed 45 (56.3%), LTFUP 27(33.8%) and 'transfer out' 8(10%). While as of 44 (15.0%) losses in the community, death accounted for 26 (59.1%), 8(18.2%) LTFUP and 10 (22.7%) were 'transfer out' to other facilities. It was also noted that most of the LTFU in the hospital (55.5%) and 50% in the community occurred during the first 6-12 months following ART initiation.

4.4 SECONDARY OUTCOME

4.4.1 RECORDED CAUSES DEATH AMONG PATIENTS ON ART IN THE COMMUNITY AND HOSPITAL PROGRAM.

Table 4.3: Causes of death among PLHA after initiation on ART in community and hospital program

		Deaths [No. (%)]	
Cause of death	**All patients (N=71)**	**Community based program: Kitovu Mobile (n=26)**	**Hospital: Uganda Cares ART Clinic-MRRH (n=45)**
Tuberculosis (TB)	31 (39.4) **	6 (23.1) **	25 (55.6) **
Pneumonia	5 (6.4)	1 (3.9)	4 (8.9)
CNS WHO Stage 4	11 (16.3)	5 (19.2)	6 (13.3)
Cryptococcal meningitis	9 (13.3)	4 (15.4	5 (11.1)
Toxoplasmosis	1 (1.1)	0 (0)	1 (2.2)
Cytomegalo virus (CMV)	1 (1.95)	1 (3.9)	0 (0)
HIV related cancers	6 (9.1)	3 (11.5)	3 (6.7)
Kaposi's Sarcoma	5 (7.95)	3 (11.5)	2 (4.4)
Cancer of the Cervix	1 (1.1)	0 (0)	1 (2.2)
GIT conditions	4 (7.7)	4 (15.4)	0 (0)
Gastroenteritis	2 (1.95)	2 (7.7)	0 (0)
Liver cirrhosis	1 (1.95)	1 (3.9)	0 (0)
Peptic ulcer disease	1 (1.95)	1 (3.9)	0 (0)
Complicated Malaria	9 (14.1)	5 (19.2)	4 (8.9)
Cause not documented	4 (5.3)	1 (3.9)	3 (6.7)

**Tuberculosis (p<0.0001)

Table 4.3 shows the recorded cause of death among patients on ART. Overall mortality was 71 (12.1%) both facilities, of which 45 (63.4%) deaths occurred in the hospital compared to 26 (36.6) deaths in the community ART program. The majority of patients 31(39.4%) died of tuberculosis, 11(16.3%) died from central nervous system (CNS) stage 4 AIDS defining conditions such as cryptococcal meningitis,

toxoplasmosis and cytomegalo virus. These were noted to have occurred in patients who started ART in 2007 making 48 months during the study. Other causes of death included complicated malaria (14.1%), AIDS related cancers, in particular, Kaposi's sarcoma (7.85%) and gastro intestinal conditions. However, 5.3% of patients had their cause of death not documented in their medical records.

4.4.2 POSSIBLE RISK FACTORS RELATED TO MORTALITY AMONG PATIENTS RECEIVING ART.

Baseline patient characteristics and adherence on ART were assessed to see if they were the underlying risk factors associated with mortality on ART among patients receiving community and hospital care. This is because in this study death was significantly associated with patient attrition and reduced survival on treatment.

Table 4.4: Crude and multivariate Cox regression hazard model for the possible risk factors related to mortality among PLHA in community and hospital ART programs in Masaka district, 2007-2011

	Crude			Multivariate		
Risk factor	Hazard Ratio (HR)	P. value	[95% CI]	Hazard Ratio (HR)	P. value	[95% CI]
Type of facility						
Community	1.0	Referent	Referent	1.0	Referent	Referent
Hospital	1.82	0.02	1.12 -2.96	1.89	0.02	1.11- 3.22
TB Co-infection						
No	1.0	Referent	Referent	1.0	Referent	Referent
Yes	4.24	<0.001	2.65- 6.77	2.92	<0.001	1.69 5.04
Baseline WHO HIV clinical stage:						
Less advanced 1 & 2	1.0	Referent	Referent	1.0	Referent	Referent
Advanced 3 & 4	4.07	<0.001	2.02 -8.19	2.62	0.01	1.25 - 5.47
Baseline CD4 cell count						
250-350	1.0	Referent	Referent	1.0	Referent	Referent
100-249	1.91	0.86	0.31- 2.61	1.83	0.79	0.29 -2.54
<99	2.43	0.09	0.86- 6.82	1.89	0.24	0.65 -5.44
Unknown	4.77	0.02	1.28 -17.8	1.95	0.34	0.49- 7.65
Baseline ARV regimen						
AZT-3TC-NVP	1.0	Referent	Referent	1.0	Referent	Referent
AZT-3TC-EFV	2.44	0.04	1.06-5.61	0.66	0.38	0.26-1.66
TDF-3TC-NVP	3.89	0.001	1.78- 8.52	2.49	0.03	1.12- 5.56
TDF-3TC-EFV	5.33	0.001	2.82- 10.1	3.29	0.001	1.63- 6.62
D4T-3TC-NVP	1.85	0.07	0.96-3.59	1.29	0.47	0.65-2.53
Adherence						
≥95% [Good]	1.0	Referent	Referent	1.0	Referent	Referent
<95% [Fair & Poor]	3.33	<0.001	2.09 -5.31	2.97	<0.001	1.85-4.79

The Cox proportional hazard model was used to compare the chances of death associated with baseline characteristics at the start of ART and adherence to treatment during the study period. The

stepwise selection approach identified type of facility (p<0.001), tuberculosis co-infection (p=0.0002), adherence to ART (p<0.0001), baseline: WHO clinical stage (p=0.01), CD4 T cell count (p=0.008), and type of ARV regimen (p=0.002) as possible risk factors for mortality on ART. Factors with a p. value ≥ 0.05 that included patient age, gender, occupation status, baseline weight, duration before ART and type of cohort were eliminated by the step wise. The results of the crude and adjusted risk factors are shown in the **Table 4.4** above.

In both the crude and adjusted analyses, the type of facility was significantly associated with high risk of death (HR=1.82; 95%CI, 1.12-2.96, p. 0.02) and (HR=1.89; 95%CI, 1.11- 3.22, p. 0.02) respectively. Meaning that a patient who was receiving ART from the hospital program almost had 2 times the hazard of death compared to the same patient under community care. This finding was consistent with the incidence rates for death (Table 4.3). PLHA on ART with TB co-infection at the start of ART had 3 times increased the risk of death as compared to those without HIV/TB co infection (HR=2.92; 95%CI, 1.69 - 5.04, p<0.001). Baseline WHO HIV clinical stage was also significantly associated with increased of death. Patients who were started on ART when they were in stage 3 and 4 categorised as advanced stage, had 4 times at risk of death in the crude model (HR=4.07; 95% CI, 2.02 -8.19, p<0.001) and almost 3 times at risk of death in multivariate model (HR=2.62; 95% CI, 1.25 - 5.47, p=0.01). Similarly, patients who had fair and poor adherence to ART categorised by WHO as adherence ≤ 95% had the same hazard of death in both unadjusted and adjusted analyses (HR=3.33; 95%CI, 2.09 -5.31, p<0.001) and (HR=2.97; 95%CI, 1.85-4.79, p<0.001) respectively. That is if two patients were on ART, one with adherence level ≤95% and another with good adherence ≥95, the patient with adherence <95% was 3 times as likely to die compared with death patient with optimal adherence.

Baseline CD4 T cell count is the most significant indicator of the degree of immune suppression among patients with HIV. In both the crude and multivariate model, patient who started treatment with baseline CD4 T cell count below 250 cell/ul were nearly 2 times as likely to die compared to patients who started with CD4 T cell count between 250-350 cell/ul. However, there was no statistical significance in all the CD4 categories. It was however noted that patients who were initiated on ART with their CD4 count cells unknown 15 (2.6%), had the highest risk of death in the crude mode (HR=4.77; 95%CI, 1.28 -17.8, p=0.02). This is perhaps they were already in late stages HIV disease stage with probably no functional CD4 T cell count.

The type of ARVs regimen patients were given at the start of ART was also noted to be a risk factor to mortality. In the multivariate model for example, the hazard of death was twice in patients initiated on TDF-3TC-NVP (HR=2.49; 95%CI, 1.12-5.56, p. 0.03) and 3 times in patients initiated on TDF-3TC-EFV (HR=3.29; 95%CI, 1.63 - 6.62, p=0.001). This is perhaps because patients started on these regimens already have other HIV related complications such as tuberculosis, Kaposi's sarcoma, neuropathy and anaemia. Such OIs already may increases someone's risk of death regardless of which ARV regimens they are given. However, such findings may call for more studies on the safety and effectiveness of such combinations especially that contain Tenofovir Disoproxil Fumarate (TDF). The effect of these factors on survival was demonstrated in the **Figures 4.3, 4.4, 4.5, 4.6, 4.7 and 4.8** as shown below.

Figure 4.3: KM showing survival estimates in PLHA on ART with or without TB co infection in both community and hospital Program

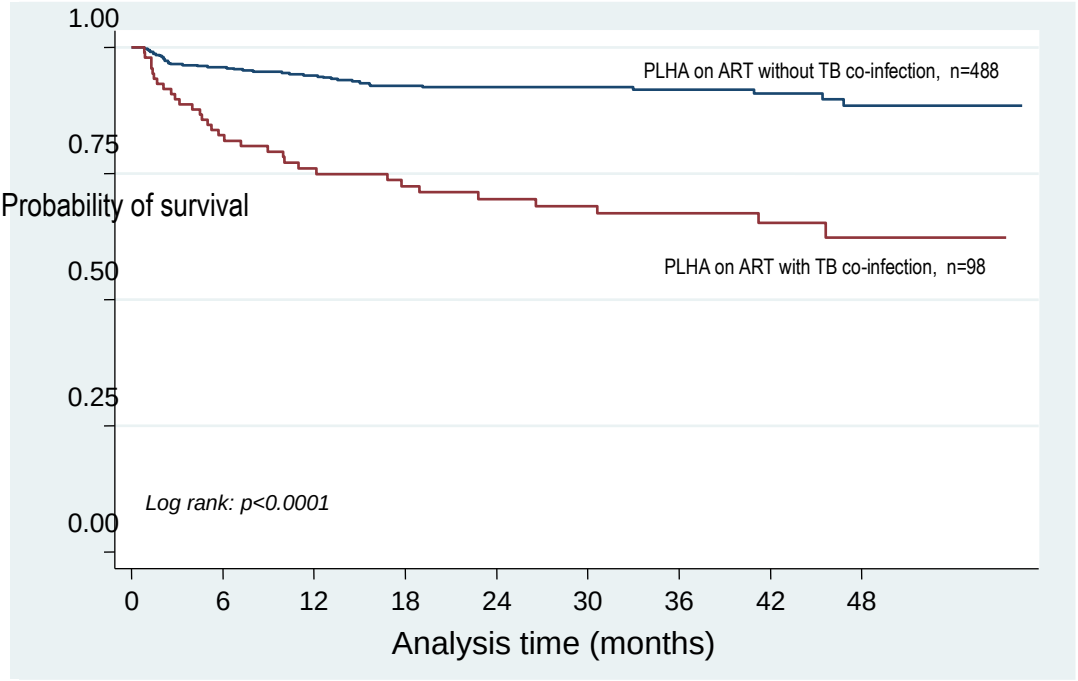


Figure 4.4: KM showing survival estimates in PLHA in less and advanced WHO clinical stage at baseline ART in both community and hospital Program

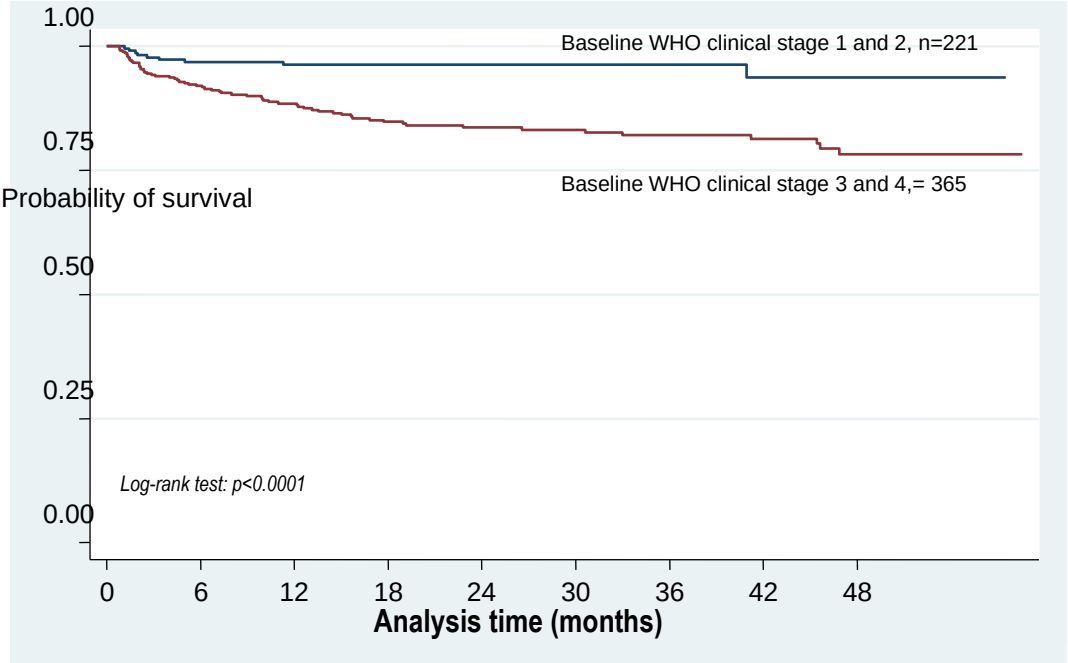


Figure 4.8: KM showing survival estimates in PLHA on ART according to the level of adherence

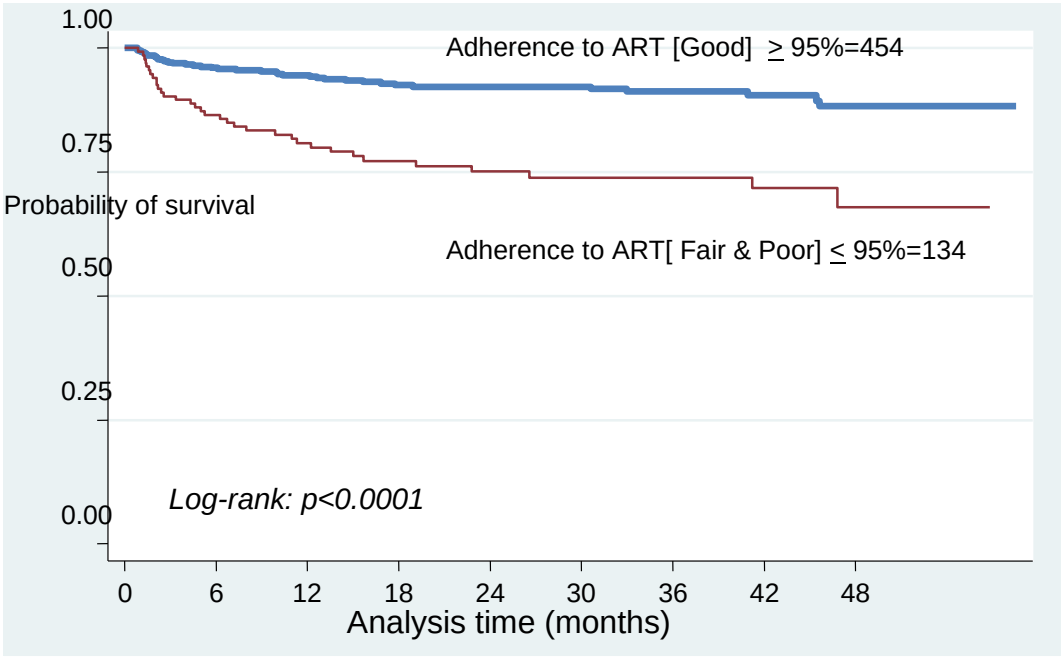


Figure 4.5: KM showing survival estimates in PLHA on ART according to the baseline CD4 T cell count

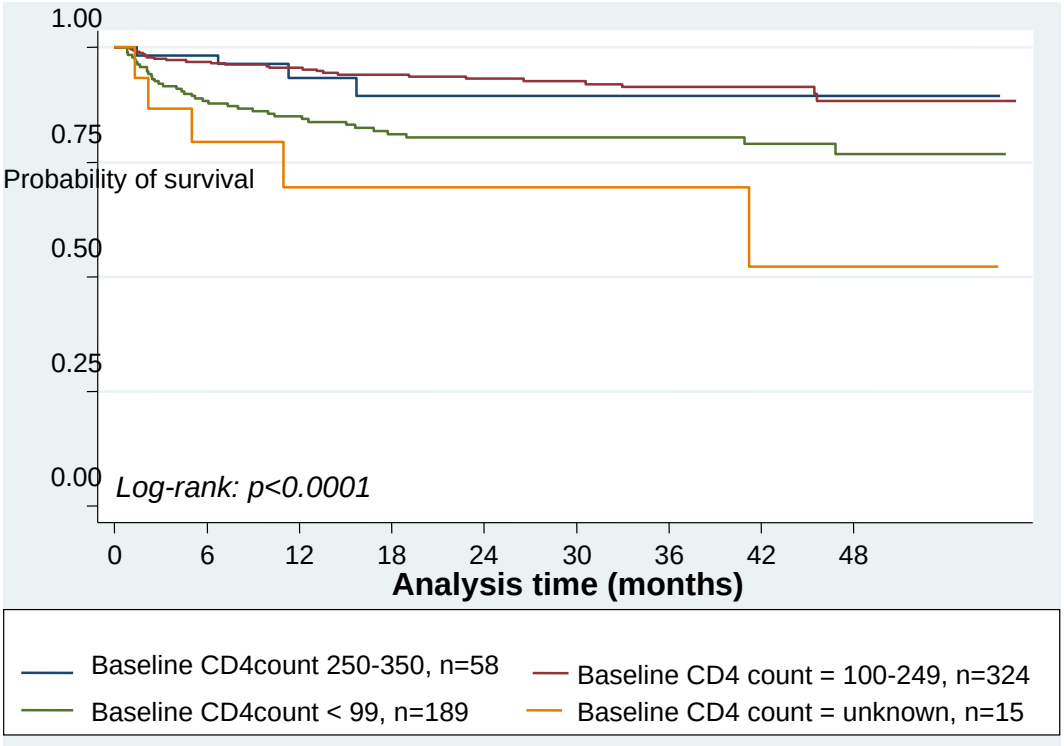


Figure 4.6: KM showing survival estimates in PLHA on ART according to the initial antiretroviral (ARVs) regimen

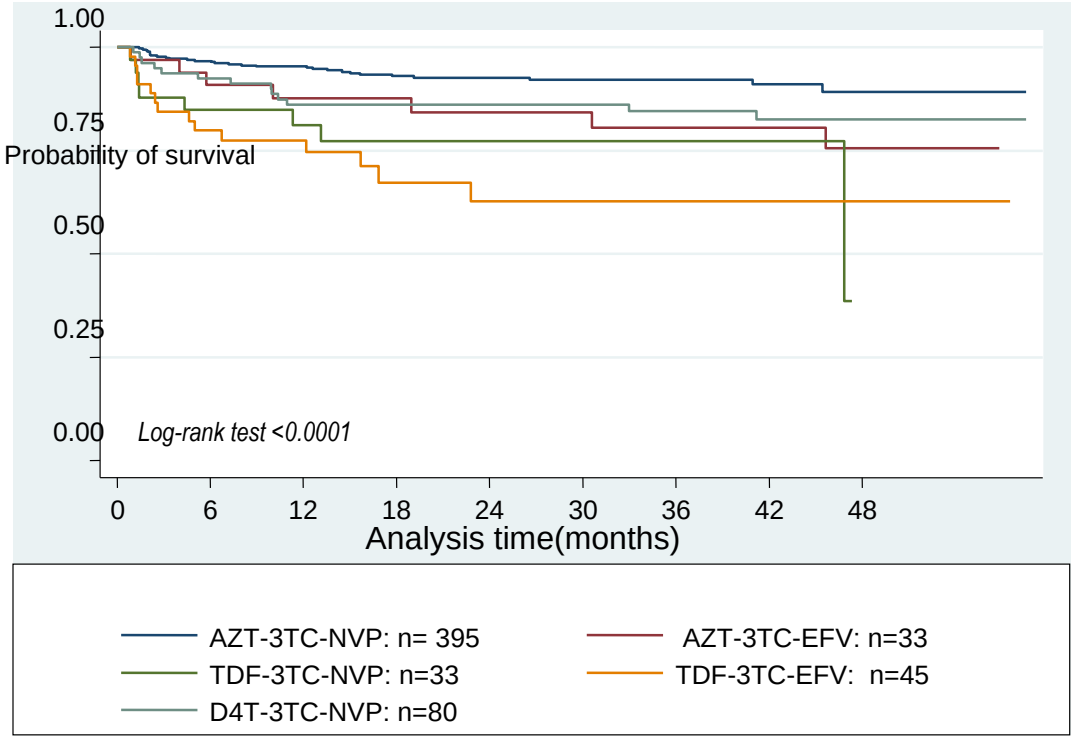
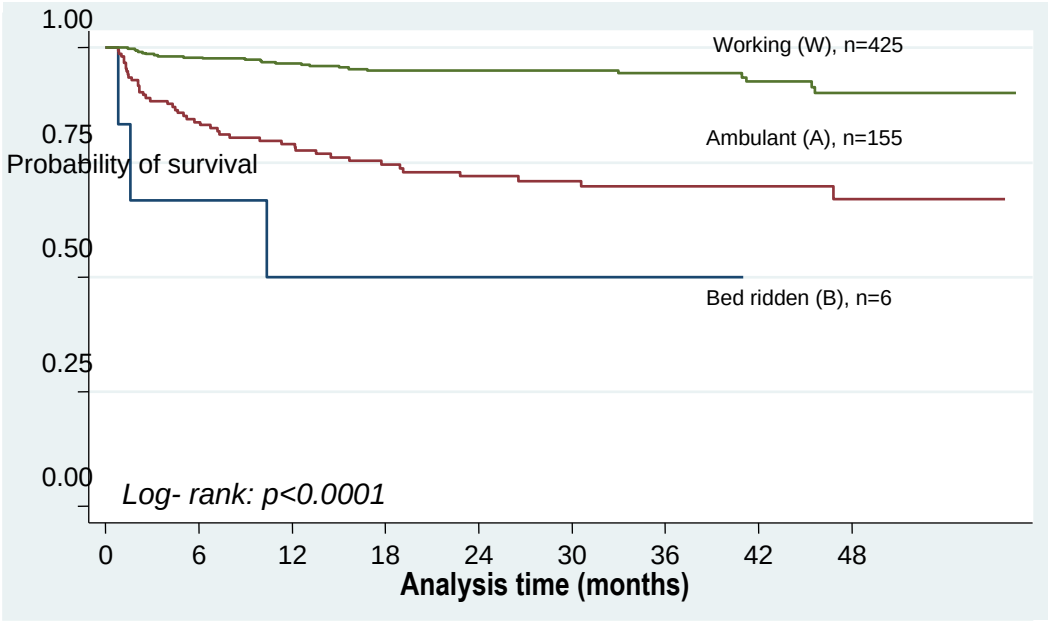


Figure 4.7: KM showing survival estimates in PLHA on ART according to their baseline function status.



CHAPTER 5: DISCUSSION

Introduction: This chapter presents the discussion of the study findings in relation to the reviewed literature and my own understanding of the concept. It highlights critical conclusions from a public health perspective that may be considered when formulating policies to scale up quality antiretroviral therapy in a resource limited setting. Similar to Chapter 4, the discussion is comparative in nature i.e. the community-based program findings are discussed first followed by a discussion of the hospital-based program findings.

5.1 PATIENT DEMOGRAPHIC AND BASELINE CLINICAL CHARATERISTICS

The majority of patients in the study were females, 206 (70.3%) and 238 (81.2%) in community and hospital care program respectively. This is explained by women's vulnerability to HIV in Uganda which is similar to other countries in SSA and internationally [1], or perhaps women sought HIV medical care earlier than men in both programs. Patients in the community program were slightly older than those in the hospital program, with an average age of 36.9±9.3 and 34.4±9.1 years. The mean age concurs with the national sero survey showing that the HIV epidemic has shifted its concentration from the age group of 24-25 years to those over 30 years and above [15, 25]. It was also noted that the majority of patients were married and cohabiting, again harmonizing with the findings of the UAC [25]. Married couples contribute to 42% of all new infections in Uganda [15]. Most of the patients (82.9%) in the community program were farmers reflecting that the program targets are predominantly rural and hard to reach areas, who are largely involved in subsistence farming.

It is worth noting that the medium baseline CD4 T cell count [IQR] for patients registered in the community was higher 169 [95-218] than that of patients who started ART in the hospital 134 [52-198]. This was true for all treatment cohorts under the study, suggesting that patients in the hospital were sicker (more immune suppressed) at the start of ART compared to those in the community. This may also explain the observed mortality proportions in the hospital (15.4%) compared to the community program (8.9%). It could be attributed to the empowerment and involvement of community volunteers who participate in the sensitisation and mobilisation of communities on the importance of early HIV testing, thus perhaps HIV positive people were identified earlier during the course of the disease in the community rather than those in the hospital program. It could also be related to the additional care and support for example nutritional support provided to registered clients in community programs as suggested by Zachariah R et al [33]. However, when patients were categorised according to their documented WHO HIV clinical staging, findings showed that 88 (30.0%) in community program versus 133 (45.4%) in hospital were categorised in the least advanced WHO clinical stage 1 and 2 while 205 (69.9%) versus 160 (54.6%) were categorised in the advanced stage 3 and 4 (p. 0.001). This implies that staging of HIV patients may be subjective depending on whether, it has been done by an experienced clinician or nurse with the ability to categorise opportunistic infections (OIs) according to the right WHO staging criteria. Therefore, monitoring patients with CD4 T cell count is perhaps the most appropriate test in decision making for initiation of ART and for follow up care. It also justifies why the majority of patients in both facilities had a baseline CD4 count at the start of ART in this study. The findings are similar to those of MOH Uganda in the national assessment of trends of ART treatment

outcomes [27]. It provides evidence for scaling up HIV services that includes the continuous mentoring clinical staff in all HIV programs and laboratory services to improve the quality care.

In both clinics in the study, it was observed that 100% of all HIV patients were assessed for tuberculosis at every clinic visit. However, the difference in the proportion of patients with a confirmed TB diagnosis 12.6% versus 20.8% (p. 0.008) in the programs could perhaps be due to the increased capacity of the hospital to assess and investigate patients for TB. For example, the Uganda Cares ART clinic is directly linked to the hospital TB Clinic unlike Kitovu Mobile, where sputum samples are collected in communities and brought to the hospital for screening. In this study like other studies patients with TB co-infection had a higher probability of death [6].

Our findings show that there were significant differences in the proportion of clients on the different ARVs regimens between the two facilities (p. 0.001). The MOH Uganda National ART Treatment guidelines recommend use of AZT-3TC-NVP as the preferred first line ARVs regimen [16]. This was reflected in this study by the larger proportion of patients, 198 (67.6%) in community and 197 (67.2%) in the hospital. This is because evidence demonstrates the efficacy in viral suppression and cost benefits of this regimen compared to other alternative regimens given in case of failure or side effects. It was also noted in this study that the proportion of clients who started on D4T-3TC-NVP in both facilities were those who started treatment in the early treatment cohorts of 2007 and 2008 before it was phased out by the MOH due to its associated toxicities.

5.2 TREATMENT OUTCOMES, SURVIAL AND RETENTION ON ART

This is the first study to compare over all treatment outcomes, survival and risk factors of mortality among patients registered in both community and hospital ART programs in Masaka district, Uganda. Standardised ART treatment outcomes measured in terms of alive and active on ART, death, LTFUP (defaulters) were significantly better among patients who received community care and support compared to those who were accessing ART from hospital the setting. There was no difference in the number of patients transferred out from both clinics to other facilities. It is recommended by the MOH that ART facilities try as much possible to retain patients in care in order to maximise follow up on treatment outcomes and reduce the development of resistance to ARVs [40]. With the rapid and massive scale, up of HIV testing in Uganda, it is expected that the number of eligible patients in need for ART will continue to increase and as suggested by Kober K, et al [22], that expansion of HIV programs should be balanced with the ability to do job. This study in particular revealed that individuals who received community care had lower incidence of mortality rates and LTFUP compared to individuals in the hospital. These results were consistent with a study done by Zachariah R, et al [33]. The probability of survival as demonstrated by the Kaplan Meir curve (Figure 4.1) at 6, 12, 24, 36, and 48 was high at all time points among patients who received community care, however at 48 months they become almost similar. As expected, the number of patients retained in care, although it was also high in the community (Figure 4.2), decreased with the duration on treatment in both facilities; similar to findings by the MOH Uganda [27]. The overall improvement in ART treatment outcomes and survival in the community ART program compared to that of the hospital is perhaps due to the type of care and follow up of clients. Antiretroviral therapy is lifelong therapy, thus the mechanisms to retain patients who start care must be well defined in all HIV facilities [17]. In this study it was noted that Kitovu Mobile

community program had a strong network of community volunteers, in particular well motivated and empowered expert clients. These expert clients play a crucial role in assisting health workers in preparation, providing adherence counselling and follow up of fellow clients in the communities. They also act as a link in the referral mechanism between patients and the clinicians especially in case of any medical problem. Such collaborative strategies with communities are perhaps the main reason for reduced numbers of clients LTFUP from the community program. It is also a model that potentially demonstrates that task shifting or sharing could potentially reduce the workforce burden in health facilities in this era when the need for universal access to ART in all SSA is evident WHO [32, 49]. Other patient support initiatives such as food security and small income business projects that are usually found in community programs could also have an impact on increasing patient support network, solidarity and stigma reduction. For instance, in Kitovu Mobile the introduction of the 'beyond ART' agricultural projects in 2008 may have played a role in improving patients' nutritional status and the retention of patients involved in the projects. In this study patients who started ART when they were ambulant had less chances of survival compared to those who were working (Figure 4.7). This is more likely be due to poor nutrition despite access to ART, although it was not possible to demonstrate whether patients' body mass index (BMI) influences treatment outcomes since patients' heights were not included in recorded data.

As noted in this study mortality contributed to the highest reduction in survival rates of patients, however it decreased with the duration on treatment in both the community and hospital ART programs. The relative contribution of death to patient attrition and poor survival was high at 6- and 12-months following ART initiation (Figure 4.1). These findings did not match with the MOH Uganda assessment on the temporal trends where mortality among these cohorts had fallen [27]. This might indicate that although there has been changes in the ART treatment guidelines that recommend starting patients earlier during the course of the disease [16], mechanisms to influence such recommendations are still limited in the country. Existing challenges with low CD4-T cell count coverage in many HIV facilities perhaps indicate that the majority of patients still get initiated on treatment when they are severely immune suppressed. For instance, in this study the medium CD4-T cell counts for patients who started treatment in all cohorts were below 250 cell/ul (Table 4.1). In addition, as ART programs are expanding, facilities may also have a decreased ability to ascertain patient mortality. Many facilities do not document or misreport the cause of death, especially when the death occurs outside the hospital setting as noted by Brinkhof M, et al [18]. Without a functional national death registration system in Uganda, it is not possible to validate such information. Inability to generate these vital statistics explains most of the current difficulties in assessing the relation of ART to mortality at facility and population level.

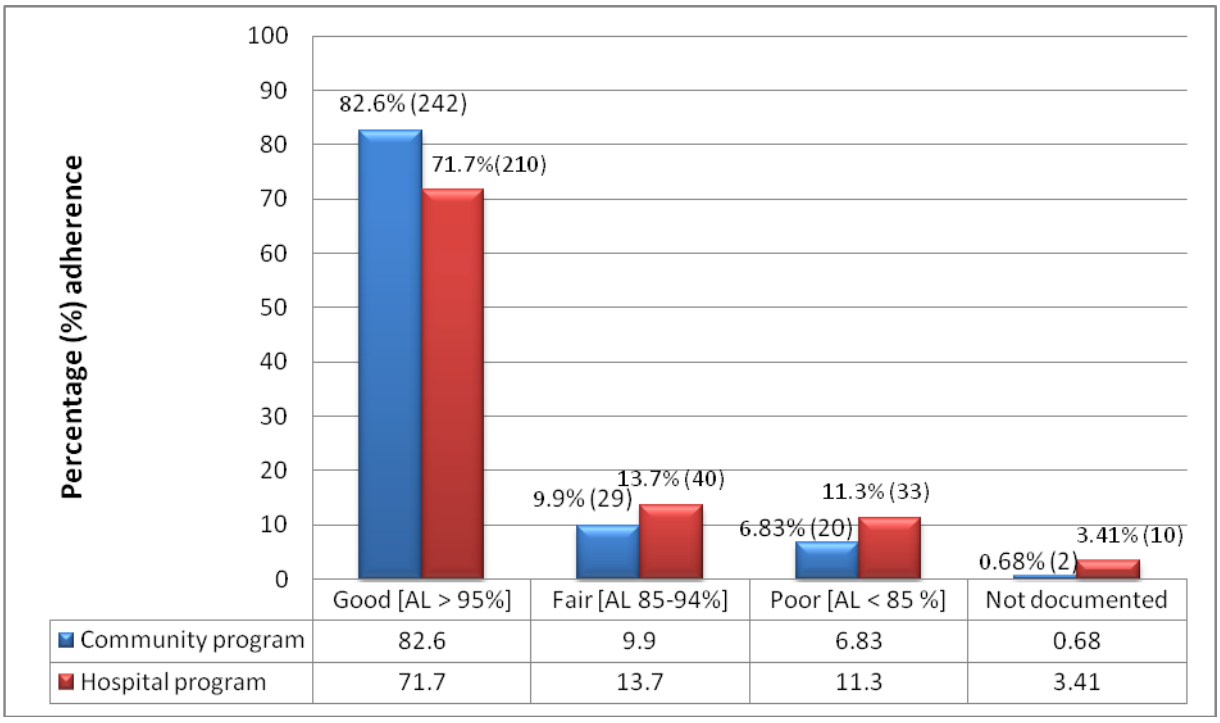
The increasing LTFU among cohorts starting treatment in recent times while programs are expanding may reflect the inability of overburdened facilities to track and retain patients on treatment as studied by WHO [32]. It may be impossible to establish whether the increasing LTFUP represents true LTFUP from health system, or patient deaths and self transfers out that is not captured by the present health system information system. The initiative for universal access to ART should be balanced with the capacity to retain and monitor patients' progress. Thus, there is a need to intensify innovative efforts by stakeholders involved in the provision of HIV/AIDS care to strengthen patient retention in care and strike balance between enrolment on ART and program capacity in terms of staff and other related cost to

provide quality services. This is critical given most countries now have ambitious efforts for accelerating ART and meet the universal access goals-coverage from 50-80% by 2015 [27].

5.3 RISK FACTORS TO MORTALITY AMONG PATIENTS ON ART

This study found that individuals who received ART from a hospital setting had an increased incidence rate and risk of mortality. It is not known why the type of facility may be a hazard to death, however as shown in Table 4.1, patients in the hospital had lower median CD4 cell count at the start of ART compared to those in the community and yet baseline CD4 count has been shown to be the most important predictor of survival [55].This finding may also be associated with the level of adherence preparation and support given to patients in care between the two facilities. For instance, although there were high proportion of patients with adherence level $\geq$ 95% in both facilities (Table 4.8), overall adherence levels were better in the community compared to hospital; Adherence less than $\leq$ 95% was significantly associated with risk of death. This concurs with Abaasa M, et al [46] that good adherence and improved survival in community care programs influences better treatment outcomes. As discussed earlier, the comprehensive community approach in Kitovu Mobile that supports patients to adhere to ART, reduced transport costs for patients since treatment is taken to the communities and regular follow up of clients including home visits, the nutrition support, may perhaps explain the low levels of patients' attrition from the program.

Figure 5.1: Adherence level (AL) to ART among receiving community and hospital care between Feb 2007-Dec 2011



Although ART has beneficial effects on mortality and lowers the incidence of OIs, tuberculosis remains the most significant opportunistic infection responsible for mortality among with HIV patients [6]. In this study the 39.4% deaths were due to TB, 23.1% in the community and 55.6% in the hospital program. TB and HIV co-infection increased the risk of death by 3 times despite enrolment on ART. These findings were consistent with the study from South Africa by Yukari C, et al [56] that showed that if ART has little

effect on AIDS outcomes in the first 6 months of treatment, it may suggest that the patient may be experiencing the effects of unrecognized active tuberculosis. Therefore, with this extra burden of TB on HIV patients, all programs need to intensify TB case finding, diagnostics, referral mechanisms and patients' awareness to detect subclinical TB before it is unmasked after initiation on ART.

In this study enrolment in care with advanced HIV disease was associated with an increased risk to mortality. In the crude analysis not shown in Cox model, a patient who started ART a short time (within one year) after HIV diagnosis had 3 times the hazard of death compared to those with duration more than 5 years (HR=3.41 95%CI, 1.83 -6.34, p<0.001). In this study 60.2% (353) patients started ART within one year of HIV diagnosis suggesting that by the time they were diagnosed with HIV, were already severely immune suppressed. In Uganda less than 30% of the population know their HIV sero status [15]. Therefore, efforts for early HIV diagnosis are critical in all SSA countries. However, the capacity and the cost of providing care to the increasingly huge number of patients remains a "global question". Thus, intensifying HIV prevention and getting back to the original behaviour change campaigns programs is likely to be the solution to this HIV global epidemic challenge [25]. These conclusions probably demonstrate a true association between baseline characteristics and survival or risk to mortality in ART programs. This is because in this study a high proportion of patients had these observations documented, therefore findings may not be due to information or selection bias.

5.4 CONCLUSION

This study has shown that overall treatment outcomes, survival and retention for patients on ART, are better and more feasible in community-based ART programs such as the Kitovu Mobile, Uganda rather than in hospital-based programs. The findings are stark in relation to mortality where the incidence rates are considerably higher in hospital-based programs. This may be because patients presented to hospital are in advanced HIV stages or it may simply be because the type of care and support in the community is such that patients on ART on a community-based program do better as our analysis demonstrates. The implication of these findings for future ART programs in Uganda is that community-based programs should be strengthened as part of an integrated health care system. However, in order for this to happen, there is a need for continued support of these programs to overcome challenges of reduced funding, staff attrition so that sustainable quality ART care and services are provided to people living with HIV and AIDS. This study will provide evidence to support this argument.

5.5 STRENGTH OF THE STUDY

The strength of this study is that the data used to asses treatment outcomes came from a 'real-life' program setting, and from the standardised MOH Uganda patient monitoring system. A relatively large number of patients on ART were included in the analysis. The average person follow-up time for patients in both groups was almost similar and thus comparable between the two study programs. Thus, the results are likely to reflect the true reality on patients' treatment outcomes, the possible risk factors that are related to mortality among patients on ART and the benefits of strengthening community care in the existing national health system in the resource limited settings like Uganda.

5.6 STUDY LIMITATIONS

The main limitation of this study is that, unlike a randomised control trial, the analysis was based on the already existing routine patients' records often constrained by missing data that would have helped to partly corroborate the observed trends in treatment outcomes and baseline characteristics. For example, there was no data on patient's viral load, height and some patients missed CD4 cell count. Also, the patient clinical condition may have been underestimated as assessment of some variables is subjective for instance the patients function status or misclassified of patients in the WHO clinical stage. In this study patients whose adherence level to ART was not documented were considered to have adherence level $\leq$ 95%. Similarly, the cause of death was not confirmed on post mortem studies leaving a doubt if the last documented clinical condition was the cause of death. Therefore, it is not possible to know the exact reasons for the differences observed in treatment outcome and survival between community and hospital programs.

Furthermore, the individual demographic level data captured in the study such as age and occupation were at enrolment into the HIV program, but there is no indication if this information changed over time, which could confound the observed association. It was also noted that the study was carried out in HIV facilities where there was an effort to provide socio-economic support such as income generating activities as well as food security projects among the support groups. Although no evidence was available on the impact of these interventions, these services may influence some outcomes of the study such as adherence and retention on treatment.

Nonetheless, this is a substantive study that will provide evidence to the MOH Uganda, community based and hospital-based ART programs and all other stakeholders in Uganda. Additionally, it adds to the literature base and supports the argument for scaling up ART programs in resource-limited settings even in an era of financial constraints.

BIBLIOGRAPHY

[1] UNAIDS, "Report on the global AIDS epidemic," Geneva, 2008 (http://www.unaids.org/en/KnowledgeCentre/HIVData/Global Report/2008, accessed 7 June 2012).

[2] World Health Organisation (WHO), UNAIDS, UNICEF "Global HIV/AIDS response. Epidemic update and health sector progress towards universal access," Geneva, Progress report 2011 (http://whqlibdoc.who.int/publications/2011/9789241502986_eng.pdf, accessed 10 june 2012).

[3] Kipp W, et al "Comparing antiretroviral treatment outcomes between a prospective community- based and hospital-based cohort of HIV patients in rural Uganda," *BMC International Health and Human Rights* 2011, vol. 11(supp 2), no. S12, 2011 (http://www.biomedcentral.com/1472-698X/11/S2/S12, accessed 23 May 2012).

[4] Hladik W, Musinguzi J, Kirungi W, et al, "The estimated burden of HIV/AIDS in Uganda, 2005-2010," *AIDS 2008,* vol. 22, no. 4, pp. 503-10, 2008 (http://journals.lww.com/aidsonline/Abstract/2008/02190/The_estimated_burden_of_HIV_AIDS_in_Uganda,.8.aspx, accessed 13 april 2012).

[5] Single A, Bairy I, Shivananda P, "Spectrum of opportunistic infections in AIDS cases.," *Indian J Med Scie,* vol. 57, pp. 16-21, 2003.

[6] Weerawat M, Suthat C, Supeda T, et al, "Survival rate and risk factors of mortality among HIV/Tuberculosis co-infected patients with and without antiretroviral therapy," *JAIDS Journal of Acquired Immune Deficiency Syndromes,* vol. 43, no. 1, pp. 42-46, 2006 (http://journals.lww.com/jaids/Abstract/2006/09000/Survival_Rate_and_Risk_Factors_of_Mortality_Among.7.aspx, accessed 5 June 2012).

[7] World Health Organisation (WHO) and UNAIDS, "Treating 3 million by 2005: Making it happen. The WHO strategy," Geneva, 2003 (HYPERLINK "http://www.who.int/3by5/publications/documents/en/3by5StrategyMakingItHappen.pdf" http://www.who.int/3by5/publications/documents/en/3by5StrategyMakingItHappen.pdf, accessed 1 June 2012).

[8] United General Assembly special Session on HIV/AIDS, "Political Declaration on HIV/AIDS," New York, United Nations, 2006 (http://data.unaids.org/pub/Report/2006/20060615_HLM_PoliticalDeclaration_ARES60262_en.pdf, accessed 20 May 2012).

[9] World Health Organisation (WHO), UNAIDS, and UNICEF, "Towards universal access: Scaling up priority HIV/AIDS interventions in the health sector," Geneva, Progress report, 2009 (http://www.who.int/hiv/pub/tuapr_2009_en.pdf, accessed 29 May 2012).

[10] Ministry of Health (MOH) Uganda, "Status report on the global fund grants in Uganda," Kampala Uganda, 2011 (http://health.go.ug/MOHweb/wp-content/uploads/2011/08/global-fund-status-report-final.pdf, accessed 30 December 2011).

[11] Edward C. Green, Daniel T. Halperin et al "Uganda's HIV Prevention Success: The Role of Sexual Behaviour Change and the National Response, AIDS and Behaviour," vol. 10, no. 4, 4 July 2006, (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1544373/pdf/10461_2006_Article_9073.pdf, accessed 31 December 2011).

[12] United Sates Agency for International Development (USAID), "What Happened in Uganda? Report on the Declining HIV

Prevalence, Behaviour Change, and the National Response," Washington DC, 2002.

[13] Ministry of Health [MOH] Uganda, STD/AIDS control programme "The status of Antiretroviral Therapy Service Delivery in Uganda, Quarterly report for July-September 2010," Kampala, Uganda, 2010.

[14] Edward C. Green, Ph.D, "Faith-based Organisations: Contributions to HIV Prevention, Report by the Synergy Project implemented by TvT Global Health and Development Strategies, a division of Social and Scientific Systems," 2003 (HYPERLINK "http://www.catholic.org.tw/theology/prochastity/e-paper/20070325/text/fbo.pdf" http://www.catholic.org.tw/theology/prochastity/e-paper/20070325/text/fbo.pdf, accessed 15 May 2012).

[15] Ministry of Health (MOH)Uganda, Calverton, Maryland, USA: Ministry of Health and ORC Macro, "Uganda HIV/AIDS Sero-behavioural Survey 2004-2005," 2006 (HYPERLINK "http://pdf.usaid.gov/pdf_docs/PNADG508.pdf" http://pdf.usaid.gov/pdf_docs/PNADG508.pdf, accessed on 1 January 2012).

[16] Ministry of Health (MOH)Uganda, National Antiretroviral Treatment and Care Guidelines for Adult and Children, Third Edition, Kampala, Uganda, June 2009.

[17] Rosen S, Fox MP, Gill J, "Patient retention in antiretroviral therapy programs in sub-Saharan Africa: a systematic review," *PLoS Med ,* vol. 4, no. 10 e298, pp. 1691-1701, 2007 (HYPERLINK "http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.0040298" http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.0040298, accessed 12 June 2012)

[18] Brinkhof W, Pujades-Rodriguez M, Egger M, "Mortality of patients lost to follow-up in antiretroviral treatment programmes in resource-limited settings: systematic review and meta-analysis," *PLoS ONE,* vol. 4, no. 6: e5790, pp.1-9 2009 (HYPERLINK "http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0005790" http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0005790, accessed 5 July 2012).

[19] Yu JK, et al "What happens to patients on antiretroviral therapy who transfer out to another facility?," *PLoS ONE,* vol. 3, no.4: e2065, 2008 (HYPERLINK "http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0002065" http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0002065, accessed 9 May 2012).

[20] Makombe SD, et al "Assessing the quality of data aggregated by antiretroviral treatment clinics in Malawi. Bulletin of the World Health Organization," vol. 86, no.4, pp. 310–314, 2008 (http://www.scielosp.org/pdf/bwho/v86n4/v86n4a16.pdf, accessed on 26 May 2012).

[21] Global Fund to Fight AIDS, Tuberculosis and Malaria, "Final report for the data quality audit for HIV/AIDS in Mali," 2008.

[22] Kober K, Van Damme W, "Scaling up access to antiretroviral treatment in southern Africa: who will do the job?," The Lancet, vol. 364, no.9428, pp. 103-107, 2004 (HYPERLINK "http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(04)16597-5/fulltext" http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(04)16597-5/fulltext, accessed 29 May 2012).

[23] World Health Organisation (WHO), Ministry of Health (MOH) Uganda, "Scaling up Antiretroviral Therapy: experience in Uganda, Case study," 2003 (http://www.who.int/hiv/amds/case3.pdf, accessed 31 December 2011).

[24] World Health Organisation (WHO), Ministry of Health (MOH) Uganda, Participant manual, Compressive HIV/AIDS care including antiretroviral therapy. Integrated Management of Adult and adolescent Illness (IMAI), Kampala Uganda, March 2006.

[25] Uganda AID Commision (UAC), Moving Toward Universal Access: National HIV & AIDS Strategic Plan 2007/8 –

2011/12, Kampala - Uganda: Uganda AIDS Commission, 2007.

[26] Ministry of Health (MOH) Uganda, National Home Based Care Policy Guideline for HIV/AIDS, Kampala Uganda, August 2010.

[27] Ministry of Health (MOH) Uganda, STD/AIDS control programme, "Temporal Trends in Baseline Characteristics and Treatment Outcome among clients initiating ART in Uganda 2005-2010. Report of assesment of temporal trends in Antiretroviral Therapy outcomes in 227 Health facilities in Uganda," Kampala, Uganda, February 2011.

[28] United Nations General Assembly Special Session (UNGASS), "Uganda progress report January 2008-December 2009," March 2010.

[29] Mbulaiteye S, Mahe C, et al "Declining HIV-1 incidence and associated prevalence over 10 years in a rural population in south-west Uganda: A cohort study," The Lancet vol. 360, no. 9326, pp. 41-46, 2002 (http://www.sciencedirect.com/science/article/pii/S0140673602093315, accessed 20 June 2012)

[30] Edward C. Green, Ph.D, "What are the lessons from Uganda for AIDS prevention?," 2002.

[31] P. John Stover, ""The effects of behaviour change on trends in HIV incidence in Uganda and Kenya" [PowerPoint Presentation]. Presentation to USAID, Washington DC, Febuary. 5," 2002.

[32] World Health Organisation (WHO), Task shifting to tackle health workers shortage, Geneva, 2007 (http://www.who.int/healthsystems/task shifting booklet.pdf, accessed 29 July 2012).

[33] Zachariah R et al, "Community support is associated with better antiretroviral treatment outcomes in a resource-limited rural district in Malawi," Transactions of the Royal Society of Tropical Medicine and Hygiene, vol. 101, no.1, pp. 70-84, 2006 (HYPERLINK "http://www.sciencedirect.com/science/article/pii/S0035920306002057" http://www.sciencedirect.com/science/article/pii/S0035920306002057, accessed 20 December 2011)

[34] Stringer J, Zulu I, et al, "Rapid scale-up of antiretroviral therapy at primarycare sites in Zambia: feasibility and early outcomes.," *JAMA,* vol. 296, no. 7, pp. 782-93, 2006.

[35] Mininstry of Health (MOH) Uganda, National Antiretroviral Treatment and Care Guidelines for Adult and Children, First edition, Kampala, Uganda, 2005.

[36] Mininstry of Health (MOH) Uganda, National Antiretroviral Treatment and Care Guidelines for Adult and Children, Second edition, Kampala, Uganda, July 2008.

[37] World Health Organisation (WHO), Strengthening health services to fight HIV/AIDS, Guidelines on Contrimoxazole Prophylaxis for HIV related Infections among Children, Adolescents and Adults: Recommendations for a public health approach, Geneva, 2006 (http://www.who.int/hiv/pub/guidelines/ctxguidelines.pdf, accessed on 2 August 2012).

[38] Assefa Y et al, "Outcomes of antiretroviral treatment program in Ethiopia: Retention of patients in care is a major challenge and caries across health facilities," vol. 11, no. 81, 2011(HYPERLINK "http://www.biomedcentral.com/content/pdf/1472-6963-11-81.pdf" http://www.biomedcentral.com/content/pdf/1472-6963-11-81.pdf, accessed on 23 May 2012).

[39] Weidle J, Malamba S, et al, "Assessment of a pilot antiretroviral drug therapy programme in Uganda:patients' response, survival, and drug resistance," The Lancet, vol. 360, no. 9326, pp. 34-40, 2002.

[40] World Health Organisation (WHO), Ministry of Health (MOH) Uganda, Tracking HIV Drug Resistance in Facilities Providing Antiretroviral Therapy in Uganda. Report on Assessment of Early Warning Indicators for Antiretroviral Drug Resistance: 2008, Kampala Uganda, September 2009.

[41] Kitovu Mobile AIDS Organization (Kitovu Mobile) Uganda, "MOH Uganda, Comprehensive HIV Care including ART Quarterly Report: October-December 2011," 2011.

[42] Kitovu Mobile AIDS Organization (Kitovu Mobile) Uganda, "MOH Uganda, Comprehensive HIV Care including ART Quarterly Report: January-March 2011," 2011.

[43] Evan W, Robert S, "Higher baseline levels of plasma human immunodeficiencyvirus type 1 RNA are associated with increasedmortality after initiation of triple-drug antiretroviral therapy," *J Infect Dis ,* vol. 188, no. 10, pp. 1421-1425, 2003 (HYPERLINK "http://jid.oxfordjournals.org/content/188/10/1421.long" http://jid.oxfordjournals.org/content/188/10/1421.long, accessed on 16 June 2012).

[44] Edward J, Mills E, "Adherence to Antiretroviral Therapy in Sub-Saharan Africa and North America: A Meta-analysis," JAMA vol. 296, no. 6, pp. 679-690, 2006 (HYPERLINK "http://jama.jamanetwork.com/article.aspx?articleid=203145" http://jama.jamanetwork.com/article.aspx?articleid=203145, accessed on 15 August 2012).

[45] Maggiolo F, Airoldi M, et al, "Effect of adherence to HAART on virologic outcome and on the selection of resistance-conferring mutations in NNRTI- or PI-treated patients.HIV Clin Trials 2007," Malawi. AIDS , vol. 20, no. 18, pp. 2355-2360, 2006.

[46] Abaasa AM, Todd J, et al, "Good adherence to HAART and improved survival in a community HIV/AIDS treatment and care programme: the experience of The AIDS Support Organization (TASO), Kampala, Uganda," BMC Health Services Research, vol. 8, pp. 241, 2008 (http://researchonline.lshtm.ac.uk/5503/1/1472-6963-8-241.pdf, accessed 15 May 2012).

[47] Barnighausen T, Bloom E, Humair S, "Human resources for treating HIV/ AIDS: Needs, Capacities and Gaps," AIDS Pat Care STDs , vol. 21, no. 11, pp. 799-812, 2007.

[48] World Health Organisation (WHO), "The World Health Report: Working together for health," World Health Organisation (WHO), Geneva, 2006.

[49] World Health Organisation (WHO), "Interaction Between Global Health Initiatives and Health System: Evidence from Countries, The Maximising Positive Synergies Academic Consortium," June, 2009 (HYPERLINK "http://www.who.int/healthsystems/publications/MPS_academic_case_studies_Book_01.pdf" http://www.who.int/healthsystems/publications/MPS_academic_case_studies_Book_01.pdf, accessed on 13 August 2012).

[50] Uganda Bureau of Statistics (UBOS), "Uganda Population and Housing Census Main Report," Kampala, Uganda, 2002.

[51] Kitovu Mobile AIDS Organisation (Kitovu Mobile), "Evaluation report for the Kitovu Mobile Home Based Care Programme for People Living with HIV and AIDS 2006-2010," Real arketing consultant, Kampala, Uganda, 2011.

[52] Kitovu Mobile AIDS Organisation (Kitovu Mobile), "Annual Home Based Care Report for People Living with HIV and AIDS (PLHA) in Masaka, Rakai, Ssembabule and Lyantonde districts," 2011.

[53] Uganda. Cares, " Uganda Cares first year rogressive report: We egan a journey we have a direction. Antiretroviral treatment model in rural Uganda," July, 2003.

[54] AIDS Health Care Foundation (AHF) Bureau, "Annual Report," 2009/2010.

[55] Nash D, et al, "Long-term immunologic response to antiretroviral therapy in low-income countries: a collaborative analysis of prospective studies.," AIDS, vol. 17, no. 22, pp. 2291-2302, 2008 (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2794130/pdf/nihms89935.pdf, accessed 5 October 2012).

[56] Yukari C, Ronan B, et al, "Unmasked Tuberculosis and Tuberculosis Immune Reconstitution Inflammatory Disease: A Disease Spectrum after Initiation of Antiretroviral Therapy," Infectious Diseases Society of America., vol. 3, no. 199, pp. 437– 44, 2009 (http://jid.oxfordjournals.org/content/199/3/437.full.pdf, accessed 4 October 2012).

[57] Ssentongo R, Nantumbwe M, "Home Based Care Report for People Living with HIV and AIDS (PLHA) in Masaka, Rakai, Ssembabule and Lyantonde districts: 2010-2012," Kitovu Mobile AIDS Organisation, 2011.

[58] Kumar R, Research Methodology. A step-by-step guide for beginners. Third edition 2011, SAGE, 2011.

[59] World Health Organisation (WHO), Ministry of Health (MOH) Uganda, Facilitator's Guide for reparation of Expert Patient-Trainer: Integrated Management of Adult and Adolescent Illness, Integrated Management of Adult and Adolescent Illness (IMAI), Kampala Uganda, August 2005.

[60] Weerawat M, Suthat C, "Survival rate and risk factors of mortality among HIV/Tuberculosis co-infected patients with and without antiretroviral therapy," *J Acquir Defic Syndr ,* vol. 43, no. 1, pp. 42-46, 2006 (HYPERLINK "http://journals.lww.com/jaids/Abstract/2006/09000/Survival_Rate_and_Risk_Factors_of_Mortality_Among.7.aspx" http://journals.lww.com/jaids/Abstract/2006/09000/Survival_Rate_and_Risk_Factors_of_Mortality_Among.7.aspx accessed 6 June 2012).

APPENDIX 2: INDIVIDAL PATIENT DATA ENTRY TOOL IN THE STUDY ART FACILITY

UNIVERSITY COLLEGE CORK (UCC), IRELAND

DEPARTMENT OF EPIDEMIOLOGY AND PUBLIC HEALTH

MASTERS IN PUBLIC HEALTH

EH6050: COMMUNITY BASED HIV CARE AND SUPPORT IS ASSOCIATED WITH BETTER TREATMENT OUTCOMES FOR PLHA ON ANTIRETROVIRAL THERAPY (ART) IN THE RESOURCE-LIMITED SETTINGS; A COMPARATIVE RETROSPECTIVE COHORT STUDY FROM UGANDA

1.0 PATIENTS SOCIO-DEMOGRAPHIC CHARACTERISTICS

Name of facility: 1. Kitovu Mobile AIDS Organisation ☐ **2.**Uganda Cares Clinic, MRRH ☐

Type of facility: 1. Community Based Care Program ☐ **2.** Hospital Based Program ☐

Date of data collection ☐☐ - ☐☐ - ☐☐☐☐

Study ID……**Patients ID Number**.....

Gender 0. Male ☐ **1.** Female ☐ **Age** ☐

Marital status:

1. Single ☐ **2.** Married/Cohabiting ☐ **3.** Widow (er) 4 ☐ vorced/separate ☐ **5.** Others

Occupational status:

1. Unemployed ☐ **2.** Self-employed ☐ **3.** Paid Job ☐ **4.** Peasant farming ☐ **5.** Others ☐

Date of HIV test ☐☐ ☐☐ ☐☐☐

2.0 BASELINE CHARACTERISTICS AT THE START OF ANTIRETROVIRAL THERAPY (ART)

WHO Clinical stage **1.i2.** ☐ i**4.** iv ☐ 9999 ☐ ☐ ☐

CD4 count (cells/ul) 0**.** 0—99 ☐ **1.** 100-199 ☐ **2.** 200-250 ☐ 9999 ☐

Specify actual CD4 Count at baseline.....Cell/ul Date ☐☐ ☐☐ ☐☐☐☐

Weight ☐ 9999 ☐ Function status 1**.** Bedridden [B] ☐ Ambulant [A] ☐. Working [W] ☐3. Others ☐

Date of ART Start ☐☐ ☐☐ ☐☐☐☐

Initial ARVs regimen

First line ARVs regimen **1.** Yes ☐ **2.** NO ☐

1. AZT-3TC-NVP ☐ 1. AZT-3TC-EFV ☐ 3. TDF-3TC-NVP ☐ 4. TDF-3TC-EFV ☐ 4. D4T-3TC-NVP

Second line ARVs regimen **0.** No ☐

1. AZT-DDI-LPV/r ☐ **2**. AZT-3TC-LPV/r ☐ **3.** ABC-DDI-LPV/r ☐ **4.** TDF-3TC-LPV/r ☐ **5.** AZT-3TC-DDI-LPV/r ☐

3.0 MONITORING AND FOLLOW UP OF ART

Adherence to ARVs: **1.** [Fair] ☐ **2.** [Poor] ☐ **3**. [Good] ☐ 4. Unknown ☐

ART Cohort completing **1.** 6 months ☐ **2.** 12 months ☐ **3.** 24 months ☐ **4.** 36 months ☐ **5.** 48 months ☐

Most recent CD4 count.....Cell/ul: Date ☐☐ ☐☐ ☐☐☐☐

3.1 ART TREATMENT OUTCOMES

Alive on ART **1.** Yes ☐ **2.** No ☐

i. First line regimen **1.** Yes ☐ **2.** No ☐

1. AZT-3TC-NVP ☐ 2. AZT-3TC-EFV ☐ 3. TDF-3TC-NVP ☐ 4.TDF-3TC-EFV ☐ 5. D4T-3TC-NVP

2. Second line regimen **1.** Yes ☐ 2. No ☐

1. AZT-DDI-LPV/r ☐ 2. AZT-3TC-LPV/r ☐ 3. ABC-DDI-LPV/r ☐ 4. TDF-3TC-LPV/l ☐ 4. AZT-3TC-DDI-LPV/r

Current function status 0. Bedridden [B] ☐ **1.** Ambulant [A] 2. Working [W] 3. Unknown

Current Weight ☐☐☐ Kgs

Lost to follow up (defaulted) **1.** Yes ☐ **2.** No ☐ Date ☐☐ ☐☐ ☐☐☐☐

Dead **1.** Yes ☐ **2.** No ☐ Date ☐☐ ☐☐ ☐☐☐☐

Stopped **1.** Yes ☐ **2.** No ☐ Date ☐☐ ☐☐ ☐☐☐☐

4.0 MANAGEMENT OF OPPOTUNISTIC INFECTIONS (OIs)

Contrimoxazole Prophylaxis (CPT): **1.** Yes ☐ **1.** No ☐ **3.** Others ☐

Tuberculosis Co-infection: **1**. Yes ☐ **2.** No ☐ **3.**

TB Treatment Status: 1. On Treatment ☐ 2. Completed treatment ☐ 3. Defaulted 4. Others ☐

THANK YOU

APPENDIX 3: EXTRACT OF THE MOH FACILITY COMPREHENSIVE HIV CARE INCLUDING ART COHORT ANALYSIS QUARTERLY REPORT.

Name of facility: Kitovu Mobile AIDS Organisation ☐ Uganda Cares ☐

Duration on ART	**6 months**		**12 months**		**24 months**		**36 months**		**48 months**	
Patients Characteristics	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Baseline Characteristics										
No of Clients that started ART at the facility										
ART regimen • 1st line regimen • 2nd line regimen										
Transfer outs since ART start										
Net cohort and on ART										
% with Baseline CD4 T-cell count done										
% of patients with CD4 T-cell ≤ 250 cell/ul										
Median CD4 T- cell count										
Follow up Characteristics										
% with follow up CD4 T-Cell count done										
% with follow up CD4 T-Cell count ≥ 250										
Median CD4 T-cell/ul										
ART Treatment outcomes										
Still alive on ART										
Lost										
Lost to follow up (Dropped)										
Dead										
Stopped										
ART Regimen • First line regimen • Second line regimen										
Source: MOH, 2009										

APPENDIX 4: ETHICAL APPROVAL FROM UCC CLINICAL RESEARCH ETHICS COMMITTEE

UCC

Tel: + 353-21-490 1901
Fax: + 353-21-490 1919

Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 4 (o) 03/04/12

21st March 2012

Professor Ivan Perry
Head of Department
Department of Epidemiology & Public Health
Western Gateway Building
University College Cork
Western Road
Cork

Re: Community based HIV care and support is associated with better treatment outcomes for PLHA on antiretroviral therapy (ART) in the resource-limited setting; a comparative retrospective cohort study in Uganda.

Dear Professor Perry

Expedited approval is granted to analyse data from the above in:

- University College Cork.

The following documents were approved:

- Application Form
- Study Proposal Version 1 dated 22nd February 2012

We note that the co-investigators involved in this study will be:

- Samuel Walligo.

Yours sincerely

Dr Michael Hyland
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

APPENDIX 5: ETHICAL APPROVAL FROM UNCST, UGANDA

Uganda National Council for Science and Technology

(Established by Act of Parliament of the Republic of Uganda)

Our Ref: HS 1180 **8 June 2012**

Mr. Samuel Waliggo
Kitovu Mobile AIDS Organization
P.O Box 207
Masaka

Dear Mr. Waliggo,

RE: RESEARCH PROJECT, "COMMUNITY BASED HIV CARE AND SUPPORT IS ASSOCIATED WITH BETTER TREATMENT OUTCOMES FOR PLHA ON ANTIRETROVIRAL THERAPY (ART) IN THE RESOURCE-LIMITED SETTINGS; A COMPARATIVE RETROSPECTIVE COHORT STUDY FROM UGANDA"

This is to inform you that the Uganda National Council for Science and Technology (UNCST) approved the above research proposal on **15 May 2012.** The approval will expire on **15 May 2013.** If it is necessary to continue with the research beyond the expiry date, a request for continuation should be made in writing to the Executive Secretary, UNCST.

Any problems of a serious nature related to the execution of your research project should be brought to the attention of the UNCST, and any changes to the research protocol should not be implemented without UNCST's approval except when necessary to eliminate apparent immediate hazards to the research participant(s).

This letter also serves as proof of UNCST approval and as a reminder for you to submit to UNCST timely progress reports and a final report on completion of the research project.

Yours sincerely,

Winfred Badanga
for: Executive Secretary
UGANDA NATIONAL COUNCIL FOR SCIENCE AND TECHNOLOGY

LOCATION/CORRESPONDENCE

Plot 6 Kimera Road, Ntinda
P. O. Box 6884
KAMPALA, UGANDA

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TEL: (256) 414 705500, (256) 312 314800
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EMAIL: info@uncst.go.ug
WEBSITE: http://www.uncst.go.ug

APPENDIX 6: LETTER OF ACCEPTANCE FOR DATA COLLECTION FROM UGANDA CARES HIV CLINIC

General Line: 0481-420018
Causality Dept: 038-2274346
Maternity: 038-2274340
Private wing: 0481-432395
Fax line: 0481-421343
E-mail: masakarrh@gmail.com

MASAKA REGIONAL REFERRAL HOSPITAL
P.O.BOX 18
MASAKA
Uganda

THE REPUBLIC OF UGANDA

MINISTRY OF HEALTH

For any correspondence on this Subject, please quote: **ADM/ 170/04** Date: **19th July 2012**

To: Samuel Waliggo
University College Cork Ireland
Kitovu Mobile Aids Org.
P.O. Box 207
MASAKA

Dear Sir/Madam

Subject: **PERMISSION TO COLLECT DATA FROM UGANDA CARES HIV CLINIC**

Reference is made to the above captioned subject where you requested for permission to access and collect data for the study entitled;

"COMMUNITY BASED HIV CARE AND SUPPORT IS ASSOCIATED WITH BETTER TREATMENT OUTCOME FOR PEOPLE LIVING WITH HIV/AIDS ON ANTI-RETROVIRAL THERAPY IN RESOURCE LIMITED SETTING".

Permission is hereby granted to you for the noble exercise.

Tugumisirize

Dr. Tugumisirize Florence
HOSPITAL DIRECTOR

MASAKA REGIONAL REFERRAL HOSPITAL
P O. BOX 18
19 JUL 2012
MASAKA

Mission statement: To increase access of all people in Masaka region to quality, general &specialized services

APPENDIX 7: LETTER OF ACCEPTANCE FOR DATA COLLECTION FROM KITOVU MOBILE

KITOVU MOBILE AIDS ORGANISATION

Plot 4, Delhi Road
P. O. Box 207 Masaka - Uganda
Office Phone - 04814-20113
Fax - 04814-20275/20514
Email: director@utlonline.co.ug
Website: www.kitovumobile.org

23rd February 2012

University of Cork,

Department of Epidemiology and Public Health.

Re : Approval for Research Data Collection

This is to inform you that the administration of Kitovu Mobile AIDS Organisation has no objection to Samuel Waliggo using the data of the organization as part of his Applied Research in Epidemiology towards the Masters in Public Health.

He is welcome to access the data relevant to the study and he will receive the cooperation from the data staff, as is necessary.

His research question is interesting and we wish him well during the study period.

KITOVU MOBILE AIDS ORGANISATION
23 FEB 2012
P. O. BOX 207 MASAKA
TEL. 0481420113

Robina Ssentongo
Director of Kitovu Mobile

C. Brigid Corrigan
Physician to ART dept.

APPENDIX 8: LETTER OF AMENDMENT FOR THE RESEARCH TOPIC

ucc
Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

Coláiste an Leighis agus na Sláinte
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11th April, 2013

FAO: Director

Uganda National Council for Science and Technology (UNCST),

Masaka Regional Referral Hospital, Uganda Cares HIV Clinic,

Kitovu Mobile AIDS Organisation,

Masaka,

Uganda

Dear Sir/Madam,

Re: Samuel Waliggo, Masters in Public Health, Student No. 111220042, University College Cork.

I would like to confirm that Samuel Waliggo completed a Masters in Public Health here in our Department of Epidemiology and Public Health. His research topic entitled is "Community Based Care and Support is associated with Better Treatment Outcomes for People Living with HIV and AIDS on Antiretroviral Therapy in Resource Limited Setting" first approved by the Clinical Research Ethics Committee by Cork Teaching Hospitals and relevant Ethics Committee in Uganda. At my suggestion the title of this project was changed to "Comparing Antiretroviral Treatment Outcomes Between Community Based and Hospital Based Programs for HIV Patients in a Resource Limited-Setting: A Retrospective Cohort Study from Uganda" for the purpose of his thesis submission. The title of the thesis topic was changed to ensure that it accurately reflected both the research topic and the research design. This change of title has no implications for the work carried out which was in accordance with that approved by the Ethics Committees in Cork and Uganda.

I hope this clarifies the position please let me know if I can be of any further assistance to you in this matter.

Yours faithfully,

Prof Ivan Perry, MD, PhD, FRCPI

Professor Ivan J. Perry MD, PhD, FRCPI
Head of Department

Ollscoil na hÉireann, Corcaigh
National University of Ireland, Cork