PREDICTORS OF HIV AND PULMONARY TB INFECTIONS AMONG INJECTION DRUG USERS IN MOMBASA COUNTY, KENYA

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P97/13136/09

A THESIS SUBMITTED IN FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN PUBLIC HEALTH IN THE SCHOOL OF PUBLIC HEALTH, KENYATTA UNIVERSITY

DECEMBER, 2015

DECLARATION

This thesis is my original work and has not been presented for a degree in any other University.

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DEDICATION

This is a special dedication to my family members who have shaped my life.

To my husband Joseph Luttson, thank you for your incalculable support, I salute thee.

To my father, the late Aaron Leonid Budambula (BA, Makerere University), who believed in girl child education, Rest in Peace.

To my mother Zerephata, the first lady of the Budambula dynasty and a great matriarch, I salute thee. And to my sister Prof. Nancy Budambula-Mong'are who is indeed a distinguished woman without limits, I salute thee.

My special tribute to Mrs. Elizabeth Kipsang, my high school teacher (Kapsabet Girls High School), for her immense love and psychosocial support, I salute thee. My accolades to Mrs. Florence Lwoyelo (Director, Nurseconsult Services) for encouraging and empowering me to pursue post graduate education, I salute thee.

ACKNOWLEDGEMENT

I take this opportunity to thank God, my *Ebenezer* for thus this far He has brought me. I convey my sincere gratitude to my supervisors Prof. Michael Otieno and Dr. Tom Were whose support, patience and guidance have made this thesis to be successful. Further, I am grateful to the staff and management of Bomu Hospital especially Mr. Musa Mwamzuka, Ms. Ann Mwashumbe (both laboratory technicians), Ms Caroline Kai (TB clinic) and Dr. Aabid A. Ahmed (the Chief Executive Officer). I am deeply indebted to all the PWID in Mombasa who took their time to participate in the study, and to Mr. Nasser Ahmed, a rehabilitated former IDU and currently a community health worker who served as a link between the IDUs and I. My sincere appreciation to research assistants Ms. Linet Makena and Ms. Nancy Odhiambo as well as to the NASCOP team hosted at Bomu especially Ms. Caroline Omeddo.

My sincere gratitude goes to the Technical University of Mombasa (TUM) for both monetary (staff development and partial research funding) and non monetary support. I acknowledge the guidance I received from the then TUM director of research, Dr. Charles Matoka. This study was made possible through the funding received from the National Commission for Science, Technology and Innovation (NACOSTI) grant number NCST/5/003/065. To NACOSTI, thank you for making my dream come true. Since it is not possible to thank each and every individual, I am forever indebted to many who have contributed positively to this work both directly or indirectly through prayers, moral support and encouragement. To all the above I say, *Ahsante sana*.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF PLATES

LIST OF APPENDICES

ABBREVIATION/ACRONYMS

AFB	Acid Fast Bacteria
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
ARV	Antiretroviral
BMI	Body Mass Index
BMT	Buprenorphine Maintenance Treatment
CDC	Centre for Disease Control
CESAR	Centre for Substance Abuse
CI	Confidence Interval
CMI	Cell Mediated Immunity
CNS	Central Nervous System
CRF	Circulating Recombinant Forms
DEA	Drug Enforcement Administration
DFSA	Drug Facilitated Sexual Assault
DST	Drug Sensitivity Test
ECDC	European Centre for Disease Prevention and Control
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
ERC	Ethics Review Committee
FANTA	Food and Nutrition Technical Advisor
FAO	Food and Agriculture Organization
FDA	Food and Drug Administration
GABA	Gamma aminobutyric acid

GABAA	Gamma-aminobutyric acid-A
HBC	High-Burden Countries
HBV	Hepatitis B virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
IBM	International Business Machines
ICHRA	International Centre for Health Interventions and Research in Africa
IDSA	Infectious Diseases Society of America
IDU	Intravenous Drug Use/ Injection Drug Use
IDUs	Intravenous Drug users/ Injection Drug Users
IHRA	International Harm Reduction Association
IQR	Inter-Quartile Range
IRIN	Integrated Regional Information Networks
KAIS	Kenya AIDS Indicator Survey
KFSSG	Kenya Food Security Steering Group
KNBS	Kenya National Bureau of Statistics
LJ	Löwenstein-Jensen
LMIC	Low and Middle Income Countries
MDR	Multidrug Resistant
METHOIDE	Methamphetamine and Other Illicit Drug Education
MMT	Methadone Maintenance Treatment
MOH	Ministry of Health
NACADA	National Agency for the Campaign against Drug Abuse

NACC	National AIDS Control Council
NASCOP	National AIDS and STI Control Programme
NCDs	Non Communicable Diseases
NIDA	National Institute on Drug Abuse
NIH	National Institutes of Health
NMDA	N-methyl-D-aspartate
NPIN	National Prevention Information Network
NTFIC	National Tobacco Free Initiative Committee
NUUA	New South Wales' Drug User & AIDS Association's
OR	Odds Ratio
OST	Opioid Substitution Treatment
PLWA	People Living With AIDS
PLWHA	People Living With HIV/AIDS
PWID	People Who Inject Drugs
RDS	Respondent Driven Sampling
SA	South Africa
SAMHSA	Substance Abuse and Mental Health Services Administration
SIF	Supervised Injecting Facilities
SIV	Simian Immunodeficiency Virus
SNEP	Syringe and Needle Exchange Programme
SPSS	Statistical Programme for Social Scientists
SW	Sex Worker
SSA	Sub Saharan Africa

TB	Tuberculosis
VCT	Voluntary Counseling and Testing
THC	Tetrahydrocannabinol
TISS	Tata Institute of Social Sciences
UNAIDS	Joint United Nations Programme on HIV and AIDS
UNODC	United Nations Office on Drugs and Crime
USA	United States of America
USAID	United States Agency for International Development
USDA	United States Department of Agriculture
WFP	World Food Programme
WHES	World Hunger Education Service
WHO	World Health Organization
WHR	Waist to Hip Ratio

DEFINITION OF TERMS

Intravenous/injection drug user: A person who uses recreational drugs that are administered via the vein. The two terms have been used interchangeably in this study.

Blood loaning: A practice in which an IDU who cannot afford to purchase heroin injects the blood of another IDU who recently injected, in the belief that the blood contains heroin and thus can prevent withdrawal symptoms.

Cooker: Any small container, usually a spoon or a bottle cap, used to dissolve the injectable drug, most often in powder form.

Drugs: A chemical, often an illegal substance that causes addiction, habituation, or a marked change in consciousness.

Flush-blood: the practice of deliberately drawing blood into a syringe and reinjecting the blood-drug mixture.

Recreational drug use: The non medicinal use of a substance (legal, controlled, or illegal) with the intention of enhancing life (increasing euphoria, blocking unhappy memories, or creating pleasure).

Undernutrition: Insufficient provision of energy and nutrients, such as good quality protein with an adequate balance of essential amino acids, vitamins and minerals, and an inability to meet the requirements of the body to ensure growth, maintenance, and specific functions.

Serosorting: A decision to share or not to share injection equipment based on the partner's HIV status.

Sex for police protection: Occurs when vulnerable groups like injection drug users offer sex to policemen in order to avoid being arrested.

ABSTRACT

Both injection drug use (IDU) and HIV are major global public health problems. The link between IDU and HIV arises from high risk injecting and precarious sexual behaviour. Data on the socio-demographics, drug use patterns, tuberculosis (TB) prevalence, nutritional status and HIV sub-types is inadequately documented in Kenyan IDUs. This cross sectional study sought to determine the factors that predict HIV and Pulmonary TB among IDUs in Mombasa County. At Bomu Hospital 371 IDUs (HIV infected, n=157) were enrolled using respondent driven sampling, snowball and make shift methods. The study was approved by Kenyatta University Ethics Review Committee and conducted according to the Helsinki declaration. Written informed consent was obtained from each participant. Structured interview schedule was used to capture the socio-demographic characteristics and drug use patterns. Nutritional status determined using anthropometric indices. One spot and two early morning sputa were obtained on three consecutive days for TB microscopy and culture. HIV status was established by two parallel rapid antibody tests. HIV-1 pro-viral DNA was extracted from plasma, amplified using *gag-pol* primers and amplicons were sequenced from Stanford HIVdb database. Using SPSS version 20, Pearson's Chi-square, Fisher's exact, Mann-Whitney tests and binary logistic regression were utilized as appropriate. Socio-demographic predictors of HIV-1 infection were being female, sex work or working in entertainment venues, having more than five sexual partners, sex without a condom, sex for police protection and exposure to STI, all at P <0.0001. In addition marital separation and sex for drugs increased the odds of HIV infection at P <0.001. Although heroin was the most common drug at 81.7%, a vast majority of IDUs were polysubstance users. Use of Rohypnol for recreational purposes was rampant at 55.3%. Alcohol, khat and cocktail consumption predicted higher odds of HIV infection at P <0.0001, 0.007 and 0.004 respectively. On the other hand, any use of heroin or cocaine, having injected for more than three years as well as polydrug use of heroin or cocaine alongside any other four substances were predictive of HIV infection, all at P <0.0001. High levels of undernutrition were reported in this sub-population with HIV infected IDUs faring worse on height and MUAC at P <0.001 and P <0.0001 correspondingly. Additionally, having a CD4 count of less than 500 cells/μL increased the odds of undernourishment. A CD4 of less than 500 cells/μL and or BMI equal or below 18.5 kg/m^2 augmented the odds of contracting TB irrespective of HIV status. Nonetheless HIV infected IDUs were at a higher risk of TB infection than the uninfected at P <0.0001. There were nine HIV sub-types including their recombinant forms circulating namely A1, A2_AG, A1D, A2C, ABDU, B, C, D and G with A1 being the most dominant. This study has demonstrated the association between drug use, TB and HIV infections, therefore there is need to integrate HIV and TB screening as well as nutrition supplementation in drug prevention and management programmes. These findings will influence the planning and resource allocation for targeted intervention among IDUs both at National and County Government levels in order to mitigate the impact of drug abuse as well as achieve the MDGs one to six. In addition, continuous surveillance of the HIV and TB epidemiology is imperative. These interventions are key to Kenya's achievement of zero new HIV infections and AIDS-related deaths initiative.

CHAPTER ONE: INTRODUCTION

1.1 Background to the study

Injection Drug Users (IDUs) also known as People Who Inject Drugs (PWID) are among the groups most affected by the Human Immunodeficiency virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS) since the epidemic began almost over three decades ago. The link between injection drug use and HIV arises from sharing of needles, syringes, water mixing spoons, practicing flashblood and engaging in high risk sexual behaviour (McCurdy *et al.*, 2010; Uusküla *et al.*, 2010; Ulibarri *et al.*, 2011; CDC, 2012a; NASCOP, 2012a). Consequently, injection drug use is one of the most efficient avenues of transmitting HIV and other blood-borne pathogens like Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV), that spread rapidly through IDU populations and their sexual partners (Čavlek *et al.*, 2011; Orsetti *et al.*, 2013; WHO, 2013a).

Although injection drug use has previously been perceived as a European and Asian problem, evidence indicates that drug use is on the increase on the African continent. In particular the coastal cities of Nigeria, Tanzania, Kenya and South Africa are the most affected (UNODC, 2013a). Due to the illicit nature of drug use and the associated stigma, it is difficult to obtain the exact data on PWID (Needle *et al.*, 2005) however, Mombasa is estimated to have an IDU population of about 26,000 persons (IRIN, 2012; NASCOP, 2012a). Previous studies carried out and reports show that there is steady increase of injection drug use in Kenya (Odek-Ogunde *et al.*, 2003; Beckerleg and Hundt, 2004; Ndetei, 2004; Needle *et al.*, 2005; Beckerleg *et al.*, 2006; Deveau *et al*; 2006). Currently

coastal towns (Mombasa, Lamu and Malindi) as well as Nairobi are the most affected (IRIN, 2012; NASCOP, 2012a).

Globally the most common injectable drugs are amphetamines, opioids (including, heroin) and cocaine (UNODC, 2011a). In Kenya, the commonly used injecting drugs include heroin, cocaine and methamphetamine (NACADA, 2012). In Mombasa, heroin has been a street drug for over 30 years. During the 1980s, heroin (the brown sugar version) quickly spread from Mombasa to smaller coastal towns like Malindi and Watamu (Beckerleg *et al.*, 2006). Brown sugar was mostly used through inhalation of its vapour. In 1998, the injectable heroin (white crest) started to replace brown sugar. Hence by the late 1990s, heroin users were shifting from brown sugar to white crest (Beckerleg, 2004).

High risk injecting trends and sexual behaviour has been extensively documented among PWIDs. These include sharing of syringes, needles and water mixing spoons, practicing of flashblood, blood loaning, unprotected sex with partners of unknown HIV status and anal sex (McCurdy *et al.*, 2006; McCurdy *et al.*, 2010; Čavlek *et al.*, 2011). Additionally, multiple sexual partnerships, sex for drugs, group sex, sex for money to buy drugs or for drugs, sex for police protection is well documented in this sub-population (Parry *et al.*, 2008; Williams *et al.*, 2009; Brodish *et al.*, 2011; Majidpour *et al.*, 2012). Moreover, most PWID face drug-driven impaired judgment which reduces their negotiation power for safer sex (McCurdy *et al.*, 2010; Uusküla *et al.*, 2010; Ulibarri *et al.*, 2011; NASCOP, 2012a). As a result the prevalence rate of HIV among IDUs globally is alarmingly high.

In Kenya for instance, previously the HIV prevalence among IDUs ranged between 43% - 49% (Deveau *et al.*, 2006; Needle and Zhao, 2010) as opposed to the then national adult prevalence of 7.1 % (KAIS, 2007). Currently this prevalence has come down to 18% but remains high when compared to the national adult prevalence of 6.2% (NASCOP, 2013).

Drug abuse has been linked to poor nutritional status attributed to impaired nutrient absorption or altered appetite or metabolism (Hendricks *et al.*, 2010; Vogenthaler *et al.*, 2010; Tang *et al.*, 2011). Undernutrition increases the risk of HIV transmission or acquisition by compromising ones immune status as well as gut and genital mucosal integrity (Weiser *et al.*, 2008; Olsen *et al.*, 2014). Drug use, HIV infections and undernutrition lower immunity thus increasing the risk of reactivating latent tuberculosis (TB) to active TB infection in addition to exacerbating progression of HIV to AIDS (Drake, 2010; Shalini *et al.*, 2012; Mamani *et al.*, 2013; Padmanesan *et al*, 2013).

Both IDUs and non-IDUs are at a risk of developing TB due to the overlap of epidemiological and social factors associated with both drug use, HIV and TB (Deiss *et al.*, 2009; CDC, 2012d; Rüütel *et al.*, 2012). Globally, nearly 2 billion people are infected with TB. People living with HIV/AIDS (PLWHA) are more likely to develop active TB in a given year than HIV sero-negative persons due to their weakened the immune system (USAID, 2013; WHO, 2013a). Currently about 34 million people are living with HIV and at least one third are co-infected with TB. Kenya ranks thirteenth on the list of twenty two TB High Burden Countries (HBCs) in the world and has the fifth highest burden in Africa. These 22 HBCs account for 80% of the global TB burden (WHO, 2013b). In

Kenya, the prevalence of TB among HIV sero-positive patients was 44% in 2009 (WHO, 2009a; CDC, 2011a) and presently it ranges between 38.3% and 39% (MOH, 2012; MOH, 2013).

The HIV-TB co-infection is a major problem in Sub-Saharan Africa (SSA) and is commonly called the deadly duo. TB infections enhance HIV replication at the same time accelerates HIV progression to AIDS. The overlap of HIV- TB co-infection with MDR-TB and extensively drug-resistant TB presents a tremendous challenge and threatens progress in controlling TB and HIV/ AIDS as well as in eliminating the mortality associated with these diseases (USAID, 2013; WHO, 2013b). In Kenya, out of the total samples received and processed, 225 were resistant to both Isoniazid and Rifampicin (MOH, 2012). Elsewhere, outbreaks of drug-susceptible and MDR-TB have been reported among PWID (Deiss *et al.*, 2009) but this data is scanty in Kenya.

1.2 Statement of the Problem

Despite the fact that previous studies have shown that PWID are more predisposed to HIV than the general population, injection drug use remains a major public health challenge. Approximately, there 16 million PWID globally out of which 3 million are HIV infected. Globally, injection drug use accounts for at least 10% of new HIV infections (Riley *et al.*, 2005; WHO, 2013a). The HIV prevalence among PWIDs in Kenya estimated to be 18.3% is by far much higher than the national prevalence of 6.2% (NASCOP, 2008, NASCOP, 2013, NASCOP, 2014). In addition, an estimated 4% of new HIV infections are linked to injection drug use with Coastal Kenya leading at 17%

(NASCOP, 2008). The high risk of HIV acquisition and transmission in PWID largely arises from unhygienic injecting and precarious sexual practices.

Although injection drug use is a global problem, Africa is a more recent victim as it acts as a conduit of drugs from South America en route to Europe and Asia. In the process some of the drugs find their way into the local market due to laxity in enforcing drug related laws as well as corruption (UNODC, 2013a). In Kenya, more so Mombasa, drug abuse has been linked to the proximity of the port, corruption, poverty, pouching, radicalization and breakdown in family structure.

People who inject drugs like other drug users are undernourished. Undernourishment arises from food insecurity, misplaced priorities, reduced food intake and mal-absorption(Anema et al., 2010 and Tang et al., 2011). Under nutrition on its own leads to reduced CD4 and CD8 T-lymphocyte number (Drake 2010). This impairs cell-mediated immunity (CMI) which is the principle host defense against TB (Shalini *et al.*, 2012). Undernutrition irrespective of the cause increases the risk of opportunistic infections and exacerbates progression from HIV to AIDS (Cegielski *et al.*, 2010; Padmanesan *et al*, 2013). Due to overlap of epidemiological factors like poverty and overcrowding, PWID are therefore at a greater risk of contracting both HIV as well as TB infections (Deiss *et al.*, 2009; Rüütel *et al.*, 2012).

In addition, criminalization of drug use has led to marginalization of IDUs. Therefore, IDUs who are infected with either HIV or TB or both are less likely to access healthcare

and adhere to respective drug regiments. Poor adherence reduces efficacy of medicinal drugs at the same time increases the probability of developing multi-drug resistance (Muture *et al.*, 2011; CDC, 2012a; ELF, 2012; Dutta *et al.*, 2013).

In this regard, the IDU, HIV, malnutrition and TB burden is immense as well as complex. Elsewhere, determinants of HIV and TB among PWID have been identified as socio-demographics, drug use patterns, low BMI and low CD4. However, these factors are scantly documented in the Kenyan context. Unless these factors are identified and dealt with through targeted interventions, Kenya may not achieve most of the sustainable development goals.

1.3 Research questions

1. What are the social-demographic characteristic of an IDU population?
2. What are the drug use patterns of IDUs?
3. What is the nutritional status of IDUs?
4. What is the TB prevalence rate in IDUS?
5. What are the HIV subtypes causing HIV infections in IDUs?

1.4 Null hypotheses

1. Social-demographic characteristics are similar between HIV infected and uninfected IDUs.
2. Drug use patterns are invariable between HIV infected and uninfected IDUs.
3. Nutritional status is incomparable between HIV infected and uninfected IDUs.

4. TB infection rate does not vary with HIV infection in IDUs.
5. Single HIV subtype do not cause HIV infection in IDUs.

1.5 General objective

To determine the factors that predicts HIV and Pulmonary TB infections among IDUs in Mombasa County.

1.6 Specific objectives

1. To describe the social demographic characteristics of IDUs in Mombasa County.
2. To determine drug use patterns of the IDUs in Mombasa County.
3. To assess the nutritional status of the IDUs in Mombasa County.
4. To establish the TB prevalence in the IDUs in Mombasa County.
5. To identify the HIV subtypes causing HIV infections in the IDUs in Mombasa County.

1.7 Justification

Due to scanty information on the impact of injection drug use on the upsurge of HIV infections and related co-morbidities among the PWID in Kenya, the study was necessary in order to identify the predictors of HIV and TB among IDUs. This was further necessitated by the fact that risk of TB infections among IDUs is due to an overlap of epidemiological and social factors associated with both drug use, HIV and TB. In addition, the adequate control of the HIV and TB syndemic in IDUs, non-IDUs and the non drug users is the key to the long-term TB elimination target set for 2050. It was

therefore important to delineate the factors that predict HIV and TB infections in the IDU subpopulation by establishing the epidemiology of HIV and TB among IDUs in Kenya. Findings of this study will contribute to planning and resource allocation for targeted intervention among IDUs both at National and County Government levels in order to mitigate the impact of drug use as well as achieve the MDGs one to six.

1.8 Limitations

Due to stigma and the illegal nature of drug use, drug users in Kenya are hidden and were difficult to reach. It was even more difficult to access and enroll female IDUs. This limitation was overcome by working closely with various psychosocial support groups of sex workers. Since the study design was cross-sectional, it is difficult to know the time-point of HIV acquisition. A longitudinal approach would have yielded detailed information on sexual practices and drug use patterns. Drug use patterns were self-reported as no urinalysis was carried out, hence the complete set of injection and non-injection drugs used by the study participants are unknown. Furthermore, self-reported exposure to STIs and sexual practices may be confounded by recall bias.

1.9 Conceptual framework

Injection drug use in Kenya has become increasingly recognized as a public health problem, particularly in light of its association with needle sharing and undernutrition. IDUs are vulnerable to undernutrition, overcrowding and poverty. These increase the risk for both TB and HIV/AIDS infections. Most IDUS on one hand are less likely not to adhere to both antiretroviral and anti TB drugs while on the other hand they are more

likely to engage in high risk sexual behaviour such as sex work (either heterosexuality or homosexuality or bisexuality or group). Consequently, the prevalence rate of HIV and TB in the IDU population is significantly higher than that of the general population. These factors are illustrated in Figure 1.1

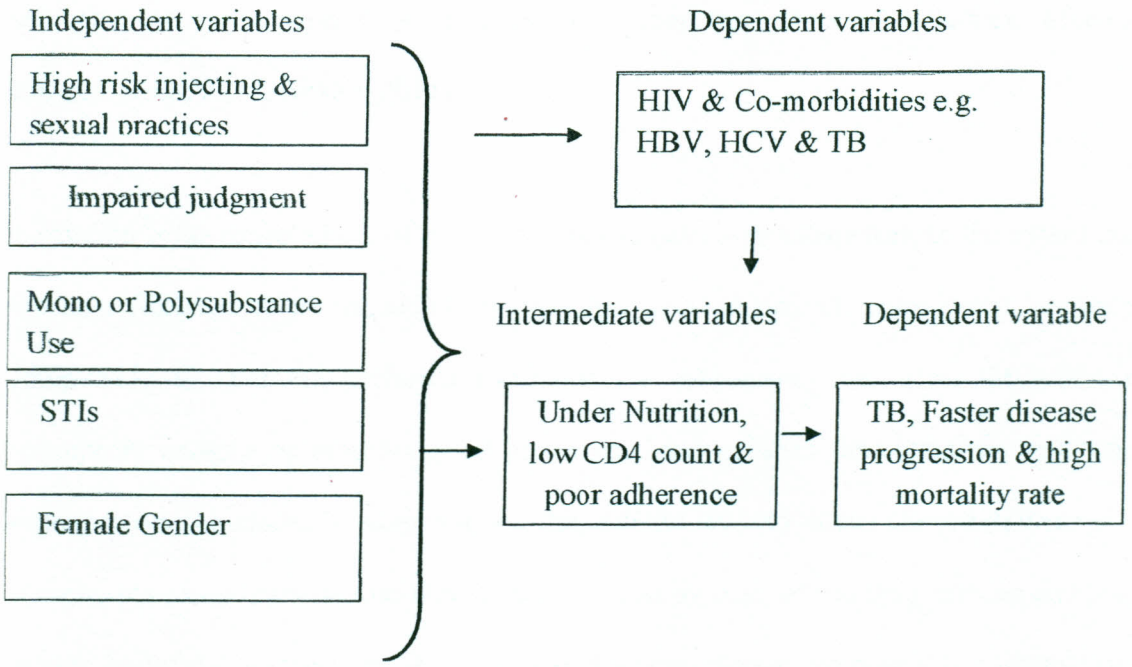

Figure 1.1 Conceptual Framework (Source: literature review)

CHAPTER TWO: LITERATURE REVIEW

2.1 Over View on Drugs Abused by Participants

Drug abuse refers to the harmful or hazardous use of psychoactive substances for mood-altering purposes. It can also be defined as the use of illicit drugs or the abuse of prescription or over-the-counter drugs for purposes other than those for which they are indicated or in a manner or in quantities other than directed (Medline Medical Encyclopedia, 2014; WHO, 2014a).

Addiction is the repeated use of a psychoactive substance or substances, to the extent that the user (referred to as an addict) is periodically or chronically intoxicated, shows a compulsion to take the preferred substance (or substances), has great difficulty in voluntarily ceasing or modifying substance use, and exhibits determination to obtain psychoactive substances by almost any means (WHO, 2014a). It can also be defined as a chronic, relapsing brain disease that is characterized by compulsive drug seeking and use, despite harmful consequences. It is considered a brain disease because drugs change the brain, its structure and how it works. These changes can be long lasting and harmful, often leading to self-destructive behaviours (NIDA, 2012).

Based on these definitions, the study focused on recreational drugs in the context of use of illegal substance(s) and pharmacological preparation (s) that is (are) taken voluntarily for personal pleasure or satisfaction rather than medicinal purposes. In addition the term drug and substance have been used as synonyms. Borrowing from both National Institute on Drug Abuse (NIDA) and Drug Enforcement Administration (DEA) recreational drugs

classification systems, drugs in this study were discussed under following topics: narcotics, stimulants, cannabinoids, depressants and alcohol. Dissociative anesthetics, hallucinogens, inhalants and anabolic steroids have not been discussed as use of these drugs was not reported by the participants (DEA 2011; NIDA, 2012).

2.1.1 Narcotics

The word narcotic is derived from the Greek word narké (meaning stupor) and is used to describe opium, opium-based derivatives and synthetic substitutes. They include opium, heroin, morphine, codeine and other opioid derivatives (DEA Museum, 2012; Opium, 2014). Narcotics have been useful in the practice of medicine for relief of intense pain since they are the most effective analgesics known. Although narcotic substances are available for medical use like in treatment of pain, epilepsy and opioid dependence, their access is controlled and limited (WHO, 2010). With respect to the context of this study, the literature review was restricted to recreational use of heroin but with a brief introduction to opium and morphine.

Opium, the first opioid, is derived from the sap of opium poppies (*Papaver somniferum*) and is obtained as the dried milky juice (Plate 2.1). Its use dates back to around 3400 BC among the Sumarians who lived in lower Mesopotamia (now western Iraq). By 1300 BC, the Egyptians were cultivating poppies for the production of opium. The opium they produced was an extremely popular commodity that they traded it as far away as Greece and central Europe (Rosso, 2010; Flascha, 2011). During the 18th century physicians in the United States of America (U.S.A) used opium as panacea (Hays, 2011).

Plate 2.1: Opium poppies (*Papaver somniferum*)

Source: Plant & Flower Encyclopedia (Botany.com)

2.1.1.2 Morphine and Codeine

In 1805, morphine was used as a cure for opium addiction since its addictive characteristics were not known. Morphine was used widely as a painkiller during the American Civil War and many soldiers became addicted. Codeine, a less powerful form of opium but can be synthesized was first isolated in 1830 in France by Jean-Pierre Robiquet to replace raw opium for medical purposes. It was used mainly as a cough remedy (DEA Museum, 2012; UNODC, 2014a).

2.1.1.3 Heroin

In 1874, German scientists developed a formula for a painkiller that they thought would be less addictive than morphine. They simply added two acetyls to morphine to form diacetylmorphine (commonly known as heroin). It was produced and marketed commercially in 1898 by Bayer Pharmaceutical Company as a panacea. Heroin is also converted into morphine once in the body. When used in medicine, it is typically used to treat severe pain, such as that resulting from a heart attack or a severe injury (Bergstrom, 2002; Scott, 2012). The chemical structure of heroin is illustrated in figure 2.1.

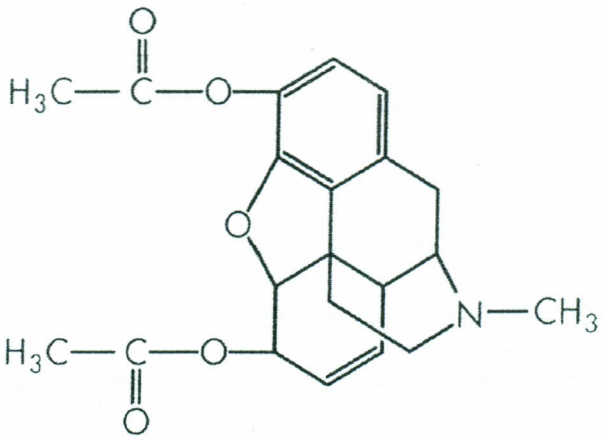

Figure 2.1: Chemical structure of heroin (diacetylmorphine)

Source: EMCDDA, 2013a

Currently United Nations Office on Drug and Crime (UNODC) estimates that there are between 12 and 21 million opiate users worldwide. Globally heroin is the most commonly used opiate. Heroin is manufactured from opium poppies cultivated in four primary source areas namely South America, Southeast and Southwest Asia and Mexico.

Europe and Asia have been reported as the key opiate consumption markets. Afghanistan remains the highest producer of opium with an estimated acreage of about 123,000 ha in 2012, that is74% of global cultivation (UNODC, 2013a). Although heroin is not cultivated in Africa, it remains the most commonly used illicit injection drug in Tanzania and Kenya (Ross *et al.*, 2008; Brodish *et al.*, 2011; Ratliff *et al.*, 2013).

Heroin is distributed in three forms namely brown, white and black tar heroin. It can be injected into a vein ("mainlining") or a muscle, smoked in a water pipe or standard pipe, mixed in a marijuana roll or regular cigarette, inhaled as smoke through a straw ("chasing the dragon,") or snorted as powder. It can also be injected under the skin also known as skin popping (Ciccarone, 2009; NIDA 2013a; Drug policy Alliance, 2014).

Brown heroin also known as brown sugar is produced mainly in the Golden Crescent (Afghanistan, Pakistan and Iran). It is less refined and burns at a lower temperature than white heroin making it ideal for smoking. When smoking, a small amount of heroin is placed on a piece of silver foil and heated from below. The heroin turns into a liquid and gives off a curl of smoke. This curly smoke is inhaled through a rolled tube of paper or straw, a practice referred to as chasing the dragon (Ciccarone, 2009; CESAR, 2013; NUUA, 2014; UNODC, 2014b).

White heroin is the most refined heroin often referred to as grade four heroin. It is produced mainly in the Golden Triangle (Burma, Laos and Thailand). The process of preparing heroin for injection can be done either heating heroin mixed with water in a

spoon over a flame ("cooking"). Alternatively it can be by dropping the heroin powder with water directly into a syringe and then applying flame from a lighter directly to the syringe (CESAR, 2013; Ciccarone, 2009; NUUA, 2014; UNODC, 2014b).

Black tar heroin is sticky like roofing tar or hard like coal. It is predominantly produced in Mexico and sold in areas west of Mississippi River. The dark color associated with black tar heroin results from crude processing methods which leave behind impurities. This impure heroin is usually dissolved, diluted and injected (Maxwell and Spence 2008; Dickson *et al.*, 2010; NIDA 2014). Black tar heroin use among PWID has been linked to an increased number of cases of wound botulism, tetanus and necrotizing soft-tissue infections due to *Clostridia* (Kimura 2007; Yuan, 2011).

Those who inject heroin use a set of paraphernalia like hypodermic needles, small cotton balls, spoons or bottle caps for heating or liquefying the drugs and a "tie-off" that the user wraps around their arm to make the veins protrude. Paraphernalia for sniffing or smoking include razor blades, straws and pipes (EMCDDA, 2013a; Palmateer *et al.*, 2014). Following injection, heroin crosses the blood–brain barrier within 20 seconds, with almost 70 % of the dose reaching the brain. Once heroin enters the brain, it is converted to morphine and binds to opioid receptors. There are three main opioid receptors: *delta*, *kappa* and *mu*. They occur throughout the central nervous system (CNS), in some sensory nerves, on mast cells and in a few gastrointestinal tract (GIT) cells. Opioid receptors are also located in the brain stem which is important for vital processes like breathing, blood pressure and arousal (EMCDDA, 2013a; CESAR, 2013; Feng *et al.*, 2012).

2.1.1.3.1 Effects of Heroin

Apart from analgesia, positive effects of diamorphine include drowsiness, euphoria and a sense of detachment. Negative effects include respiratory depression, weakened immune system, nausea, vomiting and decreased motility in the gastrointestinal tract. Moreover, heroin use leads to cough reflex suppression, hypothermia, tooth decay, inflammation of the gums, constipation, muscular weakness, partial paralysis, memory loss, impaired intellectual performance, introversion, depression as well as pustules on the face (Blum *et al.*, 2013; EMCDDA, 2013a, NIDA, 2013b).

Besides, heroin addiction has been linked to reduced sexual capacity, menstrual disturbance in women, inability to achieve sexual orgasm (in both women and men), drug induced anorexia, insomnia and coma (Schmidt *et al.*, 2013; UNODC 2014c). Long term effects include tolerance, physical dependence and overdose. Heroin is associated with far more accidental overdoses and fatal poisonings than any other scheduled substance (Bang-Ping, 2009; Chekuri, 2011; Cioe *et al.*, 2013; EMCDDA, 2013a; NIDA, 2013b).

Since heroin is addictive, sudden cessation of use in tolerant subjects leads to withdrawal syndrome also known as cold turkey. This may occur within 6 to 24 hours of discontinuation of the drug. However time frame can fluctuate with the degree of tolerance as well as the amount of the last consumed dose. Withdrawal symptoms include cold sweats, general malaise, anxiety, depression, akathisia, priapism and extra sensitivity of the genitals in females (Kenny, 2009; NIDAb, 2013). Further, excessive yawning or sneezing, cramps, watery eyes, rhinorrhea, insomnia, myalgia, bone aches and chills have

been reported. Nausea, vomiting, diarrhea, fever, cramp-like pains and involuntary spasms in the limbs are also common (EMCDDA, 2013a; Hartney, 2014).

2.1.2 Stimulants

Stimulants are drugs that excite any bodily function through stimulation of the brain and central nervous system. They include cocaine, amphetamine, methylenedioxy-methamphetamine (MDMA), methamphetamine and methylphenidate. This study focused on cocaine, khat and nicotine.

2.1.2.1 Cocaine

Coca is one of the oldest and most potent stimulants of natural origin. The ancient Incas in the Andes chewed coca leaves to get their hearts racing and to speed their breathing in order to counter the effects of living on thin mountain air as far back as 3000 BC. Natives in this region chewed or brewed coca leaves into tea for refreshment and to relieve fatigue similar to the customs of drinking tea or coffee (Gonzales, 2010; DEA Museum, 2012). Coca did not find use in Western medicine until the late 19th century when American drug companies began to research on new medicines (Gonzales, 2010; Gootenber, 2010; DEA Museum, 2012). It was first extracted from coca leaves in 1859 by German chemist Albert Niemann. Later pure cocaine was isolated in the 1880s and used as a local anesthetic in eye surgery. Many of its therapeutic applications are now obsolete due to the development of safer drugs (Gootenber, 2010; Rankin, 2010).

Cultivation of coca is concentrated in Colombia, Peru and Bolivia. In 2011, the UNODC estimated that the area under coca cultivation in 2010 amounted to 149 000 hectares (UNODC, 2011a). *Erythroxylum Erythroxylum coca* (Plate 2.2) is the most popular species in South America (Plowman, 2008; Hirst, 2014). Cocaine consignments to Europe appear to be transited through Argentina, Brazil, Ecuador, Venezuela and Mexico. In recent years, alternative routes through West Africa have been detected. Coastal cities of East Africa are some of the most provenance regions (Parry *et al.*, 2009; Peltzer *et al.*, 2009; EMCDDA and Europol, 2010; NACADA, 2010).

2.1.2.1.1 Forms of Cocaine

Cocaine ($C_{17}H_{21}NO_4$), whose chemical structure is shown in Figure 2.2 is usually distributed in three forms. These are cocaine paste, the salt form (cocaine hydrochloride also known as white crystalline powder) and freebase cocaine or crank cocaine which is a waxy solid that may be white, yellowish, or greyish. The physiological and psychoactive effects of cocaine are similar regardless of its form (NIDA, 2013c; Watson 2014).

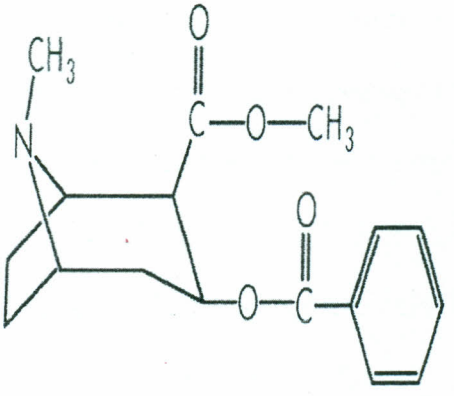

Figure 2.2: Chemical structure of Cocaine

Source: EMCDDA, 2013b

Plate 2.2: Coca Plant (*Erythroxylum coca*)

Source: DEA Museum, 2012

Cocaine paste also known as *pasta basica de cocaína* is the first crude extraction product of coca leaves thus it is the least pure form of cocaine. The leaves are mashed with an alkali like sodium bicarbonate and kerosene and then sulfuric acid or sometimes potassium permanganate. The result is off-white or light-brown paste containing 40 to 70 percent cocaine, as well as other alkaloids, benzoic acid, kerosene residue and sulfuric acid (NIDA, 2013c; UNODC, 2013a; Watson 2014).

Powdered form of cocaine (cocaine hydrochloride) is more pure than paste cocaine. It can either be snorted or dissolved in water and injected into the bloodstream. It is odourless and cannot be smoked because it is mostly destroyed by heat (Andreasen *et al.*, 2009; EMCDDA, 2010; Hall *et al.*, 2012; NIDA, 2012; Watson 2014). Crank cocaine (freebase cocaine) was first developed during the cocaine boom of the 1970's. It remains the most popular drug, as it is inexpensive to produce thus cheaper to purchase than powder cocaine. Powder cocaine when chemically changed to create crank cocaine can be smoked or snorted but cannot be injected as it is not water soluble. It is called "crack" because of the crackling sound it makes when smoked or rock (from forms of small white or yellowish rocks) and is the purest form of cocaine (CESAR, 2013; NIDA, 2013c).

Cocaine irrespective of the version is a CNS stimulant that increases levels of dopamine in brain circuits regulating pleasure and movement. Normally, dopamine is released by neurons in these circuits in response to potential rewards. It is then recycled back into the cell that released it thus shutting off the signal between neurons. Cocaine prevents the dopamine from being recycled causing excessive amounts to build up in the synapse. This amplifies the dopamine signal and ultimately disrupts normal brain communication. It is this flood of dopamine that causes cocaine's characteristic euphoria (Blaylock *et al.*, 2011; Blaylock *et al.*, 2012; NIDA, 2013c; Xiea, 2014).

2.1.2.1.2 Effects of cocaine

Cocaine produces euphoria, appetite suppression, altered metabolism, agitation, anxiety, constricts blood vessels, irregular menses in women, increased energy, mental alertness,

tremors, irritability, aggressiveness and paranoia (Dinis-Oliveira, 2012; NIDA, 2013c). It also triggers hypertension, hyperthermia, tachycardia, arrhythmias, acute coronary syndrome, myocardial infarction, increased risk of coronary diseases, cardiomyopathy, stroke and psychosis (Ersche *et al.*, 2010; CESAR, 2013; EMCDDA, 2013b)

Repeated use of cocaine leads to tolerance, addiction, loss of the sense of smell, nosebleeds, severe bowel gangrene as a result of reduced blood flow, Fournier's gangrene, priapism and undernutrition (Ersche *et al.*, 2012a; Khan *et la.*, 2013; Nidimusili *et al.*, 2013). Cocaine is more dangerous when combined with other drugs. For example, the combination of cocaine and heroin (known as a speedball if injected or moonrocks when snorted) carries a particularly high risk of fatal overdose (NIDA, 2013c; Trujilloa, 2011). The withdrawal symptoms associated with cocaine are unlike those related to opiates. The body does not become physiologically dependent, but they may produce a state of acute unease or discomfort, enhanced anxiety, depression, fatigue, insomnia and craving for more cocaine (El Hage *et al.*, 2012; UNODC, 2014d).

2.1.2.2 Khat

Khat is a stimulant drug derived from *Catha edulis,* a native plant of East Africa and southern Arabia. It is also known by street names like *qat, quat, gat, jaad, chat and miraa.* Most of the effects of chewing khat come from the two phenylalkylamines (cathinone and Cathine) which are structurally related to amphetamine (EMCDDA, 2011a; Brenneisen *et al.*, 2012). Khat (Plate 2.3) is not scheduled under the Controlled Substances Act of the United States, but since cathinone, is a Schedule I drug (a

controlled substance with no recognized therapeutic use), the Federal Government considers Khat use illegal (NIDA, 2013). In Kenya, khat has been listed as a drug by the National Authority for the Campaign against Alcohol and Drug Abuse (NACADA, 2013).

The principal active component in khat is S-cathinone, otherwise known as alpha aminopropiophenone or S-(-)-2-amino-1-phenyl-1-propanone (Figure 2.3). Cathinone is labile and is transformed within a few days of harvesting to a dimer (3,6-dimethyl-2,5-diphenylpyrazine). It is considered a natural amphetamine as it produces sympathomimetic and central nervous system stimulation analogous to the effects of amphetamine (Waleed, 2011; Wabe *et al*., 2012; CESAR, 2013).

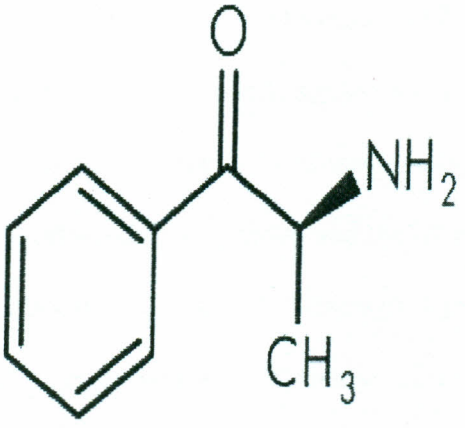

Figure 2.3: Chemical structure of Cathinone

Source: EMCDDA, 2013c

Plate 2.3: Khat Plant (*Catha edulis*)

Source: DEA Museum, 2012

Cathine (a norpseudoephedrine and phenylpropanolamine), is a further psychoactive substance that arises from the metabolism of cathinone in plants (Figure 2.4). Cathine has a milder psychostimulant action than cathinone and the effects last are short lived, so the user must chew leaves almost continuously. Although it plays only a minor role in the action of khat, cathine is responsible for the systemic effects like hypertension. The fresh leaves contain a higher proportion of desirable cathinone but on drying, it breaks down into Cathine (Krizevskiab *et al.*, 2008; Dagne *et al.*, 2010; EMCDDA, 2013c).

The constituents of khat have been shown to exert their effects on dopamine and noradrenalin. It has also been postulated that like amphetamine cathinone releases serotonin in the CNS. This increases the activity of the dopaminergic pathways. High accumulation of dopamine in the brain can cause hallucinations, schizophrenia, and hypertension (EMCDDA; 2011a; CESAR, 2013; NIDA, 2013).

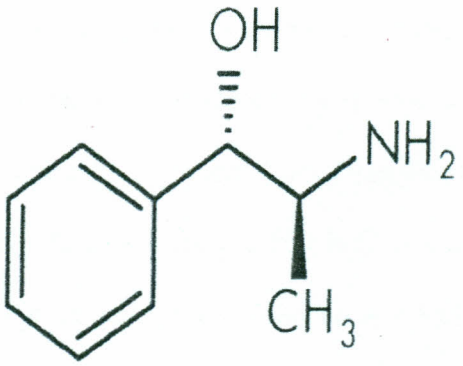

Figure 2.4: Chemical structure of Cathine

Source: EMCDDA, 2013a

2.1.2.2.2 Effects of Khat

Khat alleviates fatigue, reduces appetite while levels of alertness, euphoria, arousal and motor activity are increased. Users can quickly develop a psychological dependency to the drug, which increases their confidence, friendliness and contentment. Hallucinations, insomnia, grandiose delusions, elevated blood pressure, impaired memory and cognitive flexibility as well as paranoia have also been noted as side effects of using khat (CESAR, 2013; Getahun *et al.*, 2010; NIDA, 2013; UNODC, 2014e). This may be followed by depression, irritability, anorexia and difficulty in sleeping. Continuous use of high doses

may evoke psychotic reactions, spermatorrhoea, constipation and urine retention (EMCDDA 2011, Zeleke *et al.*, 2013; NACADA, 2014). It is unclear whether khat causes tolerance, physical dependency, addiction or withdrawal but long-term users have reported mild depression, nightmares and trembling after ceasing to chew (NIDA, 2013).

2.1.2.3 Nicotine

Nicotine is named after the tobacco plant *Nicotiana tabacum*, which in turn is named after Jean Nicot, a French ambassador to Portugal. He used to send tobacco from Brazil to Paris in 1560 as well as promoted its medicinal use (Van Hoof, 2011). Tobacco began growing in the Andes of South America about 6,000 B.C. It was used for religious and medicinal practices although not on daily basis. Tobacco was hailed as a panacea as there were claims it was effective against a host of disorders (Borio, 2010; Zagorevski and Newman, 2012; Hirst, 2014).

Tobacco is native to the subtropical and tropical Americas but there are a few species indigenous to selected areas of Africa. There are over sixty species but the most common are *Nicotiana tabacum* (Plate 2.4) and *Nicotiana rustica* (Moon *et al.*, 2009; Denduangboripant *et al.*, 2010; Van Hoof, 2011; Encyclopaedia of Life, 2012).

Plate 2.4: Tobacco plant (*Nicotiana tabacum*)

Source: Encyclopaedia Britannica Online

Tobacco leaves and the smoke generated when they are burned contain over four thousand chemicals, the best known of which is nicotine (the active ingredient responsible for addiction). Nicotine was first extracted in 1807 in Italy by the researcher Gaspare Cerioli, who called it tobacco's "essential oil." The French chemist Louis-Nicolas Vauquelin made the same discovery in 1809 without knowledge of Cerioli's work. However it is Physician Wilhelm Heinrich Posselt and chemist Karl Ludwig Reimann, who accomplished significant work in the extraction of nicotine (Erowid, 2010;

Nordqvist, 2013). Nicotine (3-[(2S)-1-methylpyrrolidin-2-yl] pyridine), as shown in Figure 2.5 is a colorless oily liquid alkaloid.

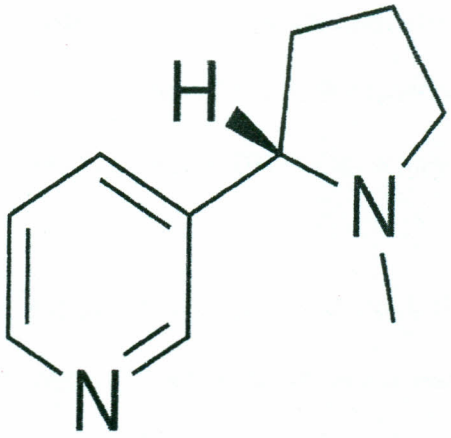

Figure 2.5: Chemical structure of Nicotine

Source: Pubchem

In Africa, the tobacco story began when it was imported from America by the Portuguese. In 1560 Portuguese and Spaniards shipped tobacco to East Africa, where it spread to Central and West Africa. By 1650s South Africa European settlers grew tobacco and used it as a form of currency (BAT, 2010; Borio, 2010). In Kenya, tobacco production can be traced back to 1935 when a tobacco industry was started by white settlers in the then Nyanza province (Campaign for Tobacco Free Kids, 2013).

In Kenya, volume and value sales of tobacco have continued to increase with time partly due to rising urbanization and changes in lifestyle especially among females where

smoking has became more acceptable. However, after passing the Tobacco Control Act in 2007, the Kenyan government began implementing enforcement of anti-smoking campaigns. Smoking prevalence dropped for the first time in 2012, after rising steadily before. Despite the decrease, non-communicable diseases (NCDs) for which tobacco is a risk factor currently account for more than 55% of the mortality in the country and 50% of the public-hospital admission (NACADA, 2012; Euromonitor, 2013).

As nicotine enters the body, it is distributed quickly through the bloodstream and crosses the blood-brain barrier. On average it takes about seven seconds for the substance to reach the brain when inhaled. Nicotine exerts its neurophysiologic action principally through the brain's reward center by binding to nicotinic receptors. The nicotine molecule increases dopamine levels in the reward circuits of the brain thus activating the reward system and generating feelings of pleasure (Whirl-Carrillo *et al.*, 2012).

2.1.2.3.1 Effects of nicotine

In general, nicotine has a psychostimulatory effect on the CNS at low doses via enhancing the actions of norepinephrine and dopamine in the brain. At higher doses, nicotine enhances the effect of serotonin and opiate activity. It exerts a calming and depressing effect (Manoranjan *et al.*, 2011; Garduño *et al.*, 2013; Koranda *et al.*, 2013). Nicotine-induced stimulation of the sympathetic nervous system causes palpitations, increased blood pressure and coronary blood flow leading to cardiovascular diseases (Chen *et al.*, 2012; D'Alessandro *et al.*, 2012; Jones *et al.*, 2013). Smoking increases the risk of respiratory, gastrointestinal, skin diseases and skeletal muscle tremors as well as a

number of tobacco-related cancers in addition to reproductive disorders (Al-Wadei *et al.*, 2012; Chakraborty *et al.*, 2014; Harte, 2014; Merritt *et al.*, 2013; Lavezzi *et al.*, 2014). Chronic nicotine use has been linked to tooth discoloration, tooth decay and gum diseases (like gingivitis) and reduced appetite as nicotine mutes taste buds as well as depresses appetite (Yann *et al.*, 2011; CDC, 2013a; Pilhatsch *et al.*, 2014).

2.1.3 Cannabinoids

Cannabinoids refers to a group of substances that are structurally related to tetrahydrocannabinol or that bind to cannabinoid receptors (NIDA, 2014). The principal constituents of *Cannabis* are delta-9-tetrahydrocannabinol (D9-THC) and cannabidiol. The former is the main psychoactive ingredient and it produces transient psychotic symptoms as well as impaired memory in a dose-dependent manner. Cannabidiol does not induce hallucinations or delusions but antagonises the cognitive impairment and psychotogenic effects caused by D9-THC (Di Forti *et al.*, 2009; Murray *et al.*, 2009).

The oldest known written record on *Cannabis* use comes from the Chinese Emperor Shen Nung in 2727 B.C. In 1545 *Cannabis* spread to the western hemisphere where Spaniards imported it to Chile as fiber. In North America cannabis, in the form of hemp, was grown on many plantations for use in rope, clothing and paper (Gumbiner, 2011; DEA Museum, 2012). There are over 200 street names for marijuana including *pot, herb, dope, reefer, grass, weed, ganja, Mary Jane and chronic* (NIDA 2013; Drugfree world, 2014). Over the course of time, marijuana has evolved into four species, *Cannabis sativa, C. indica, C. ruderalis* and *C. chinensis. C. sativa* and *C. indica* are both found in Asia but

Cannabis sativa is the dominant variety in Africa (Craker and Gardner, 2010; Abel *et al.*, 2011). *Cannabis sativa* variety *Linneaeus*, (Plate 2.5) commonly known as marijuana (with Tetrahydrocannabinol as the principle ingredient, figure 2.6) is a dioecious plant (Craker and Gardner, 2010; EMCDDA, 2013d).

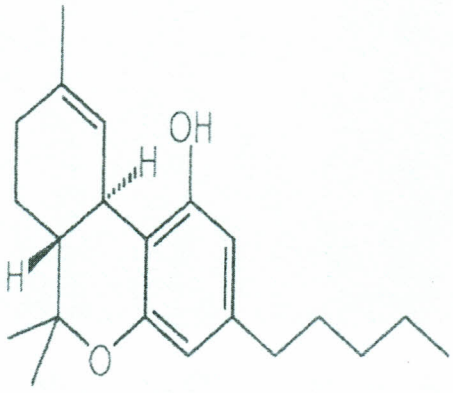

Figure 2.6: Chemical structure of tetrahydrocannabinol

Source: EMCDDA, 2013d

According to UNODC world report on drugs, *Cannabis sativa l.* remains the most widely used illicit substance globally, with an estimated annual prevalence in 2010 of 2.6-5.0% of the adult population (between 119 million and 224 million users aged 15-64 years). There was a minor increase in the prevalence of cannabis users (180.6 million or 3.9% of the population aged 15-64) as compared with previous estimates in 2009. The highest prevalence of cannabis use being reported in Oceania (Australia and New Zealand) at 9.1- 14.6%, followed by North America (10.8%), Western and Central Europe (7.0 %) and West and Central Africa (5.2-13.5%)) while in Kenya 1.2% of the population use marijuana (NACADA, 2012; UNODC, 2013a).

Plate 2.5: Marijuana Plant (*Cannabis sativa Linneaeus*)

Source: Encyclopaedia Britannica Online

Globally, *Cannabis sativa* is distributed in five forms namely, bhang (a paste of leaves of the plant or dried leaves), ganja (dried flowering stem of the plant), charas (processed from live buds), hashish (extracted from the resin covering the plant) and hash oil which is thick oil that is obtained from hashish (National Cannabis Prevention and Information Centre, 2012; NIDA, 2014). It can be smoked in cigarettes or in clay pipes (most common method in religious settings and rural areas) and in water pipes like the traditional hookah (UNODC and TISS, 2011).

Bhang consists of the dried seeded mixture of mature leaves and flowering shoots of both female and male plants, wild or cultivated. It can be ingested orally (by adding to tea and other beverages) or mixed with a combination of sugar, spices and fruit or smoked (alone

or mixed with cigarette). It is the weakest of all cannabis preparations and has a low THC concentration (DEA Museum, 2012; Drugfree world, 2014; Narconon, 2014).

Ganja (Sinsemilla) consists of the dried unfertilized flowering tops of the cultivated female cannabis plant, which become coated with a resinous exudation, chiefly from the glandular hairs as consequence of being deprived of the opportunity of setting seed. As the female plants begin to form flowers, all the large leaves on the stem and branches are also removed. The smaller leaves and the bracts of inflorescence become agglutinated into a mass called ganja (UNODC, 2014c).

Charas is processed from live *Cannabis* buds. Like ganja, it is smoked, but its THC concentration is far higher. In comparison to bhang and ganja, charas is more potent as it contains a relatively large amount of resin. Hash oil (also known as wax, nectar, full melt, honey or budder) is a resinous matrix of cannabinoids obtained from the Cannabis plant by solvent extraction which is formed into a hardened or viscous mass. Hash oil is more potent than marijuana because of its high THC content although it varies depending on the plant (Druglibrary, 2010; Hashish Centre, 2013).

Hashish is the most potent form of cannabis preparations being at least twice or as many as strong as 10 times marijuana (Encyclopaedia Britannica, 2012). It is produced by collecting and compressing trichomes (fine growths on cannabis plants that produce a sticky resin). Hashish is consumed by heating it in a pipe, hookah, bong, bubbler, vaporizer or hot knife (placed between the tips of two heated knife blades). It can be

smoked, mixed with cannabis buds or tobacco, cooked in foods or smoked as bottle tokes (DEA Museum, 2012; Hashish Centre, 2013; Narconon, 2014; UNODC, 2014d).

When one inhales marijuana, THC is absorbed into the bloodstream and later the brain. It then binds to and activates cannabinoid receptors which are activated by a neurotransmitter called anandamide. Like THC, anandamide is a cannabinoid, but found within the immune system of all animals, humans included. The THC then mimics the actions of anandamide, meaning that THC binds with cannabinoid receptors and activates neurons, which causes adverse effects on the mind and body. High concentrations of cannabinoid receptors exist in the hippocampus, cerebellum and basal ganglia. The hippocampus sits within the temporal lobe and is important for short-term memory. When the THC binds with the cannabinoid receptors inside the hippocampus, it interferes with the recollection of recent events. The THC also affects coordination, which the cerebellum controls. The basal ganglia direct unconscious muscle movements, which is another reason why motor coordination is impaired when under the influence of marijuana (EMCDDA, 2008; Bonsor, 2011; NIDA, 2014).

2.1.3.1 Effects of Marijuana

Potential consequences include euphoria, slowed thinking and reaction time, risk of developing psychiatric disorders, confusion, impaired balance and coordination, cough, frequent respiratory infections, impaired memory and learning ability. It has also been shown to cause increased heart rate, cardiovascular disease, anxiety, panic attacks, male infertility, low birth weight infants, preterm birth, foetal growth restriction, increased risk

of infant mortality, tolerance and addiction (Sharma *et al.*, 2012; Brown and Graves, 2013; Hall and Degenhardt, 2013; NIDA, 2013; NIDA, 2014; Volkow, *et al.*, 2014). In addition, it impairs human reproductive potential by disrupting menstrual cycle, suppressing oogenesis and impairing embryo development in women. In men it increases ejaculation disorders, reduces sperm count and motility, it leads to loss of libido and impotence (Bari *et al.*, 2011; Amoako *et al.*, 2013). High risk sexual behaviour, non-adherence to ART and poly-drug use has also been reported among marijuana users (Andrade *et al.*, 2013; Mimiaga *et al.*, 2013).

2.1.4 Benzodiazepines

Benzodiazepines are sedative-hypnotics used to treat anxiety, insomnia, sleep disorders and seizure disorders. Members of this class include Flunitrazepam (Rohypnol, illustrated in Figure 2.7), alpranzolam (Xanax), bromazepam chlordiazepoxide (Librium), lorazepam (Atavan) and diazepam like valium which are central nervous system depressants. Some of the street names of Rohypnol include *Date rape drug, La roche, R2, Rib, Roach, Roofenol, Roofies, Rope, Rophies, Ruffies and The forget pill* (CESAR, 2013). This study focused on recreational use of Rohypnol although medicinal use has been highlighted.

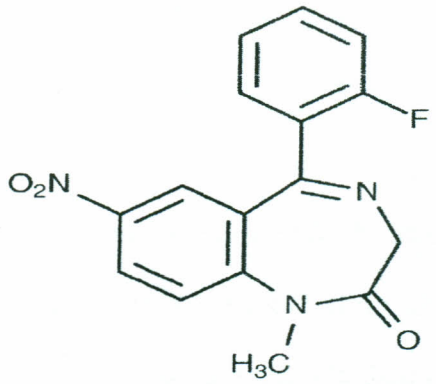

Figure 2.7: Chemical Structure of Rohypnol (Flunitrazepam)

Source: Drug Bank, 2010

2.1.4 Rohypnol

Hoffman-La Roche, a Swiss pharmaceutical company was the first company to describe and develop benzodiazepines in the 1950s. Roche modified the basic benzodiazepine structure and introduced a number of tranquilizers 1960s and 1970s, including Rohypnol in 1975 (Wick, 2013; Helmenstine, 2014). The medicinal use of flunitrazepam as a hypnotic is intended to be for short-term treatment of chronic or severe insomniacs not responsive to other hypnotics (CESAR, 2013; Helmenstine, 2014).

Since the initial composition of Rohypnol tablets was odorless, tasteless, and dissolve undetected in liquid, they were used to facilitate sexual assault. In the mid-1990s, reports surfaced that Rohypnol was being used in drug-facilitated sexual assault (DFSA) and it became known as a date-rape drug. When mixed with alcohol, Rohypnol incapacitates and induces amnesia, making one more vulnerable and unable to fight back or negotiate with rapists. In addition one may be confused or unable to remember the rape when the

drug wears off. This delays reporting of the crime, hinders law enforcement response and early medical intervention (Gemma and Fitzgerald, 2010).

In response to reports implicating Rohypnol in DFSA, the manufacturer reformulated the tablets to oblong green tablets that have a dye which turns blue when dissolved in liquid thus making the drug more easily detected in drinks (Badiye *et al.*, 2012; DEA Museum, 2012; CESAR, 2013). The use of Rohypnol for recreational studies has been reported in various studies both globally and locally (Brodish *et al.*, 2011; Fulton *et al.*2011; Irner *et al.*, 2012; Kahuthia-Gathu *et al.*, 2013; Lee *et al.*, 2014).

Rohypnol binds nonspecifically to benzodiazepine receptors BNZ1 (which mediates sleep) and BNZ2, which affects muscle relaxation, anticonvulsant activity, motor coordination, and memory. As benzodiazepine receptors are thought to be coupled to gamma-aminobutyric acid-A (GABAA) receptors, this enhances the effects of GABA by increasing GABA affinity for the GABA receptor. Binding of the inhibitory neurotransmitter GABA to this site opens the chloride channel, resulting in a hyperpolarized cell membrane that prevents further excitation of the cell (Drug Bank, 2010; EMCDDA, 2013).

2.1.4.1 Effects Rohypnol

It has powerful hypnotic, sedative, anxiolytic and skeletal muscle relaxant properties. It acts by depressing the CNS activity and brain function. This depressed CNS activity manifests as sedation, sleep, muscle relaxation, reduced anxiety and blood pressure.

When mixed with alcohol, another CNS depressant, unconsciousness, stupor, respiratory depression and death are more likely to occur. Overdose can cause drowsiness, memory impairment, low blood pressure, dizziness, headaches, nightmares, confusion, tremors and death (SAMHSA, 2010; Treweek *et al.*, 2010).

Regular use of Rohypnol results in increased tolerance while sudden cessation leads to withdrawal effects characterized by restlessness, anxiety, tremors, hallucinations, and convulsions. One may also experience headaches, muscle pain, tension, numbness, tingling of extremities, loss of identity, delirium and shock (SAMHSA, 2010; CESAR, 2013). Heroin users utilize Rohypnol to enhance the effects of low-quality heroin or to relieve withdrawal symptoms. In contrast to cocaine users who take Rohypnol to soften the negative effects of coming down from a binge (DEA, 2011; Roncero, 2013).

2.1.5 Alcohol

Alcohol (ethyl alcohol, ethanol or grain alcohol) is produced by the fermentation of yeast, sugars, fruits and starches. Ethyl alcohol (Figure 2.8) is the intoxicating ingredient found in alcoholic beverages like beer, wine and distilled spirits. Slang terms include *booze, bubbly, firewater, joy juice, sauce* and *liquid courage* (NIDA, 2012; CESAR 2013).

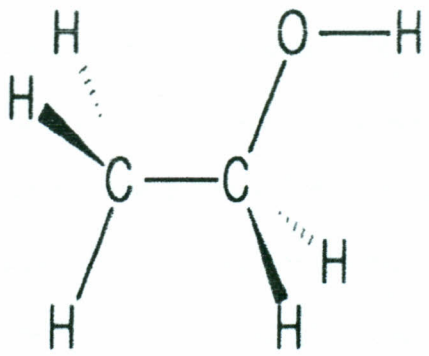

Figure 2.8: Chemical structure of Ethyl Alcohol

Source: Pubchem

According to the World Health Organization (WHO), the harmful use of alcohol is a global problem which compromises both individual and social development. It causes harm far beyond the physical and psychological health of the drinker as it affects the well-being and health of people around the drinker. Indeed it is a socio-medical problem and results in 2.5 million deaths each year. An intoxicated person can harm others or put them at risk of traffic accidents or violent behaviour, or negatively affect co-workers, relatives, friends or strangers. Thus, the impact of the harmful use of alcohol penetrates deep into society (WHO, 2011a). The current use of alcohol among 15-65 year olds in Kenya is estimated to be at 13.6% at national level and 10.6% in the coastal region (NACADA, 2012).

Ethanol appears to act by modifying cell membranes rather than by binding to specific receptor sites on neurons like other compounds. Alcohol dissolves in the lipid layer of

cellular membranes causing an increase in its fluidity. This change may modify the actions of specific receptors or ion channels, resulting in the many behavioural effects of ethanol. Gamma aminobutyric acid (GABA) and N-methyl-D-aspartate (NMDA) are receptors that are associated with the effects of alcohol. The inhibitory effects of ethanol may result from an enhancement of GABA receptor function, increasing the effects of this inhibitory receptor which causes relaxation, relief from anxiety, ataxia and lowering of inhibitions. A blockade of NMDA receptor function interferes with the effects of this excitatory receptor. However, pinpointing a site of action of alcohol effects is difficult because the drug affects virtually all neurochemical and endocrine systems (DrugBank, 2013; Adermark *et al.*, 2014; Trudel *et al.*, 2014).

2.1.5.1 Effects of Alcohol

When one consumes alcohol, it is absorbed in the stomach, enters the bloodstream and goes to all the tissues. The effects of alcohol are dependent on a variety of factors like a person's size, weight, age, and sex, as well as the amount of food and alcohol consumed (Kokavec *et al.*, 2009; CESAR, 2013; Van Zanten *et al.*, 2013). Effects of alcohol intake include dizziness, confidence, slurred speech, disturbed sleep, nausea, vomiting, impaired judgment and coordination as well as aggressiveness including domestic violence and child abuse. It can also lead to reduced performance, hangovers (characterized by headache, nausea, dizziness and fatigue) and accidents (Coskunpinar *et al.*, 2013; Kask *et al.*, 2013; National Institute on Alcohol Abuse and Alcoholism-NIAAA, 2013).

Prolonged and heavy use of alcohol leads to alcoholism. It has been strongly linked to systemic failure, malnutrition, cancer and suicide (Andrade and Gin, 2009; Camila *et al.*,

2011; NACADA, 2012). Mothers who drink alcohol during pregnancy may give birth to infants with foetal alcohol syndrome who later may suffer from mental and physical retardation (Ornoy and Ergaz 2010; Flak *et al.*, 2013). Additionally, children of alcoholic parents are at greater risk than other children of becoming alcoholics (Handley and Chassin, 2013; Hussong *et al.*, 2012; NACADA, 2010).

Sudden cessation of long term, extensive alcohol intake is likely to produce withdrawal symptoms like severe anxiety, tremors, hallucinations and convulsions (NIAAA, 2013). In Kenya alcohol use and abuse is associated with domestic violence, marital separation, child neglect, dropping out of school, loss of livelihood, idleness and crime (Githui, 2011; Birech *et al.*, 2013; Chweya and Auya, 2014). These factors are also determinants of drug abuse and HIV epidemiological trends as discussed in the next sub-topic.

2.2 Socio-demographic Characteristics

Social and economic factors shape the risky behaviours and health of drug users. They affect health indirectly by shaping individual drug-use behaviour and directly by affecting the availability of resources, access to social welfare systems, marginalization as well as adherence to medication. Drug-related activity has been associated with age, familial dysfunction, reduced productivity, unemployment, poverty, drug-related violence and gang activity (Peltzer *et al.*, 2010; Van Wyk, 2011, Trenz *et al.*, 2013).

Worldwide, most studies report the mean or median age of IDUs to be at about 30 years (Čavlek *et al.*, 2011; Ulibarri *et al.*, 2011; Majidpour *et al.*, 2012). These reports are

similar to findings of several studies in Africa (Needle *et al.*, 2008; Parry *et al.*, 2009; Nsimba, *et al.*, 2013) and Kenya (Brodish *et al.*, 2011; Tun *et al.*, 2011).

Young people are particularly at risk for psychoactive substance use, as they are at a stage in life when patterns of behaviour are being formed. They are most likely to be influenced by peers and role models who may be involved in the use of substances (UNODC, 2011b; WHO, 2013h). That is partly why UNODC advocates for prevention strategies that target working with families, schools, and communities. Such strategies ensure that children and youth, especially the most marginalized and poor, grow and stay healthy into adulthood (UNODC, 2013b). Drug education if provided in school-based and mass education programmes (like faith based institutions) has been found to reduce risk of drug abuse (NACADA, 2012; Sahin and Ersin, 2014).

Lower educational level is an important predictor of one becoming an IDU. Low educational level can be due to not enrolling in school at all, dropping out of school or not progressing to higher levels. Dropping out from school is one of the social disruption variables and a proxy indicator for initiation into drug use (Noroozi *et al.*, 2012). Studies have demonstrated that PWID with low level of education are more likely to share needles and less likely to participate in HIV interventions in contrast to those with higher educational attainment (Swe *et al.*, 2010; CDC, 2012c, Gajendra *et al.*, 2012; Medhi *et al*, 2012). This trend has been documented in Kenya, therefore the Kenya government's free primary education and subsidized secondary should be supported by all as it aids in keeping young people in school (Brodish *et al.*, 2011; NACADA, 2012).

The HIV prevalence among female IDUs (FIDUs) has been found to be higher than that of male IDUs. This HIV gender disparity is replicated in the Kenyan general population. For example, the 2012 Kenya AIDS Indicator Survey (KAIS) showed that although the adult (persons between 15 to 64 years) HIV prevalence had dropped to 5.6%, a higher proportion of women (6.9%) in the same age bracket were infected compared to their male (4.4%) counterparts (NASCOP, 2013). In addition, a study carried out in Nairobi show that females among the urban poor have remained more vulnerable to HIV-1 infection because they are more excluded from mainstream economic activities and thus more affected by the ravages of poverty (Madise *et al.*, 2012).

This gender variation could be attributed to social, cultural and biological factors. Social factors that increase the risk of HIV infection include poverty, low levels of education, intergeneration dating, early sexual debut and marital status. Moreover, most females have limited negotiating power in terms of safer sex such as consistent condom use due to male domination of sexual roles. Stereotyped gender relationships are a major barrier for females in terms of maintaining safer sex practices with their partners (Amornkul *et al.*, 2009; Ulibarri *et al.*, 2011; Munyuwiny *et al.*, 2013; NASCOP, 2013).

Although this may be a problem for females in general, but for FIDUs it is even more severe since they are marginalized by society. As a result the FIDUs often have strong feelings of powerlessness, low levels of self-esteem and self-confidence. They also experience impaired judgment while under the influence of drugs and extra sensitivity of the genitals in females during heroin withdrawal episodes. In addition, many FIDUs

engage in precarious sexual and injecting practices. Moreover, many FIDUs have a history of physical and sexual abuse (Ulibarri *et al.*, 2011; Moraros *et al.*, 2012). Globally studies and reports show that females who have been abused are more likely to use drugs and have multiple sex partners (Moraros *et al.*, 2012; UNODC, 2012). The same scenario has been documented in Africa (Ross *et al.*, 2008; McCurdy *et al.*, 2010) and Kenya as well (NASCOP, 2012a). On the other hand cultural practices like early marriages, female genital mutilation, wife inheritance and wife sharing heighten the risk of HIV infection in women (Sesay, 2010; Kemboi *et al.*, 2011; Maleche and Day, 2011).

Women's biological susceptibility to HIV can be linked to large surface area of the body parts like cervix, vagina and possibly the uterus where HIV transmission occurs in women. As compared to men, small tears occur on the penis, foreskin and urethra. In addition, HIV concentration is higher in semen than vaginal secretions and during sex a significant amount of seminal fluid enters the woman's body. Furthermore, delicate tissue of the genital tract can be damaged during intercourse, leading to increased abrasions and vaginal bleeding, consequently increased risk of transmission. Moreover, the warmth and moistness of the vagina provide HIV with an ideal place for micro-organisms to grow (Stoecklein and Osuka; 2012; Ghosh *et al.*, 2013).

Studies show that low levels of estrogen may increase a woman's risk for transmission of HIV because it makes the vaginal wall thinner. Thinning occurs during menstruation and menopause enabling HIV to penetrate more easily thus increasing vulnerability. Furthermore, increase in progesterone level that occurs due to pregnancy or use of

progesterone based contraceptives has been linked to increased risk of HIV acquisition. On the other hand women under 24 may be at higher risk of HIV infection because they may have an immature cervix and genital tract. These are characterized by thinner cells lining that tear more easily during sexual intercourse. This creates a conducive environment for HIV to penetrate more easily into the vaginal wall of younger women than in older ones. Furthermore, older women who have gone through menopause are at increased risk of infection because their lining of their uterus is thinner and their vagina drier (Carias *et al.*, 2012; Stoecklein and Osuka, 2012; Grant *et al.*, 2013).

In general, women are more prone to STIs than men as symptoms of STIs are often more difficult to detect meaning STIs are not treated early enough. The presence of STIs like candidiasis, herpes simplex virus 2 (HSV-2), bacterial vaginosis, chlamydia and the human papilloma virus (HPV) increase the risk of HIV infection (Hilber *et al.*, 2010; Cohen *et al.*, 2011; Djoba, 2014). Vaginal practices like douching and vaginal structural modification alters or destroys the friendly bacteria that protect the vagina. Douching is the practice of washing the vagina before and after sex using water, soap, lemon juice, antiseptics or other consumer douching products. Use of antiseptic or acidic liquids such as rubbing alcohol or lemon juice can irritate the lining of the vagina and create microscopic tears that HIV can pass through (Hilber *et al.*, 2011; Low *et al.*, 2011).

In SSA, vaginal practices are widespread with prevalence reportedly ranging from 6 to 98%. It has been reported in over 98 studies in 24 countries, many of which also focus on traditional medicine to preserve health and wellbeing according to local health beliefs

(Redmond, 2011). In Kenya, vaginal washing using soap, acidic and or drying agents has been reported among female sex workers. This has been shown to augment the odds of HIV acquisition by almost three to four times (McClelland, 2008; Masese *et al*; 2012).

Familial dysfunction like separation and divorce as well as being single (never married) predict a higher risk of HIV infection among IDUs. These has been reported by several studies in the USA (Heinz *et al*., 2009; Khan *et al*., 2012), Middle East (Majidpour *et al*., 2012), Africa (Drissa *et al*., 2013; Kagaayi *et al*., 2014) and Kenya (Tun *et al*., 2014). Moreover singlehood through separation, divorce or widowhood is associated with higher rates of HIV infections in the general population (CDC, 2012b).

In the Kenyan general population, marital separation has been shown to increase the risk of HIV acquisition as reported in the KAIS report of 2012 (NASCOP, 2013). In addition children from dysfunctional families are vulnerable to sexual abuse, delinquency and are more likely to lack emotional security, trust as well as healthy parent-child relationship. These factors increase vulnerability to homelessness, sex work and substance abuse (Barth, 2009; UNODC, 2009; Massey *et al*., 2014).

Furthermore, children of parents who are already drug users are likely to end up using drugs. At the same time drug use affects parenting skills and such parents may end up applying inappropriate disciplinary measures which may also trigger substance abuse among the children (NACADA, 2010; NACADA, 2012; Niccols *et al*., 2012). To break this vicious cycle of generational substance abuse, family skills training programmes that

aim at strengthening the family protective factors need to be implemented at community level (Niccols *et al.*, 2012; Kumpfer, 2013; Tlale and Dreyer, 2013).

Homeless PWID as well as those in precarious housing conditions are likely to engage in unhygienic injecting practices such as sharing injecting equipment and re-using cleaned needles (Grebely and Dore 2011). At the same time they are more vulnerable to rape, sexual assault and harassment (Mayhew *et al.*, 2009). In addition they are less likely to bargain for safer sex and access primary health care. The homeless and marginally housed HIV-positive IDUs are less likely to adherence to ARVs. Worldwide, the link between homelessness, injection drug use, undernutrition and HIV risk has been extensively documented (Hendricks *et al.*, 2010; Tang *et al.*, 2011; Cunningham, 2012; Neaigus *et al.*, 2013, Noor *et al.*, 2013; Vogenthaler *et al.*, 2013; Havinga *et al*, 2014).

In Kenya, the use of psychoactive substances among street children for survival and the high HIV prevalence in this sub-population has been extensively documented in most urban centres (Embleton *et al.*, 2012; Embleton *et al.*, 2013; Oino and Sorre, 2013; Oino *et al.*, 2014). There is therefore need to incorporate interventions that promote family relationships, family values and expectations in community based programmes.

Sex work is associated with a host of psychosocial vulnerabilities like exposure to childhood physical and sexual abuse, interpersonal violence in adulthood and substance use which are risk factors for HIV infection. The relationship between sex work and drug use is complex and inter-dependant. Drugs can be used to boost self confidence,

prolonged sexual performance as well as cope with the long and late working hours. On the other hand drug users are likely to engage in transactional sex that is sex for drugs, police protection or for money to purchase drugs. In addition substance use also helps female sex workers (FSW) feel assertive while talking with men especially when soliciting for clients (Ross *et al.*, 2008; McCurdy *et al.*, 2010; Uusküla *et al.*, 2010; Ulibarri *et al.*, 2011; Moraros *et al.*, 2012).

Female sex workers who inject drugs are also vulnerable to extortion either in cash or kind from law enforcers and pimps. This causes them to engage more in high risk sexual practices as they are more financially rewarding. Overall these multiple sexual partnerships, sex with persons of unknown HIV status, sexual assault and rape is a good recipe for HIV acquisition or transmission. Additionally, drug-driven impaired judgment, sex under duress and increased genital sensation during heroin withdrawal episodes reduce their negotiation power for safer sex (Ross *et al.*, 2008; McCurdy *et al.*, 2010; Ulibarri *et al.*, 2011; NASCOP, 2012a).

Overall sex work is associated with socio-demographic disadvantages like minority ethnic status, low income, homelessness and low education level which are also predictors of drug use as well as STIs including HIV infection in both IDU and general population (Swe *et al.*, 2010; Gajendra *et al.*, 2012; Noroozi *et al.*, 2012; Boden *et al.*, 2013; Myers *et al.*, 2013) These relationship is replicated in Africa (Kabbash *et al.*, 2012; Ademola *et al.*, 2014) and Kenya (Tegang *et al.*, 2010; Ngugi *et al.*, 2013).

The relationship between poverty and drug abuse is a complex phenomenon and is affected by many contributing factors. Beyond the insufficiency of money, poverty develops certain mindset, activities, behaviours and life conditions. These attitudes and conditions can contribute toward drug usage. Poverty deprives the people from material resources due to lack of sufficient income and as a result loose prestige and status in the society (Niazi *et al.*, 2009; Farmer and Hanratty, 2011). Social inequalities induce social exclusion, deprivation, marginalization and hopelessness which induce drug abuse. Illicit drug use can be reduced by decreasing economic and social inequality as the prevalence of drug use seems to be higher in countries with greater levels of inequality such as the USA and lower in countries with less inequality such as Japan and the Scandinavian countries (Pickett and Wilkinson, 2010; Wilkinson and Pickett, 2010; Sutin *et al.*, 2013; ThompsonJr *et al.*, 2013; UNODC, 2013b).

In Iran poverty, living in poor neighbourhoods or polluted suburbs and low level of leisure facilities have been identified as predictors of drug use (Nadjme and Nouzar, 2014). In most African countries where poverty is widespread, youths roam the streets in search of employment consequently some resort to begging as well as high risk sexual behaviour and drug abuse (Fareo, 2012; Mbwambo *et al.*, 2012). Similar scenario has been reported in Kenya (Chesang, 2013; Korir, 2013).

2.3 Drug use patterns

2.3.1 Mode of administration

A route of drug administration is a method in which a drug is taken into the body and differs from the point at which the drug interacts and affects an individual. It is

determined primarily by the properties of the drug (for example, water or lipid solubility and ionization) and therapeutic objectives like desirability of a rapid onset of action or need for long-term administration or restriction to a local site. Reasons for preferring one route over another, depends on the desired effect (like speed and intensity), effect on mood or behaviour, convenience, avoiding possible harms (for example infections and overdose), need to protect the veins, avoiding injection marks or personal preference (Harrella *et al.*, 2012; Vorobjov *et al.*, 2012).

Routes of drug administration can be categoried as topical, enteral and parenteral. Topical administration entails direct application of the drug to the area that it is needed like smoking and snorting. Enteral routes involve the digestive tract like orally taking the drug or using a suppository. Parental routes make use of other internal pathways such as subcutaneous, intravenous and intramuscular (FDA, 2009; Verma *et al.*, 2010).

Smoking is one of the most common routes of drug administration. Whenever someone smokes, the smoke goes to the lungs and is rapidly absorbed into the bloodstream. This makes it one of the fastest ways for someone to experience euphoria as the chemicals are transferred to the necessary bodily receptors in five to ten seconds (NIDA, 2011; Surratt *et al.*, 2011). On the other hand, during snorting about 30 to 60% of the snorted chemicals enter the bloodstream through the mucus membrane in the nose. The rest is swallowed and moves down to the stomach where it finally reaches the bloodstream. The euphoria is experienced within about 15 minutes (EMCDDA, 2010; EMCDDA, 2013f).

Oral ingestion allows the drug to move from the mouth to the stomach where it is absorbed by the stomach lining and then enters the bloodstream. Swallowing is one of the safest ways to take drugs as the substance is be slowly absorbed through the stomach lining resulting in effects which are less extreme and therefore less dangerous. Secondly, an individual's digestive system is designed to induce vomiting if that person ingests anything risky (Verma *et al.*, 2010; SAMHSA, 2012).

One of the riskier methods of drug intake is the use of suppositories where the substance is absorbed through the mucus membrane in the rectum. Since the mucus membranes around the rectum are very sensitive, the substance taken it can burn the lining causing irreparable damage. Additionally, inserting anything into the anus can result in the lower colon being perforated (Verma *et al.*, 2010; CESAR, 2013).

Parenteral route of administration is a recent development in the drug scene and involves injecting of drugs directly into the blood stream. This can be either subcutaneous (injecting into the soft tissue beneath the skin), intravenous (injecting into a vein) or intramuscular which entails injecting into a muscle (FDA, 2009; Verma *et al.*, 2010).

Injecting route is more popular as the full effects are felt within 3 to 5 seconds. It also bypasses many of the body's defenses and delivers the drug to the brain. That is why injecting is more dangerous as substances which would have normally been rejected by the stomach or blocked by the skin can easily enter into the bloodstream. Consequently, increased chance of infection, scarring of the veins, arterial damage, hemorrhaging, distal

ischemia, gangrene, endarteritis, thrombosis and death due to overdose may occur (Verma *et al.*, 2010; Novak and Kral, 2011; Vorobjov *et al.*, 2011; Surratt *et al.*, 2011).

Studies demonstrate that there is an increased chance of addiction for those who take drugs via injections and smoking. This is because the heightened feelings that they experience may lead them to come back and repeat the action simply to relive the previous emotions. This may explain why tobacco smoking and injecting heroin are most often associated with dependence among users. Cigarette smoking has been extensively reported among PWID although the reason for this relationship is unclear (Marshall *et al.*, 2011a; Harrell *et al.*, 2012 Methoide, 2014).

2.3.2 Monosubstance versus polysubstance use

People who use drugs (PWUD) rarely limit their use to one substance and the increasing prevalence of polysubstance use has been shown to contribute to the already devastating HIV epidemic (Wechsberg *et al.*, 2008; Floyd *et al.*, 2010). The WHO defines polydrug abuse as the concurrent or sequential abuse of more than one drug or type of drug, with dependence upon at least one and usually with the intention of enhancing, potentiating, or counteracting the effects of another drug. The term is also used more loosely to include the unconnected use of two or more drugs by the same person (WHO, 2014b).

It occurs when an individual abuses several substances over a short period of time, often in an attempt to enhance the effect of a single drug to create a more intense high. Other

individuals take a drug to counteract the effects of a drug they had taken previously like taking sedatives to come off a stimulant effects. Some combination drug users have patterned use like alcoholics who use cocaine only after they have reached a certain state of intoxication so as to avoid overuse and addicts who *speed-ball* (a mixture cocaine and heroin) for intravenous use. Polydrug use can also be due to changes in price, availability, legality or fashion (EMCDDA, 2009).

Interactions between different drugs consumed close together in time can lead to increased toxicity. This can occur due to additive or potentiation effects, pharmacokinetic factors like reduced metabolism leading to higher blood concentrations of the drug or to other interactions, such as the production of a new metabolite derived from the drugs or products. The effects of certain psychoactive substances can also lead to increased risk behaviour with another substance (EMCDDA, 2009).

The abuse of multiple substances continues to be a major public health concern in Europe (EMCDDA, 2009; Irner *et al.*, 2012), United States of America (Harrell *et al.*, 2012; Ogbu *et al.*, 2014), Latin America (Reyes *et al.*, 2012) and other countries in the world. In Africa poly substance abuse is well documented in South Africa ((Floyd *et al.*, 2010; Trenz *et al.*, 2013) and the Republic of Tanzania (Nsimba *et al.*, 2013). Although literature on polydrug abuse is scanty in Kenya, the phenomenon has recently been reported among IDUs in Nairobi (Tun *et al.*, 2014) and Malindi (Brodish *et al.*, 2012).

Studies show that risky sexual behaviour in terms of a higher number of sexual partners and higher number of self-reported STIs is influenced by the type of drug used as well as route of administration (Celentano *et al.*, 2008; Vorobjov *et al.*, 2012). Poly substance use increases the likelihood of sexually transmitted HIV and other STIs (Mimiaga *et al.*, 2008; Mayer *et al.*, 2012).

2.4 Nutrition

Undernutrition is defined as insufficient provision of energy and nutrients, such as good quality protein with an adequate balance of essential amino acids, vitamins and minerals, and an inability to meet the requirements of the body to ensure growth, maintenance, and specific functions (FAO, 2010; White *et al.*, 2012; WHES, 2012). Globally, between 842 and 870 million people or around one in eight people in the world are estimated to be suffering from chronic hunger, regularly not getting enough food to conduct an active life with Sub-Saharan Africa being the most affected region (WHES, 2012; FAO, 2014). It is estimated that 42% of the people living in the horn of Africa are food insecure and undernourished (FAO, 2010; USDA, 2012; USAID, 2014). In addition 50% of the population of Nairobi (2 million people) is food-insecure. Similarly the Coastal region of Kenya has been classified by Kenya Food Security Steering Group- KFSSG as a food insecure (GOK, 2013).

In countries like Canada and India, reports show that between 30% and 70% of drug-using individuals report some level of food insecurity and undernutrition (Anema *et al.*, 2010; Tang *et al.*, 2011). Other studies show that, regardless of HIV status, nutritional

intake of IDUs is well below the recommended dietary allowance for vitamins A, C, and E, calcium and zinc in addition to low body mass index (Hendricks *et al.*, 2009; Hendricks *et al.*, 2010; Karajibani *et al.*, 2012; Strike *et al.*, 2012).

Factors that influence nutritional status of a given population include food availability (sufficient quantities of food available on a consistent basis), food accessibility (ability to produce one's own food or buy it) and food use or quality which is the appropriate use of food based on nutritional knowledge and care as well as adequate acess to water and sanitation (Ajao *et al.*, 2010; Kimani-Murage *et al.*, 2011; Saaka and Osman, 2013; CIRAD, 2014; WHO, 2014c).

Predictors of injection drug use; like poor educational attainment, homelessness or unstable housing, unemployment or being on welfare or low income, lack of food preparation and storage facilities, mental illness, high risk sexual and injecting behaviour, social ostracization and frequent incarceration overlap with the determinants of food security and nutritional status of any given population (Hendricks *et al.*, 2009; Hendricks *et al.*, 2010; Brodish *et al.*, 2011; Tang *et al.*, 2011; Vogenthaler *et al.*, 2013). In addition these social predictors are associated with many negative social medical outcomes like elevated risk of acquiring sexually transmitted infections and blood borne pathogens like HIV, Hepatitis B and C (Majidpour *et al.*, 2012).

Undernutrition among HIV-positive drug users exacerbates an already compromised immune system (as the body lacks anti-oxidants which mop up harmful free radicals and

the nutrients needed to maintain immunity) and mitigates the effectiveness of antiretrovirals, ultimately decreasing the survival chances (Van Gaalen and Wahl, 2009; Hendricks, 2010). In addition, undernutrition irrespective of HIV status increases the risk of HIV transmission through sex and drug risk routes by compromising an individual's immune-status as well as gut and genital mucosal integrity (Weiser *et al.*, 2008).

At the same time infections increase the risk of undernutrition because sick people eat less, absorb fewer nutrients, lose nutrients (through diarrhoea and vomiting) and have increased nutrient needs especially fever. In addition, infections weaken the linings of the gut and respiratory systems making them weak and therefore can easily be invaded by pathogens (Krawinkel, 2012; MacArthur and DuPont, 2012).

Infections like HIV may result in undernutrition as a result of insufficient dietary intake, malabsorption and altered metabolism. Lack of sufficient food intake and/or malabsorption leads to weight loss, which further exacerbates the hypercatabolic nature of HIV infection and ultimately reduces the chances of survival (Koethe *et al.*, 2010; Andrade *et al.*, 2012). People living with HIV/AIDS experience weight loss, loss of muscle tissue and body fat, vitamin and mineral deficiencies. When the body mounts its acute phase immune response to HIV infection, it releases pro-oxidant cytokines and other oxygen-reactive species. These cytokines produce several results including cachexia which is characterized by involuntary weight loss due to depletion of host adipose tissue and skeletal muscle mass that is not associated with starvation (Braun and Marks, 2010; Akiibinu *et al.*, 2012; Mody *et al.*, 2014).

In addition it leads to anorexia resulting into lower food intake and fever which increases energy expenditure. An augmentation in circulating inflammatory cytokines has been implicated as a uniting pathogenic mechanism of cachexia and associated anorexia Consequently this leads to reduced immune competence and increased susceptibility to secondary infections (Braun and Marks, 2010; Shalini *et al.*, 2012; Mody *et al.*, 2014).

If the infection is prolonged, muscle wasting occurs because muscle tissue is broken down to provide the amino acids with the immune protein and enzymes they need. These processes increase energy requirements of people living with HIV/AIDS during the asymptomatic phase by 10 percent over the level of energy intake recommended for healthy, non-HIV-infected people of the same age, sex and physical activity level (Martins *et al.*, 2011; Sunguya *et al.*, 2011).

Among IDUs undernutrition is due to food insecurity, reduced food intake and food malabsorption (NIH, 2012; Strike *et al.*, 2012; DRUG INFO, 2013). In the USA between 30 to 70% of drug using individuals report some level of food insecurity (Strike *et al.*, 2012). Reduced food intake is attributed to hunger suppression, selective appetite, distorted food taste and altered metabolic processes resulting in an imbalance between fat intake and storage. This has been reported among people who chew khat, heroin and cocaine users as well as tobacco smokers (Murray *et al.*, 2008; Douglas *et al.*, 2011; Mineur *et al.*, 2011; Neale *et al.*, 2012; Ersche *et al.*, 2012b; Ersche *et al.*, 2013; Rubinstein and Low, 2013).

Overall drug addiction modifies eating habits, often causing individuals to adopt poor dietary patterns such as an irregular eating schedule, eating fewer meals per week, skipping meals or fasting to prolong the effects of drugs (Neale *et al.*, 2012). Poor nutrient absorption is partly attributed to withdrawal symptoms like loss of appetite, nausea, vomiting, diarrhoea nutrient maldigestion and direct nutrient loss (WHO 2009a; Nel, 2010; Smith *et al.*, 2012).

Most IDUs face competing demands between addiction and subsistence, which in return hinder access to groceries and food selection. As a result major components of IDU diets have been reported as foods of low nutritive value which are mostly cheap and easy to prepare foods, high-fat diets or ready to eat sweet and salty snacks while the minor components are fruits, vegetables, grains and dairy products and hence undernutrition (Hendricks *et al.*, 2010; Alves *et al.*, 2011; Saeland *et al.*, 2011).

Under nutrition enhances susceptibility to infection in both HIV infected and uninfected persons with the former faring worse. Malnourishment is associated with an increased risk of progression from latent to active TB because of the negative impact of micro and macronutrient deficiencies on the cell-mediated immune system. Low BMI is a risk factor for TB. In HIV mono infected patients a higher BMI is associated with better survival outcomes and a lower BMI is a predictor of mortality (Knut *et al.*, 2010; Maro *et al.*, 2010; Padmanesan *et al.*, 2010; Semba *et al.*, 2010).

It is important to note that under nutrition irrespective of the cause reduces CD4 and CD8 T-lymphocyte number leading to impaired cell-mediated immunity (CMI) which is the principle host defense against TB (Drake, 2010; Shalini *et al.*, 2012). Both IDU and HIV/AIDS are characterized with undernutrition which is a predictor of the health status of a population and exacerbates progression from HIV to AIDS (Shannon *et al.*, 2011; Shalini *et al.*, 2012; Padmanesan *et al*, 2013).

Although information on food security and nutrition status of African as well as Kenyan populations are well documented (FAO 2010; USDA, 2012; GOK, 2013; USAID 2014) data on the same for the IDU subpopulation in this region is scanty. To the best knowledge of the researcher there is no documented study on nutritional status and food security of injection and non injection drug users in Africa as well as Kenya.

2.5 Tuberculosis

Tuberculosis is one of the world's deadliest diseases and it is estimated that one third of the world's population is infected with TB. In 2013 alone, 9 million people around the world had active TB and around 1.5 million TB-related deaths were reported 360 000 of whom were HIV-positive. Tuberculosis is slowly declining each year and it is estimated that 37 million lives were saved between 2000 and 2013 through effective diagnosis and treatment. Since most deaths from TB are preventable, the death toll from the disease is still unacceptably high and efforts to combat it must be accelerated if the 2015 global MDG targets are to be met (CDC, 2014; WHO, 2014d).

Kenya ranks thirteenth on the list of twenty two TB High Burden Countries (HBCs) in the world and has the fifth highest burden in Africa. These 22 HBCs account for 80% of the global TB burden (WHO, 2013b). In 2013, Kenya observed a sharp decline of TB cases, having a total number of 89,760 a 9.48% decline from the 99,159 cases observed in 2012. Additionally, there was a reduction in the prevalence of TB among HIV sero-positive patients from 44% in 2009 (WHO, 2009a; CDC, 2011a) to between 38.3% and 39% (MOH, 2012; MOH, 2013).

Globally it has been shown that both IDUs and non IDUs are at high risk of contracting tuberculosis irrespective of their HIV status (Haileyesus *et al.*, 2013). Recreational drug use is a risk factor for TB as a result of the overlap of epidemiological and social factors associated with both drug use and TB (Deiss *et al.*, 2009; CDC, 2012d; Rüütel *et al.*, 2012). Most IDUs are faced with undernutrition, poverty, homelessness and overcrowding which are also risk factors for both HIV/AIDS and TB infections (Arema *et al.*, 2010; Tang *et al.*, 2011; Strike *et al.*, 2012). Although the higher risk of TB observed in IDUs is usually the result of associated HIV infection, the non IDUs are at a higher risk attributable to the sharing of drug equipment such as marijuana water pipes, smoking and living in cramped conditions or in dwellings with poor ventilation (Deiss *et al.*, 2009; Getahun *et al.*, 2012).

Furthermore, PLWHA who inject drugs have been found to be 85% more likely to have HIV-associated tuberculosis than those who were not injecting drug users. This higher TB rates among PWID support evidence that IDUs are at higher risk of TB (Odendal,

2011; Baddeley, 2013). Since there are very few mono-substance users, polysubstance use contributes to the already devastating HIV epidemic which in turn affects the epidemiology of TB (Kalichman *et al.*, 2006; Kedia *et al.*, 2007; Wechsberg *et al.*, 2008; Floyd *et al.*, 2010).

Furthermore drug use, HIV infections and undernutrition lower immunity thus increasing the risk of reactivating *Mycobacterium tuberculosis* infection. Low body mass index (BMI < 18.5 kg/m^2) and anaemia have been shown to predict high mortality among TB patients. Moreover, patients with poor weight gains during TB treatment are at an increased risk of treatment failure, relapse and premature death (Drake, 2010; Shalini *et al.*, 2012; Mamani *et al.*, 2013; McDermid *et al.*, 2013; Padmanesan *et al.*, 2013).

In South Africa, drug-related activity has been associated with poverty, reduced productivity, unemployment, familial dysfunction, political instability, drug-related violence, gang activity, escalating rates of blood-borne illness such as HIV/AIDS, TB infections, injury, and premature death (Parry *et al.*, 2009; Peltzer *et al.*, 2010; Van Wyk, 2011; Trenz *et al.*, 2013).

In Tanzania, IDUs have been shown to be at high risk for both TB and HIV with outbreaks of drug-susceptible and multidrug resistant TB being reported in this sub population (Gupta *et al.*, 2014). At the time of this study, data on TB among IDUs in Kenya was not available nevertheless drug use has been identified as a predictor of poor adherence to TB treatment in the general population (Muture *et al.*, 2011).

Since PLWHA are more likely to develop active TB in a given year than HIV sero-negative persons due to their weakened immune system, TB screening is critical for the IDU subpopulation (Hwang *et al.*, 2009; USAID, 2013; WHO, 2013a). Recognizing the important relationship between TB and drug use, the WHO, Joint United Nations Programme on HIV/AIDS (UNAIDS) and the UNODC recently issued a set of guidelines to better coordinate TB care among drug users (WHO, UNODC and UNAIDS, 2012).

2.6 HIV

Despite the global massive expansion of HIV interventions, HIV burden remains a major public health challenge. In 2013, 35.0 million people were living with HIV up from 29.8 million in 2001 due to continuing new infections, people living longer with HIV and general population growth. In the same year, 1.5 million people died of AIDS which is a 35% decrease since 2005. This decline is partly due to antiretroviral treatment (ART) scale-up (UNAIDS, 2014).

Sub-Saharan Africa, the hardest hit region is home to 71% of people living with HIV. In 2013 alone, there were 24.7 million people living with HIV in SSA with women accounting for 58% of the total number of people infected. Swaziland has the highest HIV prevalence rate (27.4%) in the world. This high rate in SSA is fueled by poverty, extensive sexual networks of men, cultural practices, unemployment, labour migration and displacement as a result of conflicts (Fox, 2010; Coburn *et al.*, 2013; Ramjee and Daniels, 2013; UNAIDS, 2014).

Although Kenya has one of the largest HIV epidemics in the world, it is still widely regarded as one of sub-Saharan Africa's success stories where HIV prevention is concerned. Annual new HIV infections are roughly one third of what they were at the peak of the country's epidemic in 1993. For example, in 2012 there were an estimated 100,000 new HIV infections in Kenya. Furthermore, during the same period the HIV prevalence among adults aged 15 to 64 years decreased nationally from 7.2% as measured in KAIS 2007 to 5.6%. At the same time, the distribution of HIV infections varied across the country with Mombasa region reporting an HIV prevalence of 4.3% from 7.1% in 2007 (NACC and NASCOP, 2012; UNAIDS, 2013; NASCOP, 2014).

2.6.1 HIV and Injection Drug Use

In the context of HIV epidemiology, people who inject drugs are classified as the most at risk populations (MARPs). Their vulnerability is attributed to precarious injecting practices, high risk sexual activities, under utilizatition of health services and poor adherence to treatment (Uusküla *et al.*, 2010; Čavlek *et al.*, 2011; Muture *et al.*, 2011; Ulibarri *et al.*, 2011; CDC, 2012d; Orsetti *et al.*, 2013; WHO, 2013a).

Sharing mainly occurs because the needles and syringes are either not enough, available, accessible or affordable to IDUs. The accessibility of new needles and or syringes is hindered by various structural factors like refusal by pharmacy operators to sell needles or syringes to IDUs. Furthermore, geographic locations (like distance between shooting galleries and pharmacies), perceptions about stigma and concerns about confidentiality hinders accessibity. Sometimes sharing occurs due to drug impaired judgment or as a sign

of brotherhood (Chakrapani *et al.*, 2011). In addition, when heroin is scarce or resources are limited, some IDUs seek partnerships with others to enhance their ability to raise funds to purchase drugs and such efforts often lead to group injection (Mateu-Gelabert *et al.*, 2010).

High risk sexual activities among PWID include multiple sex partnerships, having unprotected sex with partners of unknown HIV status and engaging in sex for drugs or for money to purchase drugs as well as survival. Besides, sex for police protection, group sex, anal sex, sexual assalt, unconsented sex and partner sexual violence have been reported in this population (Mayhew *et al.*, 2009; Swe *et al.*, 2010). The higher prevalence of HIV among women than men, together with a lower prevalence of HCV provides evidence of sexual transmission of HIV among IDUs. This is of considerable concern given that SSA has the world's largest population of individuals living with HIV (Bowring *et al.*, 2012; UNAIDS, 2012).

In Africa unsafe sexual and injecting practices among IDUs are well documented. For example in South Africa, drug use has been linked to increased risk of HIV acquisition and transmission with IDUs being more at risk than the non- IDUs. In Egypt, high risk behaviours like multiple partnerships with men who have sex with men, female sex workers and other regular or casual partners has been reported (Soliman *et al.*, 2010).

Closer home, Tanzania has been identified as one of the sub-Saharan African countries experiencing significant changes in the patterns of illicit drug use. These include both

non-injecting and injecting drug use in addition to increasing prevalence of unsafe injection and sexual practices. For example blood flashing and sharing, sex for drugs as well as sexual multiple partnerships has been reported among PWID in Tanzania (McCurdy *et al.*, 2010; Atkinson *et al.*, 2011; Bowring *et al.*, 2012).

High risk injection practices have been documented among Kenyan IDUs. These practices include syringe and needle sharing, using pre-filled needles and syringes, front or back loading, sharing of preparation water, sharing equipment and drawing drugs from a common container (Brodish *et al.*, 2011; NASCOP, 2012a; Tun *et al.*, 2014). Precarious sexual tendencies like multiple sexual partnerships with persons of unknown HIV status have been reported. These include rape, sexual assault, unprotected sex which could be consented or unconsented due to drug impairment, sex for police protection, sex for drugs and sex for money to buy drugs as well as survival (Tegang *et al.*, 2010; Brodish *et al.*, 2011; NACADA, 2012; Kahuthia-Gathu *et al.*, 2013; NASCOP, 2013).

2.6.2 HIV Subtypes: Global Outlook

There are two types of HIV which have been distinguished genetically and antigenically. The HIV-1 sub-type is the cause of the worldwide pandemic while HIV-2 is predominantly found in West Africa. The HIV-2, which is transmitted in the same ways as HIV-1 is less lethal than HIV-1 but otherwise clinically the diseases are very similar. HIV-1 and HIV-2 are thought to have arisen from two natural hosts both harboring Simian Immunodeficiency Virus (SIV). The closest relative of HIV-1 is SIVcpz which infects wild-living chimpanzees (*Pan troglodytes troglodytes*) and gorillas (*Gorilla*

gorilla gorilla) in west central Africa while HIV-2 is SIVsmm harbored by sooty mangabeys, *Cercocebus atys* (Sharp and Hahn, 2010; Sharp and Hahn, 2011).

There are three sub-groups of HIV-1, M (main or major), N (new) and O (outlier). Type O HIV-1 is mostly found in Cameroon and Gabon while the rare N sub-group is found in Cameroon. It is very likely that SIVcpz infected humans on separate occasions to give rise to the three sub-groups. In addition, there are at least ten different HIV-1 subtypes within the M group and they are designated A to K (Hunt, 2010; Sharp and Hahn, 2011; Kerina *et al.*, 2013).

Most sub-types are found in sub-Saharan Africa with A and D dominating Central and Eastern Africa and C in Southern Africa (Jung *et al.*, 2012; Kiwelu *et al.*, 2012). This subtype C is also predominant in India and Nepal. It is also the cause of most infections worldwide and is linked to mother to child HIV transmission (Zhanga *et al.*, 2009; Shen *et al.*, 2011; Alcântara *et al.*, 2012). Sub type B is majorly in North America, Latin America, the Caribbean, Europe, Japan and Australia (Junqueira *et al.*, 2011; Abecasis *et al.*, 2013; Mendoza *et al.*, 2014). Type E has been isolated in Thailand and central Africa while type F is predominant in Brazil and Romania. On the other hand, type G has been reported in Russia and Gabon while type H is found in Zaire and in Cameroon (Alcântara *et al.*, 2012; Fayemiwo *et al.*, 2014). Subtype K has been isolated in the Congo and Cameroon (Sharp and Hahn, 2011). Although subtype I was a name given to an apparent sub-type found in Cyprus but the name is no longer used since it is now classified as a recombinant (Hunt, 2010; Kousiappa *et al.*, 2011).

In some countries, mosaics (recombinants) between different subtypes have been found. These arise when two different subtypes infect a person at the same time and recombination occurs. For example, the former subtype I is a circulating recombinant form (or CRF) that is a recombinant of subtypes A, G, H and K. In addition, the polymerase genes of HIV-1 strains from Ghana are made up of recombinants of several CRF 02-AG strains from Ghana, Senegal and Cameroon (Sagoe *et al.*, 2009; Kerina *et al.*, 2013; Palm *et al.*, 2013).

Based on laboratory studies, different HIV-1 subtypes can be transmitted by different routes. For example, type B may be transmitted more effectively by homosexual intercourse and via blood (as in injection drug use) whereas types C and E may be transmitted more via a heterosexual route. This is because types C and E replicate better in Langerhans' cells found in the mucosa of the cervix, vagina and penis while type B replicates better in the rectal mucosa. It also appears that type E is more readily transmitted between sexual partners than type B (Haaland *et al.*, 2009; Almeida *et al.*, 2012; King *et al.*, 2013). Subtype D appears to be more virulent than subtype A. In addition subtypes D and C seem to be transmitted more effectively from mother to child than subtype A (Krivine *et al.*, 2009; Hunt, 2010; Ryland *et al.*, 2010; Zhang *et al.*, 2010).

2.6.3 HIV Subtypes in Kenya

In Kenya, HIV-1 subtype A has been reported as the dominant strain in southern part of the country with over 30% recombinants while subtype C is more predominant in

northern part. Subtypes A, B, C, D and G together with their recombinants have also been described in various parts of the country. Irrespective of the region, subtype A remains the principal strain but there is an increase in the prevalence of subtype C (Khamadi *et al.*, 2009; Lihana *et al.*, 2009; Kageha *et al.*, 2012; Lihana *et al.*, 2012; Muriuki, 2012; Kiptoo *et al.*, 2013; Nyamache *et al.*, 2013; Bezemer *et al.*, 2014). Kenya appears to have an array of subtypes that co-circulate courtesy of increased human migration in and around East and Central Africa (Hue *et al.*, 2012; Lihana *et al.*, 2012).

2.6.4 HIV Subtypes in the IDU population

Due to both high risk sexual and injecting practices, IDUs are likely to have diversified HIV types and recombinants. Globally the explosive outbreak of HIV-1 circulating recombinant forms among IDUs has been extensively documented for example in Afghanistan, China, Greece, India and Taiwan (Sanders-Buell *et al.*, 2010; Yen-Ju *et al.*, 2010; Sarkar *et al.*, 2011; Paraskevis *et al.*, 2011; Han *et al.*, 2013).

In Kenya investigation on the molecular epidemiology of different HIV-1 subtypes and their associated risk factors among IDUs is limited. Despite this constraint, Osman *et al.* (2013) has reported subtypes A1, B and C to be circulating among IDUs in Mombasa. Mombasa which is a coastal cosmopolitan city has the largest number of MARPS. These include PWIDs, men who have sex with men (MSM) and sex workers (NASCOP, 2012a). Due to their high risk injecting and sexual behaviour the probability of HIV co-infections as well as super infections is high. This key sub-population does not operate in

exclusion but instead acts as a bridge to the general population thus fueling HIV epidemics in the region.

2.7 Drugs and Immunity

Previous and ongoing studies as well as reports indicate that drug use diminishes immunity. For example, use of opiates (like heroin and opium) affects several components of the immune system and thus modulates host immunity increasing susceptibility to infections (Ramsin *et al.*, 2008; Haghpanah *et al.*, 2010). In addition, nicotine use has been shown to suppress the immune system there by increasing the risk of infection and poor disease prognosis (Comer *et al.*, 2014; Padmanesan *et al.*, 2013; Van Zyl-Smit *et al.*, 2014). Furthermore, cathinone and cathine reduces post-translational modifications of intracellular signal transducers in T-lymphocytes, B-lymphocytes, natural killer cells and monocytes leading to impaired immunity (Bredholt, 2013).

Weakened immunity can be as a direct result of using drugs or indirectly due to binging which causes the user to be ill and dehydrated. The impact of dehydration, mental and physical exhaustion, sleeplessness and lack of food depletes the immune system (Molina *et al.*, 2010). Diminished immune system in addition to sharing of drug equipment such as marijuana water pipes, smoking as well as living in poorly ventilated dwellings increases the risk of acquiring tuberculosis (Deiss *et al.*, 2009; Getahun *et al.*, 2012).

Beside PWID are less likely to access healthcare facilities as well as adhere to long term TB and HIV therapy (Dutta *et al.*, 2013; Singer, 2014). Therefore, drug use, exposure to HIV and TB as well as undernutrition combined or separately leads to reduced immunity

and thus inability to resist or withstand infections. By and large drug use reduces quality of life and productivity in addition to increased risk of contracting infections as well as premature death. Moreover, drug users are more likely to develop mental disorders even after rehabilitation. Consequently, recreational drug use should be dealt with as a socio-medical problem and not a criminal offence.

2.8 Other Common Co-morbidities

2.8.1 Hepatitis B and C

2.8.1.1 Hepatitis B

The term hepatitis simply means inflammation of the liver and humans are the only reservoir of hepatitis B virus (HBV). The virus is transmitted by percutaneous and permucosal exposure to infected blood and other body fluids, mainly semen and vaginal fluid. This can happen through sexual contact with an infected person or sharing needles, syringes, or other drug-injection equipment. Hepatitis B can also be passed from an infected mother to her baby at birth (WHO, 2013c; Hoffmann *et al.*, 2014; Moezzi *et al.*, 2014; Ramezani *et al.*, 2014). Hepatitis B can be prevented via vaccination which is 95% effective in preventing infection (CDC, 2013d; WHO, 2013d).

2.8.1.2 Hepatitis C

Hepatitis C is a liver disease caused by the hepatitis C virus (HCV). The HCV is most commonly transmitted through exposure to infectious blood. This can occur through: receipt of contaminated blood transfusions, blood products, organ transplants, injections given with contaminated syringes and needle-stick injuries in health-care settings,

recreational injection drug use, beauty treatments and being born to a hepatitis C-infected mother (CDC, 2013c; Villar *et al.*, 2013; WHO, 2013e; Ramezani *et al.*, 2014).

There is no vaccine for Hepatitis C but can be prevented by avoiding behaviours that can spread the disease, especially sharing drug needles or personal items such as toothbrushes, razors, and nail clippers with an infected person (CDC 2012c; Hepatitis Foundation international, 2013; WHO, 2013e).

2.8.2 Tetanus

Tetanus is an acute illness caused by the toxin of *Clostridium tetani.* Soil, street dust and intestinal content of animals and humans are the normal habitat of the organism, but contamination of any wound can result in tetanus. Tetanus among PWID has been reported worldwide (CDC, 2011). Drug injection provides several potential sources for infection with *C. tetani*, including the drug itself, its adulterants like contaminated heroin, injection equipment and unwashed skin. Although recommendations to prevent transmission of HIV among IDUs may limit infection from contaminated injection equipment, these measures may not be effective against spores inoculated from the skin or contained in the drug (WHO, 2009a; Health Protection Agency, 2011). So far, there is no cure for tetanus but it can be prevented by the administration of tetanus toxoid (WHO, 2009a; CDC, 2013e, WHO, 2013f WHO, 2013g).

2.8.3 Dermatological disorders

Skin and soft tissue bacterial infections are a common complication of IDU due to injection of drugs into the fatty layer under the skin. Additionally, leakage of drugs out of

veins during injection (extravasation) and necrosis as a result of toxic materials in drugs as well as increased numbers of bacteria on the skin surface lead to dermatological disorders. Continued use of intravenous drugs can damage both the skin at the site of injection as well as internal organs. A case in point is recurrent suppurative skin infections as a result of subcutaneous administration of drugs being associated with Amyloid A amyloidosis which leads to progressive loss of renal function (WHO, 2009a; Tomlinson, 2010; Nayer, 2014).

Although skin infections usually present as areas of redness, warmth and tenderness (inflammation), the appearance in IDUs is often atypical. Infections usually affect the arms or legs as these are the sites used most frequently for injection. Unusual sites may be involved like the abdomen, back, groin, scrotum and neck due to injecting in the jugular or femoral veins. A more recent study carried out in Glasgow, United Kingdom reported a high prevalence (60%) of skin disease and surprisingly high rates of leg ulceration (15%) among PWID (WHO, 2009a; EMCDDA, 2011b; Coull *et al.*, 2014).

2.9 Prevention and Management of drug use and addiction

It is time for drug abuse to be seen as public health problem and not a criminal problem. The consequences of drug abuse and addiction are costly in terms of preventable health care, law enforcement and crime among other costs. In Kenya, it has been note that drug treatment reduces likelihood of HIV infection by 6 fold in injecting drug users at the same time presents opportunities for screening, counseling, and referral (NACADA, 2012). According to UNODC, for every dollar spent on prevention, at least ten can be

saved in future health, social and crime costs (UNODC, 2013b). The best approach to reducing the tremendous toll from substance abuse is to prevent the damage before it occurs. These strategies include demand reduction, supply reduction and harm reduction.

2.9.1 Demand reduction

Reducing demand consists of creating an environment where the vast majority of people who have never taken drugs continue to resist any pressures to do so, and making it easier for those that do to stop. Drug and substance abuse prevention intervention programmes should target risk factors and enhancing protective factors at all levels therefore reducing demand for drugs. Moderators that need to be promoted in order to prevent drug use include but are not limited to substance and drug abuse awareness, improvement of school enrollment and retention rate, drug resistance skills, personal self-management skills, general social skills, positive peer pressure, good parenting skills, strengthening of the family fabric, poverty eradication and wealth creation as demonstrated in Srikala and Kishore (2010), Mahmoudi and Moshayedi (2012), Niccols *et al.* (2012), Crowley *et al.* (2014) and Massey *et al*, (2014).

2.9.2 Supply reduction

The basic goals of supply reduction and drug law enforcement agencies are to minimize the supply of drugs to illicit markets and to increase the price and inconveniences of acquiring drugs. A fundamental aspect of the drug market is that supply responds to demand and vise versa in accordance with basic economic theory. By targeting to reduce production, distribution, and sales of drug at street level, distributing and selling illicit

drug will be more risky and shortage of drug will increase the price to drug users. In addition, this strategy should be directed towards regulating and enforcing access to legal drugs and substances, particularly those that are of a high probability for abuse, including pharmaceuticals and other precursors and essential chemicals (UNODC and TISS, 2011; Werb *et al.*, 2011; Sahin and Matusitz, 2012; Werb *et al.*, 2013; Sahin and Ersin, 2014).

2.9.3 Harm reduction

Harm reduction refers to approaches to psychoactive drug use that aim to reduce the harms associated with drug use for people who are unable or unwilling to abstain. The prevention of harm is given the highest priority rather than achieving indefinite abstinence from illicit drug use regardless of the unintended negative consequences. Its approach to drugs is based on a strong commitment to public health and human rights (International Harm Reduction Association- IHRA, 2010; UNODC and TISS, 2011). Comprehensive harm- reduction services benefits people who use drugs, their families and the community as is associated with reversal of a rapidly emerging epidemic of HIV among PWID (Sharmin, 2013; Huang *et al.*, 2014).

The concept of harm reduction and minimization for drug users was born in 1986 with the realization that the HIV virus was being spread through the sharing of syringes amongst heroin injecting users. To reduce the risk of an increase in AIDS cases, Australia took the bold step and led the world into implementing the availability and distribution of new syringes to IDUs. As a result, Australia has the lowest incidence of HIV amongst

injecting drug users in the world, less than 2% compared to figures up to 90% in some other countries (Commonwealth of Australia, 2011).

The harm-reduction approach applies various strategies which include but are not limited to addiction counseling, STIs treatment and HIV testing including linkage, educational interventions, needle syringe exchange programmes, detoxification, oral substitution therapy-OST (like methadone and buprenorphine treatment) and Supervised Injecting Facilities [SIFs].

Research indicates that majority of PWUD have an underlying mental health condition, significant emotional or psychological difficulty and thus require both addiction and general counseling (Munro and Allan, 2011; UNODC and TISS, 2011; NIDA, 2012). A good counseling programme incorporates family therapy as drug addiction does not only affect the user's life but the whole family (Centre for Addiction and Mental Health - CAMH, 2010). Studies show family therapy results in lower relapse rates, increased happiness in the family and better functioning in children of addicted parents (Munro and Allan, 2011; UNODC and TISS, 2011; Evans *et al.*, 2012).

Screening of STIs and respective treatment in addition to HIV testing and linkage is an important aspect of harm reduction as some STIs cause open wounds or ulcers to form in the genital area. These openings provide a way for HIV to enter the blood stream. Although some STIs don't cause open wounds but the presence of the STI causes the body to increase the concentration of CD4 cells in the genital area which provide HIV with a favourable target for infection. In addition, people infected with STIs have

increased concentrations of HIV in their genital fluids, increasing the possibility of HIV transmission (CDC, 2010; Cohen *et al.*, 2012; Zhang *et al.*, 2013a). It is imperative to prevent and manage STIs including HIV infections in this sub-population as most PWID tend to engage in precarious sexual practices,

Peer education is a strategy whereby individuals from a target group provide information or training to their peers. These groups can be determined by socio-demographic characteristics (like age, education, type of work) or by risk-taking behaviour (like injection drug use, sex work and sexual orientation). Peer networks increase the credibility and effectiveness of the message being presented (Research to Prevention, 2010; UNODC, 2011b; Jain *et al.*, 2014).

Syringe and needle exchange programmes (SNEP) exemplify harm reduction because they reduce the harms from drug use to drug users, their families and community without requiring a change in the consumption of drugs. These programmes work on the philosophy of providing sterile and new needles and syringes to IDUs in exchange of old used and potentially infected ones. The exchange component has multiple benefits as it ensures that all the used injecting equipments have been collected from the IDUs and destroyed under supervision, minimizing the risk of reuse and accidental exposure. Secondly, it provides an opportunity for frequent contact with IDUs, during which not just needles and syringes but education and other services can be delivered (Global Commission on Drug Policies, 2011; UNODC and TISS, 2011). Furthermore, SNEP

encourage the entry of PWID into drug detoxification and treatment programmes (Alkiviadis *et al.*, 2010; O'Gurek and Kirchner, 2010; Aspinall *et al.*, 2014).

Detoxification services can help to ensure that withdrawal is safe and comfortable and warn drug users of the risk of an overdose on relapse. It is a prelude to treatment and not distinct a form of treatment (Global Commission on Drug Policy, 2011; Katz *et al.*, 2011; Chandra and Madison, 2012; NIDA, 2012).

Methadone and buprenorphine treatment have been endorsed by the WHO and UNAIDS as opioid substitution treatment (OST) for heroin dependence (WHO, 2009b; UNAIDS, 2011; UNODC, 2013c; Wu and Clark, 2013). Both epitomize harm reduction because they reduce the harms of street heroin use without requiring the drug user to abstain from the use of mood altering drugs. The effectiveness of OST in treating opiate addiction, reducing drug use, reducing the frequency of sharing potentially HIV-contaminated syringes and needles, and preventing HIV infection has been well documented. Strong evidence indicates that appropriate doses of methadone or buprenorphine relieve cravings, block the effect of illicit opioids and prevent withdrawal. Reduce frequency of injecting drugs, reuse of syringes and needles has also been reported (Kimber *et al.*, 2010; ECDC, 2011; MacArthur et *al.*, 2012; Wang *et al.*, 2014).

Research into treatments for stimulant (like amphetamine and cocaine) addicts lags far behind as compared to treatments for heroin dependence. Dexamphetamine substitute treatment for amphetamine dependence shows promise and appears to be effective and

safe. Use of dextroamphetamine has been associated with higher rates of sustained amphetamine and cocaine abstinence (Castells *et al.*, 2010; Galloway *et al.*, 2011).

Supervised Injecting Facilities also known as Supervised Injection Sites (SIS), Safe Injection Site, Safer Injection Facility (SIF), Drug Consumption Facility (DCF), Drug Consumption rooms (DCR) or Medically Supervised Injection Center (MSIC) are legally sanctioned and medically supervised facilities where injection drug users are allowed to inject pre-obtained drugs in a more protected, hygienic and less stressful environment compared with most other private and public settings. The first injection room appeared in Bern, Switzerland, in 1986. In the decade that followed, SIFs spread to other cities in Switzerland as well as cities in Germany and the Netherlands. Since 2000, SIFs have been introduced in Spain (Madrid and Barcelona), Australia (Sydney) and Canada (Vancouver). These facilities are exempted from the application of the criminal code or other legislation that governs the use of controlled substances (Csete, 2010; Davies, 2010; Hedrich *et al.*, 2010; UNODC, 2012).

Their aim is to establish contact with hard-to-reach populations of drug users, provide an environment for more hygienic drug use, reduce morbidity and mortality risks associated with drug use (in particular street-based drug injecting), lessen overdose episodes and promote drug users' access to other social, health and drug treatment services (Salmon *et al.*, 2010; Marshall *et al.*, 2011b; De Vel-Palumbo *et al.*, 2013; EMCDDA, 2013g).

It is imperative to note that promoting harm minimization does not condone illicit drug use. It acknowledges that many people are not able to give up drug use without help. It is a means of reducing the risk of harm to a person so that they are kept alive and if they eventually decide to stop their drug use, they will not suffer serious consequences from their drug use (DeBeck *et al.*, 2011). Despite good evidence for its effectiveness in HIV prevention, several countries remain resistant to harm reduction (Rhodes *et al.*, 2010).

2.9.4 Rehabilitation

The WHO defines rehabilitation as the process by which an individual with a substance use disorder achieves an optimal state of health, psychological functioning, and social well-being. The general intent is to enable the patient to cease substance abuse, in order to avoid the psychological, legal, financial, social, and physical consequences that can be caused, especially by extreme abuse. Drug users have a right to voluntary rehabilitation. After rehabilitation they are expected to be socially reintegrated into the wider community (Gifford, 2014; Reif *et al.*, 2014; WHO, 2014b).

2.10 Challenges

Globally, harm reduction strategies addressing drug issues are so unpopular amongst politicians, policemen, magistrates and bureaucrats. In many countries publicly supporting an innovative harm reduction strategy like SIF is considered political suicide. The Global Commission on Drug Policy has been urging politicians to courageously speak out on effective drug policies (Global Commission on Drug Policy, 2011).

The situation is not better in Kenya as most decision makers like politicians (primarily law makers), police (law enforcement officers), magistrates and judges (criminal justice authorities), technocrats, bureaucrats and religious leaders are not willing to support harm reduction strategies in letter and spirit. The criminalization of drug use promotes arbitrary arrests of PWID which it leads congestion in prisons which in return facilitates drug use among inmates, some who are first time users (Kinyanjui and Atwoli, 2013).

People who inject drugs are likely not to optimally adhere to long term treatment. This has been attributed to delayed access to health facilities, competing comorbid diseases, stigma, discrimination, poverty, criminalization of drug use and poorer long-term adherence (Caylà *et al.*, 2009; Muture *et al.*, 2011; DeSilva *et al.*, 2013). In addition, the potential interactions between methadone and buprenorphine with substances of abuse as well as medicinal drugs like Nevirapine, efavirevz, and Rifampicin reduce the efficacy of OST (Lee *et al.*, 2012; McCance-Katz *et al.*, 2013; Vilas-Boas *et al.*, 2013).

Besides, in Kenya there are limited government funded rehabilitation centres and most clients seeking rehabilitative services end up being held in unsuitable venues like the medical or psychiatric wards. Besides most government funded rehabilitation centres do not admit FIDUs. Moreover, MAT is mostly available in privately owned facilities.

2.11 Conclusion

Since drug and substance abuse is a socio-medical problem, public health interventions aimed at improving the health of drug users must address the social factors that

accompany and exacerbate the health consequences of illicit drug use. People who use drugs have the same human rights as people who have never used drugs. These rights include the right to the highest attainable standard of health, to social services, to work, to benefit from scientific progress, to freedom from arbitrary detention and freedom from cruel inhuman as well as degrading treatment.

CHAPTER THREE: MATERIALS AND METHODS

3.1 Study Design

This study was carried out in Mombasa County with an objective of determining the predictors of HIV and pulmonary TB among PWID. It was a cross sectional study which focused on assessing a representative subpopulation of PWID at one specific point in time. Disease and exposure status were measured simultaneously. This study design has been used for similar studies like in Čavlek *et al.* (2011), Majidpour *et al.* (2012) and Karajibani *et al.* (2012).

3.2 Variables

The independent variables (risk factors) were high risk injecting and sexual practices, mono or polysubstance use and exposure to STIs while the dependent variables HIV infection, low BMI, low CD4 count, TB and HIV sub-types.

3.3 Target and Study Population

The target population was a community living in a cosmopolitan coastal city while the study population was PWID living in Mombasa County, Kenya.

3.4 Study Site

The study was carried out in purposively Mombasa County based on the fact that it has the largest number of PWID in Kenya. Mombasa acts as a conduit of drugs from South America en route to Europe and Asia and in the process some of the drugs find their way

into the local market. The IDU participants were recruited from Bomu Hospital as it has support groups for recreational drug users as well as PLWHA.

Mombasa is a cosmopolitan coastal city with the largest port in East Africa and lies between latitudes 3° 80' and 4° 10' S and longitudes 39° 60' and 39° 80' E, with a total land mass of 229.6 km^2 and inshore waters covering 65 km^2 (as shown in Figure 3.1 and Appendix 1). Mombasa County has a population of 939,370 people of which 486,924 are male and 452,446 are female (KNBS, 2010). The County consists of 6 constituencies namely, Kisauni, Mvita, Changamwe, Likoni, Jomvu and Nyali (IEBC, 2012). The cosmopolitan nature of Mombasa combined with the presence of a youthful population has created a suitable environment for commercial sex, child tourism and recreational drug use (Kahuthia-Gathu *et al.*, 2013; Korir, 2013).

Bomu Hospital is a registered non-governmental healthcare organization situated in Changamwe Sub-County close to the Moi International Airport (at latitudes 40 1' 28' South of Equator and longitude 39° 46'57" East of the Greenwich Meridian). It is a project of the Mkomani Clinic Society (MCS). In addition, MCS runs three other satellite clinics in South Coast, Mariakani and at Wema Centre in Kisauni Sub-County. Bomu Hospital offers a large range of programmes like separate Comprehensive Care Centres for adults and children (MOH, 2011; Bomu Hospital, 2013).

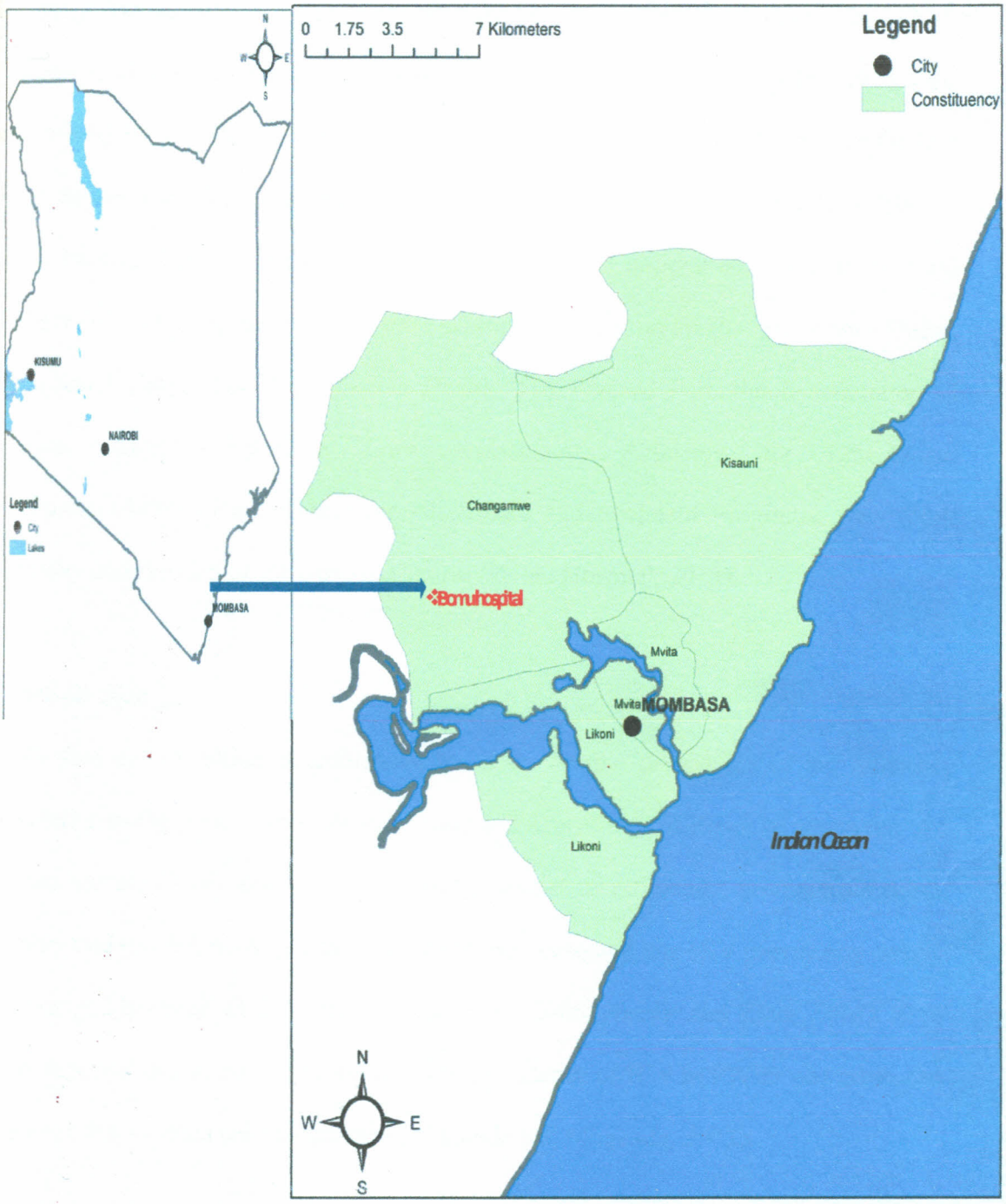

Figure 3.1: Map of Kenya and Mombasa County

Source: Courtesy of Regional Centre for Mapping of Resources for Development

Currently, Bomu provides free comprehensive medical services to more than 23,500 PLWHA from all over the Coast region through the hospital and its satellite clinics that are assisted by the President's Emergency Plan for AIDS Relief (PEPFAR) funding. Other donors include United States Agency for International Development (USAID), Kenya Family Health Program, Japanese International Cooperation Agency, Canadian International Development Agency, Pathfinder's International, European Union, International Center For Reproductive Health, The Planned Parenthood Federation of America, African Palliative Care Association, Academy for Educational Development/International Center for AIDS care and treatment Programs, New York University and the Center for Disease Control (Bomu Hospital, 2013).

3.5 Sample Size

Sample size determination is influenced by study design, prevalence of the attribute, accessibility to the participants, ethical issues and availability of financial resources. An optimum sample is one that fulfills the requirements of efficiency, representativeness, reliability and flexibility. At per time this study was designed, the HIV prevalence among PWID ranged between 43% - 49% (Deveau *et al.*, 2006; Needle and Zhao, 2010). Both authors reported this as an underestimate. The prevalence of HIV in PWID was estimated to 50% and the formula below was used (Mugenda and Mugenda, 2003).

$$n = \frac{Z^2pq}{d^2}$$

Where

n =the desired sample size (since the target population is greater than 10,000).

z = the standard normal deviant (as per area under normal curve at confidence level 95%),

p = the proportion in the target population estimated to have the attributes being measured.

q = 1-p

d = the level of statistical significance set

$$n = \frac{(1.96)^2 . (0.5) . (1 - 0.5)}{(0.05)^2}$$

n = 384 participants.

A total of 384 participants were to be recruited. Due to circumstances beyond the control of the researcher like the general elections in 2013 and arbitrary eviction of drug users from their havens by the County government, only 371 IDUs were enrolled.

3.6 Sampling Procedure

Respondent driven sampling (RDS), traditional snowball sampling and makeshift outreach methods were used to recruit IDUs.

3.6.1 Respondent driven sampling

The RDS method is based on snowball sampling and allows researchers to make estimates about hidden population such as the injection drug users, sex workers, and men

who have sex with men. This sampling technique has been used by several researchers (Atkinson *et al.*, 2011; Ulibarri *et al.*, 2011; Medhi *et al.*, 2012).

Recruitment using RDS was initiated with a number of purposefully selected "seeds" (individuals belonging to the study population who have influence over other members being interviewed). Each seed was given three uniquely coloured coupons with which to recruit peers (other eligible PWID) into the study. These recruited peers were considered as the first wave of participants. Each participant in the first wave who completed the interview was then provided six coupons with which to recruit their peers. Successive waves of recruitment continued until the waves died (no more participants were being enrolled) before the desired sample size was achieved. At this stage only 142 PWID had been recruited. Snowball sampling and makeshift outreach methods were then used.

3.6.2 Snowball sampling

Snowball sampling is a non-probability recruitment technique that is appropriate to use in hidden populations. The recruited PWID were asked to assist researchers in identifying other potential subjects. The chain referral system continued until it was exhausted. This method has been used by researchers targeting similar groups (Rafiey *et al.*, 2009; Atkinson *et al.*, 2011; Shannon *et al.*, 2011; Suohu *et al.*, 2012).

3.6.3 Makeshift outreach method

To cover up for the deficit, makeshift outreach method was used. This involved direct recruitment from drug havens by a rehabilitated former IDU. Among others, the method

has previously been used by Gyarmathy *et al*, (2009), Williams *et al*, (2009) and Suohu *et al*, (2012).

3.7. Data Collection Methods

The IDUs were defined as persons who injected drugs for recreational purpose at least once a day regularly in the last one month prior to the commencement of study. Observation of the needle scars was a necessary criterion for their enrollment. Data collection methods varied depending on the objective as follows:

3.7.1 Interview Schedule

Structured interview schedule was used to capture the socio-demographic characteristics and drug use patterns. The information was collected by research assistants who are trained community health workers. They read the questions exactly as they appeared on the interview schedule to the participants in English or Swahili. The choices of answers to the questions were both fixed (close-ended) as well as open-ended as shown in Appendix 2.

3.7.2 Anthropometric Measurements

Nutritional status was determined using anthropometric measurements which included weight, standing height, bust, waist circumference, hip circumference and mid- upper arm circumference as per anthropometry procedures manual by National Health and Nutritional Examination Survey (CDC, 2009). In addition, in order to assess the heamoglobin level a full haemogram was carried out.

Height was measured in centimeters using Health O Meter PORTROD, Professional Wall Mounted Height Rod. Participants were asked to remove their shoes, stand straight with both feet facing flat-forward and their back against the wall. To measure weight (in kilograms), each respondent was requested to remove their shoes, purse and anything else that was heavy. The respondent stood on the scale platform, facing the vertical portion of the scale with weight evenly distributed between both feet (CDC, 2009).

To determine bust circumference, a tape measure was placed around the back and across the nipples. It was wrapped around loosely. The waist circumference was determined by first identifying the lowest point of the last rib and the crest of the ilium (top of the hip bone). Once the upper hip bone was located, a tape measure was placed around the abdomen horizontally and at the belly button or just above it. The tape measure was snug but tight enough not to cause compressions on the skin. The hip circumference was obtained by positioning the tape measure horizontally around the maximum circumference of the buttocks. For women this was at groin level while for men it was 2 - 4 inches below the navel. All measurements were recorded in centimeters. Waist hip ratio (WHR) was obtained by dividing waist circumference by hip circumference.

The mid-upper arm circumference (MUAC) was obtained using MUAC tape measure. With the arm bent and held against the torso, the summit of the shoulder (the acromium) to the tip of the elbow (the olecranon) was measured; the mid-point was marked and this is where the circumference measure was then taken. The arm was left to hang in a relaxed position and the armband (strip) was contacting the entire circumference of arm, this was

done by applying finger pressure. It was not so tight to cause the skin to bulge around the tape and neither was there any space left between the tape and the skin. The circumference was recorded to the nearest millimeter (CDC, 2009; WHO, 2011b).

Body mass index (BMI) also referred to as Quetelet index, is a statistical measurement which compares a healthy body weight based on how tall a person is. It was determined using the universally formula of kg/m^2. Based on the WHO guidelines, a BMI of less than 18.5 kg/m^2 was considered underweight indicator of undernutrition, while a BMI greater than 25 was considered overweight and above 30 was considered as obese (FANTA, 2013).

To determine the heamogloblin (Hb) level, approximately 5 ml of venipuncture blood was drawn a full haemogram was carried out using Midray Analyzer (BC-5380, Mindray Medical International Limited). Haemoglobin that was equal or more than 12 g/dL for women and 13 g/dL for men was considered as non-anaemia while Hb of less than 12 g/dL in women or 13 g/dL in men was classified as anaemia (WHO, 2011c).

3.7.3 Tuberculosis Diagnostic Methods

All the participants received health education on TB and those who had a self reported history of persistent cough for more than two weeks, fever, chest discomfort and sweating at night were screened for TB infection (CDC, 2012f). The screening process was carried out by a registered medical practitioner while the sputum was obtained by a

registered laboratory technologist. The TB samples were handled at a Physical Containment Level 3 (APC3) laboratory which had bio-safety cabinets.

3.7.3.1 Collection of Sputum

The patients were given instructions on how to collect the sputum. One spot and two early morning 5 ml specimens of sputum were obtained on three different consecutive days for TB diagnosis (WHO, 2008a). This was done in a Sputum Collection Booth (model VCM-1500N 2) to prevent TB from spreading.

3.7.3.2 TB Sputum for Acid Fast Bacteria (AFB) Microscopy

Using an application stick, the most mucoid part of the sputum was placed on the slide in an oval shape (2-3 cm in length and 1-2cm width). Carbol Fuchsin was applied on the slide which was gently heated until it steamed. The hot slide was allowed to sit for 3 to 5 minutes and afterwards rinsed with tap water. The slide was flooded with a decolorizor (3% hydrochloric acid in isopropyl alcohol) and rinsed subsequently with tap water. The slide was next flooded with Methylene Blue (in order to provide a contrasting background), rinsed with tap water and blot dried. The non-acid-fast bacteria picked up Methylene Blue, to become blue while the acid-fast bacteria retained Carbol Fuchsin colour and appeared red when viewed under the microscope. A drop of oil was put on one end of the smear and the slide was viewed under oil immersion lens (APHL, 2009).

The findings were reported as negative where no AFB was found in at least 100 fields and exact figure out of 100 in slides with 1–9 AFB per 100 fields while slides with 10–99

AFB per 100 fields were reported as (+). On the other hand, slides with 1–10 AFB per field with count of at least 50 fields were reported as (++) while slides with more than 10 AFB per field with count of at least 20 fields were reported as (+++) as guided in APHL (2009). A bacteriologically confirmed TB case was defined as a positive by smear microscopy, culture or WHO-approved rapid diagnostics such as Xpert MTB/RIF (WHO, 2013i). The clients who tested TB positive were enrolled into the TB programme at Bomu Hospital or Coast PGH for treatment and psycho-social support. Infectious waste was collected in an autoclavable bag and autoclaved before incineration.

3.7.3.3 Drug Susceptibility Testing

Drug susceptibility testing (DST) of *Mycobacterium tuberculosis* was carried out after culture was isolated from clinical specimens. Löwenstein-Jensen (LJ) media was used for mycobacterial culture. A homogeneous suspension of growth was inoculated into growth control (GC) tubes and drug-containing LJ media tubes. The proportion method (critical proportion of 1% of growth for all the four drugs) was used to determine the percentage of growth (number of colonies) of a defined inoculum on a drug-free GC media versus growth on culture media containing the critical concentration of an anti-TB drug (Table 3.1). This was followed by incubation of the media at 36 ± 1 °C. The inoculated media were examined for contamination after 1 week of incubation and for DST interpretation after 4 and 6 weeks of incubation. Results after 4 weeks were considered as provisional while after 6 weeks were definitive and interpretation of results was based on the later.

Drug	Isoniazid	Rifampicin	Ethambutol	Pyrazinamide
Critical concentration (µg/ml)	0.2	40	2	4

Table 3.1: Critical concentrations of first-line drugs

Source: (WHO, 2008b).

A strain was considered to be resistant if the medium containing the critical concentration of the corresponding drug showered more colonies than the growth control (GC) with the 1% inoculum. The result was interpreted and reported as susceptible or resistant. Borderline cases (about 1% growth on drug-containing medium) were reported as resistant and retested (WHO, 2008b).

Growth of more than 20 colonies on control tubes and no growth on drug tubes were reported as sensitive to all drugs. Growth of more than 20 colonies on control tubes and number of colonies on Isoniazid, Rifampicin, Ethambutol and Pyrazinamide tubes of more than or equal number of colonies on control corresponding tubes of 1/100 was reported as resistant to Isoniazid, Rifampicin, Ethambutol and Pyrazinamide respectively. Growth of more than 20 colonies and number of colonies on Isoniazid, Rifampicin, Ethambutol and Pyrazinamide tubes of less number of colonies on respective control tubes 1/100 was considered as sensitive to Isoniazid, Rifampicin, Ethambutol and Pyrazinamide correspondingly. In cases where there was no growth on control tubes or less than 20 colonies on GC and no growth on drug tubes, it was reported as invalid result and the process was repeated. Multi drug resistant TB was defined as resistance to

isoniazid and rifampicin, with or without resistance to other first-line drugs (WHO, 2008b; WHO, 2012b; TB CARE I, 2014).

3.7.4 HIV Testing

All the participants received free HIV education after which they were allowed to make personal informed choices on either to undergo an HIV test or not. Upon obtaining written informed consent, they completed the interview schedule after which each participant underwent pre-test HIV counseling. Provider-Initiated HIV Testing and Counseling was carried out by trained VCT counselors. The HIV testing was purely on voluntary basis and those who decided not to undergo the test at this stage were not included in the study.

3.7.4.1 Blood Collection

Approximately, 5 ml of venipuncture blood was drawn from each participant in EDTA anticoagulant tubes and used for conducting other tests cited within this study like full haemogram, CD4 count and viral load. A drop of the blood was used for HIV testing. The HIV-1 status was determined using Determine™ (Abbott Laboratories, Tokyo, Japan) and positive serological results were confirmed by Unigold™ (Trinity Biotech Plc, Bray, Ireland) as per the Kenya National Guidelines for HIV Testing and Counseling (NASCOP, 2010). The results were ready within 5 to 10 minutes. Each participant received post test counseling and those who tested HIV positive were referred to the Comprehensive Care Centre and enrolled into the HIV ART treatment and psychosocial

support program at Bomu hospital or Coast General Hospital. All participants were encouraged to join the recreational drug users support group hosted by Bomu hospital.

3.7.4.2 RNA Extraction and Quantitation of HIV-1 Viral Load

The HIV-1 viral load was quantified using the automated Abbott m Sample Preparation System (m2000sp) that has automated sample extraction, amplification and detection according to the manufacturer's instructions (Abbott Molecular Inc., Illinois, U.S.A). This was achieved via RNA extraction from 0.2 mL of plasma using the 0.2 mL plasma RNA extraction and master mix addition protocol by the Abbott m2000sp sample preparation system. The master mix containing the viral RNA (vRNA) was then transferred to Abbott m2000rt instrument for viral load detection using the program for 0.2mL RNA amplification with a lower limit of quantitation at 150 (2.18 log10) copies/ml of plasma. This method has been previously by Thao *et al.* (2012).

3.7.4.3 Reverse Transcriptase-PCR

To convert vRNA to cDNA, 5 µL from the remaining 13µL of the RNA extract in the Abbott m2000sp deep well plate was used as a template and 0.16 µM each of primers; Nyupol_7 (5'-GGGAATTTTCTTCAGAGCAG-3') and Nyupol_8 (5'-TCTTCTGTCAATGGCCATTGT-3'). This was performed by one-step RT-PCR in a 25 µL reaction consisting of; 0.5 µL SuperScriptTM III one step RT/PlatinumH Taq high Fidelity Enzyme Mix in a 1x reaction buffer mixture containing Mg2+ and deoxyribonucleotide triphosphates (dNTPs) (Invitrogen, Carlsbad, CA). Thermocycling conditions for reverse transcriptase PCR were set with an initial cycle RT step at 55^{0}C for

30 min and 94^{0}C for 2 min, followed by 40 cycles of PCR at 94^{0}C for 15 sec, 46^{0}C for 30 sec, 72^{0}C for 1 min and an extension at 72^{0}C for 5 min.

The amplified viral cDNA encording the partial *pol-gag* gene was nested in a 25 µL master mix reaction consisting of 1X P 1.5mM MgCl¬2, 1U/µL Taq polymerase (KemTaq®), 200 µM of each dNTP (Invitrogen, Carlsbad, CA), 3µl of template DNA and 0.5 µM of each inner primer; Nyupol_9 (5'-TCCTTAACTTCCCTCAAATCACT-3') and Nyupol_10 (5'-CTGGCACGGTTTCAATAGGACT-3'). Amplification was done with an initial denaturation of 94°C for 4 minutes followed by 40 cycles of 94°C for 15 seconds, 46°C for 30 seconds, and 72°C for 1 min, with a final extension of 72°C for 5 minutes. The resulting PCR products were electrophoresed in 1.5% ethidium bromide stained agarose gel and visualized under ultraviolet light. Presence of 297 bp fragment was indicative of successful amplification.

3.7.4.4 DNA Purification and Sequencing

The resulting PCR amplicons were purified with QIAquick PCR purification kit (Qiagen, Valencia, CA) following manufacturer's instructions (5.7.3). Direct sequencing of the PCR amplification products was performed using the inner primers (Nyupol_9 and Nyupol_10) with the Big Dye Terminator sequencing chemistry in both directions. The sequencing products were analyzed on an ABI PRISM® 3100 Genetic Analyzer and DNA base calling performed using the DNA Sequencing Analysis software V3.7. The sequence data was then imported into the Genetyx-Windows computer software version

9.1.0 (Genetyx Corporation, Tokyo, Japan) to assemble the two sequence segments into a single contiguous sequence.

3.7.5 Hematological Profile

Full haemogram was determined using a BC-3200 mindray haematologic analyser (Mindray Inc., NJ). These included: leucocyte counts (total leukocytes, and numbers and percentages of lymphocytes, monocytes, neutrophils, eosinophils and basophils); erythrocyte indices (red blood cells [RBC], haemoglobin [Hb] levels, haematocrit [Hct], mean corpuscular Hb [MCH], mean corpuscular Hb concentration [MCHC], mean cell volume [MCV] and red cell width [RDW]); and thrombocyte indices (platelets, mean platelet volume [MPV], PCT and platelet width [PDW]).

3.7.6 CD4+ T Cell Enumeration

Baseline $CD4^+$ T cell counts were determined using a FACSCalibur flow cytometer (Becton-Dickinson, NJ) equipped with automated acquisition and analysis software. This was done by placing 5 µl of whole blood samples in a tube and RBC lysis buffer was added. After 5 minutes incubation, the cells were washed and fluorescent-tagged antibodies anti-CD3, anti-CD4, anti-CD19 and anti-CD45 were added. The cells were incubated for 30 minutes after which the samples were washed and CD4+ T cells enumerated on the flow cytometer. Individual test results were reviewed to confirm the accuracy of the automated software analysis.

3.8 Vital Signs

3.8.1 Body Temperature

It was measured using a clinical thermometer which was placed under arm with the bulb in the center of the armpit. The arm was pressed against the body for 5 minutes. The thermometer was removed and readings recorded in degrees Celsius. Pulse rate which is the beat of the heart that can be felt in any artery that lies close to the skin per minute. It was determined by placing the tips of the index and second fingers of one hand on the inside wrist of the participants hand. The fingers were positioned just below the base of the thumb to take the radial pulse at the wrist for one minute.

3.8.2 Blood Pressure

To obtain blood pressure, participants were asked to remove any constricting clothing from their upper left arm, to sit straight up in a chair with their feet resting flat on the floor and not cross their legs. The blood pressure cuff was loosened and slid on their left arm through it until it was positioned about 1/2 inch above the elbow. The cuff was inflated by rapidly pumping the inflation bulb until the correct pressure was reached. The inflation bulb was slowly released until the numbers came to rest, then the current blood pressure readings were recorded.

3.9 Pilot Study

A pilot study was carried out from Bomu Hospital (Wema centre satellite clinic in Kisauni Sub-County) to assess whether the proposed methods and procedures were applicable. This was to help in testing logistics that could have exposed any deficiencies

to the main study. The quality and the efficiency of the main study were improved. The participants from this centre were not included in the actual study.

3.10 Inclusion Criteria

1. Only individuals who had practiced injection drug use in the last 1month were included in this IDU study.
2. These individuals were all adults.
3. They must have consented to voluntarily participate and undergo an HIV test.
4. Those with visible needle scars.

3.11 Exclusion Criteria

1. Other drug users who were non IDUs were excluded from the study.
2. Injecting drug users who were minors were not included.
3. Participant who were not willing to give a written consent or undergo an HIV test were excluded.
4. Those without needle scars were excluded.

3.13 Ethical Consideration

The study was conducted according to the Helsinki Declarations and ethical approval for the study was sought and granted from Kenyatta University Ethical Review Committee (PKU019/116 of 2012, Appendix 4). Permission was granted from Ministry of Health, Mombasa County (MOH Ref:ADM.3/5/37/121, Appendix 5). Written informed consent

either in English or Swahili was obtained from each participant before enrolment (Appendix 6 and 7 respectively).

Confidentiality was ensured as no individual name was used instead the participants were assigned study numbers. The participants benefited from free health education on HIV, tuberculosis, hepatitis B and C, STIs, personal hygiene and nutrition. The HIV positive, TB positive as well as HIV-TB co-infected participants were referred to the comprehensive care unit of either Bomu Hospital or the Coast General Provincial hospital depending on participant's preference. All participants were encouraged to join the recreational drug users support group hosted at Bomu Hospital.

3.14 Data Analysis

Data analyses were conducted using SPSS, version 19 (IBM SPSS Inc., New York, USA), all tests were two-tailed and $P<0.05$ was used for statistical inferences for objectives one to four. Pearson's Chi-square or Fisher's exact tests (where the expected frequency was less than five) were used for comparing distribution in the proportions of categorical variables between HIV infected and uninfected participants.

Age comparison between HIV infected and uninfected was performed using the Mann-Whitney test. In order to identify predictors of HIV infection, binary logistic regression analyses were performed using HIV status as the dependent variable and the socio-demographic, sexual practices and drug use information as the independent that is the predictor variables. Since age, education, employment, religion and residence are associated with injection drug use, the potential confounding effect of these variables was

controlled for (Brodish *et al.*, 2011). Only variables found to be significantly associated with HIV infection at P<0.1 in the Chi-square and Fisher's exact tests were included in the regression analyses.

Data for nutritional status was presented as medians (IQR) or proportions (n %) while anaemia, BMI, CD4 and viral load classification were based on WHO criteria. Statistical comparison between groups was performed by Mann-Whitney test. Comparative distribution in the proportions of categorical variables between non-IDUs and IDUs was analysed using Pearson's Chi-square test. Fisher's exact test was used where the expected frequency was less than five. Only variables found to be significantly associated with nutrition at P<0.1 in the Chi-square and Fisher's exact tests were included in regression. Binary logistic regression was conducted using BMI<18.5 kg/m^2 (malnourished) as dependent variable and BMI≥18.5 kg/m^2 as the reference group controlling for age and gender in HIV negative IDUs and age, gender and ART use in the HIV positive IDUs. Data are presented as odds ratios (OR) and 95% confidence interval (CI).

Data the tuberculosis prevalence was presented as percentage, n (%) and Fisher's exact test was used in comparing proportions between the groups. All tests were two-tailed and P<0.05 was used for statistical inferences. Binary logistic regression controlling for age and gender in HIV negative IDUs and age, gender and ART use in the HIV positive IDUs was carried out. Data were presented as odds ratios (OR) and 95% confidence interval (CI). Data for HIV Subtypes was tabulated and presented as number (%) of participants as illustrated in the next chapter.

CHAPTER FOUR: RESULTS AND DISCUSSION

4.1 The Social-demographic Characteristics and Sexual Practices of the PWID in Mombasa County

The distribution of socio-demographic factors in the HIV infected (n=157) IDUs relative to HIV uninfected (n=214) IDUs as presented in table 4.1. The proportion of the female gender ($P<0.0001$), protestant religion ($P<0.0001$), marital separation ($P<0.0001$), and sex work, entertainment or beauty therapy occupations ($P<0.0001$) were significantly higher among HIV infected IDUs. Although most IDUs earned at least US$ 174 a month, the proportion of low income levels (US$ <174) was higher among HIV uninfected IDUs ($P=0.015$). However, the distribution of age ($P=0.271$), residence ($P=0.741$), education ($P=0.170$), and employment ($P=0.167$) did not differ significantly by HIV infection status (Table 4.1).

The gender distribution in the injection drug users indicated 86% HIV-1 infection rate among female IDUs. The subsequent regression analyses illustrating odds of 19 times for HIV-1 infection among the females implies that this special group was at an exceedingly high risk of acquiring HIV-1 infections. This finding was consistent with previous studies among Tanzanian injection drug users showing that females were 64% likely with odds of nearly 5 times for testing positive for HIV-1 (Williams *et al.*, 2009). Females among the urban poor in Kenya have remained more vulnerable to HIV-1 infections due to the fact that they are more excluded from mainstream economic activities. In addition, they are more affected by the ravages of poverty (Madise *et al.*, 2012).

are associated with increased odds for HIV-1 infections among IDUs. These observations are partly consistent with studies among South African IDUs illustrating that drug users exchange sex for money to buy drugs. In addition, drug injecting sex workers in South Africa frequently use drugs before, during and after sex at the same time share drugs with clients (Parry *et al.*, 2009). The observations among the Mombasa injection drug using population suggest that entertainment and beauty therapy industries are important in fueling the HIV epidemic in the population. This premise is in concordance with observations in Vietnam indicating that entertainment venues are frequent points for initiation of drug use (Thao *et al.*, 2006). The findings are also partly consistent with studies among Chinese female sex workers injecting drugs showing a higher risk of HIV infection in those working in entertainment venues, beauty salons or saunas (Wang *et al.*, 2009).

In contrast, to the sex work and entertainment or beauty therapy industries, small business and passenger service vehicle (PSV) operators were associated with lower odds for HIV-1 infections among injection drug users. These findings clearly illustrate that engaging in viable and consistent income generating occupations is an important deterrent for preventing transmission or acquiring HIV infections. Such individuals may be injecting less frequently and/or have money to buy drugs, needles and syringes hence less likely to engage in sex for money to buy drugs or sex for drugs or share injecting equipment. These occupations may thus be used for spreading HIV prevention social marketing interventions among injection drug users (Gibson *et al.*, 2010).

On the contrary, long distance truck drivers who have been associated with higher risk of HIV infection and drug use (Morris and Ferguson, 2006), PSV operators injecting drugs in the current study appear to be at reduced risk for HIV-1 infections. The reasons for this peculiar observation may be related to their long working hours and using drugs for alertness while driving and sedation when on short breaks. The bulk of PWID reporting working in small businesses were engaged in selling of household items, groceries and cart pushers. Again these are activities that are energy supping and require long working hours hence such individuals are less likely to engage in risky sexual activities.

From this study, having an income is an important element of reduced odds for having HIV-1 infection. The finding of low income levels predicting low odds for HIV-1 infection partly relates to class subsets in the drug injecting communities at this coastal region of Kenya. These results are also partly consistent with studies in Canada showing associations between stimulant drug use and engaging in low-threshold employment (Debeck *et al.*, 2011). In addition, studies among IDUs in the United States indicate that income is a key determinant of low to high use and low to high risk classes of injection drug users (Watson *et al.*, 2013). Subsequently income levels may determine the frequency of injection, affordability of drug injection equipment and involvement in risky sexual practices such as sex for drugs and/or money to buy drugs.

Category	HIV[-]	HIV[+]	*P*
Participants (*n*)	214	157	
Female, *n* (%)	14 (6.5)	86 (54.8)	**<0.0001**
Age, yrs.	31.7 (9.1)	30.6 (6.6)	0.271[a]
Residence			
Informal and low income	111 (51.9)	80 (51.0)	
Makeshift and streets	58 (27.1)	39 (24.8)	0.741
Middle and high income	45 (21.0)	38 (24.2)	
Education			
Secondary/college[b]	66 (30.8)	35 (22.3)	
Primary	138 (64.5)	112 (71.3)	0.170
None	10 (4.7)	10 (6.4)	
Marital status			
Currently married	57 (26.6)	17 (10.8)	
Divorced	26 (12.1)	28 (17.8)	
Never married	86 (40.2)	44 (28.0)	**<0.0001**
Separated	42 (19.6)	66 (42.0)	
Widowed	3 (1.4)	2 (1.3)	
Religion			
Catholic	43 (20.1)	43 (27.4)	
Protestant	20 (9.3)	36 (22.9)	**<0.0001**
Muslim	151 (70.6)	78 (49.7)	
Employment			
Informal	172 (80.4)	135 (86.0)	0.167
Formal	42 (19.6)	22 (14.0)	
Occupation			
PSV operators	102 (47.7)	34 (21.7)	
Small business	66 (30.8)	20 (12.7)	
CSW	5 (2.3)	32 (20.4)	**<0.0001**
Hospitality	17 (7.9)	13 (8.3)	
Entertainment/beauty therapy	4 (1.9)	41 (26.1)	
Others[c]	20 (9.3)	17 (10.8)	
Income, dollars/month[d]			
>231	100 (46.7)	88 (56.1)	
174-231	41 (19.2)	39 (24.8)	**0.015**
116-173	40 (18.7)	18 (11.5)	
0-115	33 (15.4)	12 (7.6)	

Table 4.1: Socio-demographic characteristics of IDUs in Mombasa, 2012-2013

Data are presented as numbers and proportions (%) of subjects, unless otherwise indicated. Statistical analyses were conducted using the Pearson's chi-square or Fisher's exact tests as appropriate. [a]Mann-Whitney test. [b]Chi-square test was based only on cells with at least 5 counts. [c]Others constituted fishermen, house helps, beggars, garbage collectors, clerks, masons, artisans and petty thieves. PSV, passenger service vehicles (Matatu drivers, taxi drivers, conductors and touts). [d]As at September 30th 2013, US$ was equivalent to KShs. 86.8. Values in bold indicate significant *P*-values.

Sexual practices were examined among IDUs presenting with or without HIV infection. Sexual orientation did not differ significantly between the groups (P=0.225). However, the proportion of IDUs reporting early age of sexual debut (P<0.0001), at least two sexual partners (P<0.0001), unprotected sex (P<0.0001), sex for police protection (P<0.0001), sex for drugs (P<0.0001) and an STI (P<0.0001) were significantly higher among those infected with HIV (Table 4.2).

Characteristic	**HIV[-]**	**HIV[+]**	***P***
Participants (*n*)	214	157	
Sexual orientation			
Bisexual	21 (9.8)	13 (8.3)	
Heterosexual	164 (76.6)	131 (83.4)	0.225
Homosexual	29 (13.6)	13 (8.3)	
Age of sexual debut			
<15	48 (22.4)	76 (48.4)	
16-20	123 (57.5)	62 (39.5)	**<0.0001**
>20	43 (20.1)	19 (12.1)	
Number of sexual partners			
0	25 (11.7)	5 (3.2)	
1	91 (42.5)	49 (31.2)	**<0.0001**
2-5	88 (41.1)	73 (46.5)	
>5	10 (4.7)	30 (19.1)	
Had penetrative sex in the past year	165 (77.1)	144 (91.7)	**<0.0001**
Had sex without condom	19 (8.9)	49 (31.2)	**<0.0001**
Had sex for police protection	6 (2.8)	37 (23.6)	**<0.0001**
Had sex for drugs	20 (9.3)	39 (24.8)	**<0.0001**
Had STI in the past year	52 (24.3)	102 (65.0)	**<0.0001**

Table 4.2: Sexual practices of PWID in Mombasa, Kenya, in 2012-2013

Data are presented as proportions, unless otherwise indicated. Statistical analyses were conducted using the Pearson's chi-square or Fisher's exact tests as appropriate. STI (sexually transmitted infections).

Analysis of sexual practices of PWID showed that nearly 50% of the individuals that reported sex debut at age less than 15 years were HIV infected. These results remained predictive of the HIV sero-positivity even after controlling for confounders in the regression analyses. At a young age an individual is still a minor and incapable of making informed decisions regarding safer sex. In addition, such underage persons are prone to sexual and or physical abuse that is frequently associated with risk of HIV acquisition. In Kenya, 21% of young adults aged 15 to 24 years are reported having had sexual debut before 15 years of age compared to 33.4% among IDUs in the current study (NASCOP, 2013). Young people in Mombasa may be engaging in drugs and prostitution at an early age to escape the ravages of poverty leading to a higher risk of infection (NACADA, 2012; NACC and NASCOP, 2012).

The study further showed that having at least two sexual partners increased higher odds for HIV infection. Multiplicity of sexual partners often increases the risk of acquiring sexually transmitted infections (STIs) including HIV (Khan *et al.*, 2012). In the current study individuals that reported experiencing an STI in the past year also had higher odds for HIV infections. Consistent with previous studies in the same area showing that IDUs report multiple past and new sex partners (Brodish *et al.*, 2012). These findings clearly indicate that multiplicity of sex partners is an important risk factor for acquisition of HIV in the drug injecting communities. Multiplicity of sex partners is one of the factors identified as fueling the HIV epidemic in Kenya mainly through increasing STIs which promote efficient transmission of HIV (NASCOP, 2013).

Sexual activity in the past 12 months and engaging in unprotected sex were also identified as important sexual practices predicting HIV infection in the present study. These findings are consistent with the results of the 2012 KAIS report for the general Kenyan population (NASCOP, 2013). Additionally, similar studies have shown associations between multiple sexual partnerships, unprotected sex and trading sex for money, in HIV sero-positive Tanzanian heroin users (Ross *et al.*, 2008; Atkinson *et al.*, 2011). Importantly, results in this study showed that sex for drugs and sex for police protection were associated with higher odds of having HIV infection. These findings are in part, parallel to previous studies in South Africa showing complex interacting economies of drugs and sex work whereby sex is exchanged for drugs (Needle *et al.*, 2008). Findings from this study also partly mirror studies in Pakistan indicating that harassment, abuse and exploitation of most at risk populations (MARPs) like PWID, sex workers and MSMs. Perpetrator of these atrocities range from non-state actors such as relatives and sex worker clients to state actors like the police (Mayhew *et al.*, 2009).

These findings were concurrent with the work of McCurdy *et al*, (2006), Parry *et al*, (2008), Williams *et al*, (2009), McCurdy *et al*, (2010), Brodish *et al*, (2011), Čavlek *et al*, (2011), Majidpour *et al*, (2012) and the 2012 KAIS report, NASCOP, (2013). The family unit, STIs and income in these studies were significant determinants of HIV infection among IDUs and should be targeted for effective interventions.

4.2 Drug Use Patterns of HIV Infected and Non- infected IDUs of Mombasa County

Heroin was the most frequently injected drug in the HIV infected and uninfected IDUs ($P<0.0001$) but the proportion of cocaine users was higher in the HIV infected group ($P<0.0001$). The proportion of IDUs using other injecting drugs, flunitrazepam and diazepam did not differ significantly between the HIV positive and negative groups ($P=0.837$). Although most of the IDUs in both groups injected for at least twice a day, the proportion of those injecting once daily was higher among the HIV infected group ($P=0.004$). In contrast, the proportion of IDUs reporting having been injecting for less than six months was higher among HIV uninfected IDUs ($P=0.001$).

The findings of polysubstance use among IDUs have been summarized in table 4.3. Among the non-injection substances, the proportion of IDUs using alcohol ($P<0.0001$), cocktail ($P=0.002$), and khat ($P=0.002$) was higher in the HIV infected group. However, mono-substance usage, that is, bhang ($P=0.464$), brown sugar ($P=0.643$), cigarette ($P=0.651$), or rohypnol tablets ($P=0.265$) was not significantly different between the groups. Additional analyses on polysubstance use showed that injection of heroin or cocaine (as a primary drug) and use of any four non-injection substances (Group V) was higher among HIV infected versus uninfected IDUs ($P<0.0001$) while injection of the primary drug (Group I), and any one (Group II), two (Group III), or three (Group IV) non-injection substance did not differ significantly between the groups ($P>0.05$ for all) as shown in table 4.3.

Category	HIV[-]	HIV[+]	*P*
Participants (*n*)	214	157	
Injection drugs			
Cocaine	19 (8.9)	42 (26.8)	**<0.0001**
Heroin	191 (89.3)	112 (71.3)	**<0.0001**
Heroin-cocaine	4 (1.9)	3 (1.9)	-
Other injection drugs			
Diazepam (valium)	16 (7.5)	10 (6.4)	0.837
Flunitrazepam (rohypnol)	12 (5.6)	2 (1.3)	-
Frequency of injection, per day			
Once	13 (6.1)	25 (15.9)	
Twice	75 (35.0)	36 (22.9)	**0.004**
Thrice	95 (44.4)	76 (48.4)	
>3 times	31 (14.5)	20 (12.7)	
Duration of injection			
<6 mos.	40 (18.7)	8 (5.1)	
6-11 mos.	30 (14.0)	21 (13.4)	**0.001**
1-3 yrs.	76 (35.5)	62 (39.5)	
>3 yrs.	68 (31.8)	66 (42.0)	
Non-injection drugs			
Alcohol	37 (17.3)	82 (52.2)	**<0.0001**
Bhang	102 (47.7)	81 (51.6)	0.464
Brown sugar[a]	30 (14.0)	19 (12.1)	0.643
Cigarette	144 (67.3)	110 (70.1)	0.651
Cocktail[b]	54 (25.2)	64 (40.8)	**0.002**
Diazepam	2 (0.9)	4 (2.5)	-
Khat	51 (23.8)	61 (38.9)	**0.002**
Rohypnol tablets	114 (53.3)	91 (58.0)	0.265
Polysubstance use			
Group I	6 (2.8)	5 (3.2)	0.999
Group II	50 (23.4)	25 (15.9)	0.089
Group III	71 (33.2)	39 (24.8)	0.086
Group IV	67 (31.3)	37 (23.6)	0.103
Group V	19 (8.9)	39 (24.8)	**<0.0001**
Group VI	1 (0.5)	12 (7.6)	-
Needle and syringe sharing	50 (23.4)	50 (31.8)	0.076
Flushing of blood	43 (20.1)	15 (9.6)	**0.006**

Table 4.3: Drug use patterns among IDUs in Mombasa, Kenyan in 2012-2013

Data are presented as proportions, unless otherwise indicated. Statistical analyses were conducted using the Pearson's chi-square or Fisher's exact tests as appropriate. [a]brown sugar, crude heroin. [b]cocktail, mixture of cigarettes and bhang. Group I, heroin or cocaine only (monosubstance). Group II, heroin or cocaine and any other substance. Group III, heroin or cocaine and any other two substances. Group IV, heroin or cocaine and any other three substances. Group V, heroin or cocaine and any other four substances. Group VI, heroin or cocaine and any other five substances. Values in bold indicate significant *P*-values.

Consistent with previous studies (Ross *et al.*, 2008; Brodish *et al.*, 2011), heroin was the most frequent injection drug reported in both HIV infected and uninfected injection drug users. In addition, at least 26% of HIV positive injection drug users reported injecting cocaine. Although heroin appears to be the most common injection drug in eastern and southern African countries (Ross *et al.*, 2008; Brodish *et al.*, 2011; Trenz *et al.*, 2013), cocaine is increasingly becoming available. While all the IDUs injected for at least twice daily, frequency of injection for once daily was higher among HIV infected IDUs. These observations are likely due to the fact that new initiates may be unaware of safer needle use practices. Additionaly, they may lack money to consistently buy new needles.

The results are also consisted with studies carried out in Tanzania that reported less frequent injection corresponded to increased risk of infection due to sharing of needles, large sexual networks, lack of financial stability and low negotiating power of younger recruits (Williams *et al.*, 2009). In contrast, longer injection duration increases the risk of exposure to HIV predominantly through increased probability of sharing infected needles and syringes since needle and syringe sharing in the current study was predictive of higher odds of HIV infection. The findings of lower odds for HIV infection for blood flushing IDUs could be related to increased awareness of HIV prevention and adherence to measures for reducing re-infections like auto-flushing or injection sero-sorting as observed among IDUs in the USA (Mizuno *et al.*, 2011).

Use of non-injection drugs among IDUs was also reported in this study. While the consumption of bhang, brown sugar, cigarette, and rohypnol tablets was similar in the

infected and uninfected population, alcohol, khat and cocktail consumption was higher in the HIV infected individuals and predicted higher odds of HIV infection. These findings are consistent with previous studies in Russia that illustrated alcohol and cocktail consumption is high in injection drug users and correlate with HIV infection (Abdala *et al.*, 2010). Of significance are findings presented here showing that alcohol, cocktail and khat consumption is also associated with higher odds of having HIV infection among the Kenyan injection drug using communities in Mombasa.

This study is possibly the first to show that khat predicts increased probability of HIV infection among IDUs in Kenya. Khat is normally chewed for recreational purposes and it contains a number of stimulants. It is possible that khat interaction with other substances consumed by the IDUs increases the desire for sex and interferes with decision making (Berhanu *et al.*, 2013; Tadesse *et al.*, 2013). In fact, khat use has been associated with younger age of sex debut and having multiple sex partners (Malaju *et al.*, 2013; Tadesse *et al.*, 2013; Tilahun *et al.*, 2013. Furthermore, alcohol use and khat chewing has been associated with HIV infection in Ethiopia (Ayenew *et al.*, 2012).

These findings are in line with other studies that have reported that proportionally more heroin IDUs declared to have used more than one drug in addition to heroin. For instance, cocaine and benzodiazepines use has been documented (Ross *et al.*, 2008; Williams *et al.*, 2009; Brodish *et al.*, 2011; Trenz *et al.*, 2013; Havinga *et al*,. 2014). Nonetheless, they deviate from the outcome of the studies by McCurdy *et al.* (2006) and McCurdy *et*

al. (2010) who reported high HIV incidence among IDUs in Tanzania who practiced blood flashing.

4.3 Association of Socio-demographic, Sexual Practice and Drug Use Patterns in Relation to HIV Status

To identify the predictors of HIV, binary logistic regression analyses were performed, controlling for age, education, employment, religion and residence. Increased odds for HIV infection was linked to females [OR, 18.609 (9.150-37.848); $P<0.0001$], marital separation [OR, 2.676 (1.487-4.817); $P=0.001$] and divorce or widowhood [OR, 2.897 (1.457-5.762); $P=0.002$]. In addition sex work [OR, 8.900 (2.610-30.350); $P<0.0001$]; entertainment and beauty therapy occupations [OR, 14.765 (3.979-54.794); $P<0.0001$] as well as having penetrative sex within the past year [OR, 3.072 (1.552-6.083); $P=0.001$] elevated the likelihood of HIV infection.

Furthermore, the risk of HIV infection increased with reported younger age (<15 years) of sexual debut [OR, 2.730 (1.340-5.560); $P=0.006$]; having two to five sexual partners [OR, 3.766 (1.348-10.520); $P=0.011$) or at least five sexual partners [OR, 11.375 (3.312-39.072); $P<0.0001$]; unprotected sex [OR, 3.683 (1.986-6.833); $P<0.0001$]; sex for police protection [OR, 8.888 (3.515-22.479); $P<0.0001$]; sex in exchange for drugs [OR, 2.762 (1.492-5.114); $P=0.001$] and STI [OR, 5.520 (3.364-9.056); $P<0.0001$].

Heroin [OR, 3.253 (1.823-5.803); $P<0.0001$] or cocaine use [OR, 3.509 (1.895-6.499); $P<0.0001$]; injection for 6-11 months [OR, 3.072 (1.149-8.213); $P=0.025$], 1-3 years

[OR, 3.869 (1.633-9.168); P=0.002], or >3 years [OR, 6.509 (2.716-15.598); P<0.0001]; needle/syringe sharing [OR, 1.712 (1.052-2.788); P=0.031]; alcohol [OR, 4.618 (2.810-7.590); P<0.0001], cocktail [OR, 1.916 (1.197-3.067); P=0.007]; khat [OR, 2.009 (1.251-3.224); P=0.004]; and use of heroin or cocaine and any four [OR, 3.045 (1.631-5.684); P<0.0001] or five [OR; 15.195 (1.870-123.473); P=0.011] non-injection substances also increased the odds of HIV infection (Table 4.4). However, small business [OR, 0.354 (0.150-0.837); P=0.018]; passenger service vehicle operators [OR, 0.377 (0.171-0.831); P=0.016]; monthly income levels of US$ 0-115 [OR, 0.451 (0.210-0.969); P=0.041] or 116-173 [OR, 0.426 (0.218-0.829); P=0.012] and flushing of blood [OR, 0.462 (0.238-0.897); P=0.024] were associated with low odds of having HIV infection among the IDUs (Table 4.4).

	HIV[+] injection drug users	
Characteristic	OR (95% CI)	*P*-value
Female gender	18.609 (9.150-37.848)	**<0.0001**
Marital status		
Separated	2.676 (1.487-4.817)	**0.001**
Divorced/widowed	2.897 (1.457-5.762)	**0.002**
Occupation		
CSW	8.900 (2.610-30.350)	**<0.0001**
Entertainment/Beauty therapy	14.765 (3.979-54.794)	**<0.0001**
Small business	0.354 (0.150-0.837)	**0.018**
PSV operators	0.377 (0.171-0.831)	**0.016**
Income, US$/mos.		
116-173	0.426 (0.218-0.829)	**0.012**
0-115	0.451 (0.210-0.969)	**0.041**
Age of sexual debut, yrs.		
<15	2.730 (1.340-5.560)	**0.006**
Number of sexual partners		
2-5	3.766 (1.348-10.520)	**0.011**
>5	11.375 (3.312-39.072)	**<0.0001**
Had penetrative sex	3.072 (1.552-6.083)	0.001
Sex without a condom	3.683 (1.986-6.833)	**<0.0001**
Sex for police protection	8.888 (3.515-22.479)	**<0.0001**
Sex for drugs	2.762 (1.492-5.114)	**0.001**
STI	5.520 (3.364-9.056)	**<0.0001**
Injecting drugs		
Any use of heroin	3.253 (1.823-5.803)	**<0.0001**
Any use of cocaine	3.509 (1.895-6.499)	**<0.0001**
Duration of injection		
6-11 mos.	3.072 (1.149-8.213)	**0.025**
1-3 yrs.	3.869 (1.633-9.168)	**0.002**
>3 yrs.	6.509 (2.716-15.598)	**<0.0001**
Needle and syringe sharing	1.712 (1.052-2.788)	**0.031**
Flushing of blood	0.462 (0.238-0.897)	**0.024**
Non-injecting drugs		
Alcohol	4.618 (2.810-7.590)	**<0.0001**
Cocktail	1.916 (1.197-3.067)	**0.007**
Khat	2.009 (1.251-3.224)	**0.004**
Polysubstance use		
Group V	3.045 (1.631-5.684)	**<0.0001**
Group VI	15.195 (1.870-123.473)	**0.011**

Table 4.4: Association of the socio-demographic characteristics, sexual practices and drug use patterns in relation to IDUs HIV status, in Mombasa County 2012-2013

Binary logistic regression was conducted such that all HIV infected injection drug users (n=157) were modeled against all of the HIV negative injection drug users (n=214) controlling for age, education, employment, religion and residence. Data are presented as odds ratios (OR) and 95% confidence interval (CI); SW, sex worker; STI, sexually transmitted infections; Group V, heroin or cocaine and any other four substances; Group VI, heroin or cocaine and any other five substances.

An overlap of socio-demographic characteristics, sexual practices and substance use patterns predicted HIV infections in this study. These include the female gender, marital separation, sex work or working in entertainment and beauty therapy venues, having had penetrative sex in the last one year, early sexual debut, high risk sexual behaviour (like multiple sexual partnership arising from sex for money, sex for police protection and sex for drugs as well as unprotected sex), exposure to STI and high risk injecting practices (like sharing of needles and syringes).

The increased risk of HIV acquisition arising from the overlap between sex work and drug use has been widely documented. Female sex workers who are drug dependent are more likely to engage in transactional sex while under the influence of substances in addition to being acquiesced to clients' demands for unprotected sex, especially if offered more money or drugs (Strathdee *et al.*, 2008; Patterson *et al.*, 2012; Shannon *et al.*, 2014). In some cases, drug use is involuntary because pimps and managers coerce sex workers into drug use as a means of control especially for under age users (Goldenberg *et al.*, 2012). Owing to the fact that both sex work and drug use are illegal, sex workers who use drugs are more vulnerable to police harassment like frequent arbitrary arrests or police misconduct like extortion and blackmail. They also face the risk of physical as well as sexual abuse which increases the odds of HIV acquisition and reduced probability of seeking medical attention (Cottler *et al.*, 2014; Odinokova *et al.*, 2014).

Although heroin was the most common drug, a vast majority of IDUs utilized more than one substance. In addition, consumption of khat, cocktail or alcohol and polysubstance

use was predictive of HIV infection. While many IDUs in this study used heroin, a depressant that tends to inhibit libido, especially in large quantities or with long-term use, they additionally consumed stimulant-type drugs such as khat, bhang and cocktail that increased sexual desire (Blum *et al*., 2013, Tadesse *et al*., 2013; Berhanu *et al*,. 2014).

4.4 Nutritional Measures of the PWID in Mombasa County

Nutritional analyses showed that body height was significantly higher among HIV-1 negative individuals compared to HIV-1 positive individuals (P=0.001). However, body weight, hip circumference, waist circumference, bust circumference, waist-to-hip ratio, and bust-to-waist ratio did not differ significantly between the HIV-1 negative and positive study groups (P>0.05 for all comparisons). Although the mid-upper-arm circumferences were significantly lower in the HIV-1 positive group (P<0.0001), the relative proportions of malnutrition based on MUAC definition (that is, MUAC cut-offs of <23.0 cm in males and <22.0 cm in females) did not vary significantly between the HIV-1 negative and positive study groups. In addition, BMI levels and malnutrition based on BMI<18.50 kg/m^2 were similar in the study groups (P>0.05 for both comparisons). Finally, haemoglobin (Hb) levels were significantly lower in the HIV-1 positive individuals compared to the HIV-1 negative groups (P=0.002). Consistent with the low Hb levels in the HIV-1 infected group, the proportions of individuals with anaemia was significantly higher in the HV-1 positive IDUs compared to the HIV-1 negative IDUs (29.3% vs. 19.2%; P=0.026) as shown in table 4.5.

Additional regression analyses for identifying the predictors of malnutrition (BMI<18.5 kg/m^2) indicated that malnutrition in the HIV negative IDU subpopulation was significantly associated with the CD4+ T cell count ≥350<500 cells/μL (OR, 3.718; 95% CI, 1.264-10.932; *P*=0.017) and CD4+ T cells/μL <350 cells/μL (OR, 2.761; 95% CI, 1.204-6.334; *P*=0.016). Among the HIV positive IDUs malnutrition was associated with CD4+ T cell count ≥350<500 cells/μL (OR, 2.031; 95% CI, 0.936-4.407; *P*=0.073) and <350 cells/μL (OR, 2.972; 95% CI, 1.117-7.910; *P*=0.029) (Table 4.7). However, HIV-1 viral loads ≥1,000<10,000 (OR, 1.808; 95% CI, 0.675-4.848; *P*=0.239); ≥10,000<100,000 (OR, 0.998; 95% CI, 0.394-2.526; *P*=0.997) and >100,000 (OR, 0.565; 95% CI, 0.568-4.312; *P*=0.387) were not significantly associated with malnutrition in the HIV positive IDUs (Table 4.6).

Characteristic	IDU		*P*
	HIV-1 Negative, n=214	HIV-1 Positive, n=157	
Height, m	1.71 (0.09)	1.69 (0.11)	**0.001**
Weight, kg	54.0 (9.0)	53.0 (8.0)	0.295
Hip circumference, cm	90.0 (7.8)	90.0 (8.0)	0.381
Waist circumference, cm	76.0 (7.0)	75.0 (9.0)	0.122
Bust circumference, cm	85.0 (7.3)	85.0 (7.0)	0.898
Waist-to-hip ratio	0.83 (0.09)	0.83 (0.08)	0.487
Bust-to-waist ratio	1.12 (0.11)	1.13 (0.10)	0.265
MUAC, cm	26.0 (3.0)	24.0 (2.8)	**<0.0001**
M<23.0; F<22.0cm, n (%)	24 (11.2)	13 (8.3)	0.385
Normal, n (%)	190 (88.8)	144 (91.7)	
BMI, kg/m^2	18.69 (2.77)	18.75 (2.17)	0.277
<18.5, n (%)	101 (47.2)	64 (40.8)	0.245
≥18.5, n (%)	113 (52.8)	93 (59.2	
Haemoglobin, g/dL	12.60 (2.30)	12.30 (2.50)	**0.002**
Anaemia, n (%)	41 (19.2)	46 (29.3)	**0.026**

Table 4.5: Nutritional status of HIV-1 infected and uninfected IDUs in Mombasa County, 2012-2013

Data are presented as medians (interquartile range, IQR) for continuous variables or number of subjects (n) and proportions (percentages, %) for categorical variables. Statistical analyses were conducted using the Mann Whitney U test for continuous variables and Fisher's exact test for comparing proportions between the groups. BMI: basal metabolic index. MUAC: mid upper arm circumference. Body mass index (BMI kg/m^2): Non-malnourished (≥18.50) and malnourished (<18.50) (FANTA, 2013). MUAC cut-offs for malnutrition: males, <23.0 cm and females <22.0 cm (UNICEF, 2011). Anaemia was defined using haemoglobin (Hb, g/dL) cut-offs previously established by (WHO, 2011c) as follows: non-pregnant women (≥15.00 yrs), Hb<12.0 g/dL; and men ((≥15.00 yrs), Hb <13.0 g/dL).

Since this is the first known study to assess nutritional status of PWID in Kenya, the findings of this study were compared to results of studies carried out in the general population in Mombasa and IDU subpopulations outside Kenya. The low height found among the HIV infected injection drug users in comparison to HIV uninfected injection

drug users signify loss of body height, a common feature in people living with HIV/AIDS (McComsey *et al.*, 2010). Similar results were reported among PWID in Chennai, South India showing that HIV infected injection drug users presented with lower body height relative to the HIV uninfected injection drug users (Tang *et al.*, 2011). In addition, the low body heights observed in the current study also parallel previous clinical studies in the USA among HIV infected non-drug using persons aged between 4 and 24 years as well as in Chinese adults showing marked reductions in body height (Jacobson *et al.*, 2010; Zhang *et al.*, 2013b).

Although the mechanisms governing the loss in body height are poorly defined, it appears that loss of bone mineral density underlies the low body height in the HIV infected injection drug users. This premise is supported by previous studies showing heightened bone mineral loss in Senegalese adults living with HIV/AIDS (Cournil *et al.*, 2012). It is also possible that chronic use of protease inhibitors contribute to bone mineral loss. This suggestion is supported by previous studies in France and Japan showing that long-term use of protease inhibitors is associated with loss of bone mineral density in adults on anti-retroviral treatment (Duvivier *et al.*, 2009; Kinai, *et al.*, 2014).

The lack of significant differences in the standard nutritional measures of body weight, hip circumference, waist circumference, bust circumference, waist-to-hip ratio, bust-to-waist ratio, and BMI between the HIV infected and uninfected injection drug users observed in this study may be related to the fact that these measures approximate both lean and fat body mass. These results are similar to a previous study among drug users

living in three US cities (Baltimore, Boston, Providence) that reported low waist circumference in both HIV infected and uninfected IDUs which was associated with low BMI as well as low body fat (Tang *et al.*, 2010). These findings suggest a lack of abdominal obesity that is measured as high waist circumference and waist to hip circumference ratio in both HIV infected and uninfected IDUs (WHO, 2011b).

However, the lower mid-upper-arm circumference (MUAC), a nutritional marker for wasting or acute malnutrition, in the HIV infected injection drug users suggests that the mid-arm-circumference is a better surrogate for assessing acute malnutrition in HIV infected IDUs. This proposition is supported by previous studies among non-drug using population of HIV infected adults in Guinea-Bissau showing that MUAC was an independent predictor of death while in Indian, MUAC as a marker was found to be 94.6% sensitive and 71.2% specific among adolescents (Dasgupta *et al.*, 2010; Oliveira *et al.*, 2012).

The low haemoglobin levels and associated high rates of anaemia in the HIV infected injection drug users is indicative of increased anaemia burden in this population. Although anaemia appears to occur in both HIV infected and uninfected injection drug users, it is possible that consumption of foods of low nutritive value, a common practice among injection drug users increases the risk of developing anaemia (Hendricks *et al.*, 2010; Alves *et al.*, 2011; Saeland *et al.*, 2011; Karajibani *et al.*, 2012). However, the higher frequency of anaemia in the HIV infected injection drug users is partly consistent with NASCOP guidelines on management of opportunistic infections (NASCOP, 2012c)

indicating that the burden of anaemia is higher in the people living HIV/AIDS in the country. Consistent with these results previous clinical studies in Brazil and India showed higher rates of anaemia in the HIV infected injection drug users (Solomon *et al.*, 2008; Brunetta *et al.*, 2013).

The mechanisms driving the increased anaemia burden in the HIV infected injection drug using people are largely undefined. This is supported by previous studies in Indonesian HIV infected adults showing that high prevalence of chronic diseases and/or iron deficiency is associated with increased risk of anaemia (Wisaksana *et al.*, 2011), and previous studies in India, Cambodia and South Africa among HIV infected adults illustrating that long-term use of antiretroviral drugs such as zidovudine is associated with increased risk of anaemia (Nigam *et al.*, 2013; Phe *et al.*, 2013; Simbarashe *et al.*, 2013). Overall, the implications of these results are that incorporation of iron supplements in the nutritional management schedules for HIV infected IDUs will reduce the risk of anaemia and other related co-morbidities leading to improved quality of life.

In order to assess the predictors of malnutrition in both HIV infected and uninfected IDUs, binary logistic regression was conducted as shown in table 4.6. Findings illustrating that low CD4+ T cells counts are predictive of high rates of malnutrition in both HIV infected and uninfected IDUs indicate suppression of cell mediated immunity, a frequent sequel of malnourished persons (França *et al.*, 2009). Similar results have been reported in injection drug using patients from Brazil and the general adult population from Germany (Brunetta *et al.*, 2013; Iliakis and Kressig, 2014). The low

CD4 count may result from malnutrition and HIV infection driven reduction in the CD4+ T cell numbers (Shalini *et al.*, 2012). This assertion is parallel to previous studies in South Africa showing correlations between the CD4 cell count and BMI among adults living with HIV/AIDS (Venter *et al.*, 2009; Evans *et al.*, 2013).

Overall, the present study revealed that IDUs experience high levels of malnutrition with HIV infected IDUs suffering even higher burden of malnutrition. Malnutrition in the injection drug using population is largely attributable to reduced dietary intake, malabsorption and or altered metabolism. Decreased dietary intake is due to abdominal pain, anorexia, chaotic lifestyles, depression, diarrhoea, poverty, food insecurity, mouth sores, nausea and vomiting (Anema *et al.*, 2010; Smith *et al.*, 2012; Strike *et al.*, 2012). Malabsorption can be linked to the HIV-induced mucosal changes, effects of drugs on absorption of specific nutrients and opportunistic gastrointestinal infections (Martins *et al.*, 2011; Sunguya *et al.*, 2011; Krawinkel, 2012). In contrast, altered metabolism is associated with the effects of injection drugs and substance consumption (like heroin and khat), fever or cytokine-induced increase in the basal metabolic rate, hormonal deficiencies, increased breakdown of lean body mass, and effects of medications on metabolism (Hendricks *et al.*, 2010; Douglas *et al.*, 2011; Mineur *et al.*, 2011; Neale *et al.*, 2012; Ersche *et al.*, 2013; Rubinstein and Low, 2013).

Characteristic	B	Wald	OR (95% CI)	*P*-value
HIV-1 Uninfected IDUs				
CD4+ T cells/μL				
≥500 (Ref)				
≥350<500	1.313	5.694	3.718 (1.264-10.932)	**0.017**
<350	1.016	5.751	2.761 (1.204-6.334)	**0.016**
HIV-1 Infected IDUs				
CD4+ T cells/μL				
≥500 (Ref)				
≥350<500	0.709	3.213	2.031 (0.936-4.407)	0.073
<350	1.089	4.756	2.972 (1.117-7.910)	**0.029**
Viral load (copies/mL)				
Undetectable<1,000 (Ref)				
≥1,000<10,000	0.592	1.386	1.808 (0.675-4.848)	0.239
≥10,000<100,000	-0.002	0	0.998 (0.394-2.526)	0.997
>100,000	0.448	0.75	1.565 (0.568-4.312)	0.387

Table 4.6: Predictors of malnutrition in HIV-1 infected and uninfected injection drug users in Mombasa County, 2012-2013

Data are presented as odds ratios (OR) and 95% confidence interval (CI). Binary logistic regression was conducted using BMI<18.5 kg/m^2 (malnourished) as the dependent variable and BMI≥18.5 kg/m^2 as the reference group controlling for age and gender in HIV negative IDUs and age, gender and ART use in the HIV positive IDUs. The CD4+ T cells were categorized using a combined CDC classification system and NASCOP thresh-hold for initiating anti-retroviral therapy for HIV-infected adults and adolescents into three groups: 1) ≥500 cells/μL; 2) 350-499 cells/μL; and 3) <350 cells/μL (CDC, 1992; NASCOP, 2012b).

4.5 The Prevalence of Pulmonary TB Infections among HIV Uninfected and Infected IDUs in Mombasa County

A total of 39 pulmonary TB cases were detected among the study participants with the HIV-1 infected individuals (18.5%) presenting with significantly higher rates compared to the HIV-1 uninfected individuals (4.5%) at (P<0.0001). Sensitivity testing of the thirty nine *Mycobacterium tuberculosis* isolates against anti-mycobacterial first line drugs

treatment demonstrated that all of the isolates were sensitive to ethambutol, pyrazinamide, rifampicin and isoniazid. A synopsis of the pulmonary TB prevalence rate is illustrated in table 4.7.

Characteristic	HIV-1 Uninfected, n=214	HIV-1 Infected, n=157	
Tuberculosis rates	10 (4.7)	29 (18.5)	<0.0001
***Mycobacterium tuberculosis* sensitivity to TB drugs**			
Ethambutol	10 (100.0)	29 (100.0)	-
Pyrazinamide	10 (100.0)	29 (100.0)	-
Rifampicin	10 (100.0)	29 (100.0)	-
Isoniazid	10 (100.0)	29 (100.0)	-

Table 4.7: Tuberculosis prevalence rate among PWID in Mombasa County, 2012-2013

Data presented are number and proportions (%) of subjects. Statistical analysis was performed using the Fisher's exact test. *antimycobacterial sensitivities were performed on all the TB positive cases.

The findings showing higher prevalence rates of TB in the HIV infected IDUs indicate that HIV-1 infection increases the risk of TB infection. However, the presence of TB in the HIV-1 uninfected IDUs, suggests that injection drug use is also a risk factor of acquiring TB. The results illustrating TB prevalence rates of 29% in the HIV-1 infected IDUs from Mombasa parallels previous findings of showing a 33.9% TB prevalence among IDUs from Chennai, India (Solomon *et al.*, 2008). The higher risk of TB in the HIV-1 infected IDUs is attributable to the lower CD4+ T cell counts detected in this group. The reduced CD4+ T cells consequently cause lowered cellular immunity that is paramount for elimination of *Mycobacterium bacilli* (Shalini *et al.*, 2012). It is also

likely that injection drug use which is associated with weakened cellular immunity increase the risk of TB infection (Deiss *et al.*, 2009; Getahun *et al.*, 2012).

Nevertheless, the *Mycobacterium tuberculosis* isolates from both groups were sensitive to all the first line anti-TB drugs. These results deviate from findings of a previous study which isolated MDR TB from injection drug users in Tanzania (Gupta *et al.*, 2014). In Kenya, the reasons underlying the continued sensitivity of anti-TB treatment in this most at risk population may be linked to the intensive surveillance and follow-up of TB cases in the general population by Division of Leprosy, Tuberculosis and other Lung Diseases (MOPHS, 2010). In addition, a declining trend of TB cases as well as high sputum conversion rate (ranging between 88% and 97%) to first line of treatment in the general population has been reported in Kenya (Kwange and Budambula, 2010; Sitienei *et al.*, 2013). However, it is also possible that severe TB cases and MDR TB among IDUs were not obtained due to the fact that sick injection drug users are less likely to access healthcare (Dutta *et al.*, 2013).

Regression analyses to identify the predictors of TB in the HIV-1 infected and uninfected injection drug users was carried out and presented in Tables 4.8 and 4.9 respectively. Findings indicated that the probability of having TB infection among those presenting with malnutrition was at least four times in both HIV-1 uninfected (OR, 4.599; 95% CI, 0.946-22.357; P= 0.059) and infected (OR, 4.077; 95% CI, 1.505-11.049; P=0.006) injection drug users. However, additional risk factors for TB did not show significant associations with TB infection in the HIV-1 uninfected (cigarette smoking, alcohol

consumption, anaemia and CD4+ T cell status) and infected (cigarette smoking, alcohol consumption, anaemia, CD4+ T cell and viral load status) injection drug users ($P>0.05$).

Results indicating a higher probability of having TB infection in both HIV-1 infected and uninfected IDUs presenting with lower BMI (<18.5 kg/m^2) indicate that malnutrition is an important risk factors for TB infection in this key population. This finding is similar to previous studies showing in the Kenyan general population low BMI was common among TB patients (Sitienei *et al.*, 2014). Malnutrition is associated with depressed cellular immunity (lowering host defense against tuberculosis) and this could be responsible for the acquisition of *Mycobacterium tuberculosis*, an intra-cellullar pathogen (Drake, 2010; Duggal *et al.*, 2012; Padmanesan *et al*, 2013). Among HIV-1 infected IDUs, malnutrition and reduced CD4+ T cells concomitantly worsen cellular immune responses increasing the risk of acquiring and developing disease against intra-cellular pathogens such as *Mycobacterium tuberculosis*.

This study demonstrated that pulmonary TB is an important problem in the IDU sub-population in Mombasa. In this, key population, TB is associated with HIV and malnutrition which are also a common burden in IDUs (Hendricks *et al.*, 2010; Tang *et al.*, 2011). Without adequate control of the TB-HIV syndemic, the long-term TB elimination target set for 2050 may not be reached.

Characteristic	B	Wald	OR (95% CI)	*P*
Malnutrition				
BMI≥18.5 kg/m^2 (Ref)				
BMI<18.5 kg/m^2	1.526	3.527	4.599 (0.946-22.357)	**0.059**
Smoking				
No (Ref)				
Yes	0.072	0.011	1.075 (0.275-4.200)	0.917
Alcohol				
No (Ref)				
Yes	0.203	0.057	0.816 (0.155-4.297)	0.811
Anaemia				
No (Ref)				
Yes	0.732	0.890	2.079 (0.455-9.505)	0.345
CD4+ T cells (×10^3/μL)				
≥500 (Ref)				
≥350<500	0.180	0.027	1.197 (0.138-10.383)	0.870
<350	1.222	0.920	3.395 (0.279-41.245)	0.337

Table 4.8: Predictors of tuberculosis among HIV-1 uninfected IDUs in Mombasa County, 2012-2013

Data are presented as odds ratios (OR) and 95% confidence interval (CI). Binary logistic regression analysis was conducted by entering tuberculosis status as the dependent variable, risk factors (malnutrition, smoking, alcohol, anaemia, and CD4+ T cells) as independent variables, and controlling for age and gender. Ref, reference. BMI, basal metabolic index.

Characteristic	B	Wald	OR (95% CI)	*P*
Malnutrition				
BMI≥18.5 kg/m^2 (Ref)				
BMI<18.5 kg/m^2	1.405	7.634	4.077 (1.505-11.049)	**0.006**
Smoking				
No (Ref)				
Yes	0.027	0.003	1.027 (0.375-2.815)	0.959
Alcohol				
No (Ref)				
Yes	0.803	1.827	2.231 (0.697-7.141)	0.176
Anaemia				
No (Ref)				
Yes	0.292	0.328	1.340 (0.492-3.646)	0.567
CD4+ T cells (x10^3/μL)				
≥500 (Ref)				
≥350<500	0.655	1.334	1.924 (0.634-5.843)	0.248
<350	0.927	1.801	2.526 (0.653-9.779)	0.180
Viral load/mL				
Undetectable<1,000 (Ref)				
≥1,000<10,000	1.002	1.899	2.724 (0.655-11.329)	0.168
≥10,000<100,000	1.009	2.383	2.742 (0.762-9.869)	0.123
>100,000	0.784	1.216	2.190 (0.544-8.828)	0.270

Table 4.9: Predictors of tuberculosis among HIV-1 infected PWID in Mombasa County, 2012-2013

Data are presented as odds ratios (OR) and 95% confidence interval (CI). Binary logistic regression analysis was conducted by entering tuberculosis status as the dependent variable, risk factors (malnutrition, smoking, alcohol, anaemia, and CD4+ T cells) as independent variables, and controlling for age and gender. Ref, reference. BMI, basal metabolic index.

4.6 The HIV Subtypes that Cause HIV Infections in IDUs Living in Mombasa County

Seventy six (48.4%) of the one-hundred and fifty seven HIV-1 infected IDUs were successfully sequenced. Genotype analysis identified the following sub-types: A1

(56.6%), C (15.8%), D (14.5%), A2-C (1.3%), ABDU (1.3%), B (1.3%) and G (1.3%) as illustrated in Table 4.10.

Subtype	Male	Female	Total
A1	18 (58.1)	25 (55.6)	43 (56.6)
C	9 (20.0)	3 (9.7)	12 (15.8)
D	7 (15.6)	4 (12.9)	11 (14.5)
A2_AG	2 (6.5)	2 (4.4)	4 (5.3)
A1D	1 (3.2)	1 (3.2)	2 (2.6)
A2C	0 (0.0)	1 (3.2)	1 (1.3)
ABDU	0 (0.0)	1 (3.2)	1 (1.3)
B	0 (0.0)	1 (3.2)	1 (1.3)
G	1 (2.2)	0 (0.0)	1 (1.3)

Table 4.10: HIV-1 subtypes circulating in IDUs from Mombasa County, 2012-2013

Data presented are number and proportions (%) of participants. Note: A2_AG, A1D, A2C and ABDU are circulating recombinants forms (CRFs).

The high prevalence of subtype A1 detected in the HIV-1 infected injection drug users signifies the dominance of this subtype transmission within the injection drug users from Mombasa. Although subtype A1 was the most frequent, the rate was lower relative to previous cross-sectional studies in Mombasa (same area as the present study) showing 89.7% prevalence in anti-retroviral treatment-exposed injection drug users (Osman *et al.*, 2013) and 70.6% prevalence among anti-retroviral treatment-naive individuals from the general population (Sigaloff *et al.*, 2012). This evident variation in the prevalence of the A1 sub-type between the current study and previous studies from the same study area may be attributable to the rapidly evolving epidemiology of HIV-1 subtypes in this most-at-risk-population that is frequently exposed to multiple subtypes.

This fact is related to the high rates of C, D and circulating recombinant forms detected in the present study compared to the previous studies in the same study area. Based on review of studies carried out in different regions in Kenya on HIV sub-types (Kageha *et al.*, 2012; Khamadi *et al.*, 2009; Kiptoo *et al.*, 2013; Lihana *et al.*, 2009; Muriuki, 2012; Nyamache *et al.*, 2013; Osman *et al.*, 2013; Sigaloff *et al.*, 2012), the present study is the first to report the presence of sub-type B in the country. This further supports the preposition that there is changing epidemiology of circulating HIV-1 subtypes in Kenya.

CHAPTER FIVE: CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

From the study, it was hypothesized that social-demographic characteristics are similar between HIV infected and uninfected IDUs. However the study findings imply that the female gender, being separated or divorced, widowhood, early sex debut, sex work, working in entertainment and beauty therapy sectors, exposure to STI and risky sexual practices were statistically more significant in the HIV infected group than uninfected IDUs. Therefore the null hypothesis is rejected and it is concluded that social-demographic characteristics vary between HIV infected and non-infected IDUs.

Longer duration of injection use, needle and syringe sharing, injecting heroin or cocaine in addition to using alcohol, khat, and cocktail as well as polydrug use increased the risk of exposure to HIV. The null hypothesis that proposed drug use patterns are invariable between HIV infected and uninfected IDUs is rejected and the researcher concludes drug use patterns differ between HIV infected and uninfected IDUs.

Although low anthropometric measurements and aneamia were common in the IDUs irrespective of their HIV status, the HIV infected IDUs fared worse than the uninfected. The null hypothesis that had proposed stating that the nutritional status was incomparable between HIV infected and non-infected IDUs is accepted. Based on the findings it is concluded that in terms of nutrition, the HIV positive injection drug users are more malnourished than the infected IDUs.

The significant high proportions of TB in HIV positive in comparison to the negative IDUs imply that HIV infected IDUs are at an elevated risk of acquiring TB infections. The null hypothesis is rejected and based on findings of the study it is concluded that TB infection rate do vary with HIV infection in the IDU subpopulation.

The assortment of HIV-1 subtypes and recombinants that co-circulate among PWID in Mombasa courtesy of high risk injecting and sexual practices point to the changing epidemiology of circulating HIV-1 subtypes in Kenya. The proposed hypothesis is rejected and supported by the findings of this present study, it is concluded that an array of HIV-1 sub-types and recombinants co-circulate in IDUs in Mombasa County.

Overall, the study demonstrated multiple trajectories of drug injection behaviours. By understanding socio-economic factors, drug use patterns, nutritional status, TB as well as HIV trends among users in this subpopulation forms the basis of preventive and therapeutic interventions.

5.2 Recommendations

From this study, empowerment of youths and women is recommended through the Ministry of Labour, Social Security and Services. Although the national government has already set aside funds to benefit the youths and women, the most vulnerable categories like those who dropped out of primary and secondary schools are yet to benefit. Empowerment is crucial as this will curtail idleness, drug abuse and high risk sexual behaviour. In addition both public and private funded rehabilitation centres ought to

integrate vocational training skills in their rehabilitation packages so as rehabilitated IDUs are empowered in order to prevent reversion to drug use, idleness and high risk sexual behaviour.

The County government, non-governmental organizations (NGOs), community and faith based organizations (CBOs and FBOs respectively) should plan for targeted activities that will aim at educating sex workers. In addition, they should be empowered to venture into alternative income generating activities.

Given that female IDUs are vulnerable to HIV infections; it is recommended that the County government of Mombasa to design female friendly IDU services as currently none of the public funded rehabilitation centres admit female clients. In view of the fact that female exposure to HIV has a direct implication on mother to child HIV transmission, there is need to put in place appropriate interventions targeting FIDUs.

The NGOs, CBOs and FBOs in Mombasa, should upscale targeted programmes that promote family unit as it moderates the probability of one engaging in drugs as well as high risk sexual behaviour.

The County government should invest in friendly drop-in centres for IDUs, non IDUs and their partners in order ensure accessible compressive primary health care services (PHC). In addition, integrated approaches are required in advocating for behaviour

change and early diagnosis as well as treatment of STIs in order to curb the high HIV rates among the IDUs and their sexual partners by extension.

The Nationa Authority for the Campaign against Alcohol and drugs in conjunction with Mombasa based NGOs and CBOs should start monitoring drug use patterns. For example, seasons when drugs are consumed most, type of drug(s) taken, polydrug use as well as mode of administration. This will help in developing targeted interventions like integrating prevention of alcohol, cocktail and khat consumption in injection drug use and HIV intervention programs.

In addition the Pharmacy and Poisons Board should flex its muscles and withdraw licenses or black list the pharmacy operators who dispense prescription drugs Rohypnol and valium on over the counter basis.

Overall to moderate drug use, the National government ought to step up the war against drugs by targeting the drug supply chain starting with the barons, distributors and peddlers so as to reduce supply of drugs in the market. In accordance with the law of supply and demand, reduced supply will lead to increase in drug prices and fear of being arrested hence reduced demand.

Since malnutrition is an important correlate of the immune status of PWID, it is recommended to Ministry of Health (MOH) to facilitate food assistance and micronutrient supplementation programmes as well as nutritional education to IDUs in

order to improve their nutritional status and immunological outcomes, especially, among the HIV infected IDUs as an adjunct for the antiretroviral therapy regimens.

It is recommended to the County of government to integrate active TB screening into drug prevention and management programmes as well as in targeted outreach activities. These services should work in close tandem with the MOH in order to facilitate early diagnosis and effective treatment of TB among injecting drug users. This will also help in the achievement of MDG 6C and MDG 1C that seeks to halt the TB burden as well as reduce by half the proportion of population below minimum level of dietary energy consumption respectively.

In addition, continued surveillance for MDR-TB by the MOH ought to be up scaled to reach the hidden subpopulations like IDUs that are unlikely to utilize PHC services.

To both the National and County governments, the up-scale HIV education is recommended in order to reduce infection and re-infection rates within the IDU sub-population as well as the general population. This will contribute greatly towards achieving MDG 7 that calls for the halting and reversing of the spread of HIV/AIDS and the achievement of universal access to treatment for HIV/AIDS.

As part of way forward, it is recommended that the National government, research stations and independent researchers to work together in continuous surveillance of the HIV epidemiology.

5.3 General recommendations

The researcher recommends health education to the public that should be initiated and facilitated by both National and County governments. This can be achieved through substance and drug abuse awareness starting at an early age for example at primary school level. Such an approach can form the basis of responding to substance use before one starts using substances. In addition, this strategy could help to discourage or stop use in those who are already experimenting or using. Such programmes can be extended to proprietors and workers of entertainment venues as well as beauty parlours. Substance and drug abuse awareness will help in reducing demand for drugs which in return will lead to supply reduction.

Additionally, it is imperative for police education programs to be designed in order to align policing with public health efforts targeting vulnerable populations (MARPS). This will minimize incidents of sex for police protection as well as arbitrary arrests from law enforcers since fear of arrest drives PWID away from HIV testing and primary healthcare services. Moreover it disrupts antiretroviral therapy resulting in elevated HIV viral load and subsequent HIV trans-mission as well as increased antiretroviral resistance.

Other state actors like lawmakers (including but not limited to Members of Parliament and Members of County Assemblies) and criminal justice authorities (like magistrates and judges) should also be provided with educational programs on human rights and public health interventions.

Both the County and National government are advised to support harm reduction interventions by developing policy and guidelines on harm reduction at the same time implementing them. These interventions may include counseling, syringe and needle exchange programmes (SNEP), methadone assisted treatment (MAT) and provision of safe injecting facilities (SIF).

The County government is advised not to ignore the plight of PWID or persecute them through arbitrary arrests but instead facilitate their voluntary rehabilitation. This can be achieved through partnership with NGOs, CBOs, and FBOs as well as the private sector.

Additionally, the community and affected families need to be encouraged to accept back the rehabilitated IDUs. This will help to break the vicious cycle of rejection and stigma associated with IDU.

As a parting to all the parties mentioned in these recommendations, people who use drugs have the same human rights as people who have never used drugs. These rights include the right to the highest attainable standard of health, to social services, to work, to freedom from arbitrary detention and freedom from cruel inhuman as well as degrading treatment. A time has come for all mankind to stop focusing on the sin but what happens to the sinner.

5.4 Suggested Further Research

Since this was a cross sectional study no causal relationships could be established. Therefore further research needs to be carried out using a longitudinal and experimental approach. There is a possibility that drug use pattern was not well captured due to the structure of the interview schedule. In future studies it is advisable an elaborate list of drugs should be included so that the participants can respond to the items on the list. In addition, both drug use patterns and exposure to STIs were self-reported and hence may be confounded by recall bias. Future studies should include toxicological analysis of urine in order to a certain the complete set of injecting and non-injecting drugs used by the study participants. Moreover, future studies should include comparative groups like non-injecting drug users and non drug users.

Although both MUAC and BMI are good nutritional markers, it is imperative that additional nutritional markers like biochemical, body composition measurements and dietary intake assessment be examined. It is suggested further research be carried out on TB and HIV epidemiological patterns in both high risk as well as general population. While the present study has shed light on predictors of HIV and Pulmonary TB among PWID, more studies need to be carried out to reinforce or refute the findings of this study.

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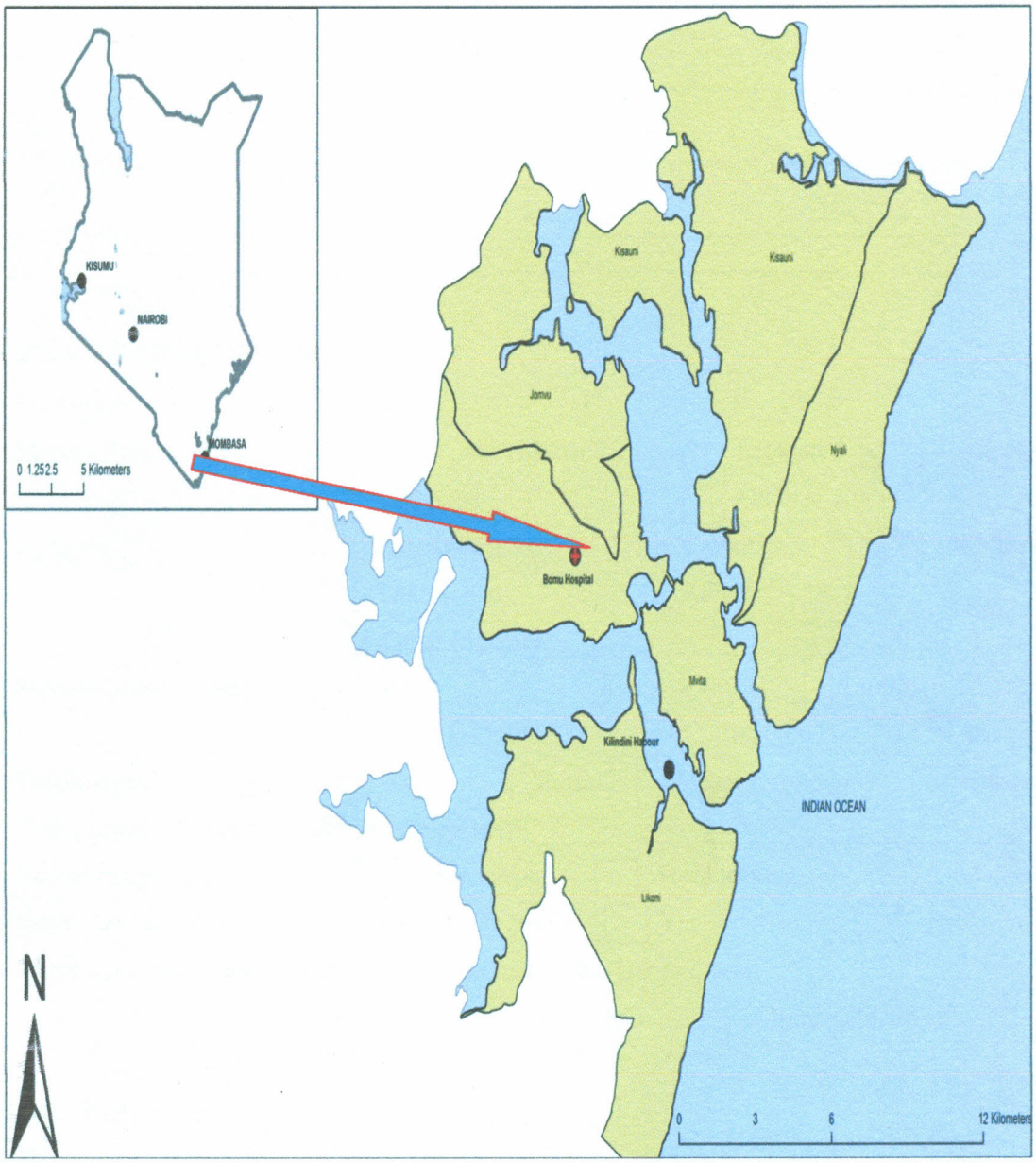
APPENDICES

Appendix 1: Map of Kenya and Mombasa County



Source: Courtesy of Regional Centre for Mapping of Resources for Development

Appendix 2: Interview Schedule

This interview is part of a PHD research paper by Valentine Budambula (KU). Your participation is completely voluntary. Response to this interview will be taken as your acceptance to participate. Please be assured that the information you provide will be treated in the strictest confidentiality.

DATE: DAY----------MONTH----------YEAR----------
CENTRE ----------
CODE: ----------
DATE OF BIRTH: DAY----------MONTH----------YEAR----------
GENDER: M ☐ F ☐
P/ADDRESS: ----------
TEL: ----------

PART A: SOCIO-ECONOMIC STATUS

1. Education: None 1^0 2^0 3^0
2. Marital Status: ☐ Single ☐ Married ☐ Separated ☐ Divorced ☐ Widowed ☐ Other
3. Religion: ☐ Protestant ☐ Catholic ☐ Muslim ☐ Traditionist ☐ Atheist ☐ Other (Specify _____)
4. Income/Month (Ksh): ☐ Nil ☐ < 5000 ☐ 5001-10, 000 ☐ 10, 001-15, 000 ☐ 15,001-20,000 ☐ ≥ 20,001
5. Employment ☐ None ☐ Formal ☐ Self Employment ☐ Student
6. If employed what is your current occupation? _____
7. Sexual orientation: ☐ Heterosexual ☐ Homosexual ☐ Bisexual
8. Have you had penetrative sex in the last one year? ☐ Yes ☐ No
9. If yes, how many sexual partners have you had in the last one year:

   ☐ 1 ☐ 2-5 ☐ >5 ☐ Impossible to tell

10. Age of first sexual encounter _____
11. Have you ever been forced to have sex without using a condom? ☐ Yes ☐ No
12. During the last 12 months, how many times have you avoided arrest by providing the police officer with a sexual favour ☐ None ☐ twice ☐ 3-5 times ☐ > 5 times
13. In the last 12 months have you had sex in exchange for drugs Yes ☐ No ☐
14. If yes, how many times? ☐ Once ☐ twice ☐ 3-5 times ☐ > 5 times

15. Have you ever been diagnosed with a STI within the last

	Yes	No
Six months		
1 year		
2-3 years		
>3 years		

16. If yes, which STI were you diagnosed with?

☐ Syphilis ☐ Gonorrhea ☐ Trichomoniasis

☐ Chlamydia ☐ Herpes ☐ Others (specify_____)

PART B: ANTHROPOMETRIC DATA

	Measurement		Unit
1	Weight		(kg)
2	Standing Height		(cm)
3	Waist Circumference		(cm)
4	Buttocks (Hip) Circumference		(cm)
5	Mid- Upper Arm Circumference		(cm)
6	Bust		(cm)

PART C: KNOWLEDGE, ATTITUDE AND PRACTICES

17. Which injection drug (s) do you use?

a) _____ c) _____

b) _____ d_____

18. Which non injecting drug do use?

a) _____ c) _____

b) _____ d) _____

19. When did you start injecting? ☐ < 6 months ☐ 6-11 months ☐ 1-3 yrs ☐ >3 yr

20. How many times do you inject per day?

☐ ONCE ☐ TWICE ☐ THRICE ☐ >3 TIMES

21. Have you ever shared syringes? ☐ YES ☐ NO

22. Have you ever heard of Flashblood? ☐ YES ☐ NO

23. Have you ever practiced Flashblood? ☐ YES ☐ NO

24. Name some of the health related risks associated with needle/syringe sharing or flashblood.

1_____; 2_____; 3 _____

25. Do you know of any drug rehabilitation centre? ☐ YES ☐ NO

26. If yes name some of them

1_____; 2_____; 3 _____

27. Would you like to be referred to a rehabilitation centre for treatment? ☐ YES ☐ NO

If yes, Reason----------

If no, Reason----------

PART D: MEDICAL HISTORY

I) SELF REPORTED MEDICAL HISTORY

28. Have you experienced any of the following in the last **TWO** weeks?

Fever ☐ Vomiting ☐ Diarrhoea ☐ Headache ☐ Coughing ☐

29. Have you been on any medication in the last **TWO** weeks? ☐ YES ☐ NO

30. If yes please specify ARVs ☐ Antibiotics ☐ Others_____

31. When did you start using ARVs? ☐ < 6 months ☐ 6– 11 months ☐ 1-3 yrs ☐ >3yrs

II) MEDICAL EXAMINATION

32. Vital signs

Vital sign	Reading
Temperature	
Pulse rate	
Blood pressure	

33. TB Screening and testing

a) Physical screening		
Chest examination		
Coughing		
b) Sputum Analysis	**AFB (-VE)**	**AFB (+VE)**
On spot sputum		
Early morning sputum		
Early morning sputum		

34. Drug Sensitivity Testing

Drug	**Sensitive**	**Resistant**	**Borderline**	**Comment**
Isoniazid				
Rifampicin				
Ethambutol				
Pyrazinamide				

Appendix 3: ERC clearance

KENYATTA UNIVERSITY
ETHICS REVIEW COMMITTEE

Fax: 8711242/8711575
Email: kuerc.chairman@ku.ac.ke
kuerc.secretary@ku.ac.ke
Website: www.ku.ac.ke

P. O. Box 43844,
Nairobi, 00100
Tel: 87[illegible]1-12

Our Ref: KU/R/COMM/51/32-4

Date: June 6th, 2012

Valentine Budambula
School of Public Health,
Kenyatta University
P.O. Box 43844, Nairobi.

Dear Ms. Valentine

APPLICATION NUMBER PKU019/116 of 2012 - **'HIV/Pulmonary TB co-infection amongst intravenous drug users in Mombasa, Kenya. Version 4.**

1. IDENTIFICATION OF PROTOCOL

The application before the committee is with a research topic **'HIV/Pulmonary TB co-infection amongst intravenous drug users in Mombasa, Kenya'**, Version 4. Dated 19th May, 2012.

2. APPLICANT

Valentine Budambula
School of Public Health,
Kenyatta University
P.O. Box 43844, Nairobi.

3. SITE

Mombasa County, Kenya.

4. DECISION REACHED.

The committee has considered the research protocol in accordance with the Kenyatta University Research Policy (section 7.2.1.3) and the Kenyatta University Ethics Review Committee Guidelines, and is of the view that against the following elements of review,

i. Scientific design and conduct of study,
ii. Recruitment of research participant,
iii. Care and protection of research participants,
iv. Protection of research participant's confidentiality,
v. Informed consent process,
vi. Community considerations.

AND APPROVED that the research may proceed for a period of ONE year from 6th June, 2012.

5. ADVICE/CONDITIONS

i. Progress reports are submitted to the KU-ERC every six months and a full report is submitted at the end of the study.

ii. Serious and unexpected adverse events related to the conduct of the study are reported to this board immediately they occur.

iii. Clearance must be obtained for transportation of any biological material out of the country i.e. Kenya.

iv. Notify the Kenyatta University Ethics Committee of any amendments to the protocol.

When replying, kindly quote the application number above.

If you accept the decision reached and advice and conditions given please sign in the space provided below and return to KU-ERC a copy of the letter.

PROF. NICHOLAS K. GIKONYO
CHAIRMAN ETHICS REVIEW COMMITTEE

I Valentine B. Nzomo ..... accept the advice given and will fulfill the conditions therein.

Signature..... Dated this day of..... 2012.

cc. Vice-Chancellor
Director: Institute for Research Science and Technology

Appendix 4: Ministry of Health, Mombasa County Clearance

MINISTRY OF PUBLIC HEALTH & SANITATION

Telegrams: "PROVMED",
MOMBASA
Tel: Mombasa: 2226006/2222867
Fax: 2226006
Email: pdphscoast@yahoo.com
When replying please quote

OFFICE OF
THE PROVINCIAL DIRECTOR
OF PUBLIC HEALTH &
SANITATION SERVICES /COAST
PROVINCE
P. O. BOX 90233-80100
MOMBASA

Ref: ADM.3/5/37/121

Date: 12TH JULY 2012

District Medical Officers of Health
- **Mombasa**
- **Kilindini**

RE: REQUEST TO CARRY OUT DATA COLLECTION ON HIV/PULMONARY TB CO-INFECTION AMONGST INTRAVENOUS DRUG USERS IN MOMBASA

The bearer of this letter, Valentine Budambula is a PhD student at the Department of Community Health, Kenyatta University (KU), Nairobi and also a lecturer at Department of Environment and Health, Mombasa Polytechnic University College.

She wishes to carry out data collection in health institutions and rehabilitations centres within Mombasa County for a period of one (1) year with effect from 6th July 2012.

Kindly accord her the necessary support.

Dr. Anisa Omar, **OGW**
M, B, Ch. B M. Med (paed) H. Dip.HSM (Israel)
Provincial Director of Public Health and Sanitation,
COAST PROVINCE

Appendix 5: Consent Form- English Version
Study Title: HIV/Pulmonary TB Co-Infection amongst Injection Drug Users in Mombasa, Kenya.

Dear participant,
You are invited to take part in this research study because you have a history of injection drug use. This form tells you why this research study is being done, please read then can decide if you want to join this study or not. The Principal Investigator in this study is a PhD student at Kenyatta University. A study team will be working closely with principal investigator and the study will run for 2 years.

The purpose of this study is to determine the factors associated with HIV and pulmonary TB co-infections among injection drug users. If you choose to participate in this study, the team will require 3ml of blood (HIV voluntary testing and Complete Blood Count) and three early morning sputum (for TB testing) from you. No drug or chemical will be introduced into your body. You can decide whether to take part in this study or not. You are free to say yes or no. If you say no, your regular medical care will not change. Even if you join this study, you do not have to stay in it, you may stop at any time. It is important to note that there is no financial benefit for participating in this study at the same time there will be no any cost implications to you. Participation in this study is important as the findings of the study have the potential of being used to lobby for funding for antiretroviral drugs (ARVs) and primary healthcare for drug users.

The risks in this study include possible discomfort due to questions on health and personal behaviour/history. In addition, discomfort may be experienced while a blood sample is being obtained. Every effort will be made to keep your study records confidential but we cannot guarantee it. No funds have been set aside to pay any costs if you are harmed because of this study. If you think that you were harmed because of this study, contact the Principal Investigator.

By signing my name below, I confirm the following:

1. I have read (or been read to) this entire consent document. All of my questions have been answered to my satisfaction.
2. The study's purpose, procedures, risks and possible benefits have been explained to me.
3. I agree to let the study team use and share the health information and other information gathered for this study.
4. I voluntarily agree to participate in this research study. I agree to follow the study procedures as directed.
5. I have been told that I can withdraw from the study at any time.

Participant's Name_____sign_____Date_____

Principal Investigator _____sign_____Date _____

Note: Below are some of the key contacts

1. *Principle investigator – Valentine Budambula 07222822448*
2. *KU-ERC kuerc.chairman@ku.ac.ke*

Appendix 6: Consent Form- Swahili Version

Mada Ya Utafiti : Uambukizo pamoja wa virusi vya HIV na Kifua kikuu kati ya watumiaji wa mihadarati kwa kujidunga, Mombasa Kenya.

Kwako mhusika,

Unaalikwa kushiriki kwenye utafiti kwa sababu uko na historia ya utumiziaji wa mihadarati kwa kujidunga shindano. Fomu hii inakuelezea kwa sababu gani utafiti huu unafanywa. Tafadhali soma fomu hii halafu uamue kama utashiriki kwenye utafiti huu. Mtafiti mkuu ni mwanafunzi wa shahada ya philosophia(PHD) katika chuo kikuu cha Kenyatta. Timu ya utafiti itafanya kazi kwa karibu na mtafiti mkuu, na utafiti mwenyewe utachukua muda wa miaka miwili.

Inia hasa ya utafiti huu nikutathimini au kuamua sababu zinazohusishwa na uambukizo pamoja wa virusi vya HIV na kifua kikuu kati ya watumiaji wa mihadarati kwa kujidunga. Ukichagua kushiriki kwenye utafiti huu, hii timu ya watafiti itahitaji kiasi cha mililita 3 za damu kutoka kwako(kwa ajili ya upimaji wa hiyari wa virusi vya HIV na hesabu ya kiwango cha damu) na pia watahitaji makohozi ya asubuhi (kwa ajili ya upimaji wa maambukizi ya kifua kikuu). Hakuna dawa ama kemikali zozote zitakazoekwa kwa mwili wako. Unaweza kutoa uamuzi wa kushiriki kwenye utafiti huu au la, pia uko huru kusema ndio ama la. Ukisema la matibabu yako ya kawaida hayataathirika. Si lazima kubaki kama mshiriki unaweza ukakatiza kushiriki wakati wowote. Ni muhimu kufahamu kwamba hakuna faida za kifedha kwa kushiriki kwenye utafiti huu. Wakati huohuo hautagaramika kivyovyote kifedha kwa kushiriki. Kushiriki katika utafiti huu ni muhimu kwa sababu, uvumbuzi ama majibu ya utafiti huu yatasaidia kupigania au kushawishi misaada ya kifedha kwa dawa za kuvunja makali ya virusi na pia afya ya msingi kwa watumiaji wa mihadarati.

Hatari zinazoambatana na kushiriki katika utafiti huu ni kama usumbufu kutokana na maswali ya kiafya na ya kibinafsi hasa tabia na historia yako. Kadhalika utahisi usumbufu hasa wakati wakutolewa damu. Juhudi zote zitafanywa kwa ajili ya kuhifadhi habari na jumbe zako zote kwa njia ya usiri wa hali ya juu. Lakini hatuezi kuhakikisha hili. Hakuna fedha ambazo zimehifadhiwa kwa ajili yakukufidia endapo utadhurika kutokana na utafiti huu. Kama unafikiria kwamba ulidhurika kutokana na utafiti huu wasiliana na mtafiti mkuu.

Kwa kuweka sahihi jina langu nathibitisha yafuatayo:-

1. Nimesoma (ama nimesomewa) karatasi hii ya kutoa idhini ya kukubali, na maswali yangu yote yamejibiwa na nimeridhika.
2. Nia, mitindo,hatari pamoja na faida zinazoambatana na utafiti huu zimeelezwa kwangu.
3. Nakubali na kuruhusu timu ya utafiti kutumia na kugawa habari za kiafya ama aina yoyote ya habari zitakazo kusanywa kutokana na utafiti huu.
4. Nimekubali kwa hiyari kushiriki kwenye utafiti huu.
5. Nimeelezwa kwamba ninaweza kukoma kushiriki wakati wowote.

Jina la mshiriki _____ Sahihi_____ Tarehe_____

Mtafiti mkuu _____Sahihi _____ Tarehe_____

Zaidi; wasiliana na wafuatao

1. Mtafiti mkuu: Valentine Budambula kwa nambari ya rununu, 07222822448
2. KU-ERC: Kupitia barua pepe kuerc.chairman@ku.ac.ke

Appendix 7: PCR protocol

QIAquick PCR Purification Kit Protocol

This protocol is designed to purify single- or double-stranded DNA fragments from PCR and other enzymatic reactions. For cleanup of other enzymatic reactions, follow the protocol as described for PCR samples or use the MinElute Reaction Cleanup Kit. Fragments ranging from 100 bp to 10 kb are purified from primers, nucleotides, polymerases, and salts using QIAquick spin columns in a microcentrifuge.

Important points before starting

i. Add ethanol (96–100%) to Buffer PE before use (see bottle label for volume).
ii. All centrifugation steps are carried out at 17,900 x g (13,000 rpm) in a conventional tabletop microcentrifuge at room temperature.
iii. Add 1:250 volume pH indicator I to Buffer PB (i.e., add 120 µl pH indicator I to 30 ml Buffer PB or add 600 µl pH indicator I to 150 ml Buffer PB). The yellow color of Buffer PB with pH indicator I indicates a pH of ≈7.5.
iv. Add pH indicator I to entire buffer contents. Do not add pH indicator I to buffer aliquots.
v. If the purified PCR product is to be used in sensitive microarray applications, it may be beneficial to use Buffer PB without the addition of pH indicator I.

Procedure

1. Add 5 volumes of Buffer PB to 1 volume of the PCR sample and mix. It is not necessary to remove mineral oil or kerosene. For example, add 500 µl of Buffer PB to 100 µl PCR sample (not including oil).
2. If pH indicator I has beein added to Buffer PB, check that the color of the mixture is yellow. If the color of the mixture is orange or violet, add 10 µl of 3 M sodium acetate, pH 5.0, and mix. The color of the mixture will turn to yellow.
3. Place a QIAquick spin column in a provided 2 ml collection tube.
4. To bind DNA, apply the sample to the QIAquick column and centrifuge for 30–60 s.
5. Discard flow-through. Place the QIAquick column back into the same tube. Collection tubes are re-used to reduce plastic waste.
6. To wash, add 0.75 ml Buffer PE to the QIAquick column and centrifuge for 30–60 s.
7. Discard flow-through and place the QIAquick column back in the same tube. Centrifuge the column for an additional 1 min.

   IMPORTANT: Residual ethanol from Buffer PE will not be completely removed unless the flow-through is discarded before this additional centrifugation.

   PCR Purification
8. Place QIAquick column in a clean 1.5 ml microcentrifuge tube
9. To elute DNA, add 50 µL Buffer EB (10 mM Tris·Cl, pH 8.5) or water (pH 7.0–8.5) to the center of the QIAquick membrane and centrifuge the column for 1 min. Alternatively, for increased DNA concentration, add 30 µL elution buffer to the center of the QIAquick membrane, let the column stand for 1 min, and then centrifuge.

   IMPORTANT: Ensure that the elution buffer is dispensed directly onto the QIAquick membrane for complete elution of bound DNA. The average eluate volume is 48 µL from 50µL elution buffer volume, and 28 µL from 30µL elution buffer.

Appendix 8: Work plan

EVENT	Sept 2010– Aug 2011	Nov – June 2012	July 2012	Aug-Dec 2012	Jan 2013- June	July- Dec 2013	Jan14 -July	Aug 2014	Sept- Dec 2014
Proposal processing									
Clearance by ERC									
Training of research assistants									
Data collection									
HIV geno-typing									
Data analysis									
Thesis writing									
Manuscript preparation									
Results Presentation									
Thesis submission									
Thesis defense									

Appendix 9: BUDGET: DATA COLLECTION COSTS

	Item	Description	Cost(Kshs)
1	Photocopy (Consent forms)	400 copies Kshs. 3	1, 200.00
2	Photocopy (questionnaire)	400 copies x 5 pages xKshs.3	6, 000.00
3	Email/airtime		8, 000.00
4	Determine kits	4 pkts @ 6000	24, 000.00
5	Unigold	2 pkts @ 8000	16. 000.00
6	surgical gloves	8 pkts @ 600	4, 800.00
7	syringes	450 @ 17	7, 650.00
8	needles	450 @10	4, 500.00
9	Slides	200 pieces @ Kshs 30	6, 000.00
10	Glycene envelops	150 @ 12	1, 800.00
11	filter papers (for DBS)	300 @16	4, 800.00
12	Ziplock bags	Assorted	3, 600.00
13	Desiccants	Assorted	3, 500.00
14	Humidity indicator	1 tin	2, 500.00
15	ETDA tubes	450 @ 20	9, 000.00
16	Plain tubes	450 @ 20	9, 000.00
17	Cryovials	9 boxes @ 1900	17, 100.00
18	Pippettes	196 pieces @ 60	11, 760.00
19	Field visits	2 fuel tanks/ month for 6 months	48, 000.00
20	Field assistants	2 research assistants and 2 lab t	80, 000.00
21	Field assistants	2 IDU field mobilizers	40, 000.00
22	CD4 Testing	361 IDU @ 1000	361, 000.00
23	Full haemogram	361 IDU @ 400	144, 400.00
24	Bus fare reimbursement	361 IDU @ 250	90, 250.00

BUDGET: HIV GENOTYPING EXPENDITURE

	ITEM	**Cost Kshs**
1	UltraPure DNAse/RNAse-Free Distilled Water (1x0.5litre)	2,376.00
2	One-Step Reverse transcriptase	34,956.00
3	AmpliTaq Gold DNA Polymerase, with Gold Buffer {Chemically modified enzyme for automated Hot Start PCR. Includes10x PCR Gold Buffer (500mM KCl, 150mM Tris/HCl pH 8.0) and 25mM MgCl 2 solution for 200 x 50µl reactions}	32,883.00
4	MicroAmp Optical 96-Well Reaction Plate (1 PKT/10)	10,241.00
5	AmpliTaq Gold PCR Master Mix (200 rxs) Each tube of AmpliTaq Gold PCR Master Mix is at 2X the recommended usage concentration, and contains the following: AmpliTaq Gold DNA Polymerase 250 U (0.05 U/µL) GeneAmp PCR Gold Buffer, 30 mM Tris/HCl, pH 8.05, 100 mM KCl dNTP, 400 µM each MgCl2, 5 mM Stabilizers	50,440.00
6	BigDye ® Terminator v1.1 Ready Reaction Cycle Sequencing Kit [200µL Tube of BigDye® Terminator v1.1 Ready Reaction Mix,Tube M13 (-21) Primer,Tube pGEM Control DNA, 1mL Tube of 5x Sequencing Buffer]	44,405.00
7	0.2 mL Polypropylene PCR Tubes (2xCase of 250)	34,073.00
8	15 mL Polypropylene Centrifuge Tubes (1xcase of 500)	56,706.00
9	DNA MW Marker, 100 bp Ladder (100bp-1.5kb (1x250µl)	40,120.00
10	Powder-less hand Gloves (Large) (case of 1000)	7,480.00
11	20 µl micropipette tips (500)	13,260.00
12	1000 µl micropipette tips (500)	1,955.00
13	200 µl micropipette tips (1000)	1,955.00
14	Eppendorff microcentrifuge tubes (1.5mL, assorted colours and sterile) (1 bag)	1,955.00
15	10X TBE (1 litre)	8,840.00
16	Ethidium bromide (5 g)	11,900.00
17	Denatured Ethanol (molecular biology grade, 1 litre)	6,120.00

18	Sodium Acetate (molecular biology grade, 500g)	4,250.00
19	Highly deionized (HiDi) Formamide (100 ml)	4,335.00
20	POP 6 polymer (3ml)	5,525.00
21	Sequencing tray (96 well sequencing plate, 3 sets)	19,720.00
22	Bench fee	130,900.00
23	One-step Rtase	50,150.00
24	PRIMER SET-1	
25	5'-GGAAACCAAAAATGATAGGGGGAATTGGAGG-3'	12,750.00
26	5'-TGACTTGCCCAATTTAGTTTTCCCACTAA-3'	9,775.00
27	5'-GTAGGACCTACACCTGTTCAACATAATTGGAAG-3'	
28	5'-CCCATCCAAAGAAATGGAGGAGGTTCTTTCTGATG-3'	9,775.00
	PRIMER SET-2	
29	5'-TCCTTAACTTCCCTCAAATCACT-3'	
30	5'-CTGGCACGGTTTCAATAGGACT-3'	9,775.00
31	5'-GGGAATTTTCTTCAGAGCAG-3'	
32	5'-TCTTCTGTCAATGGCCATTGT-3'	9,775.00
	PRIMER SET-3	
33	5'-TCTTAGGAGCAGCAGCAGGAAGCACTATGGG-3'	
34	5'-AACGACAAAGGTGAGTATCCCTGCCTAA-3'	9,775.00
35	5'-ACAATTATTGTCTGGTATAGTGCAACAGCA-3'	
36	5'-TCCTACTATCATTATGAATATTTTTATATA-3'	9,775.00

	PRIMER SET-4	
37	5'-GGGTCACCATATTCTTGGG-3'	
38	5'-CA (A/G) AGACAAAAGAAAATTGG-3'	9,775.00
39	5'-GAACAAGAGCTACAGCATGGG-3'	
40	5'-CCACTGCATGGCCTGAGGATG-3'	9,775.00
41	Research Assistants (2) @ 20, 000 per month	40,000.00
	SUB-TOTAL	**705,495.00**
	PLUS DATA COLLECTION COSTS	**904,860.00**
	GRAND TOTAL	**1,610,355.00**