MODELING SURVIVAL RATE OF DRUG ABUSERS IN KENYA

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DECLARATION

STUDENT DECLARATION

I hereby declare that this thesis is my original work and has not been presented for degree in any other university.

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DEDICATION

This thesis is dedicated to my family for their prayers and moral support that they offered me throughout the course of my studies. To my dad and mum I am extremely grateful for the sacrificial love and teaching me discipline, value of hard work and above all believing in me. May God Almighty give you many more years to see the success of your children. To my brothers may you continue with this spirit and reach the highest levels of academic studies.

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I thank the almighty God for allowing me to undertake this study. My sincere gratitude also goes to my parents for the good upbringing. Your everlasting love has been the greatest treasure of my life. Your value for education has sincerely pushed us as a family to the limits of academic excellence. To my brothers and sisters, thank you for taking your time to remind me of the goals that our parents wanted us to achieve. Special thanks also go to my supervisors; Prof. Joseph Arap Koske and Dr. Mathew Kosgei for their indispensable guidance in writing this thesis. This document is what it is due to your dedicated professional guidance. I therefore extend my gratitude to you for accepting to invest your knowledge in me. I am also grateful to my classmates who morally encouraged and supported me. I also thank MOI University and the entire staff for giving me an enabling environment to undertake my studies.

God bless you all.

ABSTRACT

Drug and substance abuse is a serious health problem in many countries. In Kenya drug abuse is one of the leading causes of mortality. The government and other stakeholders have made efforts to fight the problem of drug abuse. However there are no significant results that have been drawn from these efforts. This study sought to model the survival rate of drug users in relation to drug and substance abuse. The objectives of this study were to formulate survival model for drug users using a Kaplan-Meier and Cox proportional hazards model, to establish the recovery rates of drug users under medication, to perform sensitivity analysis on the model parameters to determine the significant predictors of drug use and compare survival rates based on significant predictors. The dependent variable was survival time to recovery of the subject and the independent variables were age, gender, residence, marital status, job status, mode of drug abused and the type of drug abused. The study used secondary data on drug use obtained from Mathari National Hospital. Data was collected from specialized registers containing the drug users' medical information provided by the hospital. Data was fitted to the survival model using R statistical software. Kaplan-Meier and Cox Proportional Hazard methods were used to formulate a survival rate model for drug users. Sensitivity analysis of the model parameters was performed to determine an optimal model for the study. Kaplan-Meier model was used to establish the rate of recovery of drug users. The optimal model revealed that age, gender, marital status and job status were significant predictors .Female drug users had higher survival rates (80.95%) compared to male drug users (19.05%).The overall survival rate was 36.37% recovery rate increased with progression of treatment. The study recommended that campaigns against drug abused should be more focused towards treating male subjects since they have lower survival rates compared to female subjects.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

CNS	Central Nervous System.
MLE	Maximum likelihood estimator
NIDA	National Institute on drug abuse
AOD	Alcohol and other drugs
NACADA	National Authority for the campaign against Alcohol and Drug Abuse
IRB	Institutional Review Committee
MOH	Ministry of Health
UNODC	United Nations of Drugs and Crime
AIC	Akaike Information Criteria
BIC	Bayesian Information Criterion
SCAD	Smoothly Clipped Absolute Deviation
LASSO	Least Absolute Shrinkage

CHAPTER ONE

INTRODUCTION

1.1 Background of the study

This chapter presents the background of the study which covers entry of drug abuse and the trends in drug abuse, the research problem, the objectives of the study, significance of the study and the scope of the study.

A drug is any substance other than food that when inhaled, injected, smoked, consumed, absorbed through a patch on the skin or dissolved through a tongue causes a physiological change in the body (WHO, 2018). Drugs can be useful for treatment of disease when proper prescription is followed. Medical research has developed a variety of drugs that have had a profound effect on humans by curing, preventing or at least slowing diseases and therefore enabling humans to live healthier and happier lives. For instance, antibiotics have improved treatment of infections, vaccines prevent the spread of diseases such as measles and algesics lessen or eliminate pain.

However if proper prescription of drugs is not followed then they become harmful. This is referred to as drug abuse. Drug abuse is a lifestyle disease and a chronic and enduring phenomenon, which is among the important challenging and costly health problems, leading to physical, mental and psychiatric outcomes in persons, families and communities (UNODC, 2017). Continued drug abuse leads to addiction, which is defined as a chronic, relapsing disorder characterized by compulsive drug seeking and use despite adverse consequences. It is considered a brain disorder, because it involves functional changes to brain circuits involved in reward, stress, and self-control, and those changes may last a long time after a person has stopped taking drugs. Continued use of drug abuse has drawn attention to the general public as it threatens the health and

socio-economic wellbeing of individual and countries. It degrades detoxification process during treatment procedures (Metsch and Pollack, 2005).

In general the term drug abuse is, more applicable when the drug is used for other purposes other than for medicinal purposes. Such a drug intake or abuse affects the individual's perception and mood. Therefore abused drugs can be classified as psychoactive. That is, they influence how the brain or more precisely how the mind processes information. Inglis (1975) notes that psychoactive drugs have been in use as far as human history is concerned. Research by scholars shows that continued abuse of drugs adapts the human brain to the use of such drugs (Erickson, 2007). These frequently abused drugs are termed as illicit drugs, to differentiate them from those drugs that have medicinal value. When drugs are abused they affect the individual using it on an equal measure. That is they do not discriminate or respect any boundary or obey any laws. They destroy whatever they came into contact with effectively erasing health, sanity, families and eventually people's lives (collet, 2003).

Illicit drugs can be categorized into hard and soft drugs.Most teenagers get involved in drugs through use of soft drugs such as alcohol and tobacco (Weil, 1972). While most school going children are alcohol addicts. This leads them to use of hard drugs. This means that soft drugs are a get way substance to the use of hard drugs such as cocaine and heroin, (Papalia,Olds and Feldman (2001).

The most common type of "soft" drug is alcohol. Alcohol abuse has been extensively documented (Berkowitz & Perkins 1986; Ham & Hope, 2003) and is a significant problem (Globetti, Haworth- Hoeppner, & Marasco, 1993). Heavy drinking, alcohol-related problems and associated risky and illegal behaviors peak during late adolescence and early adulthood (Baer, 1993). Alcohol consumption patterns contribute to a number of serious personal, relational, academic, and legal problems for

youth adults (Globetti et al., 1993). The most evident effects of alcohol misuse are injuries, specifically vehicle injuries, which remain a leading cause of death, (Wechsler et al., 1998). Although research has been successiful in documenting the incidence and prevalence of alcohol use and abuse (Pullen, 2001) there exists an ongoing need to examine the factors associated with this problem (camatta, and Nagoshi, 1995). Evidence from studies of college samples consistently suggests that drugs are abused for different physhologiacal effects in different contexts. It is important to better understand the factors associated with drug abuse in youth adults because this period is an important juncture in the etiology of drug use and depence (Orwa, 2015).

The population of drug users may be regarded as a "hidden" population. Drug abusers tend to hide their drug use from the public. The main reason is due to the fact that abused drugs are illegal. Therefore the users buy and consume these drugs in secret places. Therefore the users buy and consume these drugs in secret places. Another possibility for having such hidden population is because generally non-users don't like being associated with drug users. As a result, the subjects who are drug users find it hard to cope with nonusers. Due to lack of advice from nonusers they tend to continue with the use of the illicit drugs (Ndetei, Khasukhala, Mutiso, Ongecha and Kokonya (2009).

The contemporary studies on drug abuse have blamed the increasing menace of drug abuse on failure of governments to enact adequate laws prohibiting drug abuse and failure to place strict border controls to prevent entry of drugs (Sambo, 2008). Other studies have blamed social media and modernization as key players towards the current trends of drug abuse. However it should be noted that drug abuse is a historical issue tracing its roots from the ancient times when few or no drug manufacturing factories existed. With the growing need to differentiate between licit and illicit drugs several

laws have been developed that target decriminalization of drug abuse (Csete , 2016). This draws the attention of the need to properly define drug abuse as the intake of any drug without a medical reason. As such, a drug of abuse is deemed to have no medicinal value. This definition has been a bone of contention for several countries over the years. For example drugs such as khat (locally known in Kenya as miraa) is legal in Kenya and illegal in other countries like Tanzania and recently in the United Kingdom who banned its importation terming it as an illicit drug (Kiambuthi, 2005). Such a contrast may be drawn against Tanzania where bang is legalized when it is an illicit drug in many countries, Kenya inclusive.

1.1.1 Entry of drug abuse

Subject to the porous borders in the Eastern African countries, there has been tremendous increase in the trafficking of drugs within these countries particularly in Kenya (UNODC, 2017). Most of the drug peddlers have exploited the weak justice system in the country compounded by cover ups they receive from the political class and other elite personalities to contact their business. The result of the influx of these drugs has no doubt caused a rapid increase in the number of drug abusers in the country. These undercover groups working with the drug peddlers have ensured limited availability of drug abuse information that can inform the public and relevant stakeholders in the fight against drug trafficking and abuse (UNODC, 2017). It is sufficient to say that currently the Eastern African countries are the key drug trafficking routes as shown in Figure 1.1.1. As such, Kenya is termed as a main hub due to the existence of key ports for transit of the drugs. These ports have connections between West Africa and the cocaine-producing countries in South West and South East Asia. There is also an increasing use of postal and courier services for cocaine, heroin and hashish. Many of these products, sometimes imported without authorization, are sold

by hawkers in street-markets (Lisakafu ,2018). The international airports in Nairobi, Kenya, and Addis Ababa, Ethiopia are key entry points for illicit drugs into the region, primarily due to the frequent commercial flights from Asia and the Middle East. The seaports of Dar es Salaam and Mombasa are also entry points favored by drug traffickers (UNODC, 2017).

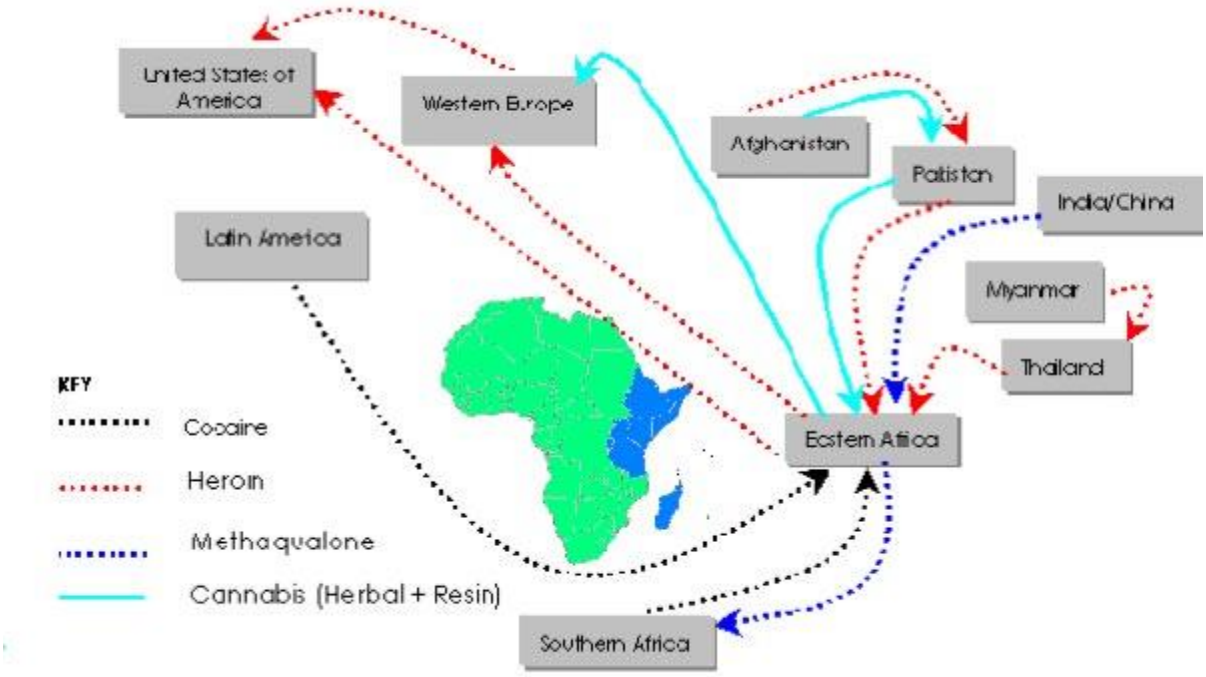

Figure 1.1.1 Drug trafficking routes in East Africa (UNODC, 2017)

A review of drug seizures from 1998 to date indicates an increase in the trafficking of drugs to eastern African countries from Pakistan, Thailand and India. Increased seizures of heroin with Nigerian connections bound for Uganda, Tanzania and Kenya through Ethiopia have been noted as well (UNODC, 2017). West African syndicates, with their experience in cannabis and heroin smuggling, are actively networking in Latin America, and are responsible for the emergence of cocaine trafficking and abuse in eastern Africa (Okoye, 2001).

African drug trafficking routes have been nicknamed “Smack Track” signifying circuitous route to smuggle drugs from Asia to Europe, passing through east Africa. For example, two drug busts in November, 2015, netting 712kg of the stuff, closed a record year for heroin seizures off the coast of Kenya. In April, 2014, an Australian warship while on surveillance in the coastal waters of Kenya found a whooping one ton of heroin hidden inside sacks of cement on a dhow in the coastal waters (Okoye, 2001). The discovery with an estimated street value of $240m was equivalent to the entire heroin seized off East Africa between 1990 and 2009. In November, 2017, the Kenyan police deported thirty drug peddlers who pretended to be foreign students. In 2014, cocaine seizure was at 11.30kg, 5.96 kg in 2015 and was record high in 2016 at 106.3 kg in 2016. The estimated number of people using illicit drugs increased steadily as a result (UNODC, 2017).

1.1.2 Trends of drug abuse

Globally, the trends of drug abuse have continued to increase at an alarming rate with an estimated population of 20 million people currently using drugs. In Europe for example the latest trends released up to the year 2011 show a steady increase in the use of illicit drugs as shown in Figure 1.1.2 (a). These trends are an indication of increasing prevalences of drug abuse in the target regions(Morgensten, 2013).

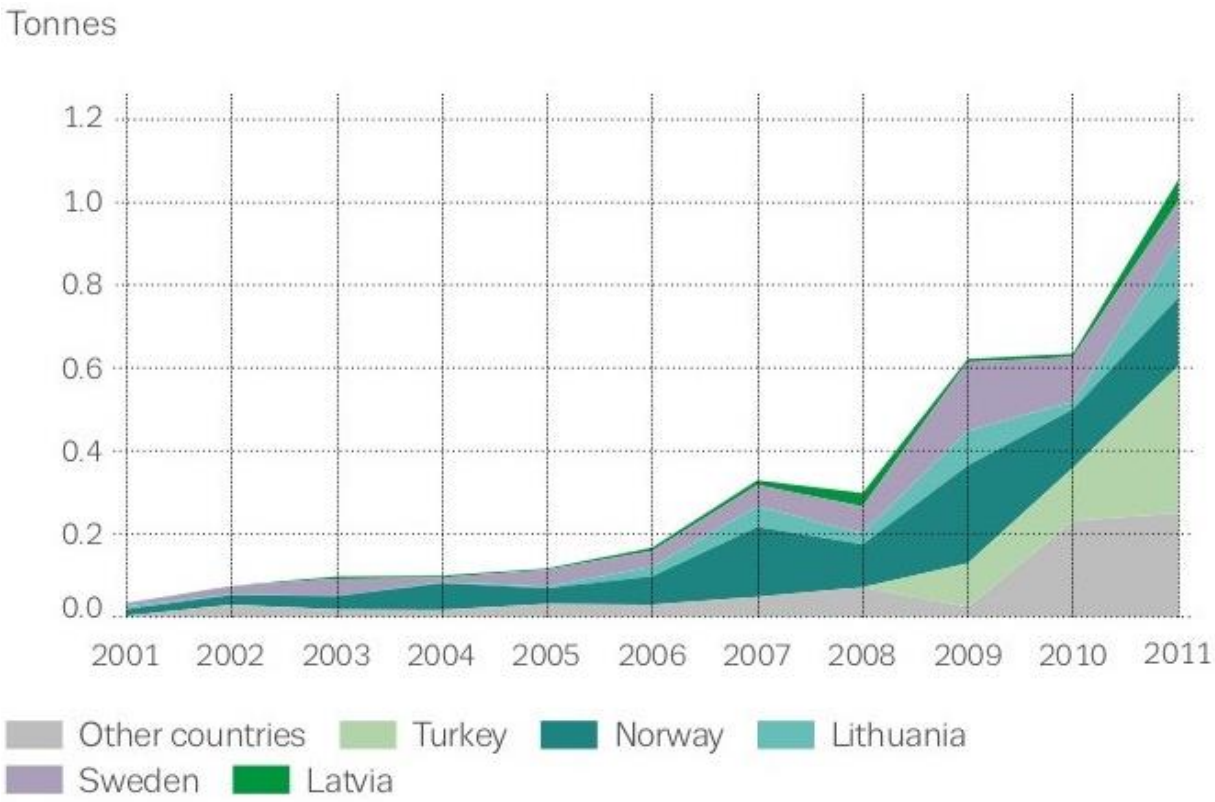

Figure 1.1.2 (a) Reported prevalence of drug abuse (UNODC, 2017)

Similar trends are evident in Africa as given in table 1.1.2.Latest figures released by UNODC (2017) show Africa as emerging market for drug abuse and trafficking. The figures show Africa as a major consumer of the various types of cannabis drug at an almost 50% consumption level. According to the report of UNODC (2017), the East Africa region where Kenya is a member tops the list in the influx of drugs of abuse signifying continued increase in prevalence of use of these drugs.

Table 1.1.2 Africa drug abuse statistics Source (NACADA, 2017)

	Heroin	Cocaine	Cannabis Herb	Cannabis Plant	Cannabis Resin	Amphetamines	Ecstasy
East	137.9	17.0	225,340.6	32,236.1	2.3	N/A	0.0
North	78.6	91.2	146,490.5	427.7	118,523.6	2.1	1.0
Southern	29.7	363.4	637,227.9	145,751.6	54.8	315.4	22.9
West and	107.6	14,578.9	207,820.0	928.4	10,426.0	517.7	3.5
Africa	353.8	15,050.6	1,216,879.1	179,343.7	129,006.8	835.1	27.5
World	705,789.4	5,239,695.3	1,340,507.5	1,024,828.6	43,171.5	4,510.7	103,991.6
African	0.3%	2.1%	23.2%	13.4%	12.5%	1.9%	0.6%

In Kenya, drug abuse was reported as the third leading cause of disease burden for males in 2013. According to the recent national survey of drug abuse, 4 million of addicts need treatment services in Kenya. Alcohol, cannabis and cocaine were reported as the main drugs of abuse, respectively (NACADA, 2017).The trends of drug abuse have continued to grow exponentially within the country as shown in figure 1.1.2 (b)]. However, little is being done currently to help control the situation. Policy makers especially the political class have not shown adequate cooperation in this fight against drug abuse. As a result more studies on the rates of survival of drug abusers attending

medication would provide a stepping stone to the concerned medical community and the public as a whole (Mokaya, 2016).

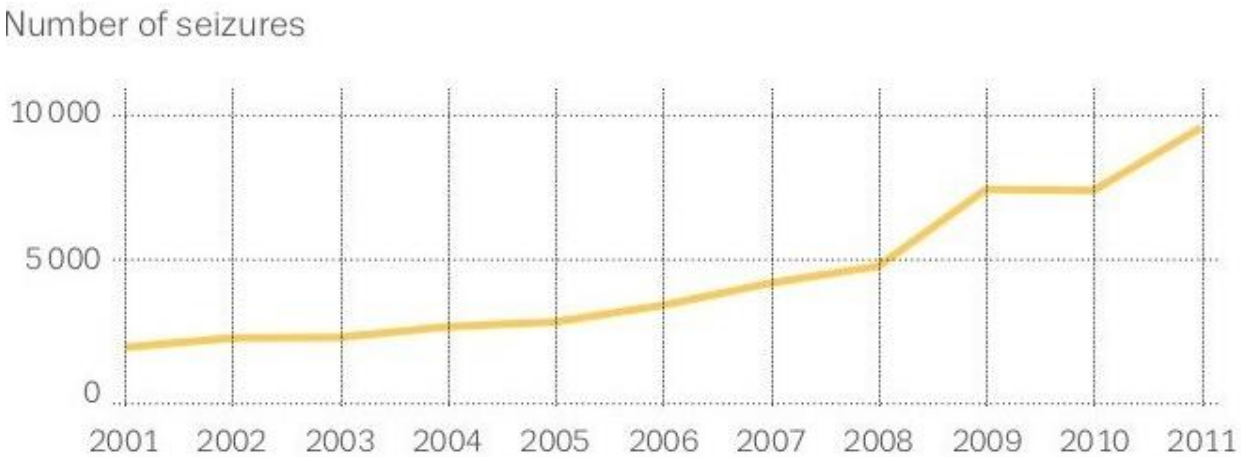

Figure 1.1.3: Drug use seizures in Kenya (NACADA, 2017)

Alcohol still remains the primary and most preferred substance of abuse in Kenya. According to NACADA (2017) high percentages of patients reporting to treatment are as a consequence of alcohol abuse at specialist treatment centers across the country. In Kenya alcohol is consumed in various categories. Chang'aa famously known with a street name of "kill me quick" - often contains methanol, a toxic, non-drinking type of alcohol (Ndetei et al., 2009). Chang'aa is a distilled beverage locally made and consumed in Kenya. Chang'aa can be made from a variety of grains malted millet and malted maize being the most common. Its alcoholic content ranges from 20 to 50%. This illegal traditional liquor is produced in clandestine distilleries and consumed by people who cannot afford beer. This type of alcohol has been known to cause blindness and even death. Most of the abusers of this brand are dwellers from poverty-stricken rural and slum areas and are particularly vulnerable to its effects (Ndetei et al., 2009). Kenyans also are drinking brand-name spirits and beer, though, in addition to traditional liquors and cheap manufactured alcohol. Other types of locally produced beer include, Busaa, traditional beer made from finger millet malt, Palm wine, consumed in the

coastal region of Kenya and Banana beer which is prepared from bananas, mixed with cereal flour (often sorghum flour) and fermented to an orange, alcoholic beverage(Mokaya,2016).

According to WHO(2011) about 2.5 million people die annually, and more people die as a result of illness and injury, due to harmful alcohol use. According to UNODC (2017) prolonged abuse of alcohol has been proved to have damaging effects on the brain as shown in Figure 1.1.2 (c).

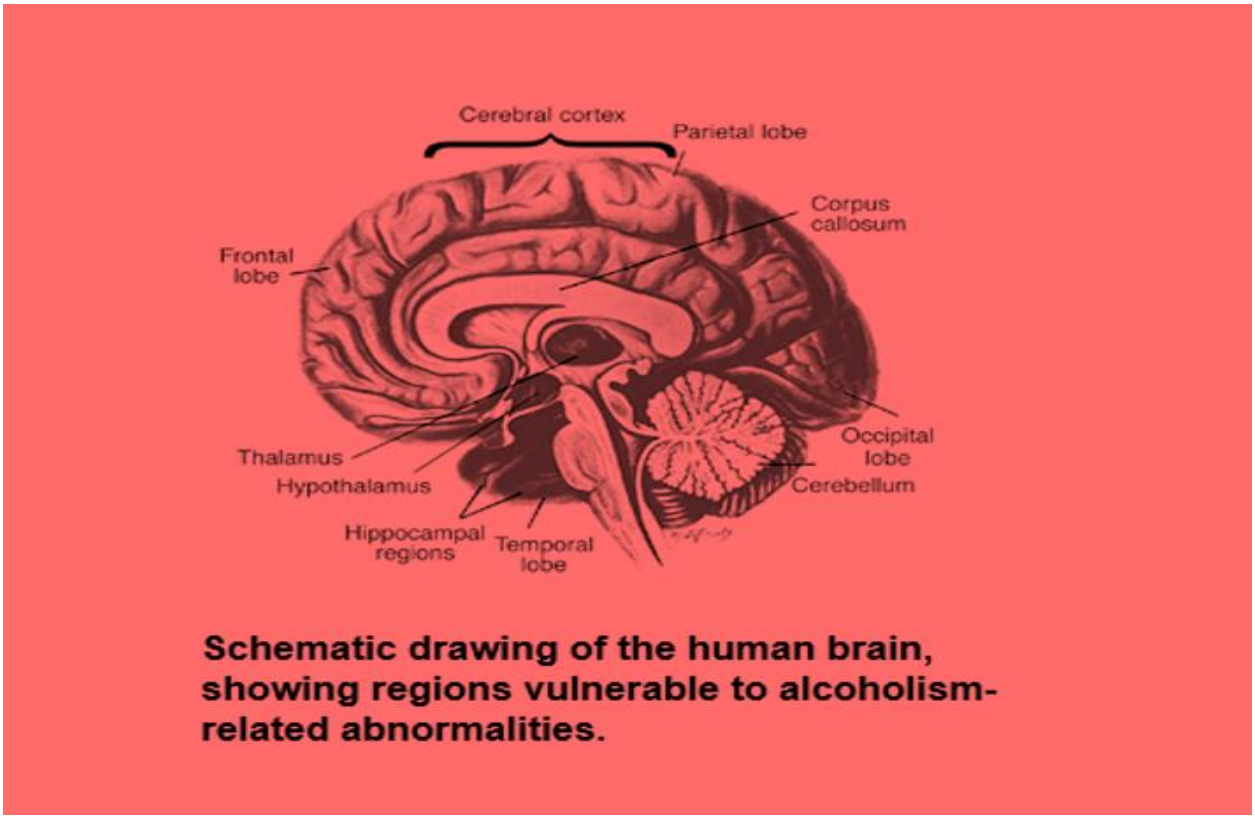

Figure 1.1.2 (c) Brain effects caused by alcohol abuse UNODC (2017)

Methamphetamine whose negative effects resemble the same effects experienced as a result of consuming cocaine causes the human brain to release dopamine, a chemical substance that causes an intense 'rush' of pleasure and prolonged sense of euphoria among methamphetamine users. After prolonged use, the dopamine receptors eventually get depleted and destroyed (Barr , 2006). Hence limiting feelings of pleasure.

Although the pleasure centers may recover with time, the effects of methamphetamine on the cognitive abilities of the user is simply irreversible. Intake of methamphetamine also triggers the brain to release adrenaline, a hormone produced by the adrenal glands during high stress or exciting situations. Adrenaline hormone increases blood flow to the body muscles and oxygen to the lungs by stimulating the heart rate, contracting blood vessels, and dilating air passages. The excitement that accompanies the release of these chemical hormones greatly contributes to the popularity of methamphetamine among its users (Asante, 2017).

Similarly Cocaine is a strong central nervous system stimulant that increases levels of dopamine, a brain chemical associated with pleasure and movement, in the brain's reward circuit (Ciccarone, 2011). Certain brain cells, or neurons, use dopamine to communicate. Normally, dopamine is released by a neuron in response to a pleasurable signal (such as the smell of good food), and then recycled back into the cell that released it, shutting off the signal between neurons. Cocaine acts by preventing the dopamine from being recycled, causing excessive amounts of dopamine to build up, amplifying the message, and ultimately disrupting normal communication (Ciccarone, 2011). It is this excess of dopamine that is responsible for cocaine's euphoric effects. With repeated use, cocaine can cause long-term changes in the brain's reward system and in other brain systems as well, which may eventually lead to addiction. With repeated use, tolerance to the cocaine high also often develops. Many cocaine abusers report that they seek but fail to achieve as much pleasure as they did from their first exposure. (Avois, 2006) notes that some users will increase their dose in an attempt to intensify and prolong the euphoria, but this can also increase the risk of adverse psychological or physiological effects.

(Pluddemann, Parry and Myers, 2014) note that low dosages of methamphetamine and cocaine is accompanied by such effects as increased alertness, concentration, and energy. Higher dosages arouses excessive excitement, enthusiasm, increased blood pressure, paranoia, aggression, extreme mood swing, lack of sleep and occasionally hallucination. Such individuals bear increased self-esteem and intense desire for sexual intercourse (Pluddemann et al., 2014). Excessive dosage of methamphetamine and cocaine results into abuse and addiction; robbing users their looks, sexual desires, physical health and cognitive abilities. Chronic cases witness physical damage such as cardiovascular damage as a result of overdose and severe psychological harm such as impaired concentration and memory, paranoia, insomnia, extreme aggression and withdrawal; as a consequence of methamphetamine induced neurotoxicity. Moreover, withdrawal often results into depression, abdominal cramps and increased appetite. Research evidence indicates that long term use of methamphetamine may increase risk of contracting HIV/AIDS (Siphokazi et al., 2017). As a consequence of drug injection and increased libido, users of methamphetamine and cocaine are more likely to indulge in risky sexual behaviors coupled with impaired judgment stemming from abuse of methamphetamine and cocaine. Addicted users are most likely to engage in unprotected sex, or engaging in sex with several partners or even exchange sex for drug, which is prevalent among prostitutes and sex workers.

According to Stewart (2008) chemicals in the brain such as dopamine and adrenaline which are triggered by methamphetamine and cocaine not only provide the users with the required sense of desirability, confidence and stamina during sexual intercourse, but also impair judgment centers and leads to more aggressive sex for even longer periods of time, increasing chances of injury and the danger of spreading infections. Many users take the drug intravenously, thereby enhancing their chances of contracting diseases such as HIV/AIDS and Hepatitis B and C (NIDA, 2002).. Some of the physical damages

resulting from methamphetamine and cocaine abuse include discolored and rotten teeth, popularly known as 'meth mouth'. Other effects include older skin, as it easily loses its luster and elasticity, making the users appear older than they should be (NIDA, 2002). Like elsewhere, the use of cocaine among commercial sex workers is also rampant in Kenya. Similar to cannabis and cocaine, methamphetamine abuse is popular among commercial sex workers and homosexuals (Orwa, 2015). High consumption of cocaine or methamphetamine have been shown to bear damaging effects on the brain as shown in figure 1.1.2 (d).

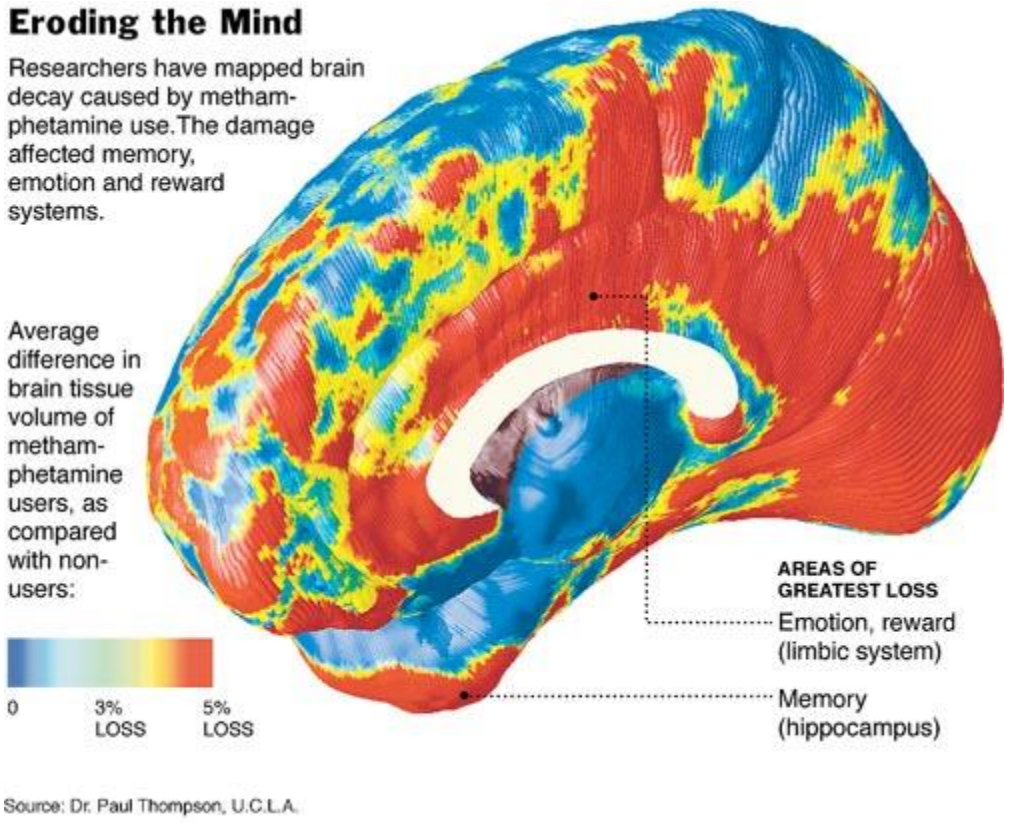

Figure 1.1.2 (d) Damaging effects of Methametaphine of brain UNODC (2017)

Emerging trends in drug abuse show many drug users engaging in use of more than one drug. More precisely they use a combination of drugs (WHO, 2011). Drugs that are readily available can always be used as substitute for drugs that aren't easily obtainable. For example, substituting cocaine with alternative stimulant such as amphetamine. According to (Chang, Alicata, Ernst, & Volkow, 2007; Kalechstein, Newton, & Green,

2003; Nordahl, Salo, & Leamon, 2003) psychoactive substances users usually not only overuse one drug of choice but also increasingly take several other drugs in combinations that pose serious health dangers and create hazards for detoxification programs. The use of multiple drugs has more devastating health and social consequences. It progressively worsens medical symptoms among their hosts. However despite major negative effects on the users, poly drug abuse has continued to be the norm for people heavily involved in drugs/substance abuse.

Orwa (2015) notes that diagnosis of poly drug abuse continues to be complex due to the fact that most treatment programs are tailored for specific drugs of abuse, as most of the patients on drug abuse, admit to abusing only one drug. This makes diagnosis for poly drug abuse even more difficult and complicated. Gold (2011) argues that even with proper diagnosis, detoxification of multiple substance-abuse is still not fully solved. For example, during withdrawals, individuals are shown to be in danger of experiencing brain seizures upon multiple use of alcohol and tranquillizers unless the specific treatment is addressed to the individual's condition. Scientifically, assessing the dangers of poly drug abuse is complicated as a result of a wide range of competing factors involved. Several research work has indicated that there are many approaches to multiple drug treatment (Chang et al., 2007). However, due to the dangerous reactions during withdrawal, the process of detoxification should take place both at the rehabilitation center and at homes. Worse still, drug abuse specialists are not well prepared to deal with poly drug abuse. Both theoretical and practical results reveal some effective relationships between alcohol and methamphetamine abuse (Newton and Green, 2003).

In comparison to single drug effects, methamphetamine-alcohol combination produced a greater elevations of heart rate which is arguably a motivation for the drug users who consider such effects as positive impacts of the drug combinations (Kirkpatrick,

Gunderson, R Frances, Foltin, & Hart, 2012). Their study showed that methamphetamine combined with alcohol produced a profile of effects that was different from the effects of either drug alone. The combination of alcohol and methamphetamine does not only produce a new psychoactive substance, it also increases heart rate and blood pressure beyond that seen for methamphetamine use alone (Kirkpatrick etal., 2012). While the combination of methamphetamine with cannabis is prevalent, its combination with alcohol is the most common among multiple drug abusers. Although extensive use of multiple drugs have been associated with poorer medical conditions of the user, excessive use of methamphetamine with other drugs such as cocaine, opiates or alcohol, increases its toxicity (Kirkpatrick et al., 2012).

1.2 Problem statement

Drug abuse is a major problem facing the country as whole. Policy makers and other stakeholders have staged major efforts to fight this menace. However substance abuse and illicit drug use remain pronounced. The use of these illicit drugs and substances pose risk health behaviors that lead to disease burden and increased crime rates, as well as adverse impacts on a number of life needs such as employment and educational attainment. The rising trends in drug abuse and complex population dynamics prove difficult to monitor.

According to a study conducted by NACADA (2017), 7.9 million Kenyans aged 15 – 65 years are abusing at least one drug or other substance related problems. The study states that for a lifetime use 23.4 percent (508,132) have ever used alcohol in their lifetime. The study also shows 7.2% of the population were currently using prescription drugs; 3.2% were using tobacco, 2.6% were using alcohol, 2.3% Khat, 1.2% were using inhalants and 1.2% heroin. The study shows 20.2 percent of school pupils have used at

least one drug in their lifetime with young people leading in drug abuse. At least 17% of school going children are abusing drugs. Despite the alarming numbers there is little knowledge in the treatment outcomes of the subjects who undergo medication (Ndetei et al., 2009). A study conducted by Morgenstern et al (2013) in the United States found that survival rate for subjects enrolled in a treatment program for a one year period was at 40%. Another study conducted in Iran by Kassani (2015) found that survival rate of drug users were 30.42%. However in Kenya there is no study that has determined the survival rate of drug users. The studies that have been conducted in Kenya have focused on the prevalence of drug abuse in Kenya, (Ndetei et al., 2009; Mokaya et al., 2016 and Kiambuthi, 2005). This study sought to determine the possible survival rate of drug abusers and inform relevant stakeholders including the public so that appropriate measures can be taken to eradicate or minimize drug abuse menace.

1.3 Objectives of the study

The study was guided by the general and specific objectives.

1.3.1 General objective

The general objective of the study was to model the survival rate of drug abusers in Kenya

1.3.2 Specific objectives

The specific objectives of the study were:

i. To apply a survival rate model for drug users.
ii. To perform a sensitivity analysis on model parameters.
iii. To establish the recovery rate of drug users under medication.
iv. To compare survival rates among drug users based on the significant predictors.

1.4 Significance of the study

The study was intended to inform policy makers and other stakeholders on the statistical reality of drug abuse and therefore to guide in strengthening or adopting new intervention measures appropriate for curbing drug abuse. Knowledge on survival rate of drug abusers is essential to hospital management. They will be able isolate cases based on the risk factors that are significant in the treatment of subjects. The government through the Ministry of Health and Sanitation can use the results of this study to target susceptible drug users for early intervention. Information generated from this study also suggests decentralization of treatment services to the counties and at affordable rates.Data on survival rate would be useful to guide the development, and implementation of policies that would address the shortage of treatment center.Furthermore, identifying the covariates that could distinguish users from non-users and those at high risk for use from those at low risk could help for diagnostic purposesThis study performed statistical analysis that helped identify contributing variables to survival rate of the drug subjects. These variables were age, gender and marital status. This study could therefore contribute to the effectiveness of treatment and intervention programs. Furthermore, identifying the covariates (risk-factors) that could distinguish users from non-users and those at high risk for use from those at low risk could help for diagnostic purposes so that appropriate cases could be selected for treatment and intervention.

1.5 Scope of the study

The study used data on drug use from Mathari National hospital. Data from other drug abuse treatment centers across the country was considered through the referrals to the main National hospital. The time of commencement of treatment for a subject was from

July 2013 and study period ended in June 2015. The study observed the length of time the subject took for full recovery.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

The chapter provides a review of the literature. The specific areas covered here are review of relevant studies which have been accomplished by other scholars on the concept of drug abuse, particularly, relating to prevalence of abuse, risk exposure and possibility of existing gender differences in survival rates of drug abusers. The study specifically embeds the theoretical discussions, critique of existing literature, research gap and introduces survival analysis methods applicable to the study in addition to the chapter's summary.

2.2 Theoretical literature Review

A theoretical framework is intended to provide an understanding of concepts that are relevant to the topic of any research (Swanson, 2013). It provides a sound knowledge base to support the conceptualization of causal relationships in any study. It sets out a logical structure that informs research theory. The theoretical literature helps the researcher see clearly the variables of the study provides a general framework for data analysis and help in the selection of appropriate research design (Swanson, 2013). In this section, this study reviewed the concepts of drug use continuum, drug classification, prevalence of drug use, gender differences in drug use, use of survival drug models and model development.

2.2 Overview of literature on drug use

One of the biggest drawbacks that researchers worldwide have faced is scarcity of data when studying medical data (Caetano and Clark, 1995). The situation has been due to

issues of privacy and confidentiality. As a result, social and health researchers have often relied on simple deterministic models to generate insight and understanding on the relative role of various mechanisms of disease spread. This practice has been extended to drug abuse research where data availability remains the biggest problem. The epidemiological study of substance and drug abuse is both challenging and rewarding (Hanna et al., 1993). The study provides insightful points and understanding of both the local and global nature of the drug use and misuse and its impacts on health, social, economic and political situations of communities, countries and regions. The results from drug abuse study are very handy to policy makers, social scientists and epidemiologists (Gomberg, 1994). Contrary to infectious disease epidemics, the spread of drug abuse is influenced by a combination of many factors, not the usual biological factors. Nevertheless, upon abuse, the biological and physiological factors often dominate the drug using career (Walton-Moss, 2000). Like many other social behaviors, drug abuse is characterized by both demographic and geographical features. The underlying causes of drug abuse are numerous and varied (Caetano and Clark, 1995). Some of the common causes, as some studies indicate, include but not limited to peer pressure, which is most common among the youth; curiosity, which encompasses the desire to taste or discover the actual feelings associated with drug and drug abuse; depression, individuals take drugs so as to kill depression tendencies; during sexual intercourse, individuals may use such drugs as methamphetamine, cocaine among others to boost their libido and sexual performances (Caetano and Clark, 1995). This is most common among commercial sex workers. Some drug users merely use them for the purpose of rebellion and alienation tendencies. The drug abusers not only suffer the usual social consequences of drug abuse such as personal and family neglect, but also expose their lives to numerous and adverse health consequences. For

example, the intravenous drug abusers are exposed to a high risk for contracting HIV/AIDS as well as host of other diseases (Hanna et al., 1993).

Drug abuse has evolved and changed substantially over time from patterns of abuse to modes of administration (Gomberg, 1994). Drug users have continued to indulge in more perilous modes of drug administration such as injection methods, and excessive dosages coupled with combinations of two or more substances. Clinical results have shown that the habit of using drugs in combinations increases victim's vulnerability to toxic effect, and offers greater consequences in relation to single drug abuse (Gomberg, 1994).

The fact that drug abuse and possession is considered illegal in most countries makes data on drug abuse to be scarce. The challenge in estimating the actual population of drug users is further compounded by the fact that the behavior of drug users do not exactly mirror that of individuals infected with infectious diseases. Despite these short falls, the technique of mathematical analysis has become handy in providing the necessary insight and understanding towards drug abuse epidemic (Orwa, 2015). Deterministic and stochastic models have been helpful in the understanding of the various aspects of the drug abuse dynamics from initiation, treatment to prevention measures. Previous studies by Caetano and Clark (1995) have attempted to answer such questions as: the type and amount of drug abused, trends of drug abuse, consequences of abuse, effectiveness of available policies and their corresponding costs. Policy makers on the other hand have been faced with such challenges as understanding the problem of drug abuse, designing robust intervention strategies and constructing better evaluation tools to test on the effectiveness of the desired strategies.

Unlike infectious disease epidemic model with biological parameters, drug abuse epidemic is mainly characterized by social parameters which are often transitory. It is

assumed that the rate of new 'infectious' in drug abuse epidemic is regulated by the law of mass-action which states that new cases of drug abuse are reliant on the population of drug users and the population of individuals who have never used drugs before but are at risk of being initiated into drug abuse (Orwa, 2015). Compartmental model is a powerful and well established tool that can be applied not only in the spread of diseases but also the spread of drug and substance abuse in the population of interest. The compartments are constructed such that the flow mirrors are usual dynamics and interactions in disease epidemics (Orwa, 2015). Upon sub-diving the population in each compartment over time. Collet (2003) categorized the susceptible population into 'Stayers' (those who cannot be initiated into drug abuse for one reason or another, and hence are never at risk) and 'Movers' (those who are at risk always). Upon initiation drug users undergo a process of latency, a period of hidden drug use. During the latency phase, the drug users may die, quit or continue using the drug. The hidden phase can further be split into several compartments depending on the interest of the modeler. For example, the hidden phase may be split into 'light drug use', representing initial stages of drug use and 'hard drug use', which marks the problematic stage of drug abuse (Collet, 2003). Addicts are further taken through rehabilitation which may be a success or not, and therefore this may give insight on their survival rate.

Comiskey et al., (2006) developed the first ordinary differential equation model for drug addiction. The model results from their study were vital to policy makers in targeting prevention and treatment in heroin epidemic. The original model as shown in figure 2.1, has three compartments each representing a stage in drug using career of drug user. Those individuals, who have never used drugs before but stand a chance of using them are called susceptible(S). Drug users under treatment are denoted by U1

while those that have reached the problematic phase of drug abuse are under treatment and denoted as U2.

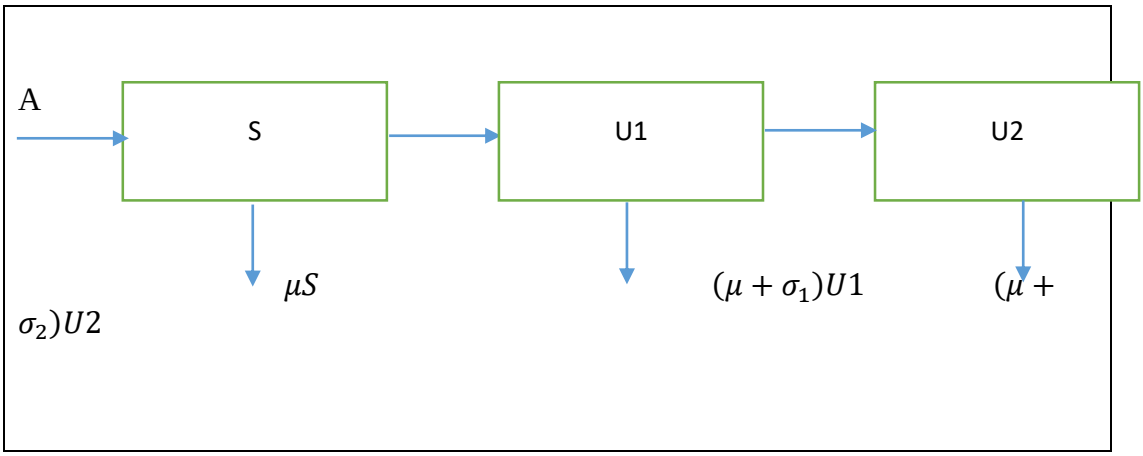

Figure 2.1 A drug abuse model (Comiskey, 2006).

Results from the sensitivity analysis identified the probability of becoming a drug user as the most influential parameter for target in the reduction of secondary cases of drug abuse. Secondly, preventive therapy was more effective as compared to treatment for maximum and effective eradication of addiction and abuse (Comiskey, 2006).

Drug abuse has been associated with men. However the trends seem to be changing. Women are increasingly getting involved in drug use. No single factor thoroughly explains why women engage in the use and abuse of alcohol and other drugs, most contemporary theories attribute drug users to gender inequalities. For example, Schultz, et al., (2000) noted that some women's subjective experiences is an institutionalized society unjustly characterized by gender inequalities can negatively impact their health. Other factors such as separation fears, over dependence, escapism, and low self-esteem may also contribute to substance use and abuse (Wingo, 2001). Any number of life stressors such as divorce, single parenting, caring for elderly parents, etc. (Boyd et al., 1998), as well as poor socioeconomic and socio-environmental conditions probably also contribute to substance use and abuse. The research literature indicates the lack of well-defined social roles among women to be highly associated with drug use and alcohol related problems. Russel (2010) found that single women drank and experienced alcohol related problems in greater numbers than did married women.

Corroborating those findings, Newcomb (1997) noted that young adult women who have prepared themselves since adolescence for marriage and child bearing but then who are unable to fulfill those roles have an increased likelihood of using drugs or alcohol to overcome resulting feelings of failure. Hanna, Faden & Harford (1993) noted that women who married or remarried decreased drinking, whereas women who separated or divorced increased their alcohol consumption. Walton-Moss (2000) also examined that the relationship does exist. Specifically, they pointed out that single women tend to drink more and experience more alcohol related problems than widowed or married women.

A number of researchers have examined whether a genetic predisposition contributes to drug use among women. Gomberg (1994) found women with family history of alcoholism were at a greater risk of becoming alcoholics than those without their family history. Hanna et al., (1993) noted that routine life stresses, which most women handle with constructive ways, are sometimes overwhelmingly complex for female children of alcoholics. Thus adult female children of alcoholics have an increased tendency to self-medicate as copying mechanism (Gomberg, 1994). According to (Miller & Downs, 1993), (Van der Walde, et al, 2002), those women often partner with men who are alcoholics or addicted to other drugs. Caetano and Clark (1995) found drinking and alcohol related problems to be associated with marital conflict, education, unemployment and childlessness (each role facilitates a sense of responsibility), family history of alcoholism, and regular psychoactive drug use to be associated with alcohol related problems among women.

The literature strongly supports the existence of gender differences among drug users. Since women tend to be overrepresented as clinical patients, they are more likely than men to use and abuse medically prescribed psychotropic drugs, and to receive dual

diagnoses. For this, comorbidity is more common among women and women (Moras,2014).

The reason for trying out drugs is different for different patients. Some patients try it because they wonder what it feels like to be high, peer pressure or to better themselves in one thing or the other (Moras, 2014). Other reasons are depression, anxiousness, or tension. Using a particular drug does not automatically mean that one is abusing. Irrespective of the amount of intake, if it results to challenges in one's daily life, school work and family, then nurses can inquire if a person has the problem of abusing drug and possibly addiction (Moras, 2014). Drug abuse is a composite disorder characterized by compulsive drug use. Although different drugs produce different effects, all abused drugs produce the same effect by changing the appearance of the bran and its use. When addicted to drugs every other thing becomes insignificant and does not matter, family and friends included. The compulsion is so strong that being on drugs or high takes the same meaning as eating, drinking and its required for survival (Robinson et al, 2014).

Drug use causes a surge in levels of dopamine in the brain, which trigger feelings of pleasure; the brain remembers these feelings and wants them repeated. In the case of addiction, the substance takes on the same significance as other survival behaviors such as eating and drinking. These changes in the brain interfere with the ability to think clearly, exercise good judgment, control behavior and feel normal without drugs. The urge to use is so strong that the mind finds many ways to deny or rationalize the addiction. Patients may drastically underestimate the quantity of drugs being taken, how much it impacts their life and the level of control they have over drug use (Comiskey, 2006).

2.2.1 Drug use continuum

A study done by Doweiko (2002) found that there are five levels on the drug use continuum. Level 0 is the first point on the continuum, representing total abstinence. This level represents individuals in the susceptible stage. They are exposed to drug use but have not yet started abusing the drugs. Level 1, is the rare use level whereby the individuals are beginning to abuse the drugs. This level represents individuals using drugs for recreational purposes. The subjects do not face any financial or medical problems. At Level 2, which is the early problem use of drugs, the individuals use drugs more regularly. The individual is beginning to face financial and medical problems. Level 3 represents heavy problem drug use. This is indicative of early addiction. At Level 4 is the severe addiction stage. The user demonstrates unprecedented addiction syndrome. The user faces a combination of legal, medical, financial, work-related and personal problems. At this stage, Doweiko (2002) noted that the individual might still try to rationalize his or her addiction or deny that the problem exists.

Individual-level theories attempt to explain addiction by reference to concepts that apply to individuals and their circumstances. Caetano and Clark(1995) notes that individuals are regarded as possessing particular dispositions and/or inhabiting particular environments that promote addiction, through either initial engagement in the addictive activity or susceptibility to the development of addiction once the individual has undertaken the activity and been exposed to its consequences. Recovery from improvement in or management of addiction involves changes to one or more of these.

Acquired need theories are prevalent in the drug abuse and conform to the popular image of addiction as a disorder in which an individual begins taking a drug because of its positive effects and then habituates to these effects, and therefore needs to escalate the dose (Simpson and Miller, 2002). However, at the same time, the physiological

adaptation means that when the drug is not present in sufficient concentrations, he or she needs to take the drug to stave off aversive withdrawal symptoms. Thus, the discomfort of withdrawal symptoms comes to drive the decision to continue to take the drug.

Drug withdrawal theory (Koob et al., 1992) is probably most commonly held theory of addiction. Under this theory, physiological adaptation occurs with the presence of a drug in the body so that, when the drug is no longer present, physiological rebound occurs, leading to unpleasant and sometimes life-threatening symptoms (Koob et al., 1992, 1998; De Vries and Shippenberg, 2002). This is often referred to as 'physical dependence'. In fact, there may be multiple physiological adaptations that lead to a range of unpleasant withdrawal symptoms and drive states that motivate activities that may have previously relieved the symptoms. Thus, under the most general form of this theory, the drive to use a drug (experienced as 'craving') could arise out of a process of physiological adaptation.

Opponent-process theory (Solomon and Corbit, 1973, 1974; Solomon, 1980) is a specific version of drug withdrawal theory. The human brain has a physiological propensity to adapt to and counter influences that disturb its homeostasis. Repeated administration of a pleasurable drug, or repeated experiences of euphoria, lead to physiological adaptive processes to restore equilibrium so that, in the absence of the drug or euphoria activity, a negative state prevails. This state is aversive and motivates activities to mitigate it.

A striking observation in those people who are addicted to illicit drugs is the proportion who suffered abuse as children (Simpson and Miller, 2002). There is also good evidence of a strong association between depression and anxiety in children and subsequent development of addiction to a range of drugs including alcohol and nicotine (Douglas

et al., 2010). This, together with self-reports of addicts, has led to the view that an important motive for taking up and continuing with an addictive behavior pattern is to meet pre-existing psychological needs. The need may involve numbing or improving adverse mood. In the case of smoking for example , it has been suggested that one reason that people with schizophrenia smoke is to help with gating of sensory inputs, which is an important factor underlying the symptoms of this condition (Adler et al., 1993, 1998). In all these cases, the presumption is that these needs contribute to the process of reflective choice, which may or may not be rational.

2.2.2 Drug Classification

A study by Erickson (2007) describes depressants as substances that dampen the central nervous system. Depressants include alcohol, barbiturates, methaqualone, and benzodiazepines. Depressants are used to treat disorders such as panic attacks, insomnia and epilepsy.

Stimulants are drugs that arouse the central nervous system (CNS), enhancing brain activity (UNODC, 2017). Stimulants include drugs such as cocaine, amphetamines, prescription weight-reducing products, nicotine, caffeine, some over-the counter (OTC) weight reducing products, minor stimulants, and amphetamine-like drugs such as Ritalin (Erickson, 2007). Amphetamines increase energy and decrease appetite. Individuals who abuse amphetamines show signs of irregular heartbeat, rapid breathing, high energy, increased mental alertness, reduced appetite and hallucinations. According to Erickson (2007), frequent use of these drugs can lead to overdoses, obsessions, and anxious episodes including panic attacks, physical addiction, severe depression and psychoses. Cannabis (marijuana) is a psychoactive agent, primarily used to produce euphoria (Erickson, 2007). This drug can be smoked or orally consumed. On the streets, marijuana may be referred to as pot, grass, reefer, weed, herb, or Mary Jane. According

to NIDA (2002), most individuals smoke marijuana in hand-rolled cigarettes called joints while others may use pipes or water pipes called bongs. Blunts are marijuana filled cigars. Marijuana is also used in brewed tea and is often mixed into foods (NIDA, 2002). The effect of the plant depends on the quality and potency. Erickson (2007) stated that the effect of the drug may produce relaxation after euphoria, loss of coordination, impaired memory, concentration and knowledge retention, and loss of appetite. More potent doses can cause disoriented behavior, psychosis, fragmented thoughts and mood swings (NIDA, 2002).

2.3 Prevalence of drug abuse

Global trends on drug abuse show increasing prevalence in drug abuse. Studies contacted in Europe showed prevalence of illicit drug use to be historically high (EMCDDA, 2011). Previous studies performed in the USA regarding illicit drugs showed that 9 % of lifetime cannabis users and 23 % of lifetime cocaine users will develop substance dependence later in life (Morgensten etal., 2013). Similar prevalence figures are found in other western countries (Anthony, Warner & Kessler, 1994; Hall, Teesson, Lynskey & Degenhardt, 1999).

Similar trends are revealed for occasional cannabis use (such as using cannabis 1-2 times).

In Kenya, data from NACADA (2017) reveals much the same trends as seen in Europe. The consumption of alcohol has increased over the last years and the most dramatic increase since 2007 is found among young people. Thus, there seems to be a trend in Kenya’s population of drug abusers towards higher lifetime prevalence of illicit drugs, more frequent usage being towards the use of cannabis and alcohol.

2.4 Gender differences and drug abuse

Female substance abusers are said to be proportionately less likely to seek treatment for their drug use than male substance abusers. Past studies have shown that female drug users experience low turnout for treatment from drug abuse. Reed (1985) found that women drug users who attended treatment were way below estimated prevalent rates. However a more recent review of treatment studies of cocaine or alcohol (Toneatto, 1992) found that there was increasing trend of women drug users seeking treatment. Carroll, Rounsaville and Keller (1992) used a larger sample of cocaine users seeking medication (n=89) and non-medication-seeking (n=89) cocaine abusers. Their study did not show gender variations between the two groups and both groups were predominant, male (67 to 69 percent).Previous studies have showed that many women who are mothers tend to avoid drug abuse treatment for fear of their children being taken away from them (Marsh and Miller 1985). Others feel ashamed and therefore they shy away from seeking treatment. This may be due to different societal expectations of being responsible parents (Kumpter 1997).

A study conducted by (Beckman, 1978) found that many women have low self-esteem over men especially when faced with challenges. This may lead them to drug abuse as a form of consolation. Depression is another common factor that leads to women entering into drug abuse (Culbertson, 1997, Keslller, 1994; Weissman and Klerman 1977). The ratios of Female to male drug abuser as shown in past studies are in the range of about 2:1 to 4:1 and statistical evidence suggests that gender differences is more likely to exist in more developed cultural settings (Culbertson 1997).

Providing treatment programs for women who chronically engage in the most dangerous forms of drug abuse have found rehabilitation efforts to be handicapped

by some women's lack of marketable skills. A study done by Platt and Metzger (1987) found that chronic women drug abusers experienced low drug survival rate due to lack of adequate job skills. Once they left drug use they eventually returned to drug use because of unemployment.

It is notable that previous studies have given conflicting findings on the gender differences in survival rate due to drug abuse. For instance a study done by Deleon (1993) found that there were no significant differences in survival rates based on gender while (Saunders, Resnick, Hoberman & Blum, 1994)) found that there was a significant difference in the rate of survival based on gender

2.5 Multiple drug/substance abuse

The scientific definition of multiple drug/substance abuse is not unique. It is dependent on both the time and the effects to the users. Time category defines multiple drug/substance abuse on the basis of time frame in which the drugs are used(Kassani, 2015). They include a case in which more than one substance is used on the same occasion called the Simultaneous Poly drug Use (SPU) and a scenario in which different drugs are used by a drug user during his/her drug using career, called the Concurrent Poly drug Use (CPU). Effect category on the other hand, defines multiple drug/substance use in terms of the effects of mixing drugs(Kassani,2015). Mixing of drugs is likely to increase or decrease the effects of each drug; or a case in which drugs are combined to generate new effects (Ives and Ghelenie, 2014).

Multiple drug/substance abuse in Kenya, like in most other parts of the world, is viewed as a 'positive' step to satisfaction by drug abusers. Data from (Pluddemann, Parry, and Myers, 2014) illustrates continued use of multiple drugs/substances by patients seeking rehabilitation services in the different rehab centers in the country. Patients not only report their primary drug of abuse but also the secondary drug of choice. Some of the

substances used in combinations in Kenya include combinations of alcohol and cocaine, marijuana, methamphetamine sleeping pills. It is important to observe that the users of multiple drugs are often addicted to two or more such drugs (Kandel, Yamaguchi, and Chen, 1992).

Treatment services should therefore be broad enough to cater for the secondary and even tertiary drugs of abuse consumed by the patient. Abuse of drugs in combinations apparently leads to increased health problems (NIDA,2014).Data collected by the National Institute on Drug Abuse indicate that about two-thirds of hospital emergency room cases admitted for drug abuse involve combinations of drugs.

The diagnosis of poly-drug abuse is however a difficult and more challenging process. During intoxication and withdrawal, multiple substance abusers may exhibit symptoms that mimic psychiatric disorders (Greenwood, Guydish and Bein (2010). In addition, since most treatment programs require patients to be drug free, poly-drug abusers often admit sadly to using only one kind of drug/substance (National Institute on Drug abuse 2014). Bower, (1985) further argues that even with the proper diagnosis, the detoxification of multiple-substance abusers is even more complicated owing to lack of uniform approach to poly drug abuse treatment. For example, individuals who use alcohol in combination with tranquillizers; drugs that are used to reduce anxiety, fear, tension, agitation, and related states of mental disturbances, are at a high risk of experiencing brain seizures during withdrawal unless treatment is tailored to the individual's condition. In order to avoid withdrawal tendencies, detoxification procedures need continue both in hospitals and at homes during rehabilitation procedures.

Multiple drug abuse among adolescents is of great concern. Some of the problems associated with multiple drug abuse and especially among the adolescents are well documented in (Czechowicz, 1998). Their research work highlights some of the merits

of concern for multiple abuse of alcohol and other drugs among adolescents. Other researchers such as Kandel, Yamaguchi, and Chen, (1992), and Bailey (1992) share the argument that alcohol abuse is very instrumental in contributing to multiple substance abuse epidemic. According to Kandel, Yamaguchi and Chen, (1992). They argued that adolescents typically use alcohol and then graduate to marijuana before progressing to other illegal drugs such as cocaine and methamphetamine. Bailey (1992) also observed that adolescents do not progress to marijuana and other drugs until they are alcohol users. Also, they observed that fewer young people use drugs such as hallucinogens, amphetamines or cocaine without initially using alcohol and marijuana (Kandel and Logan1984; Hesselbrock, Meyer and Keener (1985) observes that unlike other substances, most alcohol abusers frequently abuse other drugs in dangerous combinations. Statistics from multiple drug abuse combinations shows for example that about 30-60% of alcoholics' abuse cocaine (Tsuang, Shapiro, Smith, and Schuckit, 1994). 20-50% of alcoholics abuse marijuana (Caetano and Weisner, 1995).12-20% of alcoholics abuse benzodiasepines and approximately 7-10% of alcoholics abuse heroin (Caetano and Weisner, 1995).This view is also supported by research work by the National Institute of Drug Authority, which indicates that the majority of drug related energy room visits involve combinations of alcohol and other illicit drug use(National Institute on Drug abuse,2014).Some of the consequences associated with multiple drug abuse include low self-esteem, emotional distress, physical and sexual abuse. The specific consequences are however quite numerous. Multiple substance abuse therefore presents a range of problems to treatment and public health institutions. It also increases the likelihood of overdose and suicide among its users (Ruttenber and Luke, 1984).This is common in cases where, in an effort to balance the side effects of one drug of abuse, a drug abuser uses the secondary drug in excessive doses. Sex enhancing drugs such as methamphetamine which increases sexual energy, are taken in combination with other

substances such as alcohol before indulging in sexual escapades. Such individuals exhibit a high likelihood to indulge in unprotected sex or be unable to control themselves during sexual intercourse, creating a better opportunity for infections from other STDs and HIV/AIDS (Petry, 1999).Patients of drug abuse have very minimal chance of full recovery owing to other secondary substances, resulting into poor treatment outcome (Schuckit, 1985).

Drug abuse has been associated with men. However the trends seem to be changing. Women are increasingly getting involved in drug use. No single factor thoroughly explains why women engage in the use and abuse of alcohol and other drugs, most contemporary theories attribute drug abuse to gender inequalities. For example, Schultz et al., (2000) noted that some women's subjective experiences in an institutionalized society unjustly characterized by gender inequalities can negatively impact their health. Other factors such as separation fears, over dependence, escapism, and low self-esteem may also contribute to substance use and abuse (Wingo, 2001). Any number of life stressors such as divorce, single parenting, caring for elderly parents, among others, (Boyd, Hill, Holmes, & Purnell, 1998), as well as poor socioeconomic and socio-environmental conditions (Wingo, 2001) probably also contribute to substance use and abuse. The research literature indicates lack of well-defined social roles among women to be highly associated with drug use and alcohol-related problems. Lozina, Russell and Mudar (1995) found that single women drank and experienced alcohol related problems in greater numbers than did married women. Corroborating those findings, Newcomb (1997) noted that young adult women who have prepared themselves since adolescence for marriage and childbearing—but then who are unable to fulfill those roles—have an increased likelihood of using drugs or alcohol to overcome resulting feelings of failure. Hanna, Faden & Harford (1993) noted that women who married or remarried decreased drinking, whereas women who separated or divorced increased their alcohol

consumption. Walton-Moss (2000) also examined the relationship between marital status and substance use among women and confirmed that a positive relationship does exist. Specifically, they pointed out that single women tend to drink more and experience more alcohol-related problems than widowed or married women.

A number of researchers have examined whether a genetic predisposition contributes to drug use among women. Gomberg (1994) found women with a family history of alcoholism were at a greater risk for becoming alcoholics than those without that family history. Van der Walde, Urgenson, Weltz, and Hanna (2002) noted that routine life stresses, which most women handle in constructive ways, are sometimes overwhelmingly complex for female children of alcoholics. Thus, adult female children of alcoholics have an increased tendency to self-medicate as a coping mechanism (Gomberg, 1994). According to (Miller and Downs, 1993), (Van der Walde, et al., 2002), these women often partner with men who are alcoholics or addicted to other drugs. Caetano and Clark (1995) found drinking and alcohol-related problems to be associated with marital conflict, education, household income, employment status, and religion. Lozina, et al., (2002) found that lack of education, unemployment and childlessness (each role facilitates a sense of responsibility), family history of alcoholism, and regular psychoactive drug use to be associated with alcohol-related problems among women.

Addiction arises out of either pre-existing characteristics of individuals or the acquisition of characteristics that, together with a given set of environmental circumstances, result in powerful motivations to engage in harmful behavior patterns (Barnett, 2012).

2.6 Survival of drug users

Survival analysis refers to the analysis of elapsed time. The response variable is the time between a time origin and an end point. The end point is either the occurrence of the event of interest, referred to as a death or failure, or the end of the subject's participation in the study (Agarwal, 2012). These elapsed times have two properties that invalidate standard statistical techniques, such as t-tests, analysis of variance, and multiple regression. First of all, the time values are often positively skewed. Standard statistical techniques require that the data be normally distributed (Hazra, 2017). Although this skewness could be corrected with a transformation, it is easier to adopt a more realistic data distribution. The second problem with survival data is that part of the data are censored(Breslow,1975). An observation is censored when the end point has not been reached when the subject is removed from study. This may be because the study ended before the subject's response occurred, or because the subject withdrew from active participation. This may also be because the subject died for another reason, because the subject moved, or because the subject quit following the study protocol. All that is known is that the response of interest did not occur while the subject was being studied. When analyzing survival data, two functions of fundamental interest are the survivor function and the hazard function *(*Hosmer and lemeshow, 1999).

Several studies have been conducted with the aim of determining the rate of survival of drug users upon entry into medication programs. A study by Barnett, 2012) conducted a meta-analysis of 39 Motivational Interviewing studies on youth drug use, including two quasi-experimental studies and 37 randomized control trials (31 randomized by individuals and 6 randomized by groups) in various settings. They found that 28 of the 39 studies (72%) showed significant reductions in drug use, including seven studies on alcohol use, seven studies on marijuana use, and eight studies on other drug use.

Carroll (1994a) states that interventions targeted at relapse prevention have been tested for efficacy studies. Interestingly these studies have not shown full relapse prevention. However relapse prevention treatment tend to indicate that benefit is achieved and also that substantial room exist for better efficacy (percentage of those treated who achieve a recovery criterion). In study of cocaine users, Carroll (1994) found that 57% attained three week or more of continuous abstinence and 43% met a criterion of recovery at the end of a twelve week treatment program In a later study , Carroll (1994b) also found some evidence that gains attained during acute treatment were maintained (findings consistent with the connotation of relapse prevention) in a one year follow up of relapse prevention and pharmacotherapy for cocaine abuse. Treatment gains were maintained and even increased to some extent for the relapse prevention-alone condition. Gender differences in the efficacy of relapse prevention treatments have not been reported (Karla, 2014). In their 2014 study they found that 100 women who received inpatient or day treatment for anorexia nervosa, 41% relapsed within one year.

2.7 Cox Proportional Hazards Regression Model for survival data

To determine gender difference in the rate of survival of drug use, it was necessary to apply a survival analysis model that could show the parameter estimates and significant differences in the subgroups of gender, that is, male and female subjects. Cox proportional hazards model (Cox, 1972) was chosen for this purpose.

The Cox Proportional Hazard (PH) Model is a multivariate regression method used to determine the effect of multiple covariates on the survival of a subject. Cox (1972) proposed a semi-parametric model for the hazard function that allows the addition of covariates, while keeping the baseline hazards unspecified and can take only positive values.

The Cox proportional hazard model is popular because it allows a flexible choice of covariates: time varying, time-independent, continuous and discrete. Two other issues that make it popular are that it does not make any assumption about the underlying survival distribution and also does not require estimation of the baseline hazard rate to estimate the regression parameters.

2.7.1 Estimation of Parameters in proportional hazard model

The regression coefficients in the proportional hazards Cox model, which are the unknown parameters in the model, can be estimated using the method of maximum likelihood. In Cox proportional hazards model we can estimate the vector of parameters without having any assumptions about the baseline hazard.

2.7.2 Model development

In any applied setting, performing a proportional hazard regression analysis of survival data requires a number of critical decisions. It is likely that we will have data on more covariates than we can reasonably expect to include in the model, so we must decide on a method to select a subset of the total number of covariates. When selecting a subset of the covariates, we must consider such issues as clinical importance and statistical significance, (Hosmer and Lemeshow, 1999).

2.7.3 Selection of covariates

The methods available to select a subset of covariates to include in a proportional hazards regression model are essentially the same as those used in any other regression model. There are three methods of selecting influential covariates. These are purposeful selection, stepwise selection (forward selection and backward elimination) and best subset selection. Survival analysis using Cox regression method begins with a thorough

univariable analysis of the association between survival time and all important covariates (Hosmer and Lemeshow, 1999).

2.7.4 Recommendable procedure in selecting variables in the study

Hosmer and Lemeshow (1999) and Collett (2003) recommended the following procedure in variable selection.

1. Include all variables that are significant in the univariable analysis at the 25 percent level and also any other variables which are presumed to be clinically important to fit the initial multivariable model.
2. The variables that appear to be important from step 1 are then fitted together in a multivariable model. In the presence of certain variables others may cease to be important. Consequently, backward elimination is used to omit non-significant variables from the model. Once a variable has been dropped, the effect of omitting each of the remaining variables in turn should be examined.
3. Variables that were not important on their own, and so were not under consideration in step 2, may become important in the presence of others. These variables are therefore added to the model from step 2, with forward selection method. This process may result in terms in the model determined at step 2 ceasing to be significant.
4. A final check is made to ensure that neither significant variable is eliminated from the model nor non-significant variable is included in the model. At this stage the interactions between any of the main effects currently in the model can be considered for inclusion if the inclusion significantly modifies the model.

Interest is often in comparing between groups, for example, a clinical trial may investigate how the hazard rate in a group of patients randomized to standard therapy, compares to the hazard rate in a group of patients randomized to receive a new therapy.

To illustrate this, consider a binary covariate, X, with X = 0 representing standard therapy, and X = 1 representing a new therapy.

2.8 Recovery rate of drug users

Kaplan-Meier provides for calculating the proportion surviving to each point in time when relapse occurs (Goel , 2010). An important advantage of the Kaplan– Meier method is that it can take into consideration types of censored data, particularly right-censoring, which occurs if a patient withdraws from a study (i.e. is lost from the sample before the final outcome, relapse, is observed. The Kaplan-Meier method and life table method give identical results in the absence of withdrawals. The Kaplan-Meier (KM) estimator of the survival function (Kaplan and Meier ,1958), also called the product limit estimator, is often used to estimate the survivor and

2.9 Critique of existing literature

Most of the studies that relate to drug abuse have aimed at describing the prevalence in drug abuse. However different studies have given conflicting results on the prevalence of drug abuse. Several studies conducted in western countries have shown persistent increase in prevalence of drug abuse (Anthony, Warner & Kessler, 1994; Hall, Teesson, Lynskey & Degenhardt, 1999). Most of the studies report that the major drug of abuse is alcohol while in some other countries Cannabis is reported as the most frequently used illegal drug. (Long and Horgan, 2012). In this light it is difficult to compare results of drug abuse studies due to the complexity based on geographical regions.Past studies have shown that female drug users experience low treatment outcomes for women as compared to their male counterparts (Reed 1985). However other scholars report that female treatment outcomes surpass those of male drug abusers (Toneatto, 1992).

2.10 Gap in the literature

Previous studies have tried to explain the factors that contribute to drug abuse. For example Hemphill (2011) and Arteaga et al., (2010) studied the covariates that drive youth into drug use. However this study looks at the covariates that influence the rate of survival of drug use once the subjects are enrolled in treatment programs. Currently few studies, if any, have been done in Kenya to determine the survival rate of drug users. Several studies on the survival rate have been done in Europe. However due to complexity of the nature of drug abuse it is difficult to relate the results to the Kenyan population. This study seeks to fill the existing gap in the study by identifying covariates that significantly contribute longer rates of survival of drug use. The covariates considered in this study are age, gender, marital status, and employment status, type of drug taken, residence of the subjects and the mode of taking the drug. The overall rate of survival of the drug abuse subjects is also determined through a follow-up for a period of 2 years. The hazard rate for the drug use subjects is also determined to point out the exposure groups so that government agents and other stake holders can target them for easy recovery.

CHAPTER THREE

METHODOLOGY

3.1 Introduction

The Chapter dealt with the methods and all the procedures that were be applied in conducting this study. It explains the rsource of the data, the population of the subjects, procedure of analyzing the data, the Cox and Kaplan Meier Survival analysis methods and the model diagnostics.

The main source of the study data was Mathari National hospital registry. This hospital is used as referral center for different health centers in and across the country and the East African region. The hospital has separate departments for handling drug abuse in addition to two rehabilitation centers. The hospital started as a drug abuse treatment center in 2003. However over the past 10 years there was no proper filing system to keep medical records of subjects attending treatment. The adoption of digital filing system became effective on July 2013.

Secondary data was used for the study. The data was recorded in standard registers available at the hospital. These registers were provided by the ministry of health. The study used the routine hospital database to collect more clinical information on treatment and co-morbidity. In addition the study reviewed hospital records to ensure that no subjects were counted more than once and that there was no missing information. The subjects for the study were identified by patient ID coded from ID001 to ID162 to ensure confidentiality of the patient information. Drug abuse treatment and follow-ups were recorded obtained. The end of the follow-up time was June 2015.

Only the data that was required for the study was obtained. Data was coded to make it anonymous before the analysis stage by removing all sensitive data such as names and

addresses and replacing them with computer-generated numbers. The use of the data was approved by the Institutional Review Board (IRB). The study protocol was approved by the ethics committee of Mathari hospital. Patients were not directly contacted or involved and therefore the principal ethical consideration in this study was to avoid disclosure of personally identifiable information.

The response or outcome variable in this study was the survival time from the date of entry into the drug abuse treatment until the end of the study.The predictor variables that were considered for predicting survival rate were: age in years, gender (male, female), marital status (Never Married, Married, Others), Job status (employed, unemployed), Residence (urban, rural), Type of drug used (alcohol, cigarettes, cocaine and cannabis) and Mode of taking the drug (oral, sniffing, injecting, absorbing).

3.2 Kaplan –Meier and Cox Proportional Hazards Regression Models for survival rate for drug users

A Kaplan Meier is used in this study to obtain the survival probability curves. Based on this estimator the overall survival rate was obtained, the survival rate for males and females was also obtained. The significant differences between the survival curves would then be noticed by use of log rank statistics.

The Kaplan method also generated the life table that could clearly provide evidence on the hazard rate and the relapse rates during the course of treatment of the subjects.

The estimator is given by:

$$s(t) = \prod_{t_i, i \leq t} \left(1 - \frac{d_i}{n_i}\right). \quad (1)$$

With t_i a time when at least one event happened, d_i the number of events that happened at time t_i and n_i the individuals known to survive (have not yet had an event or been

censored) at time t_i. A plot of the Kaplan–Meier estimator is a series of declining horizontal steps which, with a large enough sample size, approaches the true survival function for that population. The value of the survival function between successive distinct sampled observations is assumed to be constant. An important advantage of the Kaplan–Meier curve is that the method can take into account some types of censored data, particularly right-censoring, which occurs if a patient withdraws from a study, is lost to follow-up, or is alive without event occurrence at last follow-up. On the plot, small vertical tick-marks indicate individual patients whose survival times have been right-censored. In order to generate a Kaplan–Meier estimator, at least two pieces of data are required for each patient (or each subject): the status at last observation (event occurrence or right-censored) and the time to event (or time to censoring).

Let σ_i be a random variable, which we think of as the time until an event of interest takes place. As indicated above, the goal is to estimate the survival function S underlying σ_i. This function is defined as

$$s(t) = prob(\sigma_i > t). \qquad (2)$$

where $\sigma_i = 0,1,\cdots,n$

Let $\sigma_1, \ldots, \sigma_n \geq 0$ be independent, identically distributed random variables, whose common distribution is that of σ: σ_i is the random time when some event i happened. The data available for estimating S is not $\sigma_i, i = 0,1, \ldots$., but the list of pairs $(\sigma_i, c_i) j = 1, \ldots, n$ where for $i \in [n] \coloneqq \{1,2,, \ldots, n\}$, $c_i \geq 0$, is a fixed, deterministic integer, the censoring time of event i and $\sigma_i = min(\sigma_i, c_i)$. In particular, the information available about the timing of event i is whether the event happened before the fixed time c_i and if so, then the actual time of the event is also available.

Cox proportional hazards model (Cox, 1972) was used to derive the parameter estimates for

drug users. Suppose the probability density function of the random variable T is given by $F(T)$. The probability distribution function of T is then given by

$$f(T) = P(t < T). \quad (3)$$

$$\int_0^T f(t)dtI. \quad (4)$$

The survivor function, $S(T)$, is the probability that an individual survives past T. This leads to

$$S(T) = P(T \geq t) \quad (5)$$

$$= 1 - F(T). \quad (6)$$

The hazard function is the probability that a subject experiences the event of interest (relapse) during small time interval given that the individual has survived up to the beginning of that interval. The mathematical expression for the hazard function is

$$h(T) = \lim_{\Delta T \to 0} \frac{P(T \leq t < (T+\Delta T) | T \leq t)}{\Delta T} \quad (7)$$

$$= \lim_{\Delta T \to 0} \frac{F(T+\Delta T) - F(T)}{\Delta T} \quad (9)$$

$$= \frac{f(T)}{S(T)}. \quad (10)$$

The cumulative hazard function $H(T)$ is the sum of the individual hazard rates from time zero to time *T*. The formula for the cumulative hazard function is

$$H(T) = \int_0^T h(u)du. \quad (11)$$

Thus, the hazard function is the derivative, or slope, of the cumulative hazard function. The cumulative hazard function is related to the cumulative survival function by the expression

$$S(T) = e^{-H(T)}. \quad (12)$$

$$H(T) = -\ln\big(S(T)\big). \quad (13)$$

We see that the distribution function, the hazard function, and the survival function are mathematically related. As a matter of convenience and practicality, the hazard function is used in the basic regression model. Cox (1972) expressed the relationship between the hazard rate and a set of covariates using the model

$$\ln[h(T)] = \ln[h_0(T)] + \sum_{i=1}^{p} w_i\beta_i. \quad (14)$$

$$h(T) = h_0(T)e^{\sum_{i=1}^{p} w_i\beta_i}. \quad (15)$$

where $w_1, w_2, w_3, \dots, w_p$ are covariates, $\beta_1, \beta_2, \beta_3, \dots, \beta_p$ are regression coefficients to be estimated, *T* is the elapsed time, and $H_0(T)$ is the baseline hazard rate when all covariates are equal to zero. Thus the linear form of the regression model is

$$ln\left[\frac{h(T)}{h_0(T)}\right] = \sum_{i=1}^{p} w_i\beta_i. \quad (16)$$

Taking the exponential of both sides of the above equation, we see that this is the ratio between the actual hazard rate and the baseline hazard rate, sometimes called the relative risk. This can be rearranged to give the model

$$\frac{h(T)}{h_0(T)} = exp\big(\sum_{i=1}^{p} w_i\beta_i\big) \quad (17)$$

$$= e^{w_1\beta_1 + w_2\beta_2 + \cdots + w_p\beta_p}. \quad (18)$$

The regression coefficients can thus be interpreted as the relative risk when the value of the covariate is increased by one unit. We note that unlike most regression models, this model does not include an intercept term. This is because if an intercept term were included, it would become part of $h_0(T)$. We also note that the method is called proportional hazards. An interesting attribute of this model is that we only need to use the ranks of the failure times to estimate the regression coefficients. The actual failure times are not used except to generate the ranks. Thus, we will achieve the same regression coefficient estimates regardless of whether we enter the time values in days, months, or years.

3.2.1 Cumulative Hazard

Under the proportional hazards regression model, the cumulative hazard is

$$H(T,W) = \int_0^T h(u,W)\,du \tag{19}$$

$$= \int_0^T h_0 e^{exp(\sum_{i=1}^p w_i\beta_i)} du \tag{20}$$

$$= exp\left(\sum_{i=1}^p w_i\beta_i\right) \int_0^T h_0(u)du \tag{21}$$

$$= H_0(T)exp\left(\sum_{i=1}^p w_i\beta_i\right). \tag{22}$$

Note that the survival time *T* is present in $H_0(T)$, but not in $exp\left(\sum_{i=1}^p w_i\beta_i\right)$. Hence, the cumulative hazard up to time *T* is represented in this model by a baseline cumulative hazard $H_0(T)$ which is adjusted by the covariates by multiplying by the factor $exp\left(\sum_{i=1}^p w_i\beta_i\right)$

3.2.2 Cumulative Survival

Under the proportional hazards regression model, the cumulative survival is

$$S(T,X) = \exp(-h(t,w)) \tag{23}$$

$$= exp(-H_0(T))exp\left(\sum_{i=1}^p w_i\beta_i\right) \tag{24}$$

$= S_0(T)exp\left(\sum_{i=1}^{p} w_i\beta_i\right).$ (25)

Note that the survival time *T* is present in $S_0(T)$, but not in $exp\left(\sum_{i=1}^{p} w_i\beta_i\right)$

The Cox model was defined as $h(t, x, \beta') = h_0(t)e^{\beta' w}$ (26)

where

$h(t, w, \beta')$ is the hazard function at time t with covariates $W = (w_1, w_2, \ldots., w_p)'$.

$h_0(t)$ is the arbitrary baseline hazard function that characterizes how the hazard function changes as a function of survival time.

$\beta' = \left(\beta_1, \beta_2, \ldots., \beta_p\right)'$ is a column vector of p regression parameters associated with explanatory variables.

$e^{\beta' x}$ characterizes how the hazard function changes as a function of subject covariates.

t is the failure time. For n subjects, each individual has its own hazard function of survival time. Then, the above model becomes

$h(t, W_i, \beta') = h_0(t)ex\,p\left(\beta_1 W_{i1} + \beta_2 W_{i2} + \cdots + \beta_p W_{ip}\right), i = 1,2, \cdots, n$ (27)

where:

n is total number of observations in the study.

$W_i = (W_{i1}, W_{i2}, \ldots., W_{ip})'$ is a column vector of measured covariates for the i^{th} individual (patient) which are assumed to affect the survival probability.

3.2.3 Estimation of Parameters in Cox model

The regression coefficients in the proportional hazards Cox model, which are the unknown parameters in the model, can be estimated using the method of maximum likelihood. In Cox proportional hazards model we can estimate the vector of parameters β without having any assumptions about the baseline hazard $h_0(t)$ .Consider *n*

independent subjects, the data that we need for the Cox proportional hazard model is represented by triplet

$(t_i, \sigma_i, W_i), i = 1,2,3, \cdots, n.$

where

t_i is the survival time for the i[th] subject, σ_i is an indicator of censoring for the i^{th} subject given by 0 for censored and 1 for recovery and W_i is a vector of covariates for individual $i\left(W_{i1}, W_{i2}, \dots, W_{ip}\right)$.The full maximum likelihood function is defined as

$$L(\beta) = \prod_{i=1}^{n} h(t_i, W_i, \beta)^{\sigma_1} S(t_i, W_i, \beta) \quad (28)$$

where $h(t_i, W_i, \beta') = h_0(t_i)e^{\beta' w_{i1}}$ is the hazard function for individual i. and

$S(t_i, W_i, \beta') = S_0(t_i)e^{\beta' w_{i1}}$ is the survival function for individual *i*.

Two tests are available for testing the significance of one or more independent variables in a regression: the likelihood ratio test and the Wald test. Simulation studies usually show that the likelihood ratio test performs better than the Wald test. However, the Wald test is still used to test the significance of individual regression coefficients because of its ease of calculation.

3.2.4 Likelihood Ratio and Deviance

The *Likelihood Ratio* test statistic is -2 times the difference between the log likelihoods of two models, one of which is a subset of the other. The distribution of the LR statistic is closely approximated by the chi-square distribution for large sample sizes. The degrees of freedom (DF) of the approximating chi-square distribution is equal to the difference in the number of regression coefficients in the two models. The test is named as a ratio rather than a difference since the difference between two log likelihoods is equal to the log of the ratio of the two likelihoods. That is, if *L* full is the log likelihood

of the full model and *L* subset is the log likelihood of a subset of the full model, the likelihood ratio is defined as

$$LR = -2\left[L_{subset} - L_{full}\right] \quad (29)$$

$$= -2\left[ln\left(\frac{l_{subset}}{l_{full}}\right)\right]. \quad (30)$$

We note that the -2 adjusts *LR* so the chi-square distribution can be used to approximate its distribution. The likelihood ratio test is the test of choice in Cox regression. Various simulation studies have shown that it is more accurate than the Wald test in situations with small to moderate sample sizes. In large samples, it performs about the same. Unfortunately, the likelihood ratio test requires more calculations than the Wald test, since it requires the fitting of two maximum-likelihood models.

3.2.5 Deviance

When the full model in the likelihood ratio test statistic is the saturated model, *LR* is referred to as the deviance. A saturated model is one which includes all possible terms (including interactions) so that the predicted values from the model equal the original data. The formula for the deviance is

$$D = -2[L_{reduced} - L_{saturated}]. \quad (31)$$

The deviance in Cox regression is analogous to the residual sum of squares in multiple regression. In fact, when the deviance is calculated in multiple regression, it is equal to the sum of the squared residuals. The change in deviance, ΔD, due to excluding (or including) one or more variables is used in Cox regression just as the partial *F* test is used in multiple regression. Many texts use the letter *G* to represent ΔD. Instead of using the *F* distribution, the distribution of the change in deviance is approximated by the chi-square distribution. Note that since the log likelihood for the saturated model is common to both deviance values, ΔD can be calculated without actually fitting the saturated model. This fact becomes very important during subset selection. The formula

for ΔD for testing the significance of the regression coefficient(s) associated with the independent variable $X1$ is

$$\Delta D_{without\ X_1 - D_{with\ X_1}} \quad (32)$$

$$= -2[without\ X_1 - L_{saturated}] + 2[with X_1 - L_{saturated}] \quad (33)$$

$$= -2\left[without\ X_1 - D_{with\ X_1}\right]. \quad (34)$$

We note that this formula looks identical to the likelihood ratio statistic. Because of the similarity between the change in deviance test and the likelihood ratio test, their names are often used interchangeably.

3.2.6 Wald Test

The Wald test will be familiar to those who use multiple regression. In multiple regression, the common *t*-test for testing the significance of a particular regression coefficient is a Wald test. In Cox regression, the Wald test is calculated in the same manner. The formula for the Wald statistic is

$$z_j = \frac{b_j}{s_{b_j}}. \quad (35)$$

where s_{b_j} is an estimate of the standard error of *bj* provided by the square root of the corresponding diagonal element of the covariance matrix,

$$V(\beta) = I^{-1}. \quad (36)$$

With large sample sizes, the distribution of *z j* is closely approximated by the normal distribution. With small and moderate sample sizes, the normal approximation is described as "adequate." The Wald test is used to test the statistical significance of individual regression coefficients.

3.2.7 Confidence Intervals

Confidence intervals for the regression coefficients are based on the Wald statistics. The formula for the limits of a 100(1−α)% two-sided confidence interval is

$$b_j \pm |z_{\alpha/2}| s_{b_j} \quad (37)$$

Hosmer and Lemeshow (1999) indicate that at the time of the writing of their book, there is no single, easy to interpret measure in Cox regression that is analogous to R^2 in multiple regression. They indicate that if such a measure "must be calculated" they would use

$$R_p^2 = 1 - exp\left[\frac{2}{n}\left(L_0 - L_p\right)\right]. \quad (38)$$

where $L0$ is the log likelihood of the model with no covariates, n is the number of observations (censored or not), and Lp is the log likelihood of the model that includes the covariates.

3.2.8 Subset Selection

Subset selection refers to the task of finding a small subset of the available regress or variables that does a good job of predicting the dependent variable. Because Cox regression must be solved iteratively, the task of finding the best subset can be time consuming. Hence, techniques which look at all possible combinations of the regressor variables are not feasible. Instead, algorithms that add or remove a variable at each step must be used. Two such searching algorithms are available in this module: forward selection and forward selection with switching.

3.3 Sensitivity analysis of model parameters

Sensitivity analysis was performed to establish the parameters that had significant influence on the model. Akaike information criteria was used to test sensitivity of the model parameters. The Akaike information criterion (AIC) is an estimator of the relative quality of statistical models for a given set of data. Given a collection of models for the data, AIC estimates the quality of each model, relative to each of the other

models. Thus, AIC provides a means for model selection. The values of the parameters of a model can be estimated by choosing for them the values which have the maximal likelihood relative to the observed covariance matrix. Analytic models with many parameters will, in general, have a larger likelihood than the models with few parameters. In the extreme case in which there are just as many parameters the equations which connect these values with the parameters will have a solution in which all the error terms have the value zero. In this case the prediction concerning the covariance matrix that the model yields will be identical with the covariance matrix which has been observed.

A model like this is a saturated model. Also more generally, a model is called saturated if it has so many parameters that it will fit the evidence perfectly, no matter what the evidence is like. When AIC is used for making a choice between two models M_1 and M_2 on the basis of a sample of some fixed size *N*, it will produce the methodological recommendation that the model M_1 should be preferred to the model M_2 if

$$AIC(M_1) < AIC(M_2). \quad (39)$$

The Akaike information criteria is written as

$$AIC(\hat{p}) = -log\hat{p} + \hat{p}. \quad (40)$$

where $\hat{p}$ is the number of free model parameters. Using AIC the model that solved

$$\hat{k} = arg\ min = AIC(\hat{p}). \quad (41)$$

where $\hat{k}$ is the number of model parameters, was considered optimal. In most settings in which residuals are studied, the dependent variable is predicted using a model based

on the independent variables. Residual analysis of the model was used to help in model selection. The formula for residual analysis is simplified if we use the substitution

$$\theta_r = exp\left(\sum_{i=1}^{p} x_{ir}\beta_i\right). \quad (42)$$

3.3.1 Cox-Snell Residuals

The residuals describe under Cox and Snell enable the study to determine if the model is a good fit or not.

The mathematical form of the residuals is given as

$$z_t = B_{\alpha 0}(T_t)\theta_t. \quad (43)$$

where there *b*'s are the estimated regression coefficients and *B*(*T*) 0is an estimate obtained by Breslow method (Breslow,1975) after cumulating the baseline hazard function. Therefore the estimate can be given as

$$B_{\alpha 0}(T_t) = \sum_{T_i \le T_t}\left[\sum_{j \le \in_{R_{Ti}}} \frac{m_i}{\theta_j}\right]. \quad (44)$$

The Cox-Snell residuals were the earliest to be studied in literature of Cox Proportional Hazards estimation. However other types of residual such as martingal residual and Sconfield residuals have since been studied.

3.3.3 Martingale Residuals

These residuals are effectively used to determine if a model is a better fit mainly in multivariate regression. The best model need not have the smallest sum of squared martingale residuals. Martingale residuals follow the unit exponential distribution. These residuals are analyzed to determine how close they are to the exponential distribution, where a lack of exponetiality would indicate a lack of fit. Another diagnostic tool is a plot of the residuals versus the fitted values. Here again, the martingale residuals cannot be used for this purpose since they are negatively correlated

with the fitted values. They have two main uses. First, they can be used to find outliers— individuals who are poorly fit by the model. Second, martingale residuals can be used to determine the functional form of each of the covariates in the model.

3.3.4 Outliers

The martingale residuals are defined as

$$M_t = C_t - r_t. \quad (45)$$

where C_t is one if there is a failure at time T_t and zero otherwise. The martingale residual measures the difference between whether an individual experiences the event of interest and the expected number of events based on the model. The maximum value of the residual is one and the minimum possible value is negative infinity. Thus, the residual is highly skewed. A large negative martingale residual indicates a high risk individual who still had a long survival time.

Martingale residuals can be used to determine the functional form of a covariate. To do this, Martingale residuals are generated from a model without the covariates. Then a plot these residuals against the value of the covariate is made. For large datasets, this may be a time consuming process. Therneau and Grambsch (2000) suggest that the martingale residuals from a model with no covariates be plotted against each of the covariates. These plots will reveal the appropriate functional form of the covariates in the model so long as the covariates are not highly correlated among themselves.

3.3.5 Deviance Residuals

Deviance residuals are used to search for outliers. The deviance residuals are defined as

$$DEV_t = sign(M_t)\sqrt{-2[M_t + c_t ln(c_t - M_t)]}. \quad (46)$$

or zero when M_t is zero. These residuals are plotted against the risk scores given by

$exp\left(\sum_{i=1}^{p} w_{ir}\beta_i\right)$. (47)

When there is slight to moderate censoring, large absolute values in these residuals point to potential outliers. When there is heavy censoring, there will be a large number of residuals near zero. However, large absolute values will still indicate outliers.

3.3.6 Schoenfeld's Residuals

A set of p Schoenfeld residuals is defined for each non-censored individual. The residual is missing when the individual is censored. The Schoenfeld residuals are defined as follows

$$r_{it} = c_t\left[x_{it} - \frac{\sum_{r\in R_t} x_{ir}\theta_r}{\sum_{r\in R_t}\theta_r}\right] \quad (48)$$

$$= c_t\left[x_{it} - \sum_{r\in R_t} x_{ir} w_r\right]. \quad (49)$$

where

$$w_r = \frac{\sum_{r\in R_t} x_{ir}\theta_r}{\sum_{r\in R_t}\theta_r}. \quad (50)$$

Thus this residual is the difference between the actual value of the covariate and a weighted average where the weights are determined from the risk scores. These residuals are used to estimate the influence of an observation on each of the regression coefficients. Plots of these quantities against the row number or against the corresponding covariate values are used to study these residuals. Hosmer and Lemeshow (1999) and Therneau and Grambsch (2000) suggest that scaling the Schoenfeld residuals by an estimate of their variance gives quantities with greater diagnostic ability. Hosmer and Lemeshow (1999) use the covariance matrix of the regression coefficients to perform the scaling. The scaled Schoenfeld residuals are defined as follows

$$r_{kt}^{*} = m\sum_{i=1}^{p} V_{ik} r_{it}. \quad (51)$$

where *m* is the total number of relapses in the dataset and *V* is the estimated covariance matrix of the regression coefficients. These residuals are plotted against time to validate the proportional hazards assumption. If the proportional hazards assumption holds, the residuals will fall randomly around a horizontal line centered at zero. If the proportional hazards assumption does not hold, a trend will be apparent in the plot.

Least absolute shrinkage and selection operator (LASSO) was also used to perform variable selection and regularization in order to enhance sensitivity of the model. LASSO coefficients that were set at zero after LASSO regression were dropped from the model since they were not sensitive to the model. Smoothly clipped absolute deviation (SCAD) was plotted to indicate the number of variables that were sensitive to the model. DFBETA statistic was also used to determine if there were unusual observations that if removing the observations could substantially change the estimate of the coefficients. DFBETA means diagnostics for influential Betas. It measures how much impact each observation has on a particular predictor. The DFBETA for a predictor and for a particular observation is the difference between the regression coefficient calculated for all the data and the regression coefficient calculated with the observation deleted, scaled by the standard error calculated with the observation deleted.

3.4 Recovery rate of drug users under medication

Kaplan-Meier method was used to determine the observed survival recovery rates of drug users over time. Kaplan-Meier provides for calculating the proportion surviving to each point in time when relapse occurs. Thus it was used to measure the length of time the subjects had taken for recovery. The Kaplan-Meier (KM) estimator of the survival function (Kaplan and Meier ,1958), also called the product limit estimator, was used to estimate the survival and hazard functions.

3.4.1 The Hazard function $h(t)$

The hazard function $h(t) \geq 0$, was given as

$$h(t)$$

$$= \lim_{\Delta t \to 0} \frac{p(an\ individual\ fails\ in\ the\ time\ interval(t, t+\Delta t)\ given\ survives\ until\ time\ t}{\Delta t}$$

$$= \lim_{\Delta t \to 0} \frac{p\{t \leq T \leq t+\Delta t | t \geq t\}}{\Delta t}. \qquad (51)$$

Relating to equation (51) and applying the theory of conditional probability, the hazard function was expressed as shown in equation (52)

$$h(t) = \frac{f(t)}{s(t)} = \frac{-d}{dt} lns(t). \qquad (52)$$

The corresponding cumulative hazard function $H(t)$ was defined as

$$H(t) = \int_0^t h(u)du = -lns(t)$$

Thus $S(t) = exp(-H(t))\ and\ f(t) = h(t)s(t).$ *(53)*

3.4.2 Survivor function S(*t*)
The survivor function, *S*(*t*) was written as

$$S\ (t) = P\ (T\ \geq t) = 1 - F\ (t), t\ \geq 0\ . \qquad (54)$$

The relationship between *f* (*t*) and *S* (*t*) was derived as $f(t) = \frac{d}{dt}F(t) =$

$$\frac{d}{dt}\big(1 - s(t)\big) = \frac{-d}{dt}s(t), t \geq 0\ . \qquad (55)$$

t ranges from 0 to infinity. Survivor functions have the characteristics that:

i. They are non-increasing

ii. At time *t* = 0, *S*(*t*) = *S*(0) = 1; which means, initially, since no one has experienced the event yet, the probability of surviving past time 0 is one and

iii. At time t→∞, $S(t) = S(\infty) \rightarrow 0$; that is, theoretically, if the study period increased without limit, eventually nobody would survive, so the survivor curve must eventually converge to zero.

3.5 Log Rank test for significance of gender differences in drug abuse

The log rank test, also called the Cox-Mantel test, is the most widely used test statistic. It was used to compare differences in survival rates based on the significant predictors of drug use. The standard test for an association between the row and column factors for *J* independent 2 x 2 tables is the Mantel-Haenzel statistic. This statistic is constructed by subtracting the expected number of failures in group subjects from the observed failures, and then standardizing this difference by the square root of the variance:

$$Z_{M-H} = \frac{\sum_j \left(d_{1j} - E\left(d_{1j}\right)\right)}{\sqrt{\sum_j \text{var}\left(d_{1j}\right)}} \approx N(0,1).$$

The square of this statistic $Q_{M-H} = Z^2_{M-H}$ has an approximate chi-square distribution with one degree of freedom and is often reported in practice.

The log rank statistic was used to determine if there were significant differences in survival rate of drug abuse based on the predictors of the model. A survival rate curve based on gender was fitted and the significant differences in the survival determined using the log rank test. If the probability value of the log rank statistic was less than 0.05 then it was an indication that the model parameters were significantly different.

CHAPTER FOUR

RESULTS AND DISCUSSIONS

4.0 Introduction

This chapter presents the findings of the study. The chapter begins by examining the descriptive survival characteristics of the subjects. The significance of age, gender, job status, residence, type of drug used, mode of drug used and marital status in contributing to survival rate of drug users is also examined. The chapter also looks at the observed and relative survival rates as well as the survival probability using a variety of Kaplan-Meier and Cox models. R statistical software is used in the analysis.

The study conducted a follow up on a cohort of drug users who had enrolled in the beginning of July 2013 to the end of the study period, that is, June 2015. Information on these subjects was obtained from referring to the subjects' medical records for the entire period that they were in or attended the hospital. Factors such as age, marital status, employment status, residence, type of drug abused, mode of taking the drug and gender of the subjects were studied.

4.0.1 Prevalence of drug abuse

The main drugs of the study were alcohol, cannabis, cocaine and multiple drug and substance use. An estimate of the percentage of alcohol users that reported for treatment during the period of study (between July 2013 and June 2015.) is illustrated by table 4.0.1.

Table 4.0.1 Percentage of alcohol users for the period July 2013 to June 2015

Year	July13	Aug13	Sep13	Oct13	Nov13	Dec13
2013	16.6	19.3	27.6	57.1	40.2	32.7
	Jan14	Feb14	March14	April14	May14	June14
2014	26.2	25.7	27.7	17.5	38.4	40.5
	July14	Aug14	Sep14	Oct14	Nov14	Dec14
	6.1	8.6	26.0	34.2	36.0	47.1
	Jan15	Feb15	March15	April15	May15	June15
2015	43.2	43.1	46.7	45.5	46.9	47.0

Table 4.0.1 shows that there was a gradual yearly increase in the number of alcohol users. The number of alcohol users was highest in the year 2015.

Figure 4.0.1 below shows the proportion of alcohol users for the period between July 2013 and June 2015, the period of our study. From the figure there is a gradual increase in the number of alcohol users seeking treatment. This can be attributed to the increased number of youths who are influenced into alcohol use. Among the drugs of abuse, alcohol is usually considered as the primary entry drug into drug abuse. This is therefore an indication that the number of alcohol users would be on the rise.

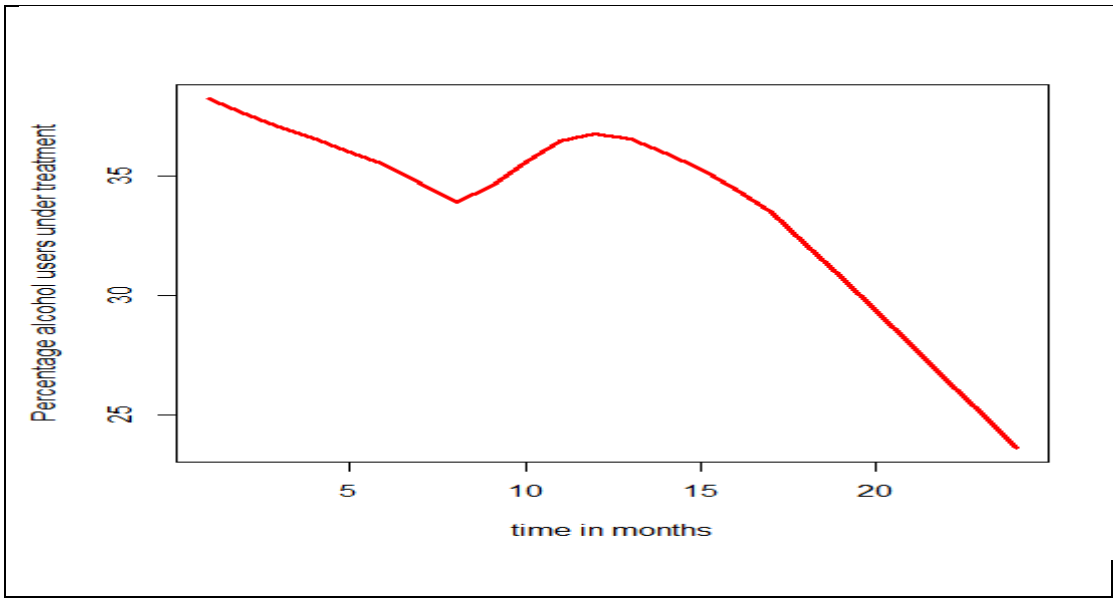

Figure 4.0.1 . Percentage of alcohol users for the period July 2013 to June 2015

Table 4.0.2 below shows a gradual yearly decrease in the number of cocaine users. The number of cocaine users was highest in the year 2014.

Table 4.0.2. Percentage of alcohol users for the period July 2013 to June 2015

year	July13	Aug13	Sep13	Oct13	Nov13	Dec13
2013	41.1	38.6	6.1	27.1	44.9	36.6
	Jan14	Feb14	March14	April14	May14	June14
2014	34.4	42.8	35.9	418	30.2	27.9
	July14	Aug14	Sep14	Oct14	Nov14	Dec14
	55.6	46.2	27.4	35.7	20.7	32.9
	Jan15	Feb15	March15	April15	May15	June15
2015	26.2	31.4	18.0	36.1	26.8	26.7

Figure 4.0.2 below shows the proportion of alcohol users for the period between July 2013 and June 2015, the period of our study. From the figure there is a gradual decrease in the number of cocaine users seeking treatment.

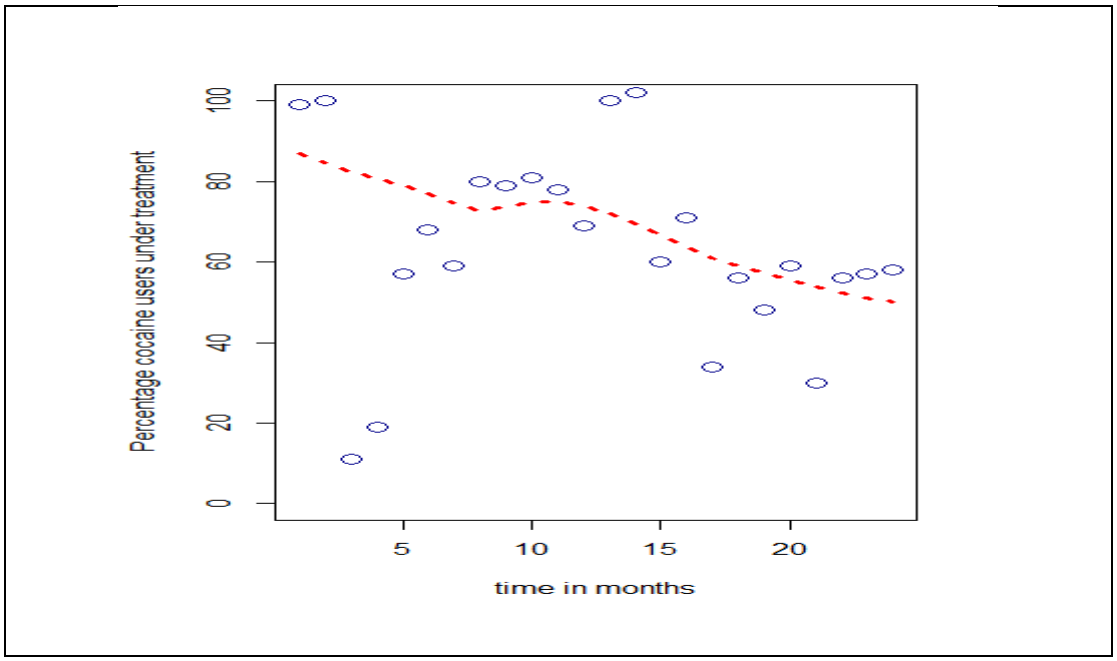

Figure 4.0.2 . Percentage of cocaine users for the period July 2013 to June 2015

Although the data is presented in terms of proportions and not actual populations, the decline in the population seeking treatment for cocaine abuse could be attributed to the fact that some cocaine drug users may have found refuge in other substances of abuse such as bhang, alcohol, and methamphetamine or use it in combination with other psychoactive stimulants. Victims of drug/substance abuse, could as a result, be experiencing greater effects of other drugs as compared to alcohol, hence increased prevalence of other drugs. The projected prevalence of cocaine abuse is shown to be on the decline as shown in figure 4.0.3.

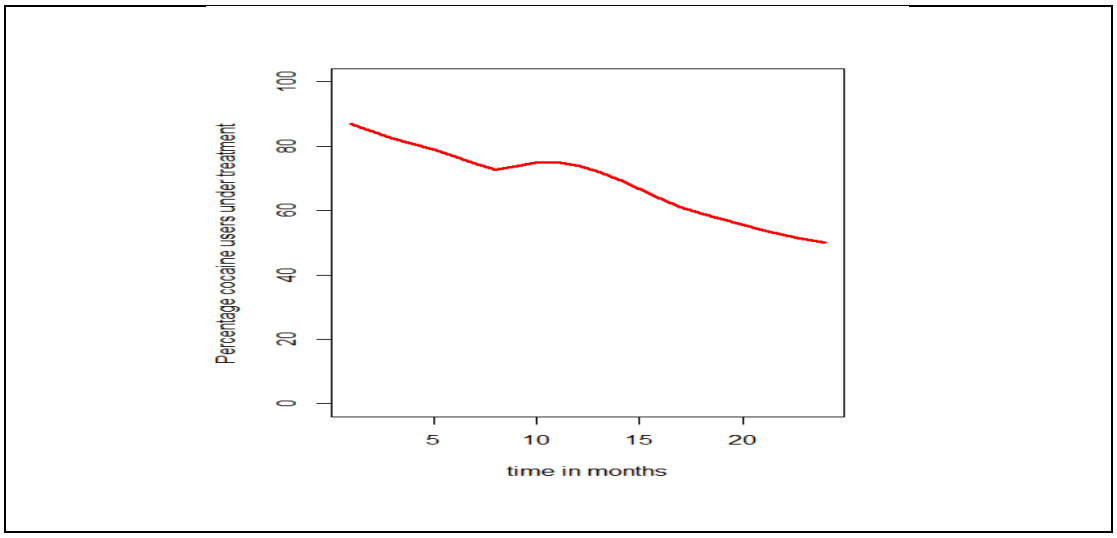

Figure 4.0.3. Percentage of cocaine users for the period July 2013 to June 2015

Table 4.0.3 . Percentage of multiple drug users for the period July 2013 to June 2015

Year	July13	Aug13	Sep13	Oct13	Nov13	Dec13
2013	42.3	42.1	66.3	15.7	15.0	30.6
	Jan14	Feb14	March14	April14	May14	June14
2014	39.5	31.6	36.4	40.7	31.4	31.6
	July14	Aug14	Sep14	Oct14	Nov14	Dec14
	38.3	45.2	46.6	30.2	43.3	20.0
	Jan15	Feb15	March15	April15	May15	June15
2015	30.6	25.5	35.3	19.4	26.3	26.3

The percentage of drug users in the year 2013 appears to be higher compared to the subsequent years of our study. However during the year 2015 there was a gradual decline on the population of multiple drug users seeking treatment.

Comparison of the population values in Table 4.0.3 reveal that in the year 2013, the population of individuals under treatment for multiple substance users was lower than that for persons under treatment for alcohol addiction. Similarly, in reference to the approximation curve in Figure 5, we observe that there were approximately 40% individuals under treatment for abuse of both alcohol and methamphetamine. Since most substance abuse treatment centers do not cater for individuals under addiction for multiple substances abuse, it is vital to observe that such population does in deed exist, and that they should not be ignored if the fight against drug abuse is to be successful. Nevertheless, treatment for multiple substance abuse is an expensive activity and will obviously require more resources as compared to those used in treatment of addicts of single substances.

The data showing the demand for treatment as a result of multiple drug abuse is shown in Table 4.0.3. Just like alcohol, the poly drug data was similarly collected July 2013 to June 2015. Figure 4.0.4 reveals that the proportion of individuals seeking treatment for poly drug abuse has been on a steady decline.

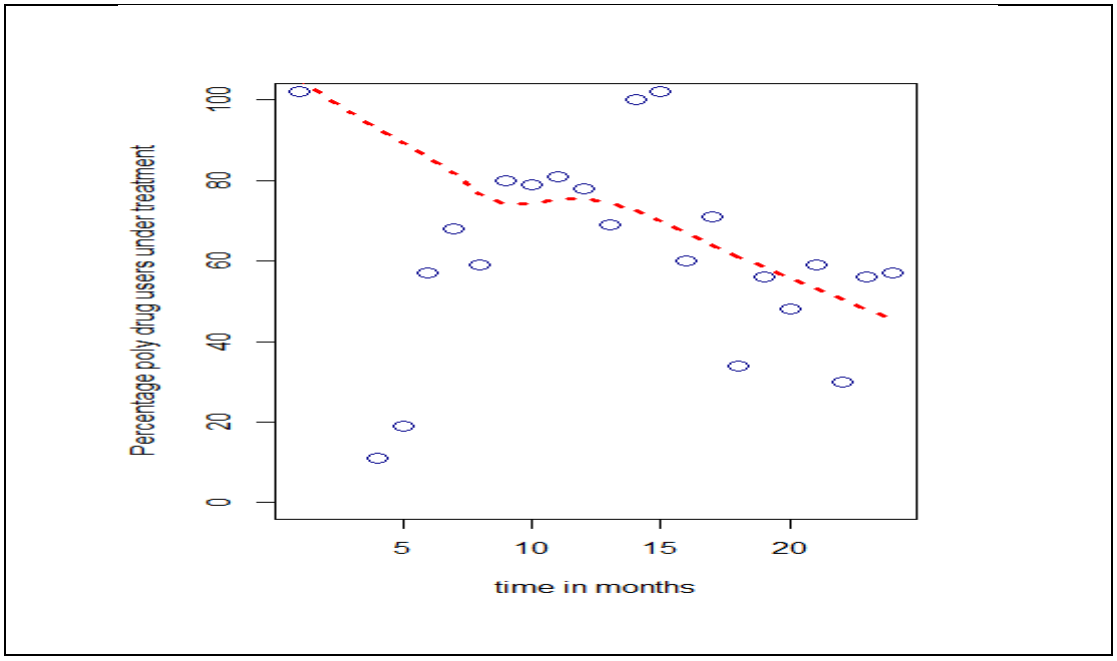

Figure 4.0.4 . Percentage of multiple drug users for the period between 2013 through 2015

Although the data is presented in terms of proportions and not actual populations, the decline in the population seeking treatment for poly drug abuse could be attributed to the fact that some poly drug users may have found refuge in other substances of abuse such as bhang, alcohol, cocaine and methamphetamine or uses it in combination with other psychoactive stimulants. Victims of drug/substance abuse, could as a result, be experiencing greater effects of other drugs as compared to poly drugs, hence increased prevalence of other drugs. The projected prevalence of alcohol abuse is shown to be on the decline, see Figure 4.0.5

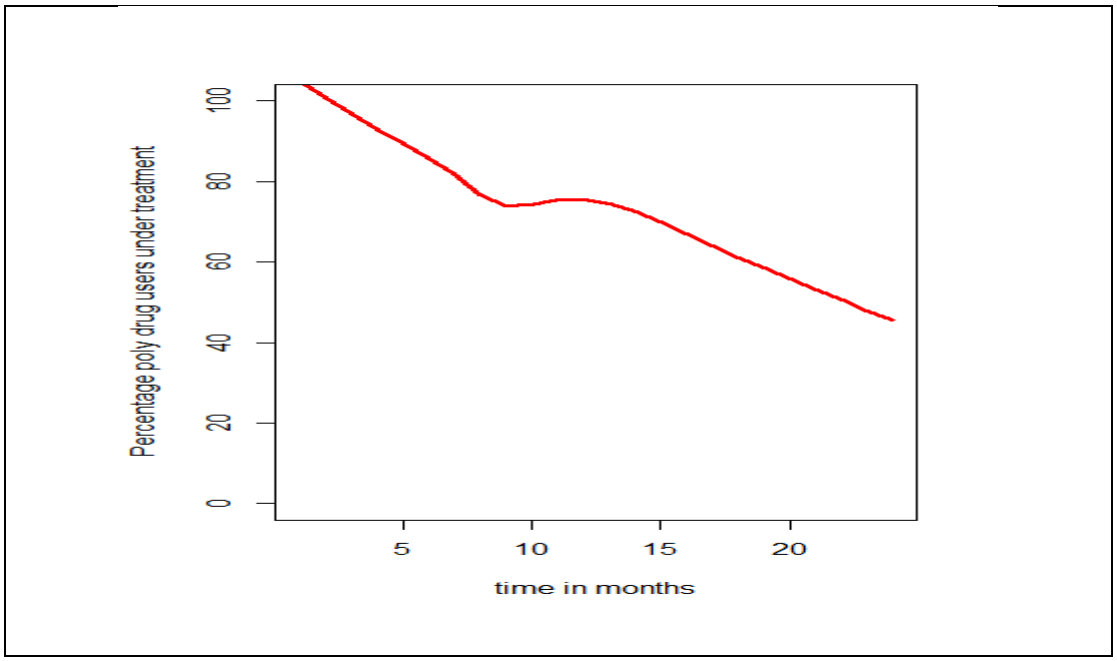

Figure 4.0.5 . Percentage of multiple drug users for the period between 2013 through 2015

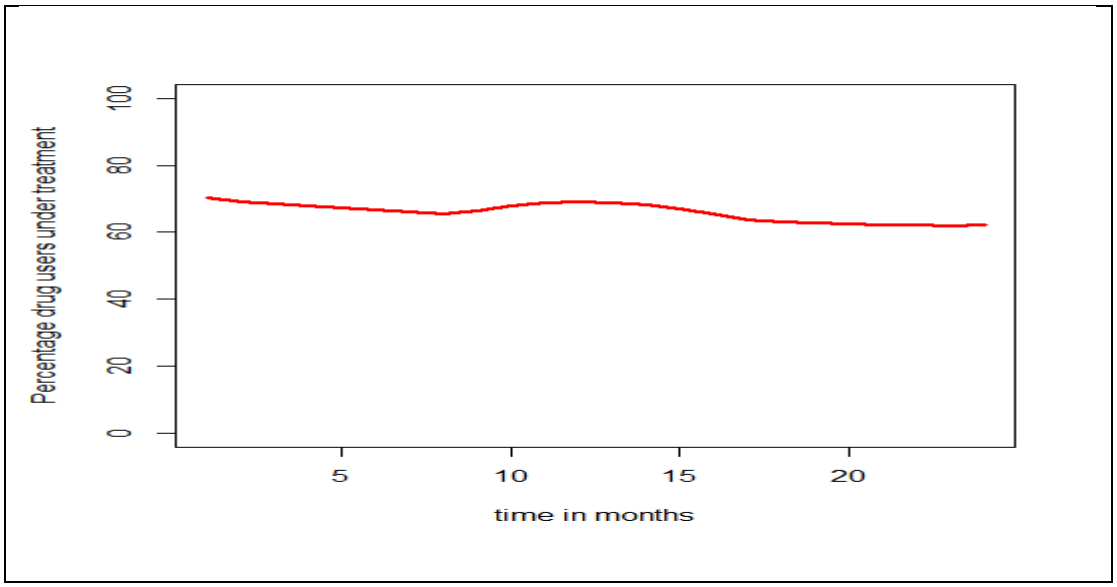

Figure 4.0.6. Percentage of average population of drug users for the period between 2013 through 2015

A combination of drug users is then generated. The red line shows the average population who use more than one illicit drug who are currently on treatment. There is gradual decline in the population. This shows that treatment is essential for curbing illicit use of drugs.

We then establish the association between inpatient drug users and outpatient drug users in terms of their survival rate and prevalence rate. The results are shown in the figure 4.0.7 below.

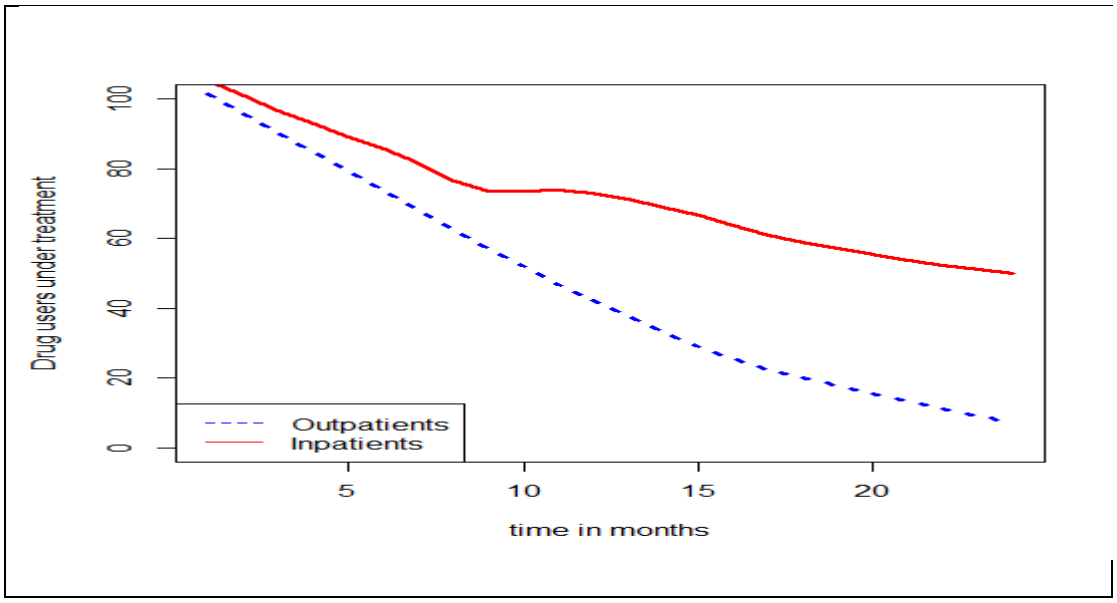

Figure 4.0.7: comparison of inpatient and outpatients duration of treatment

Figure 4.0.7 above shows that the inpatients are recovering faster from drug abuse compared to the outpatients. Therefore the inpatients have a higher survival rate from drug abuse. This could be attributed to the fact that in patient drug users are out of touch with other drug users who are currently not on treatment and also they are out of touch with their peers. The other consideration of our study was the relationship between patients who are on treatment with controls and those non treatment without controls. This is shown in figure 4.0.8 below.

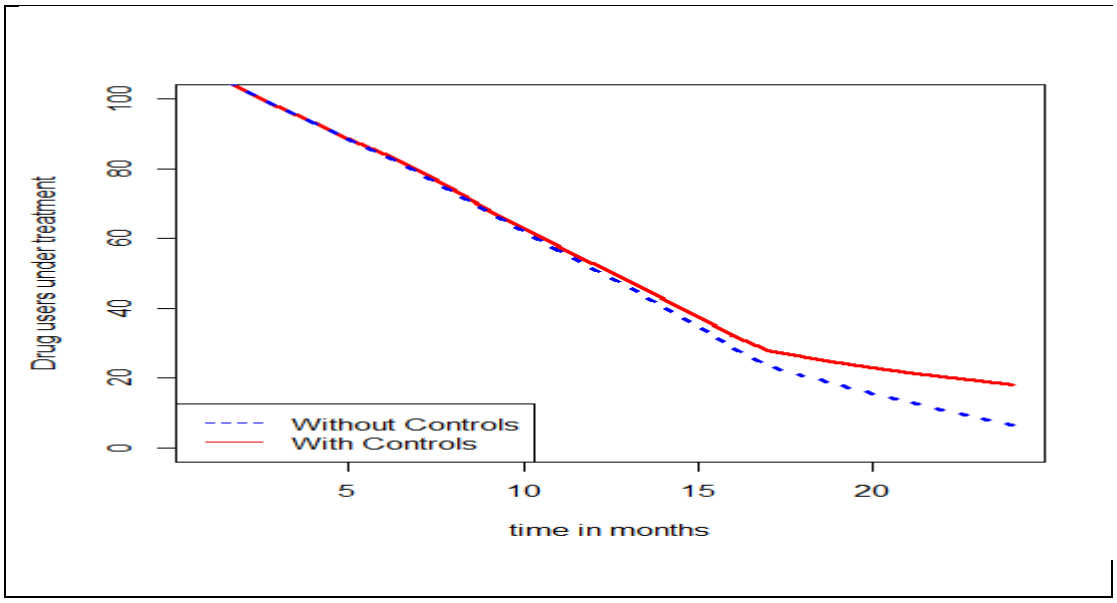

Figure 4.0.8: Comparison of outpatients' duration of treatment with and without controls

The population of subjects undergoing treatment from drug abuse is estimated as shown in figure 4.0.8 .we observe that most of the inpatients attend drug abuse control programs such as peer counselling and motivational programs from nurses and previous subjects who had been in the hospitals but have recovered. We also have anti-drug use groups who visit the hospitals to encourage the current patients to stop drug abuse. With this view the patients who are under treatment control programs have a higher survival rate. Our results are also consistent with the clinical results which have shown a strong link between the two substances of abuse, as was shown in figure 4.0.8. This trend is further consistent with the growing popularity of multiple drug use in the last few years. Therefore, increased intervention programs and rehabilitation of drug use subjects contributes to higher survival rate.

4.1 Survival rate model for drug users

As in the case for a linear or generalized model, it was desirable to determine whether a fitted Cox regression model adequately described the data. Three kinds of diagnostics that were considered were, violation of the assumption of proportional hazards, effect

of influential observations and nonlinearity in the relationship between the log hazard and the covariates.

4.1.1 Assessment of the proportional hazards assumption

The assumption of proportional hazards states that the hazard ratios are constant overtime. That is, the risk of failure must be the same no matter how long subjects had been followed. In order to test this assumption, the Cox model was employed and a graphical display used to substantiate the same. Thus, in the study, using a test based on the interaction of the covariates with the log of time and also using the plot of the scaled Schoenfeld residuals the assumption was used to see if the assumption of proportionality was violated or not. Therefore, one of the statistical tests for proportional hazards assumption was to generate time varying covariates by creating interactions of the predictors and a function of survival times, usually covariate times the log of time, and including them in the model. If any of the time dependent covariates were significant then those predictors did not exhibit a proportional effect over the study period. That is the proportional hazard assumption failed to hold. Table 4.5.1 shows the Wald chi-square value and corresponding P-values for each covariate. Since the P-value of the Wald test was greater than 0.05 for all covariates, there was no evidence against the proportionality of hazard assumption. The global test also gave a p value that was not significant suggesting that the assumption had not been violated (p=0.230). In addition, the assumption of proportionality was also assessed graphically by plotting the scaled Schoenfeld residuals of each covariate against log time.

All interactions of covariates with the logarithm of survival times were modeled together with the main effects and Wald statistic used to test the significance of the interaction terms at 5% level of significance. The result of the test indicated that none of the coefficients of interaction terms were significant at 5% level (age, P=0.22>0.05,

job status=0.397>0.05, Marital Status, P=0.192>0.05, Gender, P=0.221>0.05). The results revealed the non-significance of time-dependent covariates. On the other hand, there were no covariates which showed a trend or pattern with the time that indicated the hazard ratios would be constant over the study period. This showed that there was no sufficient evidence to reject the null hypothesis that the coefficients of the time varying covariates (interaction terms) were zero. Thus there was not enough evidence against proportionality assumption to hold. Furthermore, plotting the scaled Schoenfeld residuals of each covariate against log time was used to check whether the assumption of proportional hazards was violated or not. This plot indicated that the residuals were random and the curve was smooth and almost had zero slope.

Table 4.1.1: Assessment of proportional hazards assumption

Covariate	Rho	Chisq	Probability value
Age	0.206	1.508	0.22
Job status	0.113	0.718	0.397
Marital status	-0.176	1.705	0.192
gender	0.214	2.783	0.221
Global	NA	4.313	0.230

The results presented in table 4.1.1 suggested that the plots supported proportionality assumption to hold.

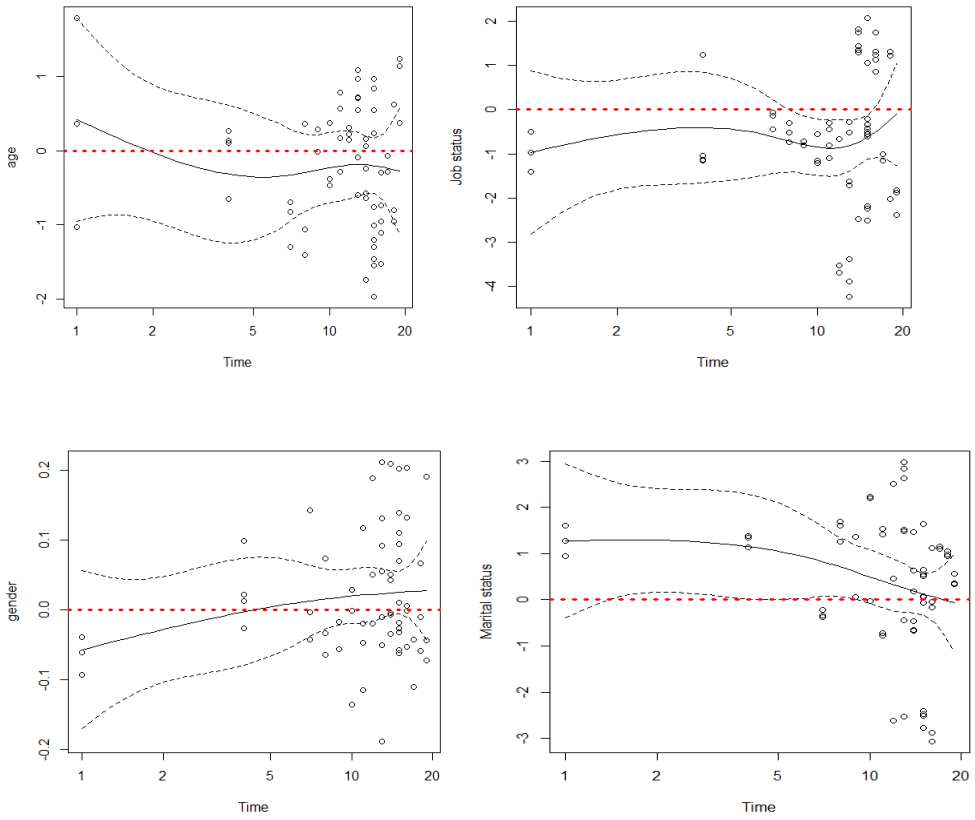

Figure 4.1.1. Assessment of proportional hazards assumption

Figures 4.1.1 showed that the schonifield residuals lie between -1 and +1 which suggested that the assumption of linearity of cox regression model was met. Therefore it was appropriate to use the model for the study. The observations were scattered around the zero line and in the range of -1 to +1.The results of the study showed that there were no observations exceeding the cut off of 1. This suggested there were no observations that needed to be dropped. Cut off of 1 means observation could be overly influential on the estimated coefficient.

4.1.2 Assessment of Influential Observations

The next diagnostic check the study carried out was to determine if there were any observations that had undue influence on the estimates of the Cox regression parameters, or had an unexpected influence on the fit of the model. Dfbeta statistic was used for measuring the influence of the i^{th} observation, defined as the one-step

approximation to the difference in the MLE of the regression parameter vector with i^{th} observation and the MLE of the regression parameter vector without the i^{th} observation. The observations were scattered around the zero line and in the range of -1 to +1.The results of the study showed that there were no observations exceeding the cut off of 1. Figure 4.1.2 suggested there were no observations that needed to be dropped.

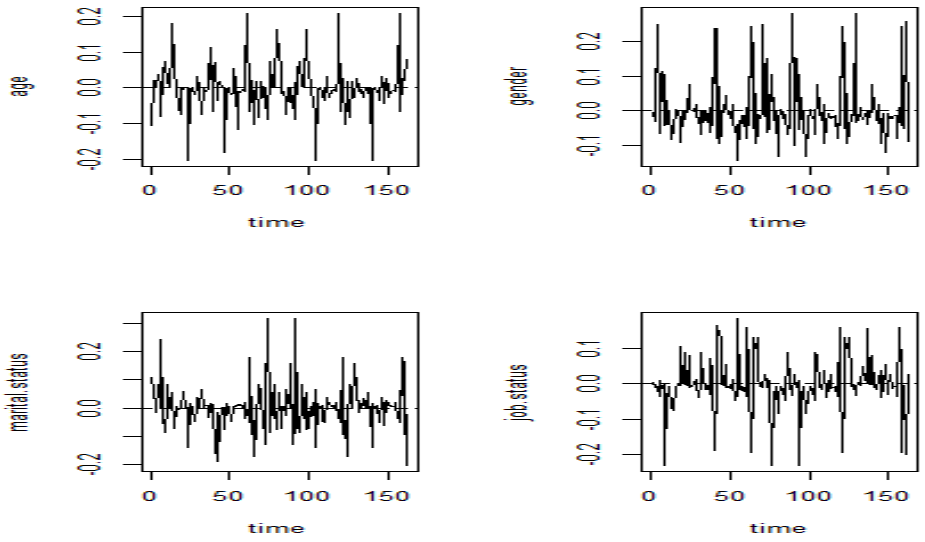

Figure 4.1.2. Assessment of Influential Observations

4.1.3 Assessment of linearity of covariates in the model

The study sought to further check whether the correct functional form of the continuous covariate held in the model proposed to describe the data. The hypothesis of interest was that the effect of the covariate was linear in the log hazard. Graphical technique of the plots of the martingale residuals was used to assess the linearity of relation of continuous covariate in which the correct functional form was understood. The study obtained plots shown in Figure 4.1.3.

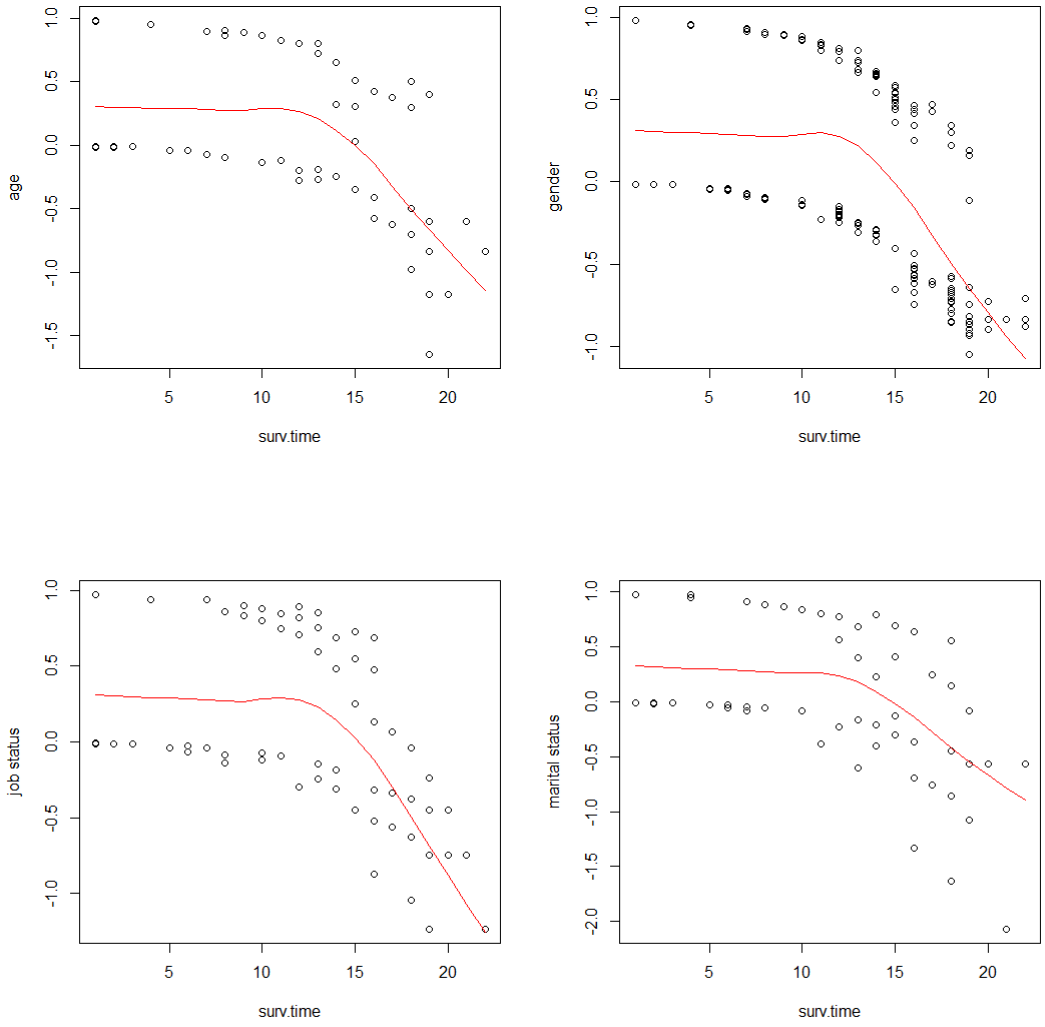

Figure 4.1.3 Assessment of linearity of covariates in the model

The figures show the plot of martingale residuals versus each covariate. For the covariates, age, gender, job status and marital status, the plots did not show systematic patterns or trend and the resulting smoothed plots were approximately between -1 and +1.

Therefore the plots of martingale residual confirmed that age, gender, job status and marital status of a patient had an approximate linear relationship with the survival time. Therefore the study concluded that the model containing covariates age, gender, job status and marital status was an appropriate model to describe the data, since it had passed all tests of fitting model. In addition, results of the likelihood ratio, score and

Wald tests for model goodness of fit displayed in table 4.1.3 suggested that the model was a good fit (significant at 5% level of significance).

4.1.4 Sensitivity Analysis of the model parameters

A Cox proportional hazards model containing the variables that were significant in univariate analysis was fitted. Differences in the categories was achieved by use of log rank statistical test which was used to test the hypothesis that there was no difference between the survival outcomes of the predictors. This was necessary to identify covariates that were statistically significant that affected survival rate of drug users. Covariates which were significant at P-value of 25% in univariate Cox proportional hazards model were used in the construction of the model. Chi square tests were conducted to test the significance of the variables. Table 4.1.3 (a) is a summary of univariate analysis used to select potential predictors.

Table 4.1.3 (a) Results for maximum likelihood estimates

Variable	DF	$se(\beta)$	Z	$p > chi$	HR	LR	Sig
x.residence	1	0.312	5.23	0.030	5.13	34.75	0.030
x.Age	1	0.133	-2.54	0.011	0.71	6.04	0.011
x.Job status	1	0.161	-4.02	0.000	0.52	15.31	0.000
x.Marital status	1	0.174	2.90	0.003	1.66	9.11	0.003
x.Drug type	1	0.066	0.80	0.23	1.05	0.64	0.235
x.Mode taken	1	0.161	-.97	0.33	0.85	0.92	0.331
x.gender	1	0.156	0.87	0.02	0.76	1.06	0.026

Those predictors that were significant were selected using the maximum log partial likelihood of the model ($-2LL$). The results showed larger reduction in $-2LL(\hat{\beta})$ for residence that reduced the value of the null model to 34.75 with a p value of 0.0300 followed by job status with a likelihood ratio of 15.31, p value of 0.0000, marital status with a likelihood ratio of 9.11, p value of 0.0036, age with a likelihood ratio of 6.04 , p value of 0.011, gender with likelihood of 1.06, p value of 0.027, drug type with a likelihood ratio of 0.64, p value of 0.2351 and finally mode of taking the drug with a likelihood ratio of 0.92 with a p value of 0.3371.

Using this procedure covariates were eliminated in accordance to their magnitude in which they reduced the $-2LL(\hat{\beta})$. Those predictors that were significant were considered for the next multivariable analysis at p-value of 0.25. These predictors included age, residence, job status, type of drug abused, gender and marital status. Age, gender, job status and marital status had strong associations with survival time of drug users at P-value less than 0.05. The Covariate that was not significant was mode taken and was therefore removed from the model. The study then fitted initial multiple Cox proportional model by considering the six covariates that were significant. This was followed by another Cox proportional regression model fitted by eliminating covariates which were not significant at p value of 0.05. From the total of seven covariates, residence, type of drug and mode of taking the drug (p-value >0.05) were eliminated from the model. The importance of the variables which were not significant in the univariate analysis as predictors or useful confounder of survival experience of patients and their effects was then assessed. The effect of those variables not significant in the analysis was also examined. These variables were added one sequentially into the cox model containing the four variables significant at 5% significance level.

Then the improvement on $-2LL(\hat{\beta})$ was determined for significance. The results showed that none of those variables were significant and therefore they were removed from the model. Then Wald test was used to assess the significance of reasonable and possible interactions. The null hypothesis tested was that the model with only main effects fitted the model equally well as the model having the main effects and their interactions as predictors. The decision for rejection of null hypothesis was reached if $-2LL_2 - (-2LL_1) > \chi^2(\alpha = 0.05) = 3.84$. Thus, the interaction of each variable was assessed. Accordingly, none of the variables had significant interaction with the other variables. The study further sought to justify the inclusion of the four predictors: age, gender, marital status and job status by applying the least absolute shrinkage (LASSO) and the Smoothly Clipped Absolute Deviation methods of variables selection. The results of these methods retained age, gender, marital status and job status as the significant predictors.

Table 4.1.3 (b) Results for Model selection using LASSO and SCAD criteria

Covariate	SCAD-criteria	LASSO-criteria
x.Intercept	1.2423	0.9416
x.Gender	0.4160	0.310
x.Age	0.350	0.270
x.Residence	0.0000	0.000
x.Marital status	0.0013	0.00190
x.Job status	0.1620	0.080
x.Drug type	0.000	0.000
x.Mode taken	0.000	0.000

The results presented in table 4.1.3 (b) shows that the non-significant predictors for the model were residence, mode of taking the drug and the type of drug and their coefficients were reduced to zero.

Figure 4.1.3 (a) showed that age, marital status, gender and marital status had Lasso coefficients greater than zero and were therefore retained in the model.

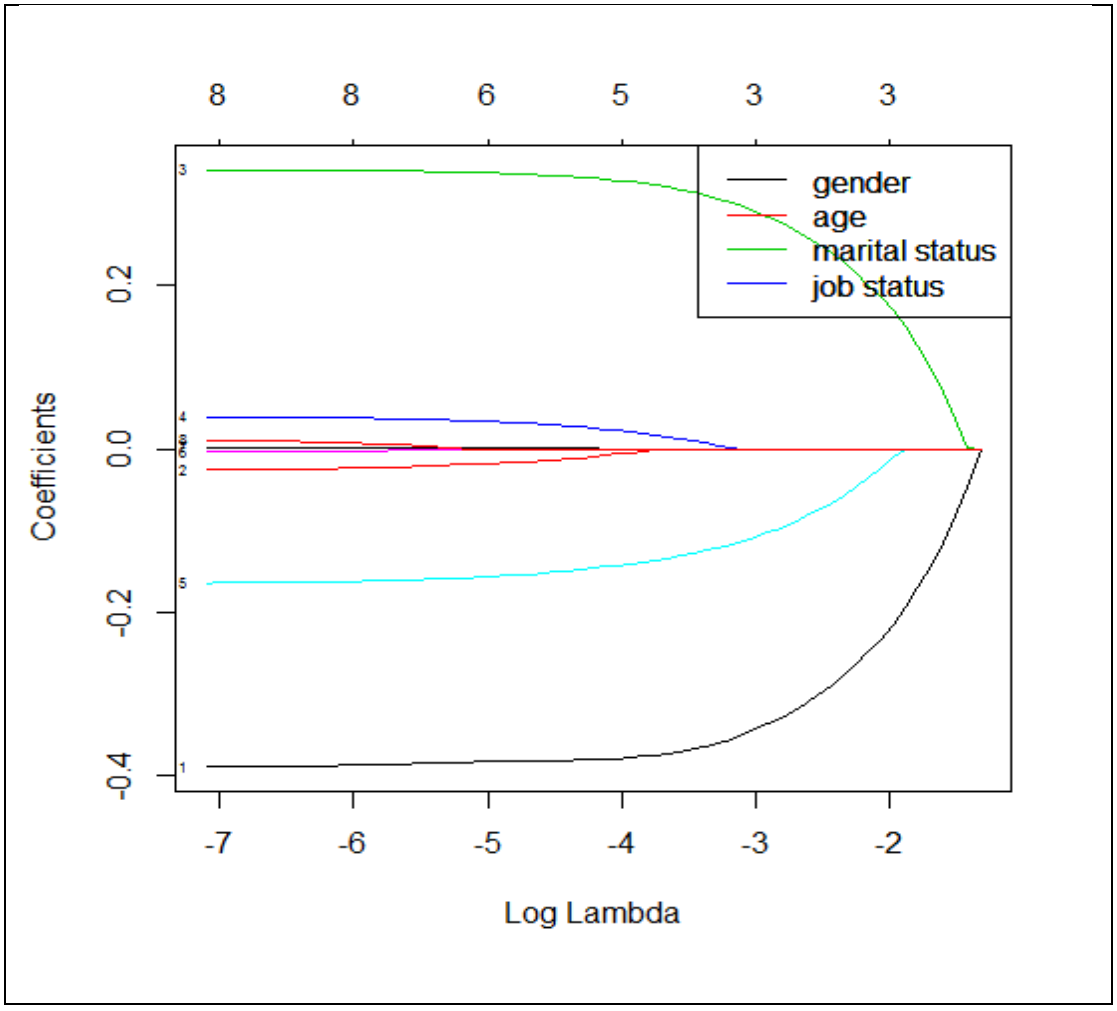

Figure 4.1.3 (a) Selected variables based on LASSO.

Figure 4.1.3 (b) shows that using the smoothly clipped absolute deviations (SCAD) it was sufficient to select four predictors out of a total of seven predictor's excluding the intercept which in the figure was coded as the eighth predictor.

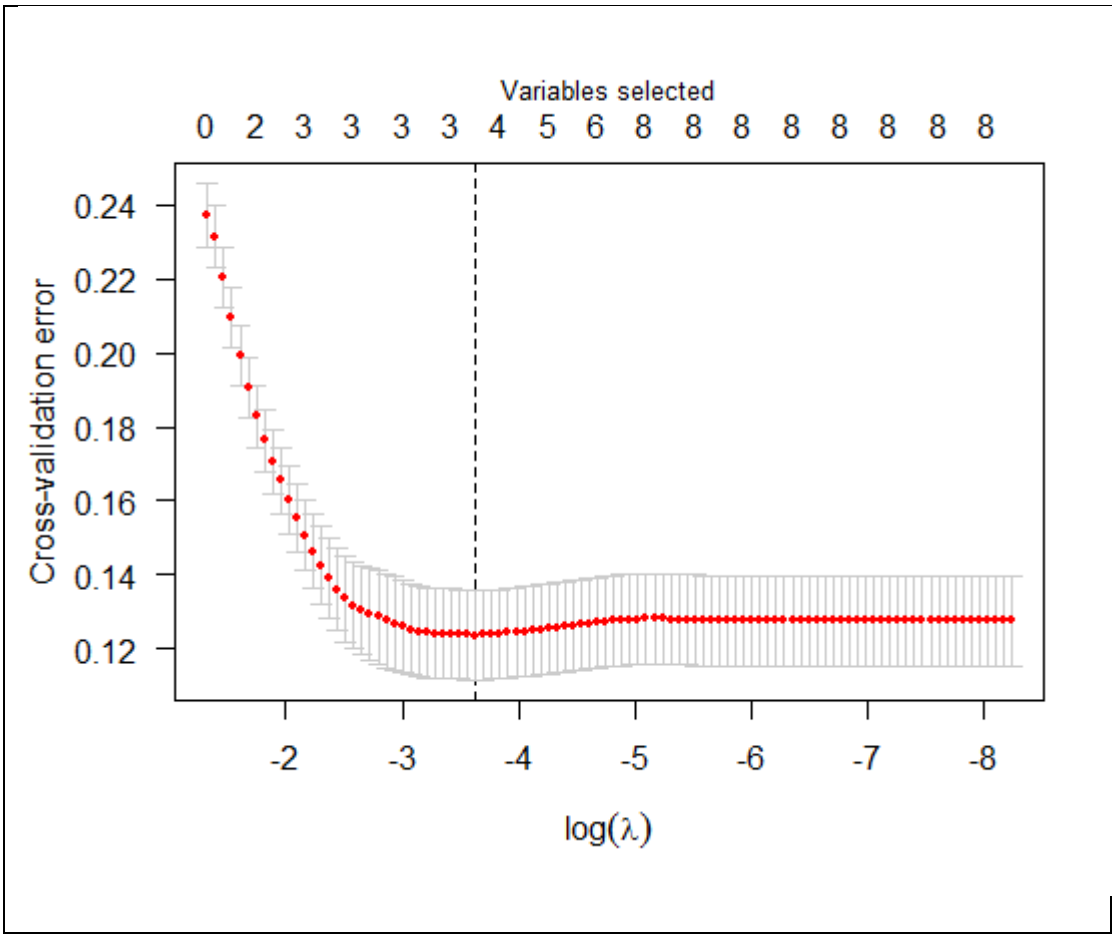

Figure 4.1.3 (b) Selected variables based on SCAD method.

The final Cox model comprised of the four covariates age, gender, job status and marital status. Table 4.1.3 (c) shows that the age of a patient, gender, marital status and job status of the subject significantly affect the survival rate of drug abuse with P value<0.05.

Table 4.1.3 (c) Analysis of maximum likelihood estimates

Variable	DF	Coef	$se(\beta)$	Sig
gender	1	0.02363	0.125	0.048
Marital status	2	0.56934	0.1704	0.0057
Job status	3	0.77103	0.1817	0.0016
age	3	0.3534	0.1326	0.0010

Therefore the fitted model was

$$h(t,w) = h_0(t)\exp(\beta_1 w_1 + \beta_2 w_2 + \cdots + \beta_p w_p)$$

$h_0(t)$ =baseline hazard rate at time t and w is the observation

β =estimated coefficient for observation w.

$ln\left(\frac{h(t,w)}{h_0(t)}\right) = 0.3534w_{age} + 0.02363w_{gender} + 0.56934w_{marital.status} +$

$0.77103x_{job.status}$.

The model results showed there was a positive relationship between age, gender, marital status and job status on survival rate of drug use as all the coefficients were positive. The parameter estimates represented the increase in the expected log of the relative hazard for each one unit increase in the predictor holding all the other predictors constant. There was a 0. 02363 units increase in the expected log of the relative hazard for each one unit increase in gender. There was a 0. 56934 unit increase in the expected log of the relative hazard for each one unit increase in marital status. There was a 0. 77103 unit increase in the expected log of the relative hazard for each one unit increase in job status. There was a 0. 3534 unit increase in the expected log of the relative hazard for each one unit increase in age.

Analysis of deviance was then carried out to test goodness of fit of the proposed model. It was found that the model was a good fit with p values less than the standard p value of 0.05 upon adding the covariates sequentially.

Table 4.1.3 (d) Results for the analysis of deviance Table

	loglikelihood	Chisquare	Df	Prob(>|Chi|)
NULL	-280.100			
x.Gender	-277.640	4.91010	1	0.02670000 *
x.age	-273.870	7.54930	1	0.00600330 **
x.Marital status	-269.500	8.73320	1	0.00312460 **
x.Job status	-262.00	19 14. 63280	1	0.00013060 ***

The results presented in table 4.1.3 (d) showed that adding covariate gender to the model had a significant impact (P value=0.0267<0.05), adding covariate age to the model with age had a significant impact (P Value=0.006), marital status had a significant impact (P value=0.003) to the model with both gender and age covariates while adding covariate job status to the model containing gender, age and marital status as covariates had a significant impact (P value= 0.000130).

The study sought to further determine if dropping one of the variables considered significant would affect the model. The results showed that the variables for optimal model were all significant and dropping one of them would affect the model optimality [table 4.1.3 (e)].From the table it was evident that dropping gender as a variable increased the AIC value to a high value of 527.93 while dropping job status would

increase the AIC value to 505.69. Thus gender was the most sensitive variable followed by job status, marital status and age.

Table 4.1.3 (e) Table showing impact of dropping a variable from the model

	Df	AIC	LRT	Pr(>Chi)
none		497.510		
x.age	1	496.910	1.3920	0.02381220
x.gender	1	527.930	32.4140	1.246e-080 ***
x.Marital status	1	499.340	3.8230	0.0505470 .
x.Job status	1	505.690	10.1770	0.0014220 **

4.2 Recovery rate of drug users under medication

Equality of survival times for all the subjects involved in the follow up study, based upon the differences in group mean, was significant (Wilcoxon statistic=103, df=27, $p = 7.44 \times 10^{-11} < 0.05$).

Table 4.3 (a) Results showing Mean and Standard deviations of the study variables

Covariate	Median time
x.age	18.0
x.gender	19.0
x.Marital status	18.0
x.Job status	19.0

The results presented in table 4.2(a) showed that the median survival time on the basis of marital status was 19 months, 18 months for employment status, 19 months for gender and 18 months for variable age.

Table 4.2 (b) Results showing differences in survival probability

variables	χ^2 value	Log rank statistics
x.age	38.440	52.250
x.gender	7.060	7.180
x.Marital status	8.550	8.870
x.Job status	17.460	18.540

The results presented in table 4.2(b) showed that using the log-rank test, the survival functions for different covariates were significantly different ($\chi 2$ = 20.0, df= 4, $p<0.050$). This was supported by log rank test statistics, which indicated that the survival rate based on age, gender, marital status and job status was significantly different.

The results of the cox proportional model were presented graphically in figure 4.2. The figure gives evidence on the recovery of drug use patients with progress up to the twenty first month. There afterwards the drug users experienced a constant survival rate.

From the entire follow up period of two years the study obtained a survival rate of 36.370% based on the total time. Relapse subjects constituted 30.90% (63 subjects) of the study, while subjects without relapse comprised of 69.10% (99 subjects).

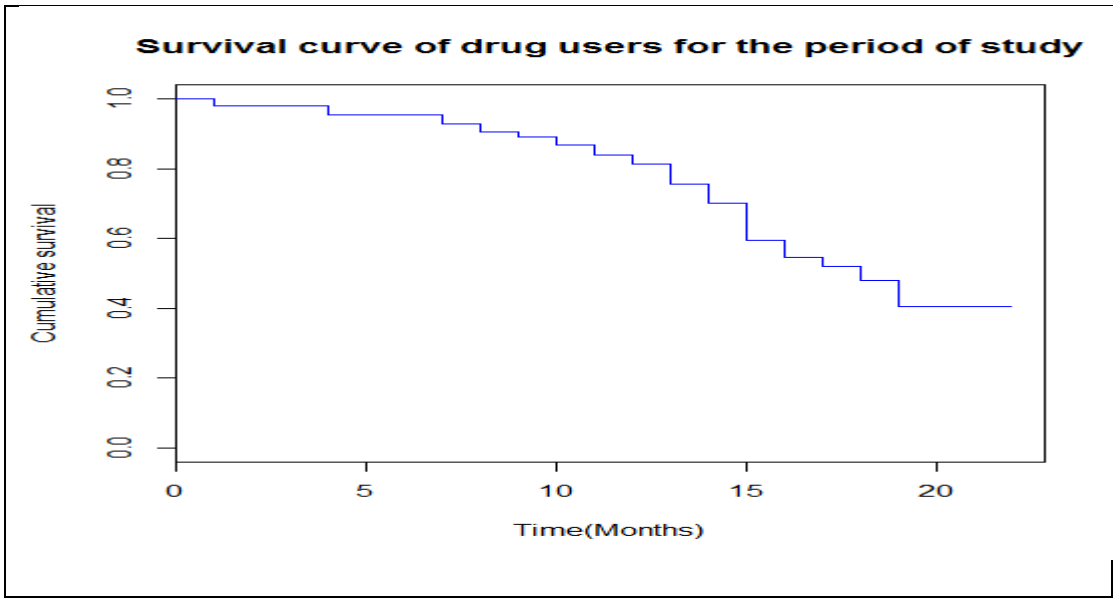

Figure 4.2: Results showing survival function for drug abuse

Table 4.2 (c) Pairwise comparison for the significant covariates

Covariate	Wilcoxon Statistic	DF	p
x.age	19.50	3.0	0.000220
x.gender	43.60	1.0	4.020×10^{-11}
x.Marital status	10.50	2.0	0.005210
x.Job status	35.80	2.0	1.690×10^{-8}

Table 4.2 (c) presents the pairwise comparison tests for the covariates. The results showed that the survival of patients based on age, gender, marital status and job status were statistically significantly different ($p<0.05$) while there were no significant differences between type of drug used, mode of taking the drug and residence of the subjects ($p>0.05$).

A life table showing survival estimates for the patients for the period of study was obtained as shown in table 4.2(d).

Table 4.2(d): survival table for drug use subjects during the study period

Interval Start Time(Month)	Number Withdrawing	Number Exposed to Risk	Relapse number	Survival rate	Cumulative survival rate	Hazard Rate
0-3	4.0	151.000	4.0	.970	.960	.010
3-6	17.0	136.500	7.0	.950	.910	.020
6-9	4.0	119.000	9.0	.920	.840	.030
9-12	19.0	98.500	16.0	.840	.700	.060
12-15	16.0	65.000	18.0	.720	.510	.110
15-18	29.0	24.500	6.0	.760	.380	.090
18-21	4.0	2.000	0.0	1.000	.380	.000

Based on the above table, the most relapses occurred within the first six months and it reduced in other intervals. In addition, cumulative survival index showed that in the first six months, about 91% of the subjects did not experience relapse due to drug abuse, while this index was around 38% in the 24th month and was consistent in the next follow-up. The minimum follow up time was 3 months and the maximum follow up time was 21 months. In the first 3 months there were 4 relapse cases, between 3 to 6 months there 7 relapses, between 6 to 9 months there were 9 relapses, between 9 to 12 months there were 16 relapses and between 12 to15 months there were 18 relapses while in the 18 months there were 6 relapses. There were no relapse cases after twenty one months. A total of 93 patients quit drug use be the end of the follow up study.

Similarly, the hazard rate showed that in the first six months, about 1% of the subjects had the risk of returning to drug use in the first 3 months, about 2% of the subjects had the risk of returning to drug use in the first 6 months, about 3% of the subjects had the risk of returning to drug use in the first 9 months, about 6% of the subjects had the risk

of returning to drug use in the first 12 months, about 11% of the subjects had the risk of returning to drug use in the first 15 months, about 9% of the subjects had the risk of returning to drug use in the first 18 months, while there was no risk of return to drug subjects after the 21st month of the study.

4.3 Survival rate for the drug users of drug users based on the significant independent variables.

4.3.1 Survival rate of drug users based on employment status

As an important comorbidity, information collected from the medical records of each patient on the history status of employment was carried out in order to study its relationship of study covariates with survival rate. The study population was divided into three groups based on the history of employment. The categories considered were the employed, the unemployed and others- those who had not been employed before or those who had lost employment. Kaplan-Meier method was used to determine the observed cumulative survival probability over time due to drug use. The prevalence of drug use among unemployed subjects was higher compared to the employed individuals.

Figure 4.3.1 shows that married individuals had higher survival rate compared to the rest of the categories. Employed individuals had a survival rate of 68.46%, unemployed individuals had a survival rate of 38.19% while the rest of the subjects had a survival rate of 7.08%. The impact of job status on survival rate has been assessed by several studies indicating that employment is associated with higher survival rate from drug use. Richardson (2009) believed that employment is usually upheld as a main consequence, indicator of the context of drug abuse treatment and recovery. This can be attributed to enabling the subject to attend treatment for drug abuse. The subject can be able to afford a higher medical care. Also the risk of losing a job due to drug abuse

may also push the subjects to attend medical care (Bauld *et al.*, 2010.). However a few studies have associated employment to increased drug abuse as the individuals can now afford to pay for the drugs of their choice.

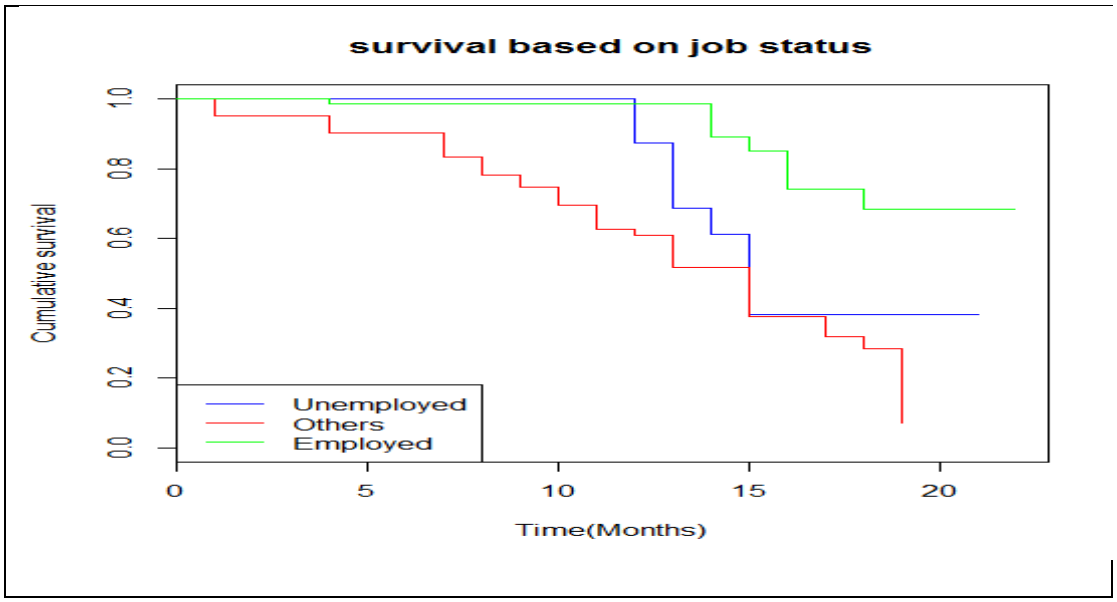

Figure 4.3.1: survival probability based on employment status

Table 4.3.1: log rank statistics for survival based on employment status

	No.	Observed N	Expected N	$\frac{(O-E)^2}{E}$	$\frac{(O-E)^2}{V}$
Job status=1	17	9	7.34	0.376	0.452
Job status=2	62	39	19.73	18.813	29.389
Job status=3	83	15	35.93	12.190	30.679

Chisq= 33.9 on 2 degree of freedom, p= 4.42e-08

Results of table 4.3.1 showed that there significance differences in survival rate among Employed, unemployed and those who specified any other category. This was supported by a Wald statistic of 33.9 which corresponded to a p value of 4.42×10^{-8} <0.05 and therefore was significant.

4.3.2 Survival probability of drug users based on marital status

Information collected from medical records of each patient on marital status was carried out in order to study its relationship of study covariates with survival rate. The study population was divided into three groups based on marital history: married, unmarried and divorced. Kaplan-Meier method was used to determine the observed cumulative survival probability over time by calculating the proportion surviving due to drug use. The results presented in figure 4.3.2 shows that married individuals had higher survival rate compared to the rest of the categories. [Married individuals had a survival rate of 67.89%, divorced or separated individuals had a survival rate of 48.86% while the single individuals had a survival rate of 29.15%. Marital status is also an important factor in helping reduce use of drugs. In most cases married individuals tend to be under pressure from their spouses to quit use of drugs and the need to care of the family also pushes the individuals to consider quitting drug abuse. This is in agreement with Ndetei et al., (2009) and NACADA (2017) who found that marriage reduces the risk of drug abuse. A study by Merete and Ann-Marie, (2008) also showed that children born from mothers who are not married are at a higher risk of drug abuse (75.6%) followed by single parents (19.5%) and the least are those who are married.

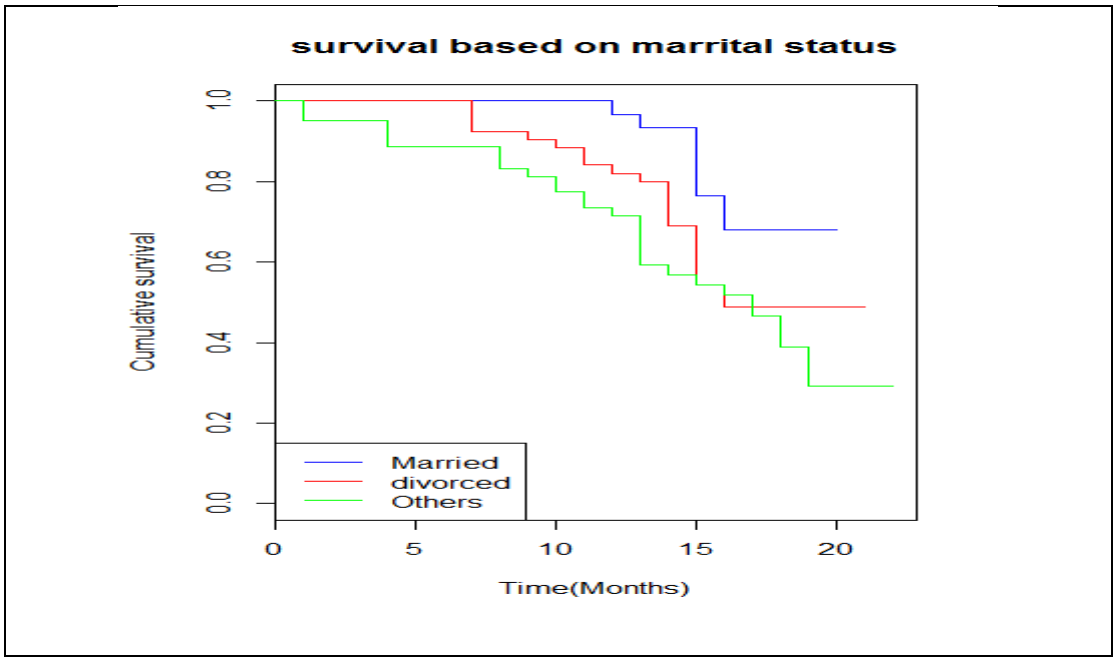

Figure 4.3.2: survival probability based on marital status

Table 4.3.2: log rank statistics for survival based on marital status

	N	Observed	Expected	$\frac{(O-E)^2}{E}$	$\frac{(O-E)^2}{V}$
Marital status=1.0	39.0	8.0	17.20	4.96e+000	7.29e+000
Marital status=2.0	61.0	23.0	23.00	4.34e-050	7.34e-050
Marital status=3.0	62.0	32.0	22.80	3.73e+000	6.35e+000
Chisq= 9.4 on 2 degrees of freedom, p= 0.00926					

Results of table 4.3.2 showed that there significance differences in survival rate among single, married, and divorced subjects. This was supported by a Wald statistic of 9.4 which corresponded to a p value of 0.00926 <0.05 and therefore was significant.

4.3.3 Survival rate based on age

Subjects aged above 40 years had a survival rate of 43.33%, those aged between35-39 years had a survival rate of 42.86%, followed by 30-34 years with a survival rate of 38.92%. This was then followed by those aged below 30 years who had the least survival times of 30.92%. This could be attributed to the fact that youth are highly exposed to many factors that contribute to drug abuse. Figure 4.3.3 shows these factors which include peer pressure, stress and unemployment. Subjects aged above 30 years usually have higher survival rate due to the fact that they are under pressure from their spouses and employers to quit drug use. The findings are in agreement with other researchers whose findings have shown that age is significant in influencing drug abuse (Sutherland, 2008, arteaga, *et al.* 2010; Trutz and Pratschke 2010; Kirby, *et al*. 2008, Healey, *et al.* 2011) and (St Vincent de Paul, 2013).

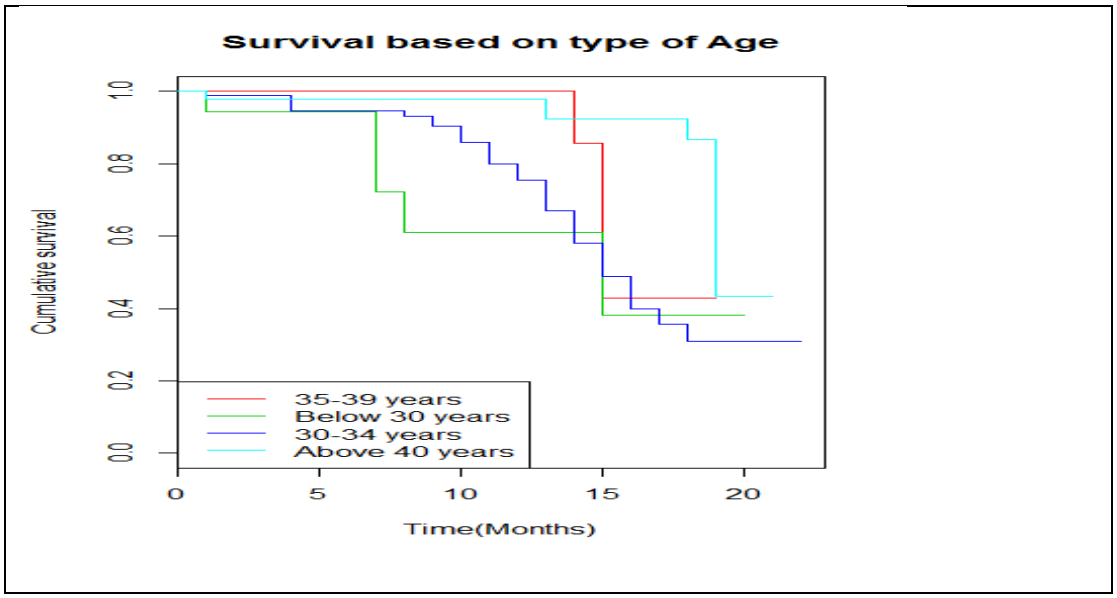

Figure 4.3.3: survival probability based on age

4.3.4 Gender differences in the rate of survival of drugs

The results were presented in table 4.3.4

Table 4.3.4: log rank statistics for survival based on gender

	N	Observed	Expected	$\frac{(O-E)^2}{E}$	$\frac{(O-E)^2}{V}$
gender=1	76	51	24.5	28.7	50.5
gender=2	86	12	38.5	18.3	50.5

$\chi^2 = 35.67$ on 1 degrees of freedom p value$= 2.341 \times 10^{-9} < 0.05$

To determine if there were gender differences in the rate of survival from drug abuse based on gender, log rank test was conducted. Results in table 4.3.4 showed a log rank test of $= 47.67$ on 1 degrees of freedom p value$= 5.209 \times 10^{-12} < 0.05$ which was significant. Therefore it was concluded that indeed there existed significant differences in the rate of survival among male and female subjects.

The results presented in figure 4.3.4 showed higher survival rates in females compared to their male counterparts. This was consistent with previous studies (Wills, Yaeger, &

Sandy, 2003; Pitel *et al.*, 2012). It was also found that females were more likely to quit drug use compared to their male counterparts. This can be attributed to the place that the society puts them. In most communities females drug users were not recognized in the society and were treated with less dignity.

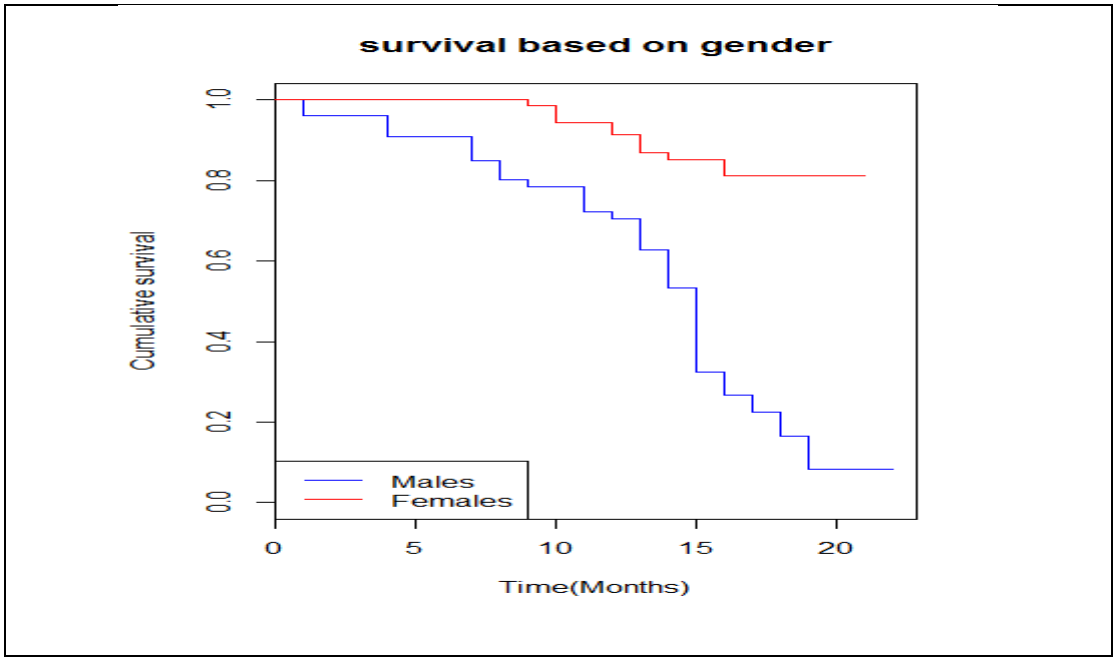

Figure 4.3.4: survival probability based on gender

4.3.5 Discussion of Results

After careful analysis the study obtained an overall survival rate of 36.370%. This was similar to the relapse rates summarized by Greenwood et al., *(2010)* and Ramo and Brown (2008). Therefore, it is necessary to monitor and supervise the addicts' treatment to reduce the relapse rate, which should be implemented more effectively and accompanied with the contribution of addicts' families. Based on the life table model, most of the relapses of drug abuse accrued in the first six months of the treatment (21 of 63 evens), which was approximately consistent with previous studies. These differences can be due to erratic and cyclic periods of relapse and abstinence in addicts. The survival accumulations at the end of 3, 6, 9, 12,15,18 and 21 months in the subjects

were 96%, 91%, 84%, 70%, 51% and 38%, respectively. In the first six months, 91% of the under treatment addicts did not return to drug abuse. There was no relapse to drug abuse (survival rate = 100%) after the 21st month of the treatment. However, accumulative survival that reveals the possibility of return to drug abuse in the previous intervals was around 38% in the 21st month and consistent after the 21st month of the treatment. In other words, the most probable time of drug abuse relapse was during one to six months following the beginning of treatment and the lowest risk to relapse was after the 21st month.

There were noteworthy differences in the survival time between the married, single and widowed or divorced subjects, which were 15.222 (CI 95%: 13.523-16.92), 18.312 (CI 95%: 17.323-19.301) and 16.768 (CI 95%: 15.437-18.1) months, respectively. Lower relapse rate in married people rather than singles and divorced or separated persons can be due to family support and financial security, which are critical for recovery and social rehabilitation. In addition, in the study of Hosseini, Moghimbeigi, Roshanaei and Momeniarbat (2014) marital duration played a significant role in survival time. The study showed higher prevalence of drug use in alcohol consumption followed by cocaine and the rest of the drug users were poly drug users. This was consistent with the study done by Olsson (2011). He noted that alcohol and cocaine misuse were the leading forms of attrition in Sweden. Lower prevalence rates were evident for poly drug users. This could be attributed to financial constraints limiting the users from affording all the illicit drugs they would to satisfy their cravings.

Most of the drug users were young and the middle aged group of subjects. The youth and the middle aged group of users also had lower survival times compared to the older generation. This could be attributed to the many factors that expose them to drug use. These may include lack of employment, curiosity and distress. Peer pressure also pushes the youth to use of drugs. This is in agreement to a study done by Dembele,

Merrer, Befort, Gardon, Filliol, Darcq, Becker and Kieffer (2012) conducted in Ouagadougou, Burkina Faso, a retrospective cohort study that showed majority of the drug users were the youth. As first study on survival rate of drug use in Kenya, this study brings interesting and important findings that should serve as a call for action to policy makers and program planners in Kenya. The study notes that the survival rates of drug use are still low despite the efforts that have so far to fight drug abuse. Drug use is a serious problem that is affecting many communities as well as organizations. Many organizations have had to lose their employees productivity due to absenteeism as a result of drug indulgence. Many families have been left with reliable source of income as one or both of the parents have entered drug abuse. Therefore the magnitude of the problem of drug abuse is big. Therefore it is important that proposed model predictors for drug use be taken into consideration when handling drug subjects.

CHAPTER FIVE

CONCLUSIONS AND RECOMMENDATIONS

5.1 Introduction

This chapter presents the conclusions and recommendations of the findings based on the study objectives. Conclusions based on the objectives of the study are presented. Recommendations are then made based on the findings of the study.

5.2 Summary of Major Findings

A Cox proportional hazard model was applied in the study. This model was significant with four predictors namely, age, gender, marital status and job status. The study obtained an overall survival rate of 36.370% in the follow up study of two years. The survival rate based on gender was significantly different. Male subjects have lower survival rates compared to female subjects. Based on the life table model, most of the relapses of drug abuse accrued in the first six months of the treatment (21 of 63 evens), which was approximately consistent with previous studies. The relapse rate of the subjects decreased with time and there zero relapses at the end of the study period. Accumulative survival that reveals the possibility of return to drug abuse in the previous intervals was around 38% in the 21st month and consistent after the 21st month of the treatment. In other words, the most probable time of drug abuse relapse was during one to six months following the beginning of treatment and the lowest risk to relapse was after the 21st month. There were noteworthy differences in the survival time between the married, single and widowed or divorced subjects during the study period. Lower relapse rate in married people rather than singles and divorced were evident.

5.3 Conclusions

This section presents notable conclusions that can be drawn from the study. First the study sought to apply a survival model in modeling the surivival rate of drug users. This objective was achieved. A Cox Proportional hazards model with four predictors namely age, gender, marital status and job status was applicable in the study. The model was significant and could be applied in identfyin underlying factors when treating drug use subjects.

The second objective was to determine the survival rate of drug users. This was achieved. The survival rate after following the subjects during the study period was 36.370%. Of course this survival rate is worrying to stakeholders but informs them on the need for putting up proper intervention mechanisms to treat subjects. The study showed higher prevalence of drug use in alcohol consumption followed by cocaine and the rest of the drug users were poly drug users. Lower prevalence rates were evident for poly drug users. This could be attributed to financial constraints limiting the users from affording all the illicit drugs they would to satisfy their cravings.

The third objective was to determine the recovery rate of drug users. This objective was achieved. The lifetable analysis showed that after the twenty first month most of the subjects had fully recovered. The median recovery rate was 18 months. Most of the drug users were young and the middle aged group of subjects. The youth and the middle aged group of users also had lower recovery times compared to the older generation. This could be attributed to the many factors that expose them to drug use. These may include lack of employment, curiosity and distress. Peer pressure also pushes the youth to use of drugs. The findings demonstrate clear rural-urban differentials in terms of knowledge of the various drugs and substances of abuse. The 2nd generation alcohol is the least known among the other categories of alcoholic drinks. Generally, Christians

have a higher total awareness level of alcohol products compared to those professing the Islamic faith. This is expected, given the religious prohibition of alcohol in Islam. People are more likely to experiment with drugs compared to older people. The recovery rate of drug use was found to be on decline in the first few months of treatment and increased gradually towards the end of the treatment. Therefore it is important to enroll the subjects in the treatment programs to increase their recovery rate.

The fourth objective was to determine the survival rates of drug users based on gender. The findings revealed significant differences in the survival rates of the subjects based on gender.

Female subjects had higher survival rates compared to the male subjects. In terms of gender, there are differences in awareness levels with more men showing a higher level of awareness compared to women, when controlling for type of drug. Thus, men tend to be more aware of the drugs compared to women. The regional differences reported in the context of this study, seem to reflect differential access to information, as well as access to the different substances of abuse.

The study contributes to the body of knowledge on survival of drug users by appying a survival drug use model, performing a sensitivity analysis on the survival model parameters, establishing a survival rate of drug users and showing that there are differences in survival rates between males and female drug users. The study confirms that policy makers and other stakeholders should embrace survival models to develop intervention procedures for overcoming drug abuse problem.

5.4 Recommendations

Based on the study results the survival rate of drug use was more in females than males. There was significant differences in the survival rates as tested using the log rank statistic. Lower survival rate were evident for males may be attributed to the fact that

male subjects enter drug use at early stages of life. This implies survival models give better clinical information that can be used by stakeholders in the fight against drug abuse. To hasten the fight against drug abuse policy makers and other stakeholders must strive to establish strong intervention programs based on survival models. The major benefit of these models is that they use real data to produce results that are reliable. Policy makers should shift from the old procedures of closing drug points to targeting specific groups of users based on information they derive from the survival models.

The recovery rates of the drug subjects also drew a point of concern. The median recovery rate was eighteen months. However during the data collection process, the study noted that most of the subjects were enrolled for rehabilitation programs for a period of three months after which they were treated as outpatients. The study recommends that the rehabilitation centers should increase their capacities and the duration in which a subject can be enrolled.

The significant differences in the survival rates of drug users based on gender implies the need for a shift in the treatment approach. Interventions should be given priority to the male drug use subjects as they have low survival rates. Campaigns against drug use should be targeted to the young males as early as possible. Policy makers should consider enhancing rehabilitation facilities at the grass roots rather than having only one central or national drug abuse treatment hospital.

The aspect of age being an important predictor should guide key players to develop more intervention programs targeting young people who are susceptible to drug use. Campaigns should also be targeted to people based on marital status so that spouse can pay closer treatment attention to their partners who are drug users. Organizations should impose strict rules against drug taking employees as well as have treatment facilities for drug use employees. Therefore , these results provide a foundation of evidence

and an essential element for raising public awareness , advocacy and improving health care service delivery with regards to drug abuse. The study recommends that further research be contacted to determine if decentralizing the treatment centers which are fully equipped would help improve the survival rates. This recommendation is based on the fact that urban residents who had faster access to the national treatment facility had higher survival rates compared to the rural residents. The study also recommends that further research can be done on modeling of the impact of family set ups in eliminating drug abuse.

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APPENDICES

APPENDIX I: R CODE

```
library(foreign)

mydata<read.spss("C://Users//Kasisi//Desktop//model31.sav",use.value.labels=FALS
E,max.value=Inf,to.data.frame=FALSE)

library(survival)

library(rms)

library(car)

library(MASS)

library(glmnet)

library(lars)

library(Metrics)

library(pROC)

library(ncvreg)

library(AUC)

library(MASS)
```

```
library(glmnet)

attach(mydata)

average<-
list(mean.surv.time=mean(mydata$surv.time),mean.age=mean(mydata$years),
mean.family.size=mean(mydata$Size.of.family),mean.addiction.history=mean(mydat
a$addiction.history))

std.dev<-
c(std.dev.surv.time=sd(mydata$surv.time),std.dev.age=sd(mydata$years),std.dev.fami
ly.size=sd(mydata$Size.of.family),std.dev.addiction.history=sd(mydata$addiction.hist
ory))

descriptives<-list(average,std.dev)

descriptives

temp1 <- table(mydata$status)

temp1[2]/temp1[1]

mydatasurv <- Surv(mydata$surv.time, mydata$status)

mydatasurvKMest<- survfit(mydatasurv~1, conf.int=TRUE)

print(mydatasurvKMest, print.rmean=TRUE)

summary(mydatasurvKMest)

mydatasurvKMest1<- survfit(mydatasurv~1, conf.int=TRUE)

mydatasurvKMest1

mydatasurvKMest2<- survfit(mydatasurv~1, conf.int=TRUE)
```

```
mydatasurvKMest2

mydatasurvKMest1 <- survfit(mydatasurv~1, conf.int=FALSE)

summary(mydatasurvKMest1)

mydatasurvKMest2 <- survfit(mydatasurv~1, conf.int=TRUE)

gender.survival <-survfit(mydatasurv~gender,data=mydata)

marriage.survival <-survfit(mydatasurv~marital.status,data=mydata)

job.survival <-survfit(mydatasurv~job.status,data=mydata)

residence.survival<-survfit(mydatasurv~residence,data=mydata)

mode.survival<-survfit(mydatasurv~mode.taken,data=mydata)

drug.survival <-survfit(mydatasurv~drug.type,data=mydata)

print(marriage.survival, print.rmean=TRUE)

print(gender.survival, print.rmean=TRUE)

print(job.survival, print.rmean=TRUE)

print(residence.survival, print.rmean=TRUE)

print(mode.survival, print.rmean=TRUE)

print(drug.survival, print.rmean=TRUE)

plot (marriage.survival,main="survival based on marrital status",ylab="Cumulative
survival",xlab="Time(Months)",col=c("blue","red","green"))

legend(x=5,y=0.2,c("Married","divorced","others"),col=c("blue","red","green","pink"
),lty=1)
```

```
plot (mode.survival,main="survival based on mode of taking
drugs",ylab="Cumulative
survival",xlab="Time(Months)",col=c("blue","red","green","pink"))

legend(x=5,y=0.2,c("Oral Users","Sniffing","Others","Injecting
users"),col=c("blue","red","green","pink"),lty=1)

marriage.survival <-survfit(mydatasurv~marital.status,data=mydata)

plot (drug.survival,main="survival based on Type of drug",ylab="Cumulative
survival",xlab="Time(Months)",col=c("blue","red","green","pink","yellow"))

legend(x=3,y=0.35,c("Others","Cocaine","Alcohol","Marijuana","Poly
use","Heroine","Cannabis"),col=c(1:7),lty=1)

plot (marriage.survival,main="survival based on marrital status",ylab="Cumulative
survival",xlab="Time(Months)",col=c(1:7))

legend(x=5,y=0.2,c("Married","divorced","others"),col=c("blue","red","green"),lty=1
)

plot(gender.survival,main="survival based on gender",ylab="Cumulative
survival",xlab="Time(Months)",col=c("blue","red"))

legend(x=5,y=0.2,c("Females","Males"),col=c("blue","red"),lty=1)

plot (job.survival,main=" Survival based on employment status",ylab="Cumulative
survival",xlab="Time(Months)",col=c("blue","red","green"))

legend(x=5,y=0.2,c("Others","Employed","Unemployed"),col=c("blue","red","green"
),lty=1)
```

```
plot (residence.survival,main="survival based on residence",ylab="Cumulative
survival",xlab="Time(Months)",col=c("blue","red"))

legend(x=5,y=0.2,c("Urban","Rural"),col=c("blue","red"),lty=1)

plot (mode.survival,main="survival based on mode taken",ylab="Cumulative
survival",xlab="Time(Months)",col=c("blue","red","green"))

legend(x=5,y=0.2,c("Oral","Sniffing","Injection"),col=c("blue","red","green"),lty=1)

plot (drug.survival,main="Survival based on type of drug",ylab="Cumulative
survival",xlab="Time(Months)",col=c("blue","red","green"))

legend(x=5,y=0.2,c("Alcohol","Cocaine","Poly
users"),col=c("blue","red","green"),lty=1)

plot (mydatasurvKMest1,main="Survival Plot",ylab="Cumulative
survival",xlab="Time(Months)",col="blue")

summary(mydatasurvKMest1)

plot(mydatasurvKMest2,main="Survival Plot",ylab="Cumulative
survival",xlab="Time(Months)",col="blue")

summary(mydatasurvKMest2)

mydatasurvKMest <-survfit(mydatasurv~gender,data=mydata,conf.type="log-log")

plot (mydatasurvKMest, lty=c(1,1),col=c("red","blue"),ylab="survival probability",
xlab="survival time (Months)",main="Drug abuse survival")

legend(x=1,y=0.1,legend=c("males","females"),col=c("blue","red"),lty=c(1,1))

my_coxph <- coxph(formula = mydatasurv ~ mydata$gender, mydata)

summary(my_coxph)
```

```
AIC(my_coxph)

BIC(my_coxph)

plot(survfit(my_coxph))

my_coxph1 <- coxph(formula = mydatasurv ~ mydata$gender, mydata)

summary(my_coxph1)

AIC(my_coxph1)

BIC(my_coxph1)

plot(survfit(my_coxph1))

my_coxph2 <- coxph(formula = mydatasurv ~ mydata$gender+mydata$years,
mydata)

summary(my_coxph2)

AIC(my_coxph2)

BIC(my_coxph2)

plot(survfit(my_coxph2))

survdiff(mydatasurv~mydata$gender, rho = 0)

logrank=survdiff(mydatasurv~mydata$gender)

logrank$var#variance-covariance matrix

survdiff(mydatasurv~mydata$age, rho = 0)

survdiff(mydatasurv~mydata$marital.status, rho = 1)

survdiff(mydatasurv~mydata$job.status, rho = 1)
```

```
logrank=survdiff(mydatasurv~mydata$gender+age)

logrank$var#variance-covariance matrix

plot(mydatasurvKMest,conf.int="log-log", col = c('red','blue'), xlab = 'Time
(Months)', ylab = 'Survival Probability')

title(main='Survival rate of drug abuse')

legend(x=1,y=0.2,c('Males ', 'Females'), col = c('blue','red'), lty = 1)

coxph.fit <- coxph(mydatasurv ~ mydata$residence+mydata$gender,
method="breslow")

coxph.fit

AIC(coxph.fit)

survdiff(mydatasurv~mydata$gender, rho = 0)

survdiff(mydatasurv~mydata$age, rho = 0)

survdiff(mydatasurv~mydata$job.status, rho = 0)

survdiff(mydatasurv~mydata$marital.status, rho = 0)

survdiff(mydatasurv~mydata$addiction.history, rho = 0)

survdiff(mydatasurv~mydata$drug.type, rho = 0)

survdiff(mydatasurv~mydata$residence, rho = 0)

survdiff(mydatasurv~mydata$family.size, rho = 0)

coxph.model<-
coxph(mydatasurv~mydata$age+mydata$marital.status+mydata$job.status+mydata$r
esidence+mydata$drug.type+mydata$mode.taken, method="breslow")
```

```
coxph.model

AIC(coxph.model)

BIC(coxph.model)

plot(survfit(coxph.model))

gender.survival <-survfit(mydatasurv~gender,data=mydata)

gender.survival

marriage.survival <-survfit(mydatasurv~marital.status,data=mydata)

job.survival <-survfit(mydatasurv~job.status,data=mydata)

residence.survival<-survfit(mydatasurv~residence,data=mydata)

mode.survival<-survfit(mydatasurv~mode.taken,data=mydata)

drug.survival <-survfit(mydatasurv~drug.type,data=mydata)

ad1<- coxph(mydatasurv
~mydata$gender+mydata$age+mydata$marital.status+mydata$job.status+mydata$res
idence+mydata$drug.type+mydata$mode.taken, method="breslow")

AIC(ad1)

BIC(ad1)

plot(survfit(ad1))

summary(ad1)

anova(ad1)
```