



**TITLE: FACTORS ASSOCIATED WITH RETENTION IN HIV CARE IN
WAKISO DISTRICT, UGANDA FROM 2008 to 2010.**

**Research report: Master of Science in
Epidemiology and Biostatistics**

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Declaration

I declare that this research report is my own work. It is being submitted in partial fulfilment of the requirements for the degree of Master of Science in Epidemiology in the field of Epidemiology & Biostatistics at the University of the Witwatersrand, Johannesburg. This research has not been submitted previously for any degree or examination to any other institution.

A handwritten signature in blue ink, reading 'Ilunga', is written over a horizontal line.

Ilunga Gil Mulumba

April 2020

Dedication

I dedicate this project to God Almighty my creator, my source of inspiration, wisdom and knowledge. He has been the source of my strength throughout this program and on His wings only have I soared.

I also dedicate this work to my loving parents, Hubert Mulumba (Pleinipo) and Justine Mulumba (Kapinga) whose words of encouragement and push for tenacity ring in my ears.

A special feeling of gratitude to my wife Badibanga Mulumba who has encouraged me all the way and whose encouragement has made sure that I give it all it takes to finish that which I have started. To my children Olivia Mulumba, Victoria Mulumba and Gilietta Mulumba who have been affected in every way possible by this quest. My love for you all can never be quantified, God bless you.

I dedicate this work to all my brothers and sisters and I and give special thanks to Serge kalala, Justine Kapinga, Dr. Patrick Kapena, Foreman Kasongo and Erick Kasongo for being there for me throughout the entire Master program. Both of you have been my best cheerleaders.

Abstract

Background

Since there is not cure for HIV/AIDS, United Nations member states embarked on efforts towards global access to adequate prevention plans, support and treatment by 2010. However, the effectiveness of HIV/AIDS treatment is subject to the retention in care of patients, which is defined as remaining connected to care and keeping all scheduled appointments. Retention in care was comparatively to this study defined as remaining connected to care and keeping scheduled appointments by attending at least one appointment in 2010.

The health system considers the retention in care for patients who have initiated ART as crucial point for improving their immunological response, to prevent HIV resistance, to avoid drug treatment interruptions and to monitor the effects of therapy.

The aim of this study is to identify factors associated with retention in care among HIV-infected patients who initiated care in primary health care centres and those who initiated care in hospital facilities in Wakiso District, Uganda from 2008 to 2010.

Methods and material

The present study was a secondary data analysis using data from the Wakiso project, a prospective cohort study carried out by MRC/UVRI & LSHTM Uganda Research Unit on AIDS in Uganda between 2008 and 2010. The study included all HIV positive patients from the 9 government health facilities who were included in the original Wakiso project (between 2008 and 2010). To compare retention in health care between HIV infected patients who initiated care in the primary health care clinics and HIV infected patients who initiated care in the hospital facilities in Wakiso district, Uganda 2008 to 2010. Descriptive analyses of the time to drop-out was carried out using survival analysis methods; the time to drop-out was graphically described using Kaplan Meier plots. To investigate factors associated with

retention in care among HIV infected patients who initiated care in the primary health care clinics and HIV infected patients who initiated care in the hospital; Cox regression models in Stata, version 15.1, were fitted.

Results

A total of 452 participants took part in the study and were all included in the final analysis. During the observation time, 21% (n=95) participants got lost to follow-up. The rate of getting lost to follow-up was 20.3 (95% CI: 16.6; 24.8) per 100 person-years. In the unadjusted model, the risk of loss to follow-up was 7 % higher from participants in peripheral health centres than those from the hospital/HC IV, although this association was not statistically significant ($p=0.750$) while in the adjusted model there was a statistically significant difference in the rates of getting lost to follow-up between the participants who received care from peripheral health center compared to those who received care at Hospital/HC IV. The risk of being lost to follow-up was lower by 40% (HR=0.62; 95% CI [0.40; 0.96]) among participants who received care from peripheral health centre compared to received care at Hospital/HC IV after adjusting for sex and whether the patient had ever been on ART. In addition, there was overwhelming evidence to suggest that participants who had ever been on ART had an 80% lower risk of being lost to follow-up relative to those who had never been on ART (HR=0.19; 95% CI [0.12; 0.32]) and this was statistically significant ($p\text{-value}<0.001$).

Discussion/Conclusion

Our results suggest that there is a significant difference in retention in care between patients who initiated care in the peripheral health centre and those in the hospital facilities. When controlling for sex and whether the participant had been on ART, participants who were recruited from the Primary Health Centres were less likely to be lost to follow-up. In addition,

the result shows that patients are much more likely to be retained in care when they are on ART.

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ABBREVIATIONS

AIDS: Acquired immunodeficiency syndrome

ART: Anti-Retroviral treatment

HIV: Human Immuno-Deficiency Virus

HC II: Health Care Centre level II

HC III: Health Care Centre level III

HC IV: Health Care Centre level IV

HCW: Health Care Worker

LTFU: Lost to Follow Up

MRC/UVRI & LSHTM Uganda Research Unit: Medical Research Council / Uganda Virus
Research Institute and London School of Hygiene and Tropical Medicine Uganda Research
Unit

VCT: Voluntary Counseling and Testing

CHAPTER 1: INTRODUCTION

1.1 Background

Although a cure for HIV/AIDS has not been found, there has been a decrease in the rate of mortality and morbidity, and an improvement in the life quality of HIV positive people due to the advent of effective antiretroviral therapy (ART) (1). The provision of ART has been made possible by an increase in funding through global initiatives and reduction in price of potent ART. United Nations member states embarked on efforts towards global access to adequate prevention plans, support and treatment by 2010. This was a goal preceded by another global commitment to treat more than three million HIV/AIDS patients with life-prolonging antiretroviral treatment (ART) by the end of 2005 (2). This goal was aimed at people living with HIV/AIDS in low and middle-income countries (3). However, the effectiveness of HIV/AIDS treatment depends on the retention in care of patients (4). The retention in care of patients is of importance since a large number of patients in low income countries requiring ART live in resource limited settings. As such, to improve the patient outcomes there is a need to retain patients in care (2).

Retention in care is complex, difficult to define and hard to measure. Some authors define “retention in care” as continuous engagement of patients with ART care (5, 6), while others define “retention in care” in terms of the proportion of patients who are alive and remaining in an ART program (7). However, what is common to both definitions is the suggestion that being retained in care means remaining connected to care and keeping all scheduled appointments. Therefore, in the present study, retention in care was defined as remaining connected to care and keeping scheduled appointments by attending at least one appointment in 2010.

Regular monitoring is required for patients both before and after initiation of ART. This reduces the risk of HIV-infected patients developing opportunistic infections (8, 9) . Retention in care for patients who have initiated ART is crucial for improving their immunological response, to prevent HIV resistance, to avoid drug treatment interruptions and to monitor the effects of therapy (10).

In Uganda the health system is structured as follows: the first level consists of village health teams /community medicine distributors (known as Health Centre I), followed by Health Care Level II Centres (HC II). HC II's provide the lowest level of service delivery and form the first point of contact with the formal health sector for the community; HC II's provide Primary Health Care (PHC) and outpatient clinical services, and serve about 5,000 people, but have no in-patient or laboratory services (11). The HC II is headed by a nurse. Health Centre level III's (HC III's) are located at the sub-county level. The HC III's provide Primary Health Care, laboratory, clinical outpatient as well as maternity services and serve about 20,000 people (11).

The HC III serves as a referral facility for the community and HC II at the sub-county level and is headed by a Clinical Officer (who has three years post-secondary school training, followed by a two-year internship). Health Centre level IV (HC IV's) are located at county level and serve a population of about 100,000 people (11). The HC IV provides PHC and clinical services, maternity services, blood transfusion and emergency services. The HC IV has a laboratory, is a referral facility for the community, HC II and HC III at the county level and is headed by a Medical Officer (who has five years post-secondary school training followed by a one-year internship). Lastly, the general hospital is a referral facility for all the lower level facilities at the district level. The general hospital offers Primary Health Care, outpatient and

inpatient services, both elective and emergency surgery, radiological services and laboratory services and is headed by a Medical Officer (11).

1.2 Literature Review

The number of new HIV infections in Uganda increased by 21% between 2005 and 2013 (8). From as early as 2004 there was globally a large increase in the number of people on treatment for HIV, which led to the rapid scale up of free ART programs in several countries including emerging countries in Sub-Saharan Africa. For example, in 2008 approximately 2.9 million people received ART in Sub-Saharan Africa, an increase from 2.1 million in 2007. Coverage among patients eligible for ART (those with CD4 cell counts < 200 cells/ μ l) increased from 30% in 2007 to 44% in 2008. Similar trends have been observed in Asian and American countries (12) .

Despite the proven and documented benefits of ART, retention of patients in antiretroviral treatment programs remained a big challenge in most sub-Saharan African countries including Uganda during the early period of ART roll-out (13). Many studies have shown that the proportions of patients that remain in care following ART initiation are low and retention in care remains a challenge in many countries with a high burden of HIV/AIDS (14). A review of 33 patient cohorts taking ART in 13 African countries suggested only 60% of patients remain in ART programs after two years with loss to follow up accounting for 56% of all attrition (15). Retention in care of patients in health facilities may be influenced by various factors, some of which are discussed and shown in conceptual framework in Fig 1 below (5, 7, 16) .

a) Health care facility.

At health care facility level, the following factors may affect retention in care.

- **Staff Shortage.**

Staff shortage may influence retention in care of patients on ART. This is because staff shortages lead to long queues at the clinic waiting area and consequently, long waiting times (17).

- **Out-of-Stock Antiretroviral Medication.**

ART clinics sometimes run low of ARV supplies, which affects the supply of medication received by the patients. Because of such inconvenience some patients get discouraged and they abandon their appointment to care .

- **Facility category**

Some patients may not adhere to their care as they would prefer to be treated at a hospital or health facility rather than at a primary health care centre (17).

b) Demographic factors

Several demographic factors have been identified as being associated with retention, and these include (18):

- **Gender**

It has been observed that men have a higher tendency of failing to be retained in care than women (19) :

- **Population group**

Evidence from pragmatic studies (applicable in broad routine clinical practice as opposed to controlled research settings) highlights certain priority populations as being at high risk of discontinuing treatment and hence being in need of retention enhancing interventions. These priority populations include men who have sex with men (MSM), African, Caribbean and Black people (ACB), women at risk (including sex workers), people who inject drugs, indigenous people and other marginalized groups (immigrants, refugees and people with precarious immigration status) (19).

c) Clinical characteristics.

Clinical characteristics that influence the retention-in-care of the patients include

- **Weight Increase as a Sign of Good Health**

Patients stop taking their medication after they notice an increase in body weight and they start to look healthy because of taking their ART. Such behavior may affect their retention in care (20).

- **Side effects**

Side effects such as nausea, vomiting and dizziness may lead to attrition from ART care (18).

- **Initiation of ART**

People who have already initiated ART may be easier to retain in care. On the other hand, patients who feel better (without AIDS diagnosis, ART, and with higher CD4 count) are at a higher risk of missing visits. Some of the people who have already initiated ART with higher CD4 count are asymptomatic and may not develop AIDS-defining illness for a prolonged period. Such people tend to miss follow-up visits at some stages (21, 22).

d) Socio economic factors.

Socio-economic factors influence retention in care and include:

- **Level of education**

People with lower education level may have less knowledge about the importance of remaining in care, consequently this could impact on their retention in care. In view of this, it has been recommended that health education be applied to emphasize the importance of care for people with lower education level to ensure and improve retention (15, 23).

- **Stigma and non-disclosure of HIV status**

HIV related stigma has been reported as one of the reasons why some patients discontinue ARV treatment or miss some pill doses. Some patients won't disclose their HIV status to either their marital partners or other members of their social network for fear of domestic violence, partner abandonment, or rejection by the community. As a result, patients are forced to stop attending the clinic for ART services (15).

- **Religious beliefs**

Religious beliefs and practices have been shown to lead to patient attrition from ART care. For instance, some church pastors who conduct healing prayers sessions in their communities may persuade patients to discontinue ART on the premise that they have been healed through prayer sessions (18).

- **Use of herbal remedies**

Patients who use herbal remedies to treat HIV related illnesses have a tendency of discontinuing their ART programs (18).

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- **Travel distance and cost of transportation**

Although ART sites do not charge for HIV related services, travel distance and additional costs incurred traveling to ART centres may contribute to patients being lost to care. Travel distance to ART centres and lack of money to pay for transport may act as barriers to accessing care (18).

- e) **Policy factors**

Aspects of policy are very important because they may affect the retention in HIV care when a new public health intervention or program is implemented (24).

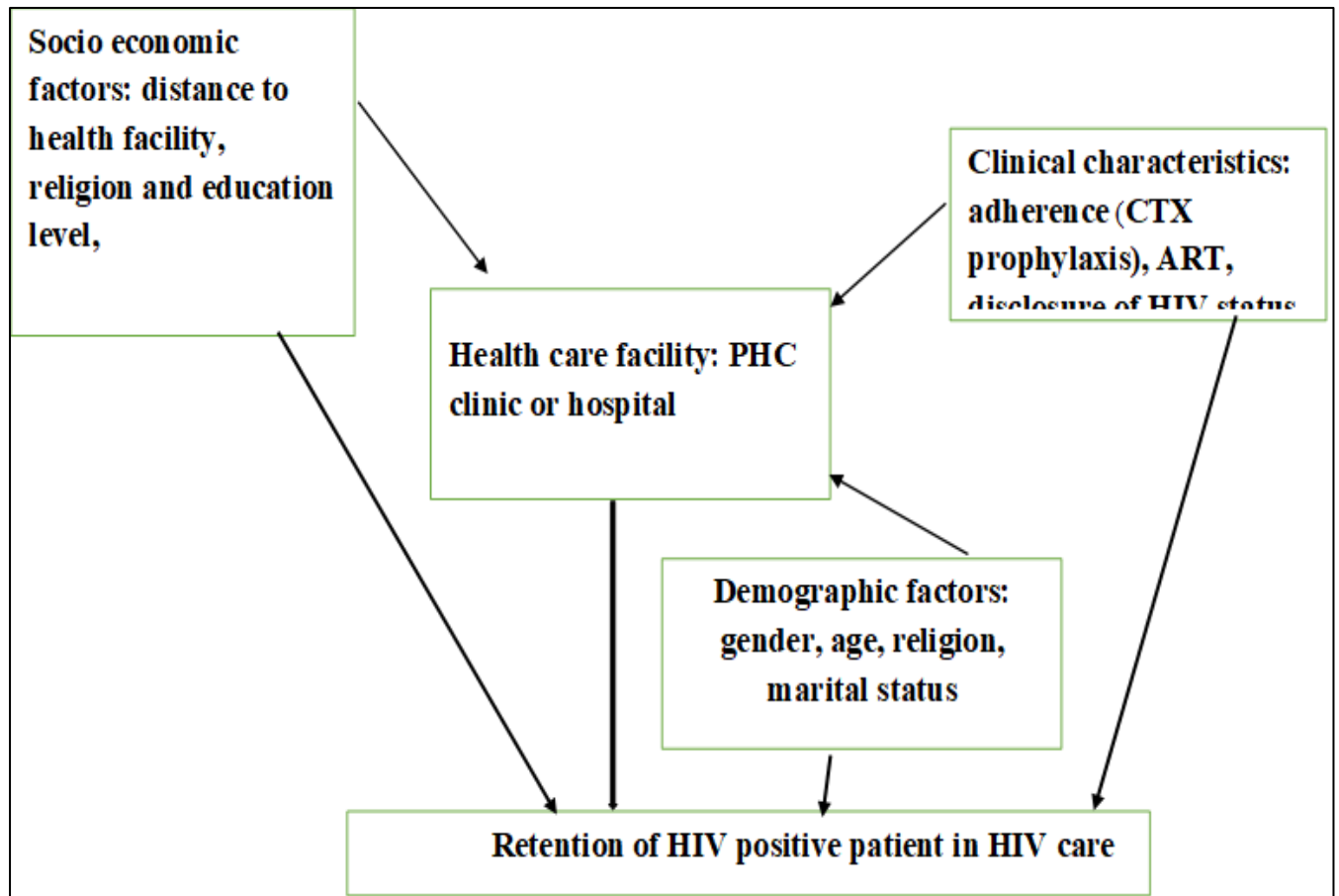


Figure 1; Conceptual Framework of factors associated with retention in care

1.3 Problem statement

As of 2008, ART in Uganda was delivered through hospitals and largely in urban areas, rather than in rural areas where health care is delivered through primary health care facilities. This made it difficult for the poor rural communities to access care as distances to the urban centres are considerable and transport is very poor and expensive (10). The severe shortage of clinically qualified staff and poor infrastructure are further barriers to reaching out to people in need of ART (10, 15, 24). Retention of patients in care, though recognized as a prerequisite for

achieving any level of adherence, has received less attention. Retention in care of patients on ART programmes is of public health importance. The Wakiso pilot project investigated whether HIV-infected patients in Uganda could be treated in Primary Health Care Centres as well as in Hospitals

1.4 Justification

To increase ART coverage in countries with limited resources, the World Health Organization (WHO) recommended decentralization of HIV care by shifting the task of HIV care to Primary Health Care centers (15, 22). Under this recommendation, HIV-infected patients in Uganda would be treated both in Hospitals and Primary Health Care Centres (15, 24). Although studies have looked at retention in different levels of healthcare system, there have been few studies on factors affecting retention in care of HIV/AIDS patients in the context of treatment delivered at the primary health care level. Therefore, this report adds information on retention in care of HIV infected patients.

1.5 Research question, aims and objectives.

Research question.

Does retention in health care among HIV-infected patients differ between patients who initiated care in primary health care centres and those who initiated care in hospital facilities in Wakiso district, Uganda from 2008 to 2010?

Aim

To compare retention in care among HIV-infected patients who initiated care in primary health care centres and those who initiated care in hospital facilities, and to identify other factors associated with retention in care in Wakiso District, Uganda from 2008 to 2010.

Objectives

1. To describe the socio-demographic characteristics of HIV-infected patients who initiated care in primary health care centers and HIV-infected patients who initiated care at hospital facilities in Wakiso District Uganda, 2008 to 2010.
2. To compare the retention in health care between HIV infected patients who initiated care in the primary health care clinics and HIV infected patients who initiated care in the hospital facilities in Wakiso district, Uganda, 2008 to 2010.
3. To investigate factors associated with retention in care among HIV infected patients who initiated care in the primary health care clinics and HIV infected patients who initiated care in the hospital facilities in Wakiso district, Uganda, 2008 to 2010.

CHAPTER 2: METHODOLOGY

2.0 Primary Study Methods

2.1 Study design

The Wakiso Pilot Project was a cohort study and this primary study was carried out by the MRC/UVRI & LSHTM Uganda Research Unit. The Wakiso project was conducted between 2008 and 2010. This project involved only HC II, HC III, HC IV levels and the hospital. In the Wakiso project, Health Centre II offered the following services: HIV prevention services, HIV counselling and screening pregnant woman for HIV. HC III's offered the same services as HCII's and in addition offered the following services: PMTCT services, monitoring patients for side effects of ARVs and using WHO clinical guidelines to stage clients (25).

In the Wakiso project, patients seen at HC III or HC IV who were deemed not yet eligible for ARVs were referred to HC II for follow up care. The HC III referred clients who were eligible for ARVs to HC IV or to the Hospital for ART initiation. Once clients were initiated and stabilized, they were referred back to HC III for treatment follow up.

The main activities of HC IV consisted of checking the clients' understanding of ARV treatment and offering further counselling where necessary. Eligible clients were initiated on ARVs at the HC IV and stabilized on treatment. Stable clients were referred back to HC III for follow up. The hospital was the final referral point. In addition, the following services were planned to be provided by the hospital: management of complex cases referred from HC IV, initiation of second line ARV treatment, taking of blood for CD4 count and viral load, provision of radiological services (25).

Each patient referred within the Wakiso Project was given a referral form to his/her next destination. The receiving health facility filled up the part showing that they had received the

patient in triplicate. The original was sent back to the referring facility. The first duplicate was sent to the research team. These were collected monthly from the health centres by the field officer and taken back to the referring health facility and also the data were entered into the computer. The HC kept the second duplicate copy.

2.2 Study population

The inclusion criteria for the primary study included all HIV positive adults who had gone through Voluntary Counselling and Testing (VCT) (at least 18 years old and above) regardless of any medical condition or pregnancy status who speak the language into which the questionnaires were translated (Luganda). Participants were drawn from 9 government health facilities in the Wakiso district and restricted to those who resided within the catchment population of each health centre for ease of follow up. The study also restricted ARVs to the participants who identified a medicine companion. The treatment companions were asked to check their client on a daily basis to observe and document at least one of the doses being taken and to help the client solve problems related to drug tolerability and scheduling. Each medicine companion received a one-day orientation to ART adherence in the health units. The inclusion criteria was all patients that were given information on Wakiso project and who met the eligibility criteria and were interested in participating in the study. These participants then provided written and verbal informed consent before they were enrolled into the study (25).

For the secondary analysis we included all participants from the primary study who were HIV positive patients in the 9 government health facilities in the Wakiso district, namely three HC-IIs, four HC-IIIs, one HC IV and one hospital, enrolled in ART between 2008 and 2010. In addition, patients who were left after the enrolment visit or those with single visits were excluded from the time to event analysis as survival analysis methods require the date of exit to be after the date of entry. (25)

2.3 Study setting

The Wakiso project was a study carried out in the Wakiso district in Uganda as shown in Figure 2. The District of Wakiso is located in Uganda's central region. This district is the second most populated district in Uganda with a population of 2,007,700 according to the 2014 census and covers a total area of 2,807.75 square kilometers. The population density is 700 persons per square kilometer and with a ratio of 90 males to 100 females. This district currently boasts a highly urbanized society with half of its population living in urban areas. This study included 9 government health facilities in Wakiso district. Three of these were level II HCs; four were level III HCs; one level IV HC and one Hospital. The health facilities included were Kitale HC II (Busiro South country, Katabi Sub-County) Nsagu HC II (Busiro South County, Ssisa sub-county) and Mutungo HC II (Kyadondo South County), Kigungu HC III (Entebbe Municipality, Division B), Kasanje HC III (in Busiro South County, kasanje Sub-county); Nakawuka HC III (Busiro South County, Ssisa Sub-county) and Kigo HC III (Kyadondo South County) Ndejje HC IV (Kyadondo South County, MakindyeSagbabo sub-county) and Entebbe hospital (Entebbe municipality) (25).

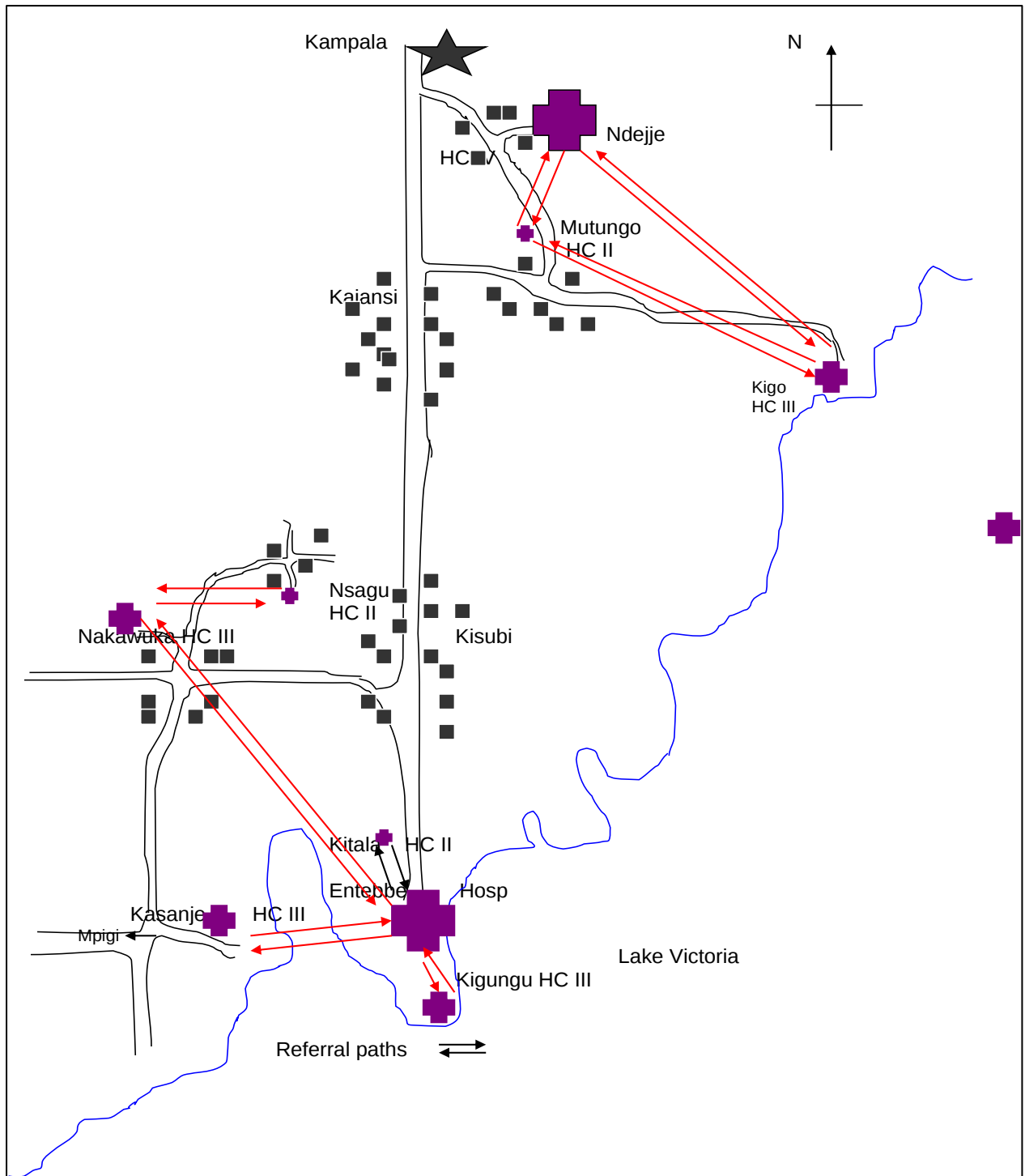


Figure 2 : Wakiso District in Uganda (25)

The health care centres were selected on the basis of their level, distance to each other and rural locations. Most of the health centres selected are in rural areas with poor road networks. In order to recruit a large enough number of participants to demonstrate the feasibility of ART delivery through peripheral health centres, a total of nine health facilities were selected (25).

Regional and national referral hospitals were not selected because these health facilities are far up the ladder of health care. They rarely receive patients directly from the peripheral health centres. Their link with the peripheral health centres is the general hospitals found in the district. Selections were limited to government health facilities where there is no charge of user fees, because recurrent costs to patients are associated with poor patient retention in care (25).

2.4 Data collection

The data of the original study was obtained through auditing of patient's clinical records, observation of health workers (HWs) at work, focus group discussions with HWs, and interview with the patients. Variables from the original data which were used in the present study are described in Appendix C.

2.5 Secondary Study Methods

2.6 Study design

The current study was a secondary data analysis using data from the Wakiso project, a prospective cohort study carried out by MRC/UVRI & LSHTM Uganda Research Unit on AIDS in Uganda between 2008 and 2010.

2.7 Sampling and sample power considerations

The study included all 452 HIV positive patients from the 9 government health facilities who were included in the original Wakiso project (between 2008 and 2010) provided the data for these patients is complete.

If we assume roughly 450 participants in the study, with 170 initiating care in a hospital and 280 initiating care at a PHC, then the study had 80% power to detect as statistically significant an absolute difference of 13% in the proportion retained in care, assuming that in the hospital group 73% were retained in care and in the PHC group 60% were retained in care.

2.8 Measurement of Variables

a) Definition of key variables

a.1) Outcome variable

Retention in the study was analysed by using as outcome variable the time to lost-to-follow-up (LTFU), in the same way that survival is analysed using time to death. In this study a patient was considered to be lost-to-follow up or not retained in care if he / she did not visit a health facility in 2010, and did not die during the study and did not formally withdraw from the study.

a.2) Explanatory variables

Explanatory variables in this study fell into one of the following four categories namely health facility level, demographic, socio-economic and clinical variables as further detailed in Table 1 below.

Table 1 : List of Variables

Health facility factors	Variable	Type of Variable	Level
	Facility	Categorical	Hospital/HC IV
			Peripheral Health Centre
Demographic factors	Sex	Categorical	Male
			Female
	Age	Continuous	
	Highest Education level	Categorical	No education
			Primary
			Secondary/Tertiary
Socio-economic factors	Religion	Categorical	Catholic
			Protestant
			Muslim
			SDA/Other
			Catholic
	Marital status	Categorical	Currently married/cohabiting
			Widowed
			Separated/divorced
			Single
	Current Alcohol Consumption	Categorical	Yes
			No
	House ownership	Categorical	Rent
			Own
			Live for free
	Roofing Material	Categorical	Corrugated Iron
			Thatch/Tiles/Other
	Distance to health facility	Categorical	<= 1 km
			2 – 3 km
			3 – 4 km

Clinical factors	When HIV status known	Categorical	< 3 months
			3 to 12 months
			>12 months
	How long attended HIV clinic	Categorical	< 3 months
			3 to 6 months
			> 7 months
	Who is medicine companion?	Categorical	Spouse/child
			Relative
			Other (neighbor/friend)
	Education level of medicine companion	Categorical	No education
			Primary
			Secondary
			Tertiary
	Is medicine companion HIV-positive?	Categorical	Yes
			No
	Disclosure to partner	Categorical	Yes
			No or no spouse/regular partner
	Disclosure to children	Categorical	Yes
			No
			Don't have children
			Children too young to understand
	Ever been on ART	Categorical	Yes
			No
	CTX prophylaxis	Categorical	Yes
			No
	Missed dose of CTX	Categorical	Yes
			No

- **Health facility level variables**

The health facility level variables included type of health facility, whether this is a peripheral health care centre (HC II or HC III) or a hospital (HV IV or district hospital),

Demographic explanatory variables.

The variables consisted of demographic factors namely age as a continuous variable, marital status, currently married/cohabiting, widowed, separated/divorced and single, and gender grouped as male and female

- **Socio-economic explanatory variables**

These consist of the socioeconomic characteristics namely education level (none, some primary, some secondary, some college/university/technical), religion (1: Catholic 2: Protestant 3: Muslim 5: Seventh-day Adventist 6: Other), current alcohol consumption (1;yes 2:no), house ownership (1:rent, 2:own: 3 live for free), roof material (1:corrugated iron, 2: thatched tiles or other). and the distance to the health facility (1: ≤ 1 km 2: 2 – 3 km 3: 3 – 4 km).

- **Clinical explanatory variables**

These consist of the following clinical characteristics: disclosure of HIV status to partner or children (yes/no), for adherence we use a proxy of whether or not the patient was on CTX prophylaxis, for those on CTX prophylaxis whether they had missed any dose, whether or not the patient is on ART (yes/no) and how long the participant had known his / her HIV status (< 3 months, 3-12 months, > 12 months), how long they attended HIV clinic (< 3 months , 3 to 6 months, >7 months), who is the medicine companion (Spouse/child, relative, other), education level of medicine companion (no education, primary, secondary, tertiary), medicine companion HIV positive (no/yes).

2.9 Data management

For the primary study, a database was created and maintained in MS-ACCESS in the Statistics section of MRC/UVRI & LSHTM Uganda Research Unit. Data was double-entered into the database. The already entered forms were stored in the archives of the statistic section, with the same security applied to all MRC/UVRI & LSHTM Uganda Research projects. For the secondary study, we received the data from gatekeepers without identification details of the participants. We used STATA version 14 (Stata Corp, College Station, Texas, USA) to clean, manage and analyse the data, by checking for data completeness, appending datasets, recoding of variables where necessary and running descriptive and inferential analysis. The multivariable analysis used a “complete case analysis approach” in which observations with a missing value in any of the terms included in the final model were omitted.

2.10 DATA ANALYSIS

Objective 1: To describe the socio-demographic characteristics of HIV-infected patients who initiated care in primary health care centres and HIV-infected patients who initiated care at hospital facilities in Wakiso District Uganda, 2008 to 2010.

Descriptive statistics were used to summarize and describe the characteristics of study participants, stratified by place where the participant initiated care - whether at a primary health care centre or at a hospital. Continuous data were summarized using both mean and standard deviation and median and interquartile range. Categorical and discrete random variables were reported as frequencies (n) and percentages (%). Study variables that were used are given in appendix B.

Objective 2. To compare the rate of loss to follow-up in health care between HIV infected patients who initiated care in the primary health care clinics and HIV infected patients who initiated care in the hospital facilities in Wakiso district, Uganda, 2008 to 2010.

We used survival analysis to measure the time to loss to follow-up from the initial time of enrollment (time zero) up to the last visit date. The survival time was measured in years. Time to loss to follow-up of participants who died or who withdrew was censored at the time of death or time of withdrawal from the study. A number of clients initially enrolled in the study and never attended a further visit (so were technically lost-to-follow up after 1 day). Those who only had one visit and who did not formally withdraw were excluded from the analysis, while those who formally withdrew had their follow-up time censored at the date of withdrawal. Patients who died while still in the system had their time to drop-out censored at death.

Descriptive analyses of the time to loss to follow-up was carried out using Kaplan Meier plots, broken down (a) by study arm (b) by whether or not the client was ever on ART during the study period and (c) by whether or not the client was ever on ART for those in the peripheral Health Centres only. Drop-out rates were estimated as number of drop-outs per 100 Person Years of Observation (PYO), broken down by subgroup, and formal log-rank tests were carried out to compare the drop-out rate between study arms and between those on ART and those who had not yet initiated ART.

Objective 3. To investigate factors associated with retention in care among HIV infected patients who initiated care in the primary health care clinics and HIV infected patients who initiated care in the hospital

Cox regression models in Stata were fitted to evaluate individual-level factors associated with retention in care in both study arms. Unadjusted analyses were used to identify important covariates. All variables that had a p-value of 0.25 or less in an unadjusted analysis (based on the Wald test) were included as candidates for the multivariate Cox regression model.

Backward elimination with a liberal P-value of $p=0.20$ was then used to choose the final model. A liberal p-value in model selection was used in order to ensure that all confounders which influenced the association with place of initiating treatment were included in the model. The proportional hazards assumption was formally tested for the final Cox regression Model.

2.11 Ethical considerations

For the primary study, ethical approval was obtained from the UVRI Science and Ethics Committee (UVRI SEC). All participants provided informed consent before their enrolment in the study. For this secondary data analysis, ethical approval was obtained from the Human Research Ethics Committee of the University of the Witwatersrand and a data agreement form with the data gatekeeper was signed. To protect the confidentiality of participants, the data sets were received in an anonymized format, only the student and his supervisor had access to the dataset. Furthermore, the data were stored in a password protected computer.

CHAPTER 3: RESULTS

This chapter presents the results of the secondary analyses.

3.0 Characteristics of Study Participants by Health facility

A total of 452 participants took part in the study and were all included in the final analysis. During the observation time, 21% (n=95) participants got lost to follow-up, with a total analysis time at risk and under observation of 468.5 years. Table 1 below shows the descriptive summary of participants by health facility.

Table 1: *Characteristics of the study participants by health facility.*

	Study Arm		Total
	Hospital/HC IV	Peripheral Health Centre	
Variable	(N = 173)	(N = 279)	(N = 452)
	N (%)	N (%)	N (%)
Lost to follow-up			
No	134 (77.5)	223 (79.9)	357 (79.0)
Yes	39 (22.5)	56 (20.1)	95 (21.0)
Age median(IQR)	35(30-41)	34(28-40)	34(29-40)
Sex			
Male	53 (30.6)	91 (32.6)	144 (31.9)
Female	120 (69.4)	188 (67.4)	308 (68.1)
Ever been on ART			
Yes	124 (71.7)	89 (31.9)	213 (47.1)
No	49 (28.3)	190 (68.1)	239 (52.9)
Highest Education level			
No education	19 (11.0)	48 (17.2)	67 (14.8)
Primary	92 (53.2)	175 (62.7)	267 (59.1)
Secondary/Tertiary	62 (35.8)	56 (20.1)	118 (26.1)
Religion			
Catholic	79 (45.7)	130 (46.6)	209 (46.2)
Protestant	46 (26.6)	94 (33.7)	140 (31.0)
Muslim	22 (12.7)	29 (10.4)	51 (11.3)
SDA/Other	26 (15.0)	26 (9.3)	52 (11.5)
Marital status			
Currently married/cohabiting	69 (39.9)	134 (48.0)	203 (44.9)
Widowed	42 (24.3)	35 (12.5)	77 (17.0)
Separated/divorced	52 (30.1)	99 (35.5)	151 (33.4)
Single	10 (5.8)	11 (3.9)	21 (4.6)
Current Alcohol use			
Yes	30 (17.3)	84 (30.1)	114 (25.2)
No	143 (82.7)	195 (69.9)	338 (74.8)
House ownership			
Rent	97 (56.1)	111 (39.8)	208 (46.0)
Own	52 (30.1)	115 (41.2)	167 (36.9)
Live for free	24 (13.9)	53 (19.0)	77 (17.0)
Roofing Material			
Corrugated Iron	169 (97.7)	246 (88.2)	415 (91.8)
Thatch/Tiles/Other	4 (2.3)	33 (11.8)	37 (8.2)

When HIV status known			
< 3 months	20 (11.6)	140 (50.2)	160 (35.4)
3 to 12 months	51 (29.5)	57 (20.4)	108 (23.9)
>12 months	102 (59.0)	82 (29.4)	184 (40.7)
How long attended HIV clinic			
< 3 months	32 (18.5)	183 (65.6)	215 (47.6)
3 to 6 months	43 (24.9)	30 (10.8)	73 (16.2)
> 7 months	98 (56.6)	66 (23.7)	164 (36.3)
Who is medicine companion?			
Spouse/child	32 (27.1)	19 (38.8)	51 (30.5)
Relative	66 (55.9)	28 (57.1)	94 (56.3)
Other (neighbor/friend)	20 (16.9)	2 (4.1)	22 (13.2)
Education level of medicine companion			
No education	8 (7.9)	5 (11.6)	13 (9.0)
Primary	36 (35.6)	27 (62.8)	63 (43.8)
Secondary	38 (37.6)	10 (23.3)	48 (33.3)
Tertiary	19 (18.8)	1 (2.3)	20 (13.9)
Is medicine companion HIV-positive?			
Yes	42 (62.7)	20 (58.8)	62 (61.4)
No	25 (37.3)	14 (41.2)	39 (38.6)
Disclosure to partner			
Yes	63 (36.4)	108 (38.7)	171 (37.8)
No or no spouse/regular partner	110 (63.6)	171 (61.3)	281 (62.2)
Disclosure to children			
Yes	62 (35.8)	77 (27.6)	139 (30.8)
No	47 (27.2)	94 (33.7)	141 (31.2)
Don't have children	20 (11.6)	27 (9.7)	47 (10.4)
Children too young to understand	44 (25.4)	81 (29.0)	125 (27.7)

The proportion of participants who were lost to follow-up was slightly lower among those who were from peripheral health centre compared to those from hospital/HC IV, 20.1% and 22.5% respectively. The median age was slightly higher for participants from the hospital/HC IV median 35(IQR=30-41) compared to those from the peripheral health centre median 34(28-40). The ratios of males to females were similar across the facilities (approximately a third of males and two thirds of females). A greater proportion of participants in hospital/HV IV (71.7%) had

been on ART compared to those from peripheral health centres (31.9%). Most of the participants reported to have completed primary education across the health facilities (53.2% and 62.7%). The Catholic religion was the most dominant among participants across the health facilities (45.7% and 46.7%). Over a third of the participants were living with a partner across the health facilities. Most participants did not consume alcohol across the health facilities (82.7% and 69.9%). Over half of the participants from the hospital/HC IV (56.1%) and 39.8% from peripheral health centres rented houses. Most of the participants lived in houses with corrugated roof material across the health facilities (97.7% and 88.2%). Over half of the participants from the hospital/HC IV and 29.4% from peripheral health centres had known their HIV status for longer time (more than 12 months). About fifty six percent of participants from the hospital/HC IV and 23.7% from peripheral health centres had attended the HIV clinic for longer duration (more than 7 months). Most participants had relatives as their medicine companions across the health facilities (55.9% and 57.1%). A higher proportion of medicine companions from hospital/HC IV (37.6%) had completed secondary education than from peripheral health centres (23.6%). Over half of the medicine companions were HIV positive across the health facilities. Majority of the participants had not disclosed their HIV positive status to their partner across the health facilities (63.6% and 61.3%). More than 25% of the participants had disclosed their HIV positive status to their children across the health facilities (35.8% and 27.6%).

3.2 Loss to follow-up Rate

The rate of getting lost to follow-up was 20.3 (95% CI: 16.6; 24.8) per 100 person-years. Table 2 below shows the loss to follow-up rates across categories of factors of the participants.

Table 2: Loss to follow-up rates across categories of factors of the participants. n(%) is the number and percentage of lost to follow-up and Y is the number of person years.

Variable	Level	n(%)	Y	Lost to follow-up rates (per 100 person years)	P-value
Facility					
	Hospital/HC IV	39 (22.5)	206	18.9 (13.8; 25.9)	0.749
	Peripheral Health Centre	56 (20.1)	262	21.4 (16.4; 27.8)	
Sex					
	Male	30(20.8)	149	20.1 (14; 28.7)	0.983
	Female	65 (21.1)	319	20.4 (16.0; 26.0)	
Highest Education level					
	No education	14 (20.9)	60	23.4 (13.8; 39.5)	0.928
	Primary	56 (21.0)	281	19.9 (15.3; 25.9)	
	Secondary/Tertiary	25(21.2)	127	19.7 (13.3; 29.1)	
Religion					
	Catholic	39(18.7)	216	18.1 (13.2; 24.7)	0.429
	Protestant	28(20.0)	146	19.2 (13.2; 27.8)	
	Muslim	14(27.5)	48	29.3 (17.4; 49.5)	
	SDA/Other	14(26.9)	59	23.7 (14.1; 40.1)	
Marital status					
	Currently married/cohabiting	40(19.7)	211	19 (13.9; 25.9)	0.758
	Widowed	20(26.0)	80	25.1 (16.2; 38.9)	
	Separated/divorced	31(20.5)	157	19.7 (13.9; 28.1)	
	Single	4 (19.1)	21	19.2 (7.2; 51.3)	
Current Alcohol use					
	Yes	28 (24.6)	100	27.9 (19.3; 40.4)	0.112
	No	67(19.8)	368	18.2 (14.3; 23.1)	
House ownership					
	Rent	48(23.1)	220	21.8 (16.4; 28.9)	0.793
	Own	34(20.4)	180	18.9 (13.5; 26.5)	
	Live for free	13(16.9)	69	19.0 (11.0; 32.7)	
Roofing Material					
	Corrugated Iron	87(21.0)	430	20.2 (16.4; 25.0)	0.936
	Thatch/Tiles/Other	8(21.6)	39	20.6 (10.3; 41.3)	
When HIV status known					
	< 3 months	43(26.9)	140	30.8 (22.8; 41.5)	0.009
	3 to 12 months	21(19.4)	116	18.1 (11.8; 27.8)	
	>12 months	31(16.9)	213	14.6 (10.2; 20.7)	

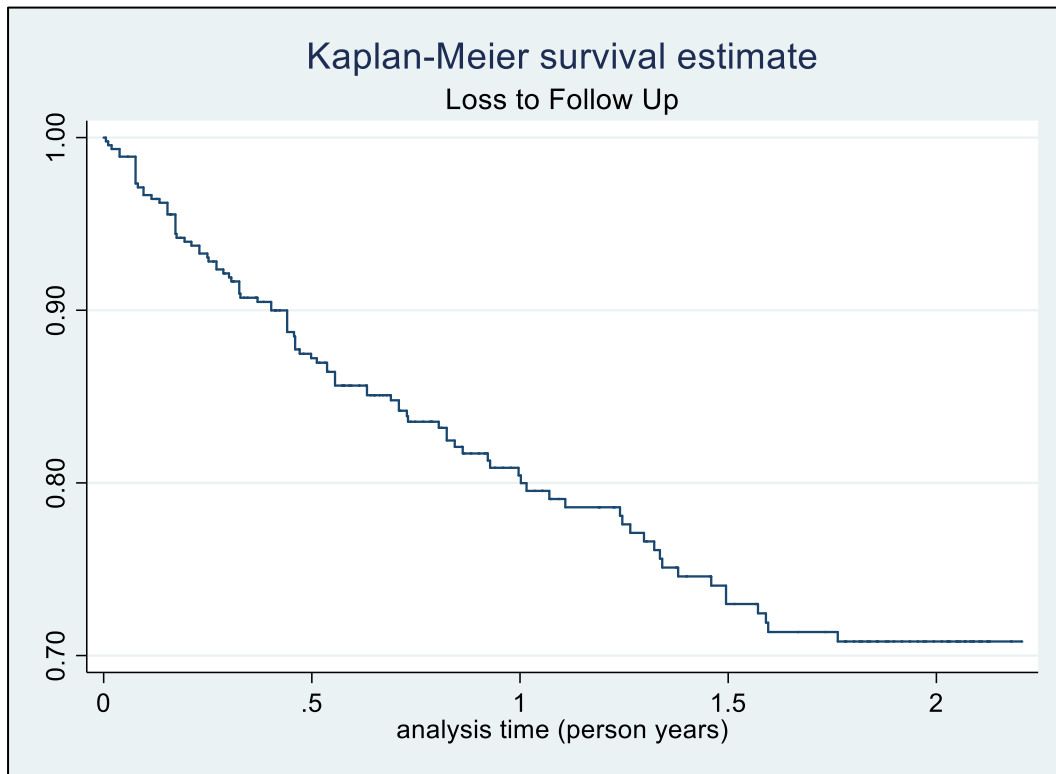
How long attended HIV clinic					
	< 3 months	54(25.1)	189	28.5 (21.8; 37.2)	0.011
	3 to 6 months	14(19.2)	82	17.1 (10.1; 28.8)	
	> 7 months	27(16.5)	197	13.7 (9.4; 20.0)	
Who is medicine companion?					
	Spouse/child	1(2.0)	68	1.5 (0.2; 10.4)	0.017
	Relative	15 (16.0)	122	12.3 (7.4; 20.5)	
	Other (neighbor/friend)	5(22.7)	25	20.1 (8.4; 48.3)	
Education level of medicine companion					
	No education	2(15.4)	20	10.1 (2.5; 40.6)	0.148
	Primary	4 (6.4)	83	4.8 (1.8; 12.9)	
	Secondary	9(18.8)	60	15.0 (7.8; 28.8)	
	Tertiary	1(5.0)	29	3.5 (0.5; 24.7)	
Is medicine companion HIV-positive?					
	Yes	8 (12.9)	82	9.8 (4.9; 19.5)	0.976
	No	5(12.8)	48	10.5 (4.4; 25.2)	
Disclosure to partner					
	Yes	30 (17.5)	185	16.2 (11.3; 23.2)	0.151
	No or no spouse/regular partner	65(21.3)	284	22.9 (18; 29.2)	
Disclosure to children					
	Yes	21(15.1)	152	13.8 (9; 21.2)	0.157
	No	32(22.7)	134	23.9 (16.9; 33.8)	
	Don't have children	9(19.2)	51	17.6 (9.2; 33.8)	
	Children too young to understand	33(26.4)	132	25.0 (17.8; 35.2)	
Ever been on ART					
	Yes	22 (10.3)	274	8.0 (5.3; 12.2)	<0.001
	No	73 (30.5)	194	37.6 (29.9; 47.3)	

There was no statistically significant difference in the rates of getting lost to follow-up between the participants who received care from peripheral health center compared to received care at Hospital/HC IV [21.4 per 100 person years (95% CI: 16.4; 27.8); and 18.9 per 100 person years (95% CI: 13.8; 25.9), respectively; Log-rank chi-square= 0.10; P-value=0.749]. There was a significant difference in the rates of getting lost to follow-up between participants who were

either on ART at the beginning of the study or initiated ART during the course of the study and those who remained ART naive throughout the study [8.0 per 100 person years (95% CI: 5.3; 12.2), and 37.6 per 100 person years (95% CI: 29.9; 47.3), respectively; Log-rank chi-square= 42.49; P-value<0.001]. Rates of lost to follow-up were significantly higher among participants who had known their HIV status for less than 3 months [30.8 per 100 person years (95% CI: 22.8; 41.5; p=0.009), who attended HIV clinic for less than 3 months [28.5 per 100 person years (95% CI: 21.8; 37.2; p=0.011) and those who had medicine companions as friends or neighbors [20.1 per 100 person years (95% CI: 8.4; 43.2;p=0.017). The lost to follow-up rate, however, appeared similar across the religious groups, sex, marital status, roofing material used, disclosure of HIV status and level of education.

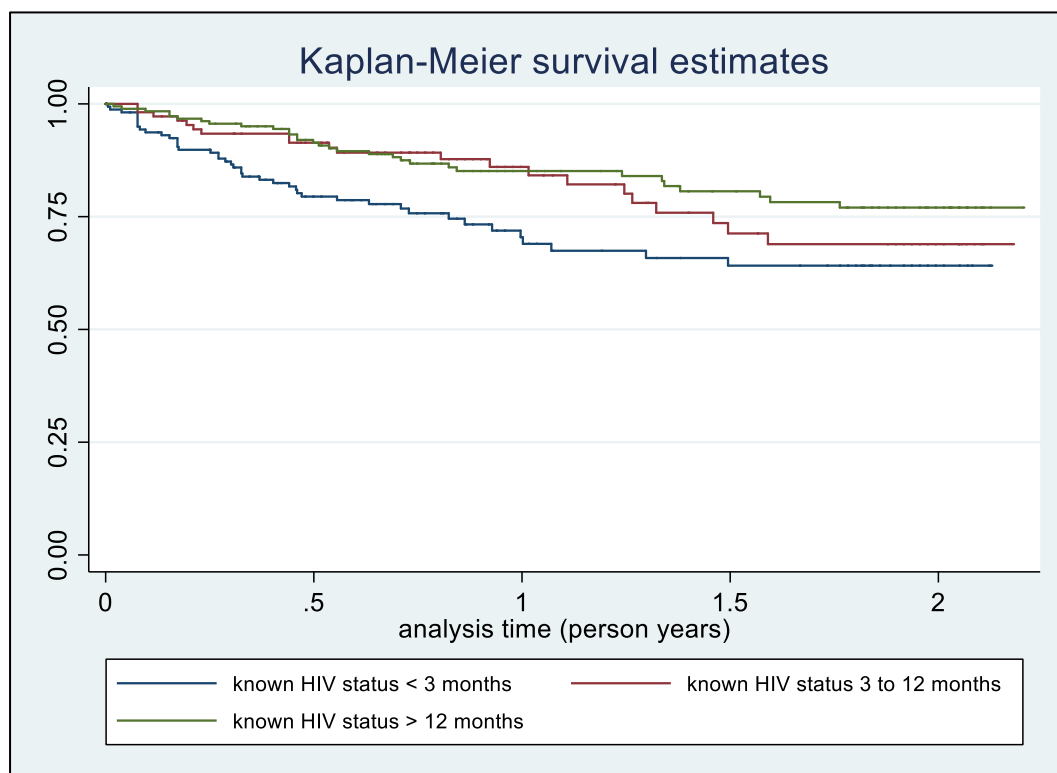
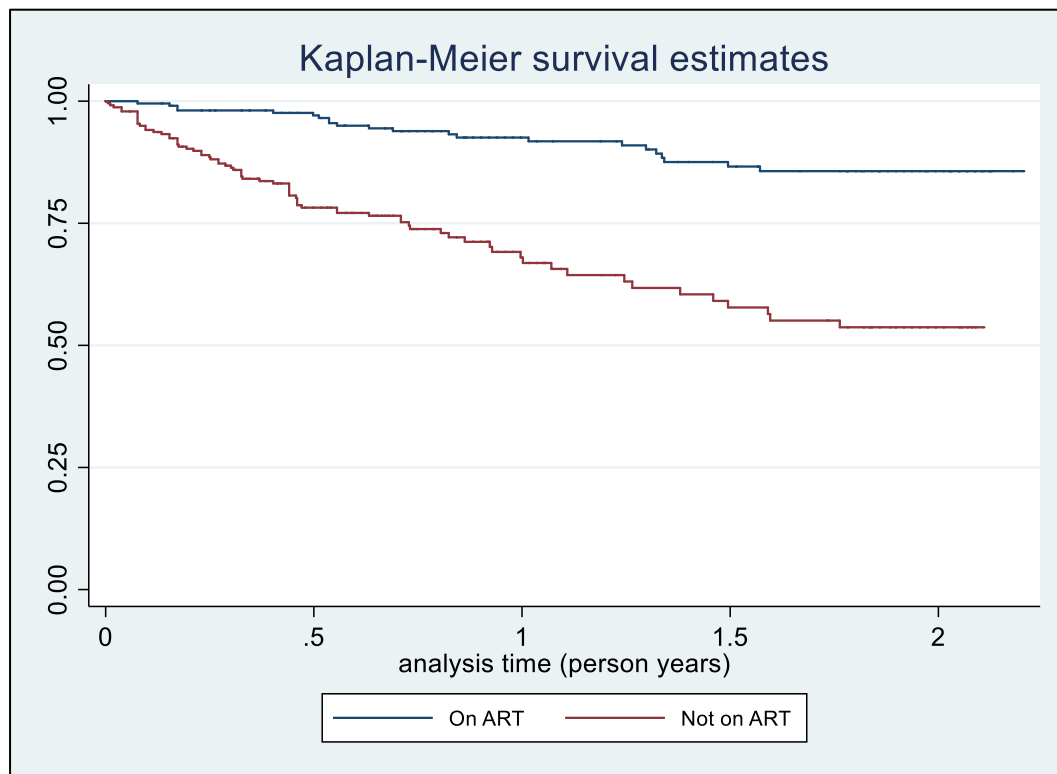
Overall retention in the study declined over time to about 70% over two years, in a roughly linear fashion as shown by Figure 1.

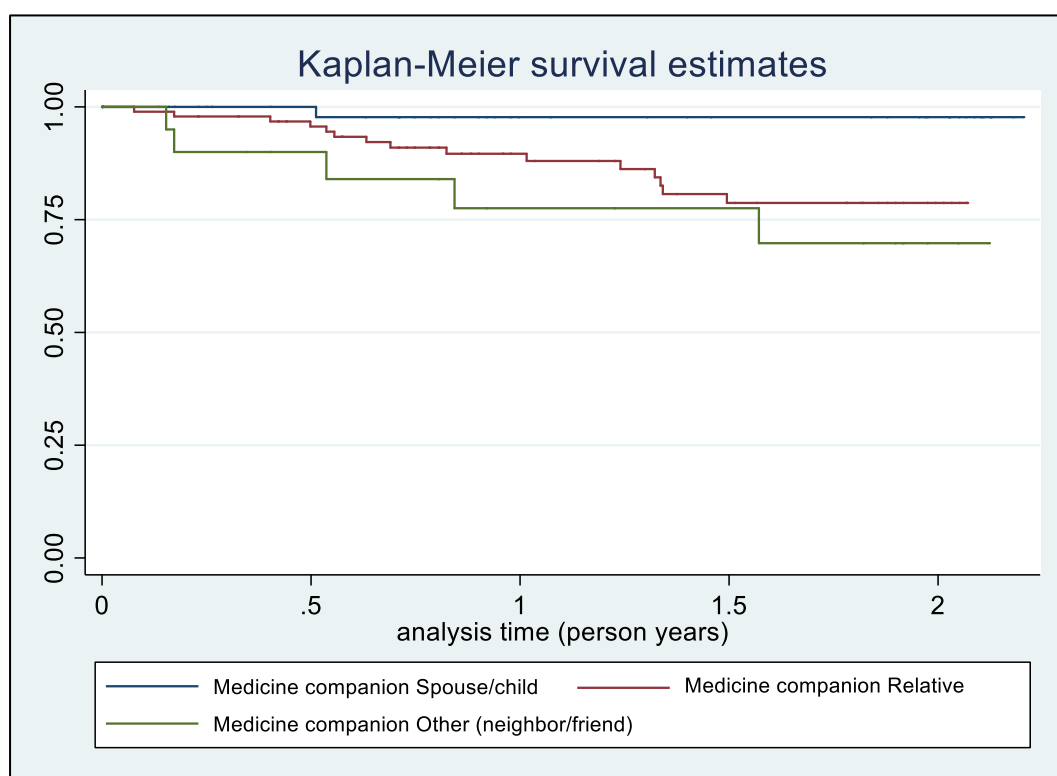
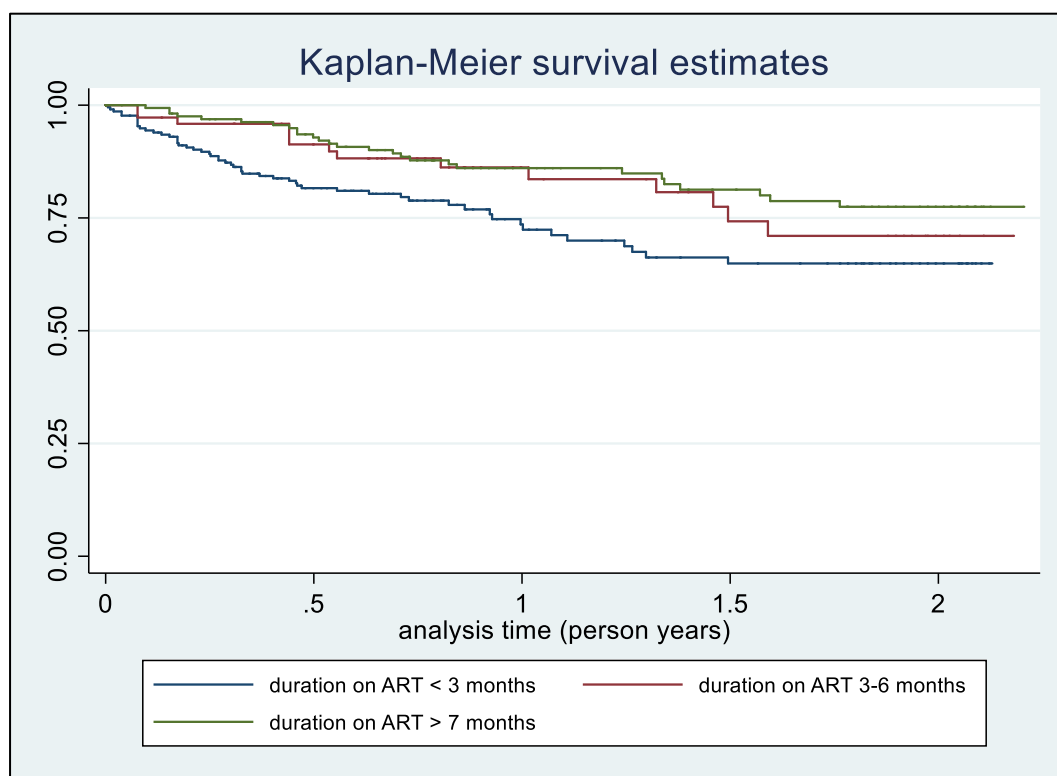
Figure 1: Kaplan-Meier plot showing retention in the study



The Kaplan-Meier plots below in Figure 2 show the retention in the study by explanatory factors. Only those that were significant are shown (time given in years).

Figure 2: Kaplan-Meier plot showing retention in the study by explanatory factors





Overall retention was lower for participants who had attended an HIV clinic for less than 3 months (approximately 60%) while it was higher for those who were on ART (approximately 85%).

3.3 Associated factors with loss to follow-up

To assess the significance of the factors to be included in the final model, Cox regression with stepwise backward elimination was used. To ensure that all important confounders were included in the model, a liberal P-value of $p=0.20$ was used. Sex was included in the final model despite not meeting the $p=0.20$ cut-off, as an a priori confounder. The choice of candidate explanatory variables to include in our final model was guided by previous literature and the univariate analyses results (Table 2). In Table 3 below, factors associated with being lost to follow-up using Cox regression are shown.

Table 3: Association between being lost to follow-up and socio-demographic and behavioural factors.

Variable	Label	unadj HR (95% CI)	P-value	adj HR (95 % CI)	P-value
Study Arm					
	Hospital/HC IV	Reference		Reference	
	Peripheral Health Centre	1.07(0.70-1.61)	0.750	0.62 (0.40; 0.96)	0.031
Sex of participant					
	Male	Reference		Reference	
	Female	1.00(0.65-1.55)	0.983	0.85 (0.55; 1.31)	0.462
Ever been on ART					
	No	Reference		Reference	
	Yes	0.23(0.14-0.37)	<0.001	0.19 (0.12; 0.32)	<0.001

In the unadjusted model, the risk of loss to follow-up was 7 % higher from participants in peripheral health centres than those from the hospital/HC IV , although this relationship was not statistically significant ($p=0.750$) while in the adjusted model, the risk of loss to follow-up was significantly lower by 40% ($HR=0.62$; 95% CI [0.40; 0.96]) among participants who received care from peripheral health center compared to received care at Hospital/HC IV. The apparent contradiction is due to the confounding effects of being on ART and sex; while the unadjusted effect of where the patient-initiated care was not significant, after adjusting for sex and whether the patient was initially on ART, the effect became statistically significant. In addition, there was overwhelming evidence to suggest that participants who had ever been on ART had an 80% lower risk of being lost to follow-up relative to those who had never been on ART ($HR=0.19$; 95% CI [0.12; 0.32]) and this was statistically significant ($p\text{-value}<0.001$). In addition, although the result was not statistically significant, females, was more likely to be retained in HIV care.

The proportional hazards assumptions checking for Cox model

We checked whether there was any evidence against the proportional hazards assumption using **phptest**. Table 4 below shows the proportional hazards assumption for individual factors.

Table 4: *Proportional hazards assumption for individual factors*

Variable	Rho	Chi-square	P-value
1b.facility			
2.facility	0.056	0.26	0.611
1b.sex			
2.sex	0.048	0.22	0.642
1.onart	0.150	1.89	0.169
2b.onart			
Global test	1.99	3.00	0.574

Our results suggest that the proportional hazards assumption was met for facility, sex and whether or not the patient is on ART. The overall p-value obtained was 0.574. Therefore, there was no evidence that the proportional hazards assumption did not hold.

CHAPTER 4: DISCUSSION

In this chapter of the research report we present a discussion, consisting of a summary of the study findings, a comparison of our findings with previous studies, the limitations experienced in the conduct of the present study, recommendations for further research and an overall conclusion

4.0 Summary of study findings

In summary, we sought to compare the retention in health care between HIV infected patients who initiated care in primary health care clinics and those who initiated care in Hospitals. In addition, for both groups of patients we investigated factors associated with retention in care, in Wakiso district, Uganda, 2008 to 2010. Understanding the factors associated with failure of retention in HIV care is of vital importance to improve treatment outcomes.

Our sample size was adequate to detect differences in effects of exposure on loss to follow-up. In the sample size calculation we actually assumed that those in the PHC arm (HC II and HC III) were more likely to be lost to follow up – the expected risk ratio was $(100-60)/(100-73)$ or $40/27 = 1.48$. The study found a rate ratio of 0.62, not as expected but the magnitude of the effect was similar to what we assumed.

In our study, there was a significant difference in retention in care between patients who initiated care in the peripheral health Centres and those in the hospital facilities. In fact, adjusting for other factors, participants who were recruited from the Primary Health Centres were less likely to be lost to follow-up. This could be that patients who initiated treatment at the HC IV / hospital were more likely to be on ART, so once the effect of being on ART is taken into account, the place of initiating treatment became statistically significant. In addition results from the Cox regression model show that the risk of being lost to follow-up is 80% lower for those participants who were on ART or initiated ART at some point in the study,

compared to those who never initiated ART (HR = 0.20 ; 95% CI 0.12 - 0.33; P<0.001). Therefore, participants who were on ART are more likely to be retained in care. There was no evidence that retention in care was associated with gender, alcohol use, education or disclosure of HIV status to a spouse or regular partner, medicine companion, known HIV status and attendance of HIV clinic. Although medicine companion, known HIV status and attendance of HIV clinic were significant in the univariate analysis, they ceased to be significant after adjustment of whether the participant had ever been on ART.

Comparison with previous studies

The poor retention in care (70% after two years) found in this study is comparable to that reported from other studies in Africa (26-28). In a study conducted by Scott and colleagues to estimate retention in care, the quantity of resources utilized, and costs for a retrospective cohort of 846 adults initiating ART under routine clinical conditions in Zambia, 75% of patients were retained in care (28). Similar to a body of literature in other sub-Saharan African countries, where retention of patients initiating ART at primary healthcare facilities was better than for those initiating ART at higher levels of care, in particular hospitals, our results show a statistically significant difference in retention between the facility categories (29-31). For instance, Fatti and colleagues conducted a retrospective cohort study including 29 203 ART-naïve adults from 59 facilities in four provinces in South Africa, enrolled between 2004 and 2007 and found that retention at the primary level of the healthcare setting was equally or more effective than in a hospital-based setting (30).

Contrary to the literature reported by other ART Programs in sub-Saharan Africa, we found no evidence of a difference in retention in care between males and females (32-34). Results from a retrospective cohort study conducted by Lowrance and colleagues to assess key 6- and 12-month outcomes among a nationally representative, stratified, random sample of 3194 adults

(\$15 years) in Rwanda who initiated ART showed that female patients were 50% more likely to remain ART at follow-up compared with similar male patients (32). In addition, the recommendation of World Health Organization (WHO) consists of test and treat i.e. that anyone who tests HIV positive should initiate ART irrespective of their CD4 count. In keeping with this recommendation, this is an important finding of our study that retention in care is better for those on ART (35).

4.1 Limitations of the study

The current study should be viewed in light of the following possible limitations: Firstly, participants themselves chose where they initiated HIV care (either at a primary health care facility or hospital facility). Hence the generalizability of the findings of this study may be limited to the populations from similar geographical settings. Secondly, the researcher had no control over the sample size, and a larger sample size with more data might have helped to identify more factors associated with LTFU. Thirdly data on CD4 count and WHO stage were not available to explore their effects, and lastly, while broader national contextual factors also influence LTFU, we were unable to measure such factors directly. We also could not further explore the effect of current use of alcohol on retention in care by distinguishing the amount of alcohol.

4.2 Recommendations for other research

If a similar study were to be done, we would recommend that participants should be randomly allocated to either a peripheral health centre facility or hospital facility to counter the bias introduced by self-selection. In addition, a study carried out in a number of districts would allow for generalization of findings. In addition, mixed methods study design has the potential to explore the reasons for retention in care among HIV infected patients. The only measure of

socioeconomic status available in this study was the roofing material, so in further studies other measures of socio-economic status could be used.

4.3 Recommendations related to the health system

The major gaps in retention in HIV care include linking individuals who test HIV positive to care and prompt initiation of ART, therefore the implementation of test and treat guideline needs to be considered. These will meet the UNAIDS 90-90-90 targets which consist of the following: 90% of HIV-positive individuals must know their status, 90% of those diagnosed must be on ART despite their CD4 and 90% of those on ART must be virally suppressed by 2020. Removing the CD4 eligibility threshold may increase the number of patients attending the clinics, which can put a strain on already overburdened healthcare systems. This fact needs to be considered (35-37).

Conclusion

In conclusion, the results obtained in this study suggest that there is a significant difference in retention in care between patients who initiated care in the peripheral health centre and those in the hospital facilities. In fact, adjusting for other factors, participants who were recruited from the Primary Health Centres were less likely to be lost to follow-up, possible reasons could be more easy access to care, lower transport costs, more supportive attitude of health workers personally known to the patient, chance and selection bias. Further work would be needed in order to decide which of these factors contributed. In addition, the result shows that patients are much more likely to be retained in care when they are on ART.

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APPENDIX



R14/49 Dr IG Mulumba

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL) CLEARANCE CERTIFICATE NO. M190209

NAME: Dr IG Mulumba
(Principal Investigator)
DEPARTMENT: School of Public Health
Epidemiology and Biostatistics Division
Medical School
University

PROJECT TITLE: Factors associated with retention in HIV care in Wakiso district, Uganda from 2008 to 2010

DATE CONSIDERED: 2019/02/22

DECISION: Approved unconditionally

CONDITIONS:

SUPERVISOR: Professor J Levin

APPROVED BY: 
Dr CB Penny, Chairperson, HREC (Medical)

DATE OF APPROVAL: 2019/07/25

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. I **agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **February** and will therefore reports and re-certification will be due early in the month of **February** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).


Principal Investigator Signature


Date

PLEASE QUOTE THE CLEARANCE CERTIFICATE NUMBER IN ALL ENQUIRIES