

**A SURVIVAL ANALYSIS APPROACH TO DETERMINE THE PREDICTORS OF  
TIME TO HIV PARTNER NOTIFICATION IN KENYA.**

**BETSY C. SAMBAI**


**W62/8622/2017**

**A THESIS SUBMITTED IN PARTIAL FULFILMENT FOR THE DEGREE OF  
MASTER OF MEDICAL STATISTICS IN THE INSTITUTE OF TROPICAL AND  
INFECTIOUS DISEASES, UNIVERSITY OF NAIROBI**

**NOVEMBER 2019**

**DECLARATION**


I declare that this research project is my original work and has not been presented in any other university or institution for academic credit.

Signed  Date 14/11/2019

Betsy C. Sambai

W62/8622/2017

This research project has been submitted for examination with our approval as the university supervisors.

Signed:  Date: 14/11/2019

Dr. David Gathara

Institute of Tropical and Infectious Disease


University of Nairobi

Signed  Date: 14/11/2019

Dr. Linda Chaba

Strathmore Institute of Mathematical Sciences

Strathmore University

Signed:  Date 14/11/2019

Prof. Carey Farquhar

Departments of Global Health, Medicine, and Epidemiology

University of Washington

## **DEDICATION**

I dedicate this work to my loving husband Mr. Enock Cheruiyot, my son Evan Kiprop, and to my parents and siblings.

## **ACKNOWLEDGMENT**

I thank God for the grace and strength to go through this process. I also wish to thank my husband Enock Cheruiyot and son Evan Kiprop for the support and encouragement through the research process. I am very grateful for my supervisors Dr. David Gathara, Dr. Linda Chaba and Prof. Carey Farquhar for their mentorship, critique and unwavering support during the development and writing of this project. I appreciate Kenyatta National Hospital and University of Washington for allowing me to use the organizations' data for my project work.

Lastly, I wish to acknowledge all my friends who have contributed immensely in my MSc program. Special thanks to Dr. Marshal Mweu for his mentorship, Dr. David Bukusi, Dr. Beatrice Wamuti, Loice Mbogo, Margaret Ndegwa and Geoffrey Omondi who have cheered me through the process. You have been of great support!

## **TABLE OF CONTENTS**

<b>DECLARATION.....</b>	<b>ii</b>
<b>DEDICATION.....</b>	<b>iv</b>
<b>ACKNOWLEDGMENT .....</b>	<b>v</b>
<b>TABLE OF CONTENTS .....</b>	<b>vi</b>
<b>LIST OF TABLES .....</b>	<b>x</b>
<b>LIST OF FIGURES .....</b>	<b>xi</b>
<b>LIST OF APPENDICES .....</b>	<b>xii</b>
<b>LIST OF ABBREVIATIONS .....</b>	<b>xiii</b>
<b>ABSTRACT.....</b>	<b>xiv</b>
<b>CHAPTER ONE: INTRODUCTION.....</b>	<b>1</b>
1.1 Background .....	1
1.2 Problem statement .....	3
1.3 Purpose of the study .....	4
1.4 Objectives .....	4
1.4.1 Broad objective.....	4
1.4.2 Specific objectives.....	4
1.5 Hypothesis .....	4
1.6 Study justification .....	5
1.7 Significance of the study .....	5

1.8 Scope and limitations of the study .....	5
1.9 Definition of terms .....	6
<b>CHAPTER TWO: LITERATURE REVIEW .....</b>	<b>7</b>
2.1 Introduction .....	7
2.2 Global and regional burden of HIV.....	7
2.3 Strategies to address HIV burden globally and within the region.....	8
2.4 Taking advantage of APS to curb the burden of HIV .....	9
2.5 Application of survival analysis in health research.....	10
<b>CHAPTER THREE: METHODOLOGY .....</b>	<b>13</b>
3.1 Introduction .....	13
3.2 Study design .....	13
3.3 Study area.....	13
3.4 Study population .....	14
3.5 Sampling method.....	15
3.6 Sample size determination .....	15
3.7 Quality assurance procedures.....	16
3.8 Ethical consideration .....	17
3.9 Data collection and analysis .....	17
<b>CHAPTER FOUR: RESULTS AND FINDINGS.....</b>	<b>21</b>
4.1 Introduction .....	21

4.2 Index socio-demographic characteristics .....	21
4.3 Partner socio-demographic characteristics .....	23
4.4 Comparison of time to partner notification between the immediate and delayed arms.	24
4.4.1 Overview of time to HIV partner notification .....	24
4.4.2 Test for equality of survival curves between immediate and delayed arms.....	25
4.4.3 Test for equality of survival curves across the socio demographic characteristics.	26
4.5 Cox regression model to determine predictors of time to HIV partner notification. ....	28
4.5.1 Shared frailty univariable Cox regression model .....	28
4.5.2 Shared frailty multiple Cox regression model.....	30
4.5.3 Testing PH assumption of the Cox regression model. ....	32
<b>CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATION .....</b>	<b>35</b>
5.1 Summary of major findings.....	35
5.2 Socio demographic characteristics of index and partners .....	35
5.3 Comparison of time to HIV partner notification between immediate and delayed arm. .....	36
5.4 Predictors of time to HIV partner notification in Kenya.....	37
5.5 Conclusion.....	39
5.6 Recommendation.....	39
<b>REFERENCE.....</b>	<b>40</b>
<b>APPENDICIES .....</b>	<b>44</b>



Appendix I: Work plan.....	44
Appendix II: Budget.....	45
Appendix III: Plagiarism Report.....	46
Appendix IV: KNH ERC Approval .....	47

**LIST OF TABLES**

**Table 4.1 Index socio- demographic characteristics ..... 22**

**Table 4.2 Partner Socio- Demographic Characteristics ..... 23**

**Table 4.3 Wilcoxon Test for equality of survival functions between the immediate and delayed arms..... 25**

**Table 4.4 Wilcoxon test for equality of survival functions across the socio demographic characteristics..... 26**

**Table 4.5 Shared frailty univariable Cox regression model. .... 28**

**Table 4.6 Shared frailty multiple Cox regression model..... 30**

**Table 4.7 Time varying effects Cox regression model ..... 32**

**Table 4.8 Effect of intervention arm, partner sex and index sex on time to HIV partner notification at different time points..... 34**

**LIST OF FIGURES**

**Figure 1.1 Assisted Partner Notification Service Conceptual Framework ..... 3**

**Figure 2.1 HIV Prevalence of adults aged 15-49 years, 2017 by (WHO) region..... 7**

**Figure 3.1 Kaplan-Meier function of time to HIV partner notification. .... 24**

**Figure 4.2 Kaplan Meier curves of time to HIV partner notification between immediate  
APS arm and delayed APS arms. .... 25**

**LIST OF APPENDICES**

**Appendix I: Work plan ..... 44**

**Appendix II: Budget ..... 45**

**Appendix III: Plagiarism Report ..... 46**

**Appendix IV: KNH ERC Approval ..... 47**

## **LIST OF ABBREVIATIONS**

AIDS	Acquired Immunodeficiency Syndrome
APS	Assisted Partner Services
ART	Antiretroviral therapy
CSV	Comma Separated Values
ERC	Ethics Review Committee
HIV	Human Immunodeficiency Virus
HR	Hazard Ratio
HTC	HIV testing and counselling
HTS	HIV testing services
IQR	Interquartile Range
K-M	Kaplan Meier
NACC	National AIDS Control Council
NASCOP	National AIDS & STI Control Programme
ODK	Open Data Kit
PH	Proportional Hazard
PN	Partner Notification
SSA	Sub-Saharan Africa
UNAIDS	United Nations Programme on HIV and AIDS
WHO	World Health Organization

## **ABSTRACT**

**Introduction:** Globally, Sub-Saharan Africa (SSA) has registered the highest Human Immunodeficiency Virus (HIV) prevalence with over 50% of seropositive individuals unaware of their HIV status. Assisted Partner Services (APS) is one of safe and cost-effective HIV testing and awareness strategy that has documented increase in uptake of HIV testing by 1.5 times. However, APS is an intense process that requires significant amount of time and many factors contribute to the amount of time spent on this process. Knowledge on time to Partner Notification (PN) and possible predictors is critical in developing individual specific strategies that could ease and quicken notification process and result in timely case finding and initiation to Antiretroviral Therapy (ART) and eventually reduction in onward transmission and HIV prevalence. APS Studies conducted in SSA have not provided a lot of information on time to PN. We therefore carried out this study to determine the possible predictors of time to partner notification among the Kenyan population.

**Methodology:** Secondary data from 1,119 HIV positive adults sampled from a cluster randomized control trial conducted in Kenya from August 2013 to August 2015 was used. The primary study randomized 9 clusters to immediate arm (that implemented APS immediately a partner was named) and the other 9 clusters to delayed arm (that implemented APS 6 weeks after a partner was named) and the outcome of measure was number of partners of an index tested for HIV, identified as HIV infected and linked to HIV care. Data analysis for this study was done using STATA version 14.2. Descriptive analysis was used to report socio-demographic characteristics. Kaplan –Meier (K-M) estimates was used to estimate time to HIV partner notification between groups and the equality of survival functions between groups

tested using Wilcoxon test. A shared frailty multiple cox regression model was fitted to determine the possible predictors of time to HIV partner notification. Time varying effects cox regression model was fitted to address the violation of Proportional Hazard (PH) assumption by three variables.

**Results:** Majority of index participants were females (61%) while males were most of the partners notified of exposure to HIV (56%). Index participants were younger (aged 30 years (IQR 25-38)) than their partners aged 31 years (IQR 26-38). There was statistically significant difference in the survival curves between immediate and delayed arms ( $p < 0.001$ ) at 5% significance level. Time to HIV partner notification was statistically associated to intervention arm (method of notification), sex of the partner and sex of the index at 5% significance level. The effects of intervention arm, sex of the partner and sex of the index on time to HIV partner notification varied with time. The intervention arm resulted in an increase in the rate of HIV partner notification at the beginning (HR=23.7) then the effects drops off with time.

**Conclusion:** Sex of partner and index are important predictors of time to HIV partner notification. Effective time to conduct partner notification is within 42 days of being named. Health care provider characteristics could be obtained in future studies because they might have an effect on time to Partner notification.

## **CHAPTER ONE: INTRODUCTION**

This section gives a background of the study, statement of the problem, objectives and hypothesis

### **1.1 Background**

#### **Late Diagnosis of HIV still presents as a burden in Sub-Saharan Africa.**

While highly active antiretroviral therapy has been successful in delaying progression into Acquired Immunodeficiency Syndrome (AIDS), late HIV diagnosis remains a major contributor to the mortality and morbidity of AIDS (Dai et al., 2015). Timely diagnosis of HIV infection is associated with reduced onward transmission of the infection, improved response to ART treatment, better immunity among those diagnosed with the infection, reduced costs for health care and ultimately reduced prevalence of HIV (Grinsztejn et al., 2014). There is however a significant proportion (25%) of HIV infected individuals globally who are diagnosed with the disease at a very late stage (Easterbrook, Johnson, Figueroa, & Baggaley, 2016). In Europe, over 54% of individual newly diagnosed of HIV were in the late stage of the disease and progressed to AIDs defining diseases six months after the diagnosis (Xie et al., 2017). Sub-Saharan Africa has also documenting late stage disease to HIV clinic, specifically Uganda found that 40% of new patients in HIV clinic had late-stage HIV disease at their initial clinic visit (Kigozi et al., 2009).

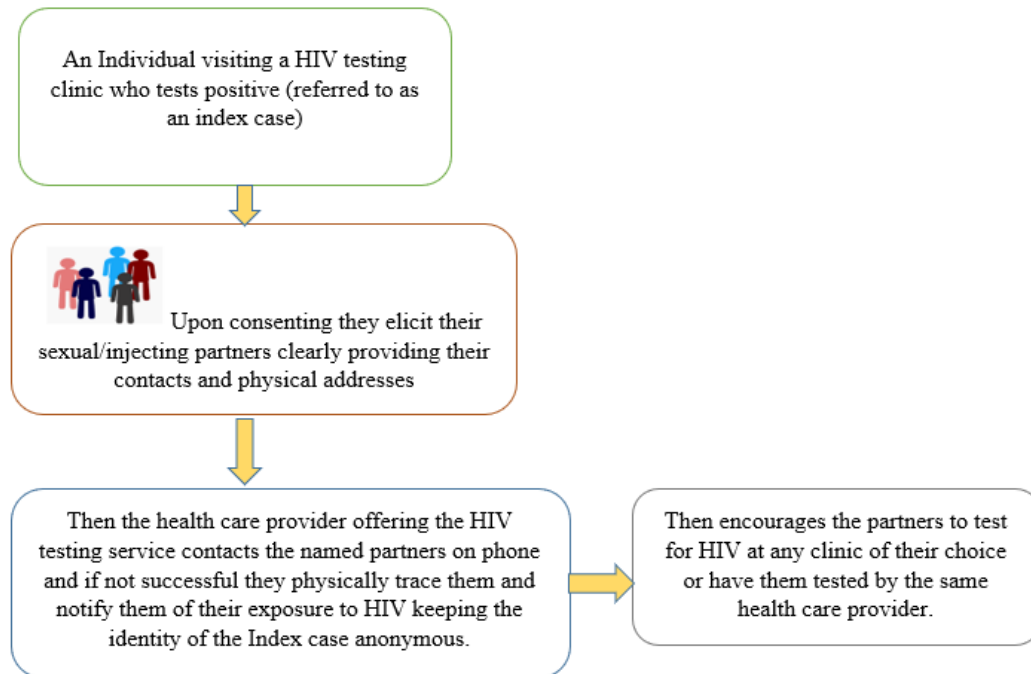
#### **Timely Partner Notification (PN) Service.**

The burden described above necessitate the study of other possible strategies that could increase HIV testing and case detection. Voluntary counselling and testing at the community level was considered a possible intervention that could increase HIV infection detection,



specifically in regions with limited access to HIV testing clinics (Sweat et al., 2011). HIV self-testing is also one of the interventions that is still new in Kenya and is being tested. Other interventions being implemented in SSA to further increase HIV testing coverage that could ultimately result in timely diagnosis of the infection is Assisted Partner Services (APS). This intervention involves the health care provider assisting HIV positive individual (index case) who consent, to disclose their status or anonymously notify their sexual/injecting partners of their possible exposure to the infection. Studies in SSA have demonstrated effectiveness of APS in increasing HIV testing and linkage to care and further 9-fold and 3-fold increase in newly diagnosing a male partner and female partner respectively (Brown et al., 2011). Results from this study have informed HIV testing guidelines and partner notification has been incorporated in the WHO HIV testing guidelines as part of the routine testing.

However, several challenges with Partner notification processes have been presented which includes the need for time and effort to successfully trace a named contact, fear for confidentiality and stigma (Adams, Carter, & Redwood-Campbell, 2015). It is therefore important to consider time as a resource that could potentially improve the effectiveness of partner notification services if implemented on large scale. The longer the time spent on partner notification, the higher the chance of onward transmission and advanced immunosuppression. It is therefore essential to think of strategies that could help minimize the time to partner notification to achieve timely case finding. Developing such strategies will entail having a clear understanding of the possible predictors of time to PN. This study therefore aimed at documenting possible factors that could influence time to successful partner tracing and notification which could provide insights on implementation of PN services in Kenya and inform the ongoing scale up of PN services.



**Figure 1.1 Assisted Partner Notification Service Conceptual Framework**

## 1.2 Problem statement

Partner tracing and notification is a very resource intense process that requires significant amount of time which directly affects the cost of implementing APS. Partner Notification (PN) practice for Sexually transmitted disease program in the US showed that 37.4% of the recorded time was spent on partner notification activities (field visits to notify a contact, interviews and treatment) with field visits accounting for the largest proportion of time spent on PN (Macke, Hennessy, McFarlane, & Bliss, 1998). Knowledge of time to HIV partner notification could inform on better strategies to timely diagnose over 50% of people living with the infection but are unaware of their status. However, most of the APS studies in Sub-Saharan Africa, Kenya included, have not documented findings on time to partner notification and the possible factors affecting time to PN.

### **1.3 Purpose of the study**

The purpose of this study was to determine the time to HIV partner notification and the factors that influence time spent on partner notification.

### **1.4 Objectives**

#### **1.4.1 Broad objective**

The overall objective of this study is to determine the predictors of time to HIV partner notification in Kenya.

#### **1.4.2 Specific objectives**

1. To determine socio–demographic characteristics of study participants at baseline and estimate median time to HIV partner notification.
2. To compare time to partner notification between the Immediate APS and Delayed APS arms.
3. To determine predictors of time to HIV partner notification in Kenya.

### **1.5 Hypothesis**

We hypothesized that there is no significant difference in time to partner notification between the intervention /immediate arm (that implemented APS immediately after a partner was named) and control /delayed arm (that implemented APS 6 weeks after a partner was named to allow time for standard process of partner notification).

## **1.6 Study justification**

Studies in SSA have demonstrated that provider initiated APS increases uptake of HIV testing by 1.5 times and that it is safe and cost-effective however it is an intense process that requires a significant amount of time(Macke et al., 1998).The longer the time to successfully notify a sexual partner on potential exposure to HIV infection, the higher the risk of onward transmission and immunosuppression. Knowledge on time to partner notification and possible factors contributing to this is necessary for developing strategies that could reduce the time to PN leading to timely case finding, initiation to ART and eventually reduction in the prevalence of HIV. APS Studies conducted in SSA have not provided a lot of information on time to PN. Therefore, this study aimed at determining possible predictors of time to partner notification among the Kenyan population that could possibly inform the ongoing implementation of APS in Kenya.

## **1.7 Significance of the study**

This study offered insights on the intensity of partner tracing and HIV notification, the time to HIV partner notification and possible factors that contribute to this. This information will be utilized in the ongoing scale up of assisted partner services in Kenya.

## **1.8 Scope and limitations of the study**

This study obtained data from a primary study that included adults from Kisumu, Nairobi and Central regions. The study population included individual from different ethnic groups of rural and urban settings.

The study was limited to few socio-demographic characteristics that were observed in the primary study which may not represent all the possible predictors of time to partner

notification. Secondly, data used in this study was obtained from only three regions of the country and might not be generalizable to other regions of the country however the study results can be used to generate evidence for future research.

### **1.9 Definition of terms**

**APS (Assisted Partner Services)** -Refers to the process in which the sexual/injecting partners of an individual who test positive for Human Immunodeficiency Virus (HIV) are notified of their exposure to the HIV infection by the health care provider who offered the testing service

**Index case-** A person who tests HIV positive and consents to give contacts of his/her sexual/injecting partners.

**Immediate /Provider referral arm-**The study arm in which the health care provider offered Assisted partner notification services within the first week a partner was named.

**Delayed /contract referral arm-** The study arm in which the health care provider offered Assisted partner notification services 6 weeks after a partner was named to allow the index case time to notify their partners as per the standard of HIV care in Kenya.

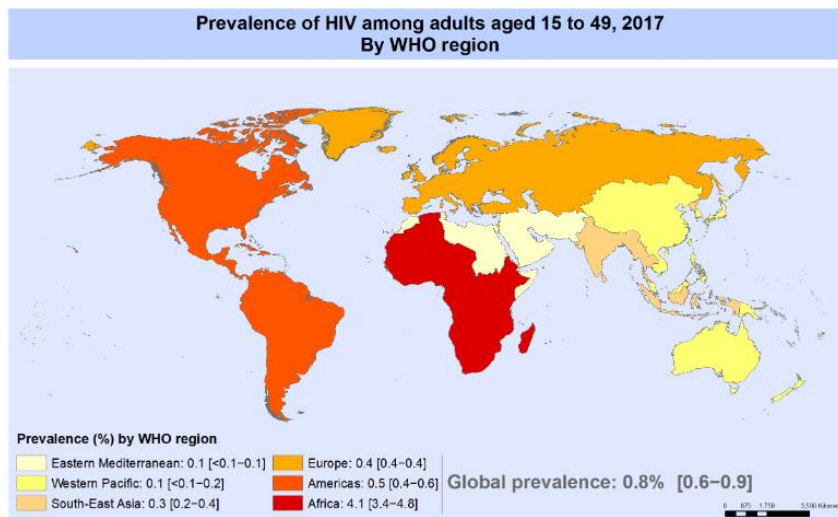
## CHAPTER TWO: LITERATURE REVIEW

### 2.1 Introduction

This section reviews literature on the research subject. It is divided into four sections: Global and regional burden of HIV, strategies to address HIV burden globally and within the region, taking advantage of APS to curb the burden of HIV and application of survival analysis in health research.

### 2.2 Global and regional burden of HIV.

Globally, the estimated number of people infected with HIV since the beginning of the epidemic is 75 million and those that have died due to the disease estimated at 32 million people (WHO, 2018) Over 37.9 million people were living with HIV end of 2018 (WHO, 2018). The Sub-Saharan countries are still reporting the highest burden of the epidemic with one in every twenty-five adults living with HIV (WHO, 2018)



**Figure 2.1 HIV Prevalence of adults aged 15-49 years, 2017 by (WHO) region.**

Out of a population of approximately 40 million people in Kenya, over 1.5 million people were living with HIV end of 2015 and the number of new infections among 15+years reported that year was 71,035 with over 51% of these new infections contributed by young people aged (15-24 years) (NACC, 2016).The National HIV Prevalence has almost stabilized at 5.6% among people aged 15-49 years with Homabay registering the highest prevalence while Wajir the lowest prevalence of 26% and 0.4 %, respectively (NACC, 2016).Even though there is a general decline in cases of new infections among those aged above 15 years by 19% between 2013 and 2015, there is however an alarming increase in new infections among young people aged (15-24 years) by 17% within the same period which calls for strategic intervention to curb this (NACC, 2016).

### **2.3 Strategies to address HIV burden globally and within the region.**

The world targets to end AIDS epidemic by the year 2030 was spelled out in the Sustainable Development Goal 3 by expanding HIV testing counselling services (HTS) and Antiretroviral therapy (ART) coverage i.e diagnosing 95% of HIV positive individuals, providing ART treatment to 95% of those testing HIV positive and 95% of those on ART treatment virally suppressed (UNAIDS, 2016). In an attempt to reach a larger population other HTS approaches have been adopted besides facility testing which includes mobile, community and homebased testing. This has resulted in over 17million people with HIV infection receiving treatment by end of 2015 however another 14.5 million remain undiagnosed (UNAIDS, 2016). A study to compare community based HIV testing (mobile, workplace and homebased) and index tracing indicated that index tracing was more effective in reaching children and identifying HIV positive individuals than the Community based testing methods (Sweat et al., 2011).

APS is one of the HTS strategy that could potentially improve HIV test uptake and case finding compared to the current standard of care. The current standard of care for partner notification is encouraging an individual testing HIV positive to disclose status to their partners and encourage them to test. A meta-analysis of randomized control trials conducted in United States, Malawi and Kenya showed that; APS resulted in 1.5-fold increase in HTS uptake among partners compared to passive referral, proportion of partners newly diagnosed with HIV higher with provider APS and higher percentage of partner linked to care among the provider initiated APS category (Dalal et al., 2017)

#### **2.4 Taking advantage of APS to curb the burden of HIV**

Scale up of APS in Sub-Saharan Africa as a strategy to close the testing gap among individuals who are not aware of their status and are at high risk of HIV has been highly recommended by WHO in the recent guidelines (WHO, 2016) and is now widely used in Kenya. Implementation of APS require significant amount of resources including money, personnel and time. A cost effective analysis of APS cluster randomized clinical trial conducted in Kenya indicated that APS could be cost effective in HIV- related mortality and morbidity and specifically reducing incident infections by 3.7% and averting 14% deaths over 10 years (Sharma et al., 2018).

One of the other resources that directly affect the cost of implementing APS is time to successful partner tracing and notification. Partner tracing is an intense process that requires significant amount of time. Partner Notification (PN) practice for STD program in the US showed that 37.4% of the recorded time was spent on partner notification activities (field visits to notify a contact, interviews and treatment) with field visits accounting for the largest proportion of time spent on PN (Macke et al., 1998). The APS study conducted in Kenya recorded an average of 40-60 minutes on APS intervention once a partner has been traced



(Sharma et al., 2018). These results have however not specifically documented the amount of time (in days/years) taken to successfully trace and notify a partner contact and the possible factors contributing to the time to partner notification. Results from an STD program in four US sites that sought to determine the predictors of time to PN showed a strong relationship between client type, STD category, outcome, mileage and time spent on PN. There was no statistical evidence to indicate an association between the demographics characteristics (age, sex and ethnicity) and time spent on PN (Macke et al., 1998). This has however not been widely researched on in APS studies carried out in SSA including the APS pilot study conducted in Kenya, from which data used in this study is obtained.

## **2.5 Application of survival analysis in health research**

Clinical outcomes take a variety of statistical formats. Some are continuous or binary outcomes analyzed using linear and logistic regression methods respectively while others are time to event outcomes analyzed using more robust methods like survival analysis. Time to event outcomes are very common in medical research. Such outcomes are analyzed using survival analysis methods which takes into account censored observations where the event of interest is not observed within the study/follow up period.

Survival models are categorized as non-parametric, semi-parametric and parametric models. The choice of survival model depends on the survival distribution of the event of interest. Kaplan-Meier estimation methods are used to plot survival curves, while Wilcoxon tests are used to compare survival curves between groups. Survival regression models like Cox Proportional Hazards model and accelerated failure time model are used to test the effect of covariates on survival time.

Some of HIV related studies have used survival analysis to model time to event data but this type of analysis has been scarcely used in partner notifications services studies because most of these studies have not included time to PN as their outcome of interest. A study to assess the effectiveness and feasibility of partner notification in Sub-Saharan Africa analyzed time to presentation of locatable partners using Cox proportion hazards regression with robust confidence intervals to account for clustering among the index client. Results of this study indicated that time to locating a named partner was associated with the method of partner notification (Brown et al., 2011). Cox regression modelling was used to assess the effects of ART on survivorship of HIV infected patients in a cohort study conducted in Spain (Garcia de Olalla et al., 2002). Survival analysis showed that patients with HIV-2 virus survived longer than those with HIV-1 virus (Whittle et al., 1994). Other studies that have analyzed time spent on PN in a US STD program have modeled time (in minutes) spent on PN activities against a set of predictors using random effects regression models (Macke et al., 1998). This type of regression model treats time (outcome variable) as a continuous variable. It is however limiting in cases where time to successful partner notification is expressed as number of days/months/years which is the case in cohort studies and where lost to follow up cases are common. Survival analysis therefore takes into consideration censored observations that are common in partner notification for instance partners whose attempt to notify them were unsuccessful which in other analysis would have been treated as missing data and excluded.

Shared frailty cox regression models are important in addressing cases of clustering in survival data. Shared frailty is the measure of the effects of unobserved covariates that a group of individuals have in common. This study therefore modeled predictors of time to partner

notification services using an appropriate multivariable method for analyzing time to event data.

## **CHAPTER THREE: METHODOLOGY**

### **3.1 Introduction**

This section describes the study design, study area, study population, sampling techniques, sample size, quality assurance procedures, ethical consideration, data collection and analysis procedures.

### **3.2 Study design**

The data used in this study was drawn from a cluster-randomized control trial conducted in Kenya from August 2013 to August 2015 (Wamuti et al., 2015). A total of 18 HIV clinics in Kenya were selected and randomized equally to intervention and control arms. The partners in the nine clinics randomized to the immediate/provider referral arm received APS from a health care provider within the first week of index case enrolment while the partners in the other nine clinics randomized to the delayed/contract referral arm received APS from the health care provider 6 weeks after index case enrolment. The purpose of the 6 weeks delay period was to allow time for the index case to notify their partners of exposure to HIV which is the current standard practice in HIV testing in Kenya. The primary outcome measured was the number of partners per index case testing for HIV, diagnosed of HIV and linked to care (Wamuti et al., 2015). However, the current study sought to determine the predictors of time to HIV partner notification using survival analysis approach.

### **3.3 Study area**

Data from 18 high volume HIV testing clinics selected in Kisumu, Central and Nairobi representing both rural and urban settings that were sampled in the primary study was used.

### **3.4 Study population**

The study population entailed HIV positive adults and their sexual/injecting partners in Kenya.

#### **Analysis inclusion criteria**

Data from at least 1,119 HIV positive adults (also referred to as index case) in Kenya who were enrolled in the primary study was drawn for analysis. We extracted index socio-demographic characteristics and index enrolment dates from both index screening data, and Index enrolment data. Sexual history information was drawn from Index sexual history data. We further extracted partner demographics from partner enrolment data.

In the analysis, we used data for;

- i. Index cases who were successfully enrolled in the primary study.
- ii. Index cases with complete sexual history information for their sexual partners.
- iii. Partners who were successfully traced and notified of exposure to HIV.

#### **Analysis exclusion criteria**

The following data was excluded during analysis;

- i. Data for index case with incomplete screening, enrolment and sexual history information.
- ii. Data for index case who was incorrectly matched to the partners.
- iii. Any data with partner enrolment date less than the date partner was named/mentioned.

### 3.5 Sampling method

All the 18 HIV testing sites were sampled and an equal number of individuals selected in each site using simple random sampling.

### 3.6 Sample size determination

The sample size of 918 index participants was arrived at using the sample size calculation formula for survival data proposed by Freedman (1982).

$$n_E = \frac{mk}{kpE+pC} \quad n_C = \frac{m}{kpE+pC}$$
$$m = \frac{1}{k} \left( \frac{kRR+1}{RR-1} \right)^2 * \left( Z_{1-\frac{\alpha}{2}} + Z_{1-\beta} \right)^2$$

Where,

- i. nE- sample size for the intervention arm (Immediate APS)
- ii. nC-sample size for control arm (Delayed APS)
- iii. k-the ratio of participants in the intervention (immediate APS) to the control arm (delayed APS) (nE/nC) which is 1.
- iv. The power of the study (1-β) set at 95%
- v.  $Z_{\frac{\alpha}{2}}$ - standard normal value for two-tailed hypothesis at α level of significance (α=0.05)
- vi. pE- probability of successfully tracing and notifying a named partner over the study period(3 years) in the intervention arm, set at 0.51(Brown et al., 2011).
- vii. pC- probability of successfully tracing and notifying a named partner over the study period (3 years) in the control arm, set at 0.51(Brown et al., 2011)
- viii. HR- postulated hazard ratio set at 1.4 (Brown et al., 2011)

## R-code

```
library(powerSurvEpi)
```

```
ssizeCT.default(power=0.95, k=1, pE=0.51, pC=0.51, HR=1.4, alpha = 0.05)
```

$$m = \frac{1}{1} \left( \frac{(1 * 1.4) + 1}{1.4 - 1} \right)^2 * (1.96 + 1.64)^2$$

$$m = 468$$

$$n_E = \frac{468 * 1}{(1 * 0.51) + 0.51}$$

$$n_E \cong 459$$

$$n_C = \frac{468}{(1 * 0.51) + 0.51}$$

$$n_C \cong 459$$

$$\text{Total sample size } (n_E + n_C) = 918$$

This analysis surpassed the targeted sample size and used data for 1,119 index participants.

### 3.7 Quality assurance procedures

To ensure quality of analysis results, the study principal investigator involved in analysis had adequate knowledge on data analysis using STATA statistical package. Data editing resulting from data cleaning was well documented. Analysis results were reviewed and critiqued by all the supervisors involved in the study to enhance credibility of the results.

### **3.8 Ethical consideration**

Permission to conduct this study was sought from Kenyatta National Hospital /University of Nairobi Ethics Research Committee. Permission to use secondary data from the primary study was sought from the Principal investigator.

### **3.9 Data collection and analysis**

Data drawn for analysis in this study was collected by the study staff using questionnaires programmed into Open Data Kit (ODK) on smart phones operating on android operating system. ODK is an electronic platform for collecting data. All the data collected was sent to the National AIDS & STI Control Programme (NASCOP) server over an encrypted connection after every interview. Data was downloaded from the NASCOP server over an encrypted connection to the local computer as Comma Separated Values (CSV) files and imported to STATA version 14 for cleaning and analysis. Data for both delayed and immediate arms were considered for analysis. The variables that were considered for analysis selected from the main dataset were;

- i. Index age in years- which was a continuous variable.
- ii. Index sex- categorized into male or female
- iii. Index marital status- categorized into single, married-monogamous, married-polygamous, Live-in partner, divorced, widow/widower.
- iv. Index occupation- categorized as unemployed, student, informal employment and formal employment
- v. Index relationship to partner- categorized as wife/husband, girlfriend/boyfriend, someone had sex with for fun, someone I had sex for money.



- vi. Index place of residence- categorized as rural and urban.
- vii. Index transport Cost to health facility- categorized as nothing, <100 shillings, 100-200 shillings and >200 shillings.
- viii. Partner Age in years- which was a continuous variable.
- ix. Partner Sex- categorized into male or female
- x. Partner marital status- categorized into single, married-monogamous, married-polygamous, live-in partner, divorced, widow/widower.
- xi. Partner occupation- categorized as unemployed, student, informal employment and formal employment
- xii. The study/intervention arms categorized as immediate and delayed.

Partner occupation, index occupation and index relationship to partner were recorded to strategic categories. The continuous variables were used as continuous and all the data selected had complete information on the variables of interest.

Data analysis involved descriptive analysis and shared frailty Cox regression model to determine the predictors of time to partner notification. Time to HIV partner notification for the two study arms were estimated using Kaplan–Meier estimates of survivor function. The Kaplan Meier estimator of time to HIV partner notification  $S(t)$  at time  $t$  is defined as:

$$S(t) = \prod_{j:t_j \leq t} \frac{(r_j - d_j)}{r_j}, \text{ for } 0 \leq t \leq t^*$$

Where,

$t_j$   $j=1, \dots, n$  are failure times (Days at which a partner is successfully notified)

$t^*$  is the final failure time ( $\text{Max}(t_j)$ ) (Maximum number of days taken to successfully notify a partner).

$d_j$  are the number of failures at time  $t_j$  (Number of partners successfully notified at that time point)

$r_j$  are the number of subjects at risk at time  $t_j$  (Number of partners who have not been successfully notified at that time point)

$I_k$  time  $(0, t^*)$  is divided into many small intervals ( $I_k$ ).

$\frac{(r_j - d_j)}{r_j}$  is the probability of surviving through  $I_k$  if alive at the start of  $I_k$  (Probability of a partner not being within the time interval  $I_k$ ) (Dohoo et al., 2012)

Wilcoxon test was used to test equality of survival functions for the two study arms. Wilcoxon test of equality of survival curves is based on a series of contingency tables of observed and expected events for each group at each time point an event occurs. The observed number of events is compared to the expected number of events and chi-square test computed. It tests the hypothesis that there no difference between the groups and is less sensitive to the assumption of proportional hazards and is more sensitive to the differences in the early time points (Dohoo et al,2012).

The Cox regression modelling approach was selected because of its advantage that no assumption is made on the shape of the baseline hazard unlike the parametric methods and that it can simultaneously evaluate effects of multiple covariates on time to HIV partner notification unlike the non-parametric methods. Specifically, the shared frailty cox regression model was

selected to take into consideration the effect of unmeasured covariates that a group of individuals in the same cluster have.

The shared frailty model is of the form;

$$h_i(t_{ij}/\alpha_i) = h_0(t_{ij}) * e^{(b_1x_1+b_2x_2+\dots+\dots\dots+b_px_p))\alpha_i}$$

where,

- i  $t$  represents the survival time (time to HIV partner notification)
- ii  $h(t)$  is the hazard function (probability of successfully notifying a partner at the time  $t$ ) determined by a set of  $p$  covariates  $(x_1, x_2, \dots, x_p)$ .
- iii The coefficients  $(b_1, b_2, \dots, b_p)$  measure the impact (i.e., the effect size) of covariates on time to HIV partner notification.
- iv the term  $h_0$  is called the baseline hazard. It corresponds to the value of the hazard if all the  $x_i$  are equal to zero (the quantity  $\exp(0)$  equals 1). The ' $t$ ' in  $h(t)$  reminds us that the hazard may vary over time.
- v  $\alpha_i$  represents the frailty of the  $i^{\text{th}}$  group on the hazard scale and is assumed to have a distribution with a mean of 1 and variance of  $\theta$  (Dohoo et al., 2012).

## **CHAPTER FOUR: RESULTS AND FINDINGS**

### **4.1 Introduction**

This chapter presents the summary of study findings and interpretation of results. The results are presented in tables and graphs.

### **4.2 Index socio-demographic characteristics**

We analyzed data for 1,119 HIV positive adults (also referred to as index) who had been randomized to immediate and delayed arms and had consented to give contact information of their sexual/injecting partners in the primary study. Of the 1,119 individuals, majority were females (61%) who had a median age of 28 years (IQR 24-33). Slightly more than half of the index participants were in married monogamous relationship (55%) who named their spouses as partners. Over half of the index participants lived in the urban setting (56%) and spent at most one hundred shillings on their transport to the health facility (48%). Approximately 21% of the index participants were unemployed. On average the index participants named two partners.

**Table 4.1 Index socio- demographic characteristics**

Variable		<b>Immediate arm n (%), N=550</b>	<b>Delayed arm n (%), N=569</b>	<b>Total n (%)</b>	
<b>Sex</b>	Males	230 (42%)	201 (35%)	431 (39%)	
	Females	320 (58%)	368 (65%)	688 (61%)	
<b>Age in years</b>	Median (IQR)	30 (25-37)	31 (26-38)	30 (25-38)	
<b>Marital status</b>	Single	103 (19%)	100 (18%)	203 (18%)	
	Married Monogamous	308 (56%)	307 (54%)	615 (55%)	
	Married Polygamous	31 (5%)	43 (8%)	74 (7%)	
	Live-in partner	21 (4%)	14 (2%)	35 (3%)	
	Divorced	66 (12%)	75 (13%)	141 (13%)	
	Widow/widower	21 (4%)	30 (5%)	51 (4%)	
	<b>Occupation</b>	Student	8 (1%)	7 (1%)	15 (15%)
	Unemployed	157 (29%)	145 (25%)	302 (27%)	
Formal employment	16 (3%)	19 (3%)	35 (3%)		
Informal employment	369 (67%)	398 (70%)	767 (69%)		
<b>Relationship partner</b>	Someone I had sex for money	7 (1%)	18 (3%)	25 (2%)	
	Someone I had sex with for fun	18 (3%)	28 (5%)	46 (4%)	
	Girlfriend/boyfriend	217 (39%)	195 (34%)	412 (37%)	
	Wife/husband	308 (56%)	328 (58%)	636 (57%)	
<b>Place of residence</b>	Rural	250 (45%)	248 (44%)	498 (44%)	
	Urban	300 (54%)	321 (56%)	621 (56%)	
<b>Transport cost to health facility</b>	Nothing	42 (8%)	26 (5%)	68 (6%)	
	<100 KES	286 (52%)	256 (45%)	542 (48%)	
	100-200 KES	194 (35%)	230 (40%)	424 (38%)	
	>200 KES	28 (5%)	57 (10%)	85 (8%)	

### 4.3 Partner socio-demographic characteristics

A total of 1,868 partners (950 in the delayed and 918 in the immediate arm) were elicited by the index participants and out of those 1,286 (69%) were successfully traced and notified of their exposure to HIV infection. Male partners notified were more than female partners (56%). The average median age of the partners notified was 31 years (IQR 26-38). Males were slightly older than females. A big percentage of partners were in married monogamous relationship (57%) and were small business owners (18%).

**Table 4.2 Partner Socio- Demographic Characteristics**

		<b>Immediate arm n (%), N=621</b>	<b>Delayed arm n (%), N=665</b>	<b>Total n (%)</b>
<b>Sex</b>	Males	313 (50%)	411 (62%)	724 (56%)
	Females	308 (50%)	254 (38%)	562 (44%)
<b>Age in years</b>	Median (IQR)	30 (26-37)	32 (28-38)	31 (26-38)
<b>Marital status</b>	Single	137 (22%)	141 (21%)	278 (22%)
	Married Monogamous	339 (55%)	400 (60%)	739 (57%)
	Married Polygamous	60 (10%)	45 (7%)	105 (8%)
	Live-in partner	27 (4%)	17 (3%)	44 (3%)
	Divorced	37 (6%)	40 (6%)	77 (6%)
	Widow/widower	21 (3%)	22 (3%)	43 (3%)
	<b>Occupation</b>	Student	7 (1%)	5 (1%)
	Unemployed	149 (23%)	115 (17%)	264 (21%)
	Formal employment	23 (4%)	46 (7%)	69 (5%)
	Informal employment	442 (71%)	499 (75%)	941 (73%)
<b>Time to PN</b>	Median (IQR)	7 (2-20)	41 (28-42)	11 (3-30)

#### 4.4 Comparison of time to partner notification between the immediate and delayed arms.

##### 4.4.1 Overview of time to HIV partner notification

The probability of successfully tracing and notifying a named partner was over 50% within the first 42 days and later drops to nearly 30% within 200 days and remains constant thereafter. This indicates that less time is taken to successfully trace and notify a named partner between 0 to 42 days compared to after 42 days. The median time between enrollment of an index to successful notification of a named partner was 7 days (IQR 2-20) in the immediate arm and 41 days (IQR 28-42) in the delayed arm.

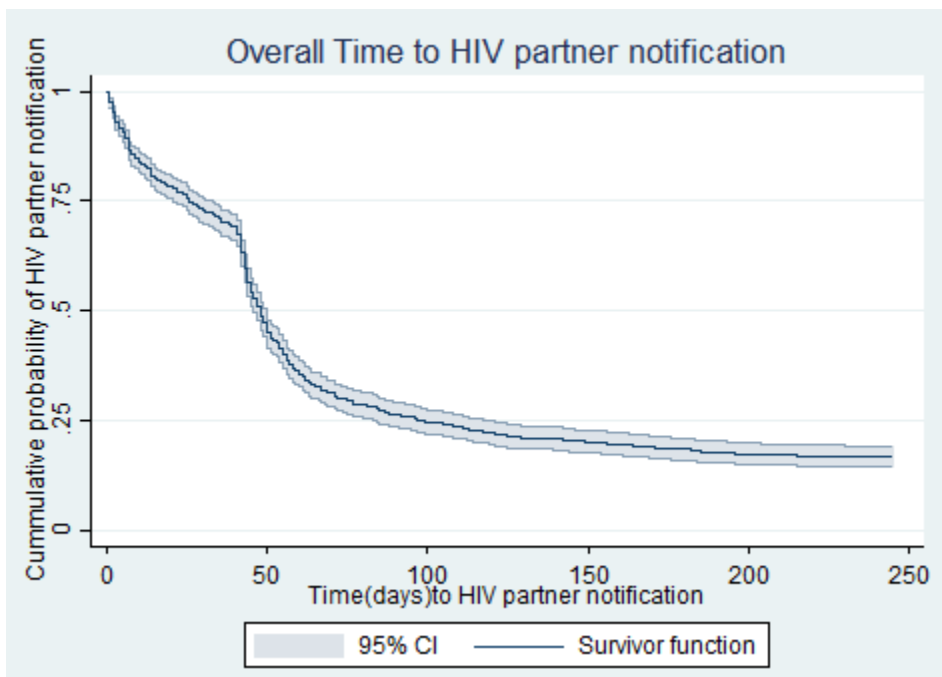


Figure 3.1 Kaplan-Meier function of time to HIV partner notification.

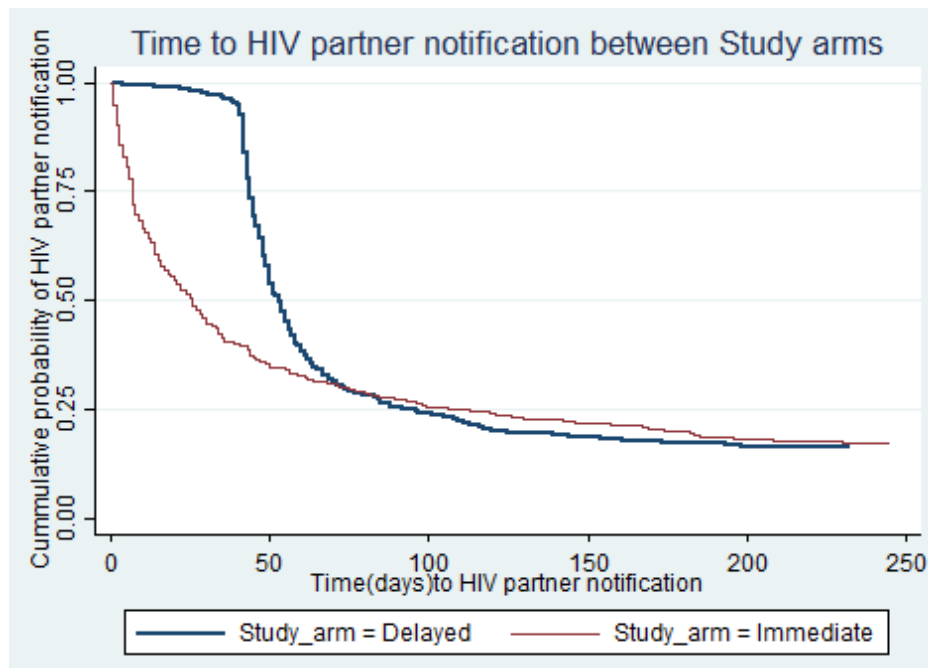
#### 4.4.2 Test for equality of survival curves between immediate and delayed arms

Results of Wilcoxon test of equality of survival curves between the immediate and delayed arms shows that there is statistically significant evidence to indicate that the survival curves were different (P-value<0.001).

**Table 4.3 Wilcoxon Test for equality of survival functions between the immediate and delayed arms.**

	Events Observed	Events Expected	$\chi^2$	P-value
<b>Delayed arm</b>	414	480	110.3	<0.001
<b>Immediate arm</b>	364	297		

The graph of survival curves indicates that less time was taken to successfully trace and notified a named partner in the immediate intervention arm compared to the delayed intervention arm in the early time points but the vice versa in the later time points.



**Figure 4.2 Kaplan Meier curves of time to HIV partner notification between immediate APS arm and delayed APS arms.**



#### 4.4.3 Test for equality of survival curves across the socio demographic characteristics.

There is sufficient statistically significant evidences to indicate a difference in survival functions between males and females among index participants ( $p < 0.001$ ), across the different index marital status ( $p = 0.009$ ), between index place of residence ( $p = 0.001$ ), between males and females among partners ( $p = 0.016$ ) at 5% significance level.

**Table 4.4 Wilcoxon test for equality of survival functions across the socio demographic characteristics.**

Variable		Events Observed	Events Expected	$\chi^2$	P- value
<b>Index sex</b>	Females	462	532	24.68	<b>&lt;0.001</b>
	Males	316	245		
<b>Index marital status</b>	Divorced	88	117	15.20	<b>0.009</b>
	Live-in partner	27	24		
	Married Monogamous	434	400		
	Married Polygamous	55	47		
	Single	142	143		
	Widow/widower	32	44		
<b>Index relationship to partner</b>	Someone I had sex for money	10	22	6.72	0.081
	Someone I had sex with for fun	22	24		
	Girlfriend/boyfriend	265	255		
	Wife/husband	481	476		
<b>Index occupation</b>	Student	10	9	0.92	0.820
	Unemployed	208	224		
	Formal employment	27	21		
	Informal employment	533	521		
<b>Index place of residence</b>	Urban	414	464	10.63	<b>0.001</b>
	Rural	364	313		

<b>Variable</b>		<b>Events Observed</b>	<b>Events Expected</b>	$\chi^2$	<b>P- value</b>
<b>Index transport cost to health facility</b>	Nothing	43	48	2.49	0.478
	<100 KES	373	372		
	100-200 KES	304	294		
	>200 KES	58	62		
<b>Partner sex</b>	Females	313	285	5.76	<b>0.016</b>
	Males	465	492		
<b>Partner marital status</b>	Divorced	28	31	5.49	0.359
	Live-in partner	22	16		
	Married Monogamous	502	500		
	Married Polygamous	58	49		
	Single	145	157		
	Widow/widower	23	23		
<b>Partner occupation</b>	Student	8	8	0.72	0.868
	Unemployed	162	158		
	Formal employment	43	44		
	Informal employment	565	566		

## 4.5 Cox regression model to determine predictors of time to HIV partner notification.

### 4.5.1 Shared frailty univariable Cox regression model

The shared frailty univariable cox regression model was fitted to assess the effects of the index and partner socio demographic characteristics on time to HIV partner notification. Time to HIV partner notification was statistically associated with the intervention arm ( $p=0.007$ ), index sex ( $p<0.001$ ), index marital status ( $p=0.017$ ), index place of residence ( $p=0.094$ ) and partner sex ( $p=0.012$ ) at 5% significance level. All the variables with a p-value  $<0.2$  were selected as candidate for multiple cox regression model.

**Table 4.5 Shared frailty univariable Cox regression model.**

Variable		Hazard Ratio (95% CI)	p-value
<b>Intervention arm</b>	Delayed (Ref)	1	<b>0.007*</b>
	Immediate	1.43 (1.11-1.16)	
<b>Index sex</b>	Females (Ref)	1	<b>&lt;0.001*</b>
	Males	1.48 (1.28-1.72)	
<b>Index age in years</b>	Age (years)	1.00 (0.99-1.01)	0.326
<b>Index marital status</b>	Divorced (Ref)	1	<b>0.017*</b>
	Live-in partner	1.31 (0.84-2.02)	
	Married Monogamous	1.39 (1.11-1.76)	
	Married Polygamous	1.52 (1.07-2.13)	
	Single	1.25 (0.96-1.64)	
	Widow/widower	0.89 (0.59-1.35)	
<b>Index occupation</b>	Student (Ref)	1	0.413
	Unemployed	1.09 (0.57-2.09)	
	Formal employment	1.45 (0.69-3.05)	
	Informal employment	1.22 (0.64-2.31))	
<b>Index place of residence</b>	Urban (Ref)	1	<b>&lt;0.094*</b>
	Rural	1.27 (0.96-1.71)	

Variable		Hazard Ratio (95% CI)	p-value
<b>Index transport cost to health facility</b>	Nothing (Ref)	1	0.959
	<100 KES	1.06 (0.77-1.48)	
	100-200 KES	1.07 (0.77-1.52)	
	>200 KES	1.02 (0.67-1.55)	
<b>Index relationship to partner</b>	Someone I had sex for money (Ref)	1	<b>0.124*</b>
	Someone I had sex with for fun	1.90 (0.89-4.03)	
	Girlfriend/boyfriend	2.13 (1.12-4.02)	
	Wife/husband	2.13 (1.13-4.01)	
<b>Partner Sex</b>	Females (Ref)	1	<b>0.012*</b>
	Males	0.83 (0.71-0.96)	
<b>Partner marital status</b>	Divorced (Ref)	1	0.997
	Live-in partner	1.03 (0.57-1.84)	
	Married Monogamous	0.99 (0.67-1.47)	
	Married Polygamous	1.04 (0.64-1.66)	
	Single	0.97 (0.64-1.47)	
	Widow/widower	1.09 (0.62-1.90)	
<b>Partner occupation</b>	Student (Ref)	1	0.986
	Unemployed	0.87 (0.42-1.78)	
	Formal employment	0.89 (0.42-1.92)	
	Informal employment	0.88 (0.43-1.79)	
<b>Partner age</b>	Age (years)	0.99 (0.99-1.01)	<b>0.200*</b>

\* Variables with a p-value<0.2 that are candidates for multiple Cox regression.

#### 4.5.2 Shared frailty multiple Cox regression model

A shared frailty multiple cox regression model was fitted with the covariates that had a p-value of <0.2 in the shared frailty univariable cox regression model. The covariates are; intervention arm, index sex, index marital status, index place of residence, partner sex, index relationship to partner and partner age.

Adjusting for the effect of all the other covariates in the model, there was a statistically significant evidence to indicate an association between time to HIV partner notification and intervention arm ( $p < 0.05$ ). Partners in the immediate arm were notified at a higher rate compared to partners in the delayed arm controlling for the effects of the other covariates (HR 2.14(95% CI 1.42 -3.22).

**Table 4.6 Shared frailty multiple Cox regression model.**

Predictor		Hazard Ratio (95% CI)	p-value
<b>Intervention arm</b>	Delayed (Ref)	1	<0.001*
	Immediate	2.14 (1.42-3.22)	
<b>Index sex</b>	Females (Ref)	1	0.289
	Males	1.31 (0.79-2.18)	
<b>Index marital status</b>	Divorced (Ref)	1	0.566
	Live-in partner	1.25 (0.81-1.96)	
	Married Monogamous	1.19 (0.92-1.54)	
	Married Polygamous	1.14 (0.79-1.66)	
	Single	1.09 (0.82-1.47)	
	Widow/widower	1.45 (0.95-2.21)	
<b>Index place of residence</b>	Urban (Ref)	1	0.743
	Rural	0.93 (0.62-1.41)	
<b>Partner sex</b>	Females (Ref)	1	0.613
	Males	1.14 (0.68-1.89)	

Predictor		Hazard Ratio (95% CI)	p-value
<b>Index relationship to partner</b>	Someone I had sex for money (Ref)	1	0.672
	Someone I had sex with for fun	0.84 (0.39-1.79)	
	Girlfriend/boyfriend	0.86 (0.44-1.66)	
	Wife/husband	0.98 (0.51-1.90)	
<b>Partner age</b>	Age (years)	0.99 (0.98-1.00)	0.392

\* Significant Variables with a p-value<0.05

#### 4.5.3 Testing PH assumption of the Cox regression model.

The Shared frailty multiple Cox regression was tested for Proportional hazard assumption. Intervention arm, index sex, index residence and partner sex were the covariates that indicated a violation of the PH assumption (the effects of covariates on time to partner notification varies with time). Therefore, another shared frailty multiple Cox regression model was fitted with the effect of four covariates allowed to interact with time on a natural log scale( $\ln(\text{time})$ ).

**Table 4.7 Time varying effects Cox regression model**

Predictor		Coef (95% CI)	p-value
<b>Intervention arm</b>	Delayed (Ref)	0	<b>&lt;0.001*</b>
	Immediate	6.45 (5.49-7.42)	
<b>Index sex</b>	Females (Ref)	0	<b>0.013*</b>
	Males	-3.28 (-5.86- -0.704)	
<b>Index marital status</b>	Divorced (Ref)	0	0.615
	Live-in partner	0.22 (-0.42-0.46)	
	Married Monogamous	0.21 (-0.49-0.46)	
	Married Polygamous	0.19 (-0.17-0.55)	
	Single	0.04 (-0.25-0.32)	
	Widow/widower	0.21 (-0.22-0.64)	
<b>Index place of residence</b>	Urban (Ref)	0	0.628
	Rural	0.11 (-0.32-0.54)	
<b>Partner sex</b>	Females (Ref)	0	<b>0.013*</b>
	Males	-3.25 (-5.82- -0.67)	
<b>Index relationship to partner</b>	Someone I had sex for money (Ref)	0	0.08
	Someone I had sex with for fun	-0.11 (-0.86-0.64)	
	Girlfriend/boyfriend	-0.03 (-0.68-0.61)	
	Wife/husband	-0.09 (-0.54-0.74)	
<b>Partner age</b>	Age (years)	-0.01 (-0.02-0.01)	0.118

Predictor		Coef (95% CI)	p-value
<b>tvc</b>			
<b>Intervention arm</b>	Delayed (Ref)	0	<b>&lt;0.001*</b>
	Immediate	-1.64 (-1.89- -1.39)	
<b>Index place of residence</b>	Urban (Ref)		
	Rural	-0.05 (-0.17-0.07)	0.456
<b>Partner sex</b>	Females (Ref)		
	Males	0.88 (0.27-1.49)	<b>0.004</b>
<b>Index sex</b>	Females (Ref)		
	Males	0.91 (0.29-1.52)	<b>0.004</b>

The interaction between  $\ln(\text{time})$  and the intervention arm, partner sex and index sex were significant which confirms that the effect of intervention arm, partner sex and index sex on time to HIV partner notification vary with time (i.e the proportional hazard assumption was violated). Therefore, to determine the effect of intervention arm, partner sex and index sex on time to HIV partner notification we obtain the hazard ratios at a number of time points. The hazard ratios at different time points is computed as follows:

Intervention arm: HR at time  $t = \exp(6.45 - 1.64 * \ln(t))$ ,  $t=2,3,4,5,6---n$

Partner sex: HR at time  $t = \exp(-3.25 + 0.88 * \ln(t))$ ,  $t=2,3,4,5,6---n$

Index sex: HR at time  $t = \exp(-3.28 - 0.91 * \ln(t))$ ,  $t=2,3,4,5,6---n$



These results in table 4.8 indicates that the immediate arm resulted in an increase in the rate of HIV partner notification at the beginning (HR=23.7) then the effects drops off with time. The sex of the partner and index resulted in a drop in the rate of HIV notification with time

**Table 4.8 Effect of intervention arm, partner sex and index sex on time to HIV partner notification at different time points**

Time (Days)	ln(time)	Hazard Ratio		
		Intervention arm	Partner sex	Index sex
<b>7</b>	2	23.71	0.006	0.006
<b>20</b>	3	4.57	0.003	0.003
<b>54</b>	4	0.88	0.001	0.001
<b>148</b>	5	0.17	0.0004	0.0004
<b>403</b>	6	0.03	0.0001	0.0001

## **CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATION**

### **5.1 Summary of major findings**

Majority of index participants were females which is consistent with global literature that women were more likely to seek healthcare services earlier compared to men(Thompson et al., 2016) and maybe a good entry point to studies. Males were however the most named partners who were notified of exposure to HIV. Index participants were younger than their partners. There was statistically significant difference in the survival curves between immediate and delayed arms. The median time(days) to HIV partner notification was 11 days with the immediate arm having a shorter period of 7 days compared to 41 days in the delayed arm. Factors that were associated with shorter period in addition to the study arm was partner sex and index sex.

### **5.2 Socio demographic characteristics of index and partners**

A total of 1,119 index participants named 1,868 partners of whom 69% of them were successfully notified of exposure to HIV. On average an index case named two partners which is similar results of a metanalysis of ten APS studies conducted in US and Malawi that indicated an average of 2 partners per index case but highest among the sex workers, injecting drug users and sex workers who are more likely to have multiple partners compared to the general population((Dalal et al., 2017). The proportion of partners successfully notified was slightly higher in the immediate/provider referral arm (59.9%) compared to delayed/contract referral arm (58.9%). Results for a randomized APS study conducted in Malawi indicated similar results where the proportion of partners returning for HIV testing was higher in the provider referral arm compared to contract referral arm however this study was randomized into three arms (Brown et al., 2011). This is an indication that provider assisted partner

notification results in reaching out to more people who might be unaware of their HIV status compared to having an index case notify their partners. The index clients mainly named spouses as their partners and the majority of the partners successfully notified were married. This is consistent with results of a study in Tanzania conducted to determine the outcomes and experiences of men and women in partner notification for HIV testing that reported marital status as a huge determinant of success in referral, with married index clients 2.5 times more likely to be successful in referring their sexual partners to test. Males were however more likely to refer their partners compared to females which is the vice versa in Kenya (Plotkin et al., 2018).

### **5.3 Comparison of time to HIV partner notification between immediate and delayed arm.**

Results from a test of equality of survival curves between immediate and delayed arms showed that there was sufficient statistical evidence to indicate that the curves were different. The hazards of the two arms were non proportional and hazard ratios were obtained by fitting a time varying effects cox regression model with the intervention arm allowed to interact with time on natural log scale which indicated that the immediate arm resulted in an increase in the rate of HIV partner notification at the beginning (HR=23.7) then the effects drops off with time. Results from the APS study conducted in Malawi also indicated a strong association between time to partner notification with the method of notification however the non-proportional hazard assumption violation was addressed by estimating the hazard ratios in the first seven days and after seven days. The rate of partner notification was higher in provider referral arm compared to the contract and passive referral arms within the first seven days. After seven days, the rate of partner notification in the provider and contract referral arms was higher than in the passive referral arm (Brown et al., 2011). The delay period in the Kenyan

study was 42 days and 7 days in the Malawi study. This is approximately the time points at which the immediate/provider referral arms (that implemented APS immediately after a partner was named) recorded an increase in the rate of HIV partner notification compared to the delay/contract referral arm.

The median time(days) to HIV notification was shorter in the provider referral arm (7 days) compared to contract referral arm (41 days) which were still higher than other APS study results that have recorded a median of 7 days and 4 days in the contract referral and provider referral arms respectively (Brown et al., 2011). This longer time to HIV partner notification in Kenya could have resulted from it being the first APS study to be conducted in Kenya and many people were not experienced with it. Another study conducted to determine the predictors of time spent on partner notification in four US sites recorded an average of 46 minutes in partner notification activities (Macke, Hennessy, & McFarlane, 2000) however this study analyzed time spent on partner notification using regression analysis which was different for this current study.

#### **5.4 Predictors of time to HIV partner notification in Kenya**

Results from this study showed that time to HIV partner notification was statistically associated with the method of notification which were similar to result of the APS in Malawi (Brown et al., 2011). The provider referral arm notified partners at a higher rate compared to contract referral arm which allowed index participants to notify their partners within six weeks. The 6 weeks delay period resulted in lower rates of notification in the early time points in the contract referral arm. Partner sex and Index sex were also significant predictors of time to HIV partner notification however their effects varied with time.

Results from this study however were different from those of a study in the US that sort to determine the predictors of time spent on partner notification using linear regression which documented that the participants demographic characteristics were not statistically significant predictors (Macke et al., 2000).

## **5.5 Conclusion**

The overall objective of this study was to determine the predictors of time to HIV partner notification in Kenya. The following are conclusions made based on the study findings.

Sex of the partner was an important determinant of time to HIV partner notification. However, the partner characteristics were not obtained at the time they were elicited but at the time they were notified.

The type of notification process was significantly associated to time to HIV notification. Immediate notification has shown to increase the rate of notification within the first 42 days.

## **5.6 Recommendation**

The following recommendation can be implemented in future APS studies to further improve the effectiveness of APS.

- i. Partner notification to be initiated by the health care provider immediately a partner is named because the probability of finding them is higher in the early time points.
- ii. It is important to also obtain the demographic characteristics of the health care provider offering APS. This could be a potential determinant of time to HIV partner notification because different providers have varying capabilities of partner notification processes.
- iii. Partner characteristics should be collected at the time they are elicited to inform decisions on better strategies for timely notification.
- iv. Gender specific partner notification strategies be developed to inform partner notification services in Kenya.

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## APPENDICIES

### Appendix I: Work plan

Activity	Time								
	December 2018	January-March 2019	April-June 2019	July 2019	August 2019	September 2019	October 2019	November 2019	December 2019
Concept Paper									
Proposal Development									
Ethical Approval									
Data Analysis									
First draft report									
Submission of Revised report for marking									
Oral Defense									
Submission of Final Thesis Report									
Manuscript Writing									
Publication									

## Appendix II: Budget

Activity	Amount
Printing of proposal for submission to Ethics Review Committee (ERC)	4,000
Fee for Ethical Approval	5,000
Printing of final report for defense	5,000
Printing and binding final thesis	6,000
Procurement of STATA software license	50,000
<b>Total</b>	<b>70,000</b>

## **Appendix III: Plagiarism Report**

## **Appendix IV: KNH ERC Approval**