MODIFIABLE FACTORS ASSOCIATED WITH ACTIVE PULMONARY TUBERCULOSIS: (A CASE STUDY OF NAKURU G.K PRISON IN KENYA)

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A thesis submitted in partial fulfillment for the Degree of Master of Science in Applied Epidemiology in the Jomo Kenyatta University of Agriculture and Technology.

2008

DECLARATION

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

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DEDICATION

To my wife Melody Kambiha and my mother Fridah Amwayi for bearing with my long absence from them and the encouragement and support they accorded me throughout this study.

ACKNOWLEDGEMENTS

I extend my sincere gratitude to my supervisors; Dr. Eric Muchiri, Dr. Gideon Kikuvi and Dr. Myat Htoo Razak. Thanks also to Dr. Douglas Klauke and Dr. Christopher Tetteh for their invaluable assistance throughout the course of this study and for their able guidance and valuable input during the development of the study protocol. I am grateful to the Nakuru Government of Kenya (G.K) prison staff and Commissioner of Prison Services in Kenya for allowing the use of prison records for this study.

My gratitude also goes to Mrs. Faith Changwony and Mr. Nahashion Mungai for their great work during the data collection period. I also convey my thanks to my class-mates; Dr. Daniel Langat, Dr. Maurice Ope, Dr. Martha Muthamia, Dan Owiti, Abade Mohamed and all the staff in the Field Epidemiology and Laboratory Training Programme (FELTP); and Institute of Tropical Medicine and Infectious Diseases for their support and encouragement. I acknowledge the Centre for Disease Control and Prevention (CDC), for providing funds for this study, through the FELTP.

May God bless the Labours of your hands.

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ABBREVIATIONS

AAFB	Acid and alcohol fast bacilli
AFB	Acid-fast bacilli
AIDS	Acquired Immune Deficiency Syndrome
AOR (MH)	Adjusted Odds Ratio (Mantel Hansel)
ART	Antiretroviral therapy
BCG	Bacille Calmette - Guerin
BMI	Body Mass Index
CDC	Centres for Disease Control and Prevention
CI	Confidence Interval
CNR	Case Notification Rate
COR	Crude Odds Ratio
CXR	Chest X-ray
DOT	Directly Observed Treatment
FELTP	Field Epidemiology and Laboratory Training Programme
G.K	Government of Kenya
HIV	Human immunodeficiency virus
ICN	International Council of Nurses
ICRC	International Committee of Red Cross
JKUAT	Jomo Kenyatta University of Agriculture and Technology
KEMRI	Kenya Medical Research Institute

MDG	Millennium Development Goal
MDR-TB	Multidrug-Resistant Tuberculosis
MLE (OR)	Maximum Likehood Estimate (Odds Ratio)
MMWR	Morbidity and Mortality Weekly report
MOH	Ministry of Health, Kenya
MOR	Matched Odds Ratio
MTB	*Mycobacterium tuberculosis*
NLTP	National Leprosy and Tuberculosis Programme
OR	Odds Ratio
PLWAs	People living with HIV/AIDS
PPM	Public–private or public–public mix
PTB	Pulmonary tuberculosis
TB	Tuberculosis
SES	Social Economic Status
STI	Sexually Transmitted Infection
WHO	World Health Organization
XDR-TB	Extensively Drug-Resistant Tuberculosis
Z-N stain	Ziehl –Neelsen stain

ABSTRACT

Prisoners constitute a high risk group for acquisition of *Mycobacterium tuberculosis* (MTB) infection compared to the general population. The living settings of prisons are very condusive for tuberculosis (TB) transmission. This poses serious danger as the spread may involve drug resistant strains. No studies investigating the factors associated with MTB in prisons have been carried out in Kenya. This study aimed at establishing the modifiable factors associated with active pulmonary tuberculosis (PTB) disease among prisoners at the Nakuru prison, in Kenya.

An age-sex matched case-control study was carried out between August and December, 2007. A PTB case was defined as "any adult prisoner who had at least two initial sputum positive acid-fast bacilli (AFB+) smear. Prisoners possessing no history of chronic cough and not treated for PTB in the previous six (6) months were enrolled as controls. Data was collected using structured questionnaire. Study subjects were checked for a typical BCG scar and their weight (in kg) and height (in meters) measurements taken. Data entry and analyses were done using Epi-Info software. Ethical approval was obtained from the relevant prison authorities and research bodies. A total of 144 subjects (Case = 48, Controls = 96) were recruited. Statistically significant factors independently associated with active PTB disease were: HIV positive {P = 0.0018}, evidence of BCG vaccination (P = 0.0059}, contact with PTB case while in incarceration {P = 0.0329}, unemployment status prior to incarceration {P = 0.0067}. A strong dose-response relationship between active PTB disease and the number of cigarettes smoked daily,

frequency of sexually transmitted infection (STI) episodes, frequency of prison transfer ($p<0.0001$) was found.

Factors associated with active PTB disease amongst adult prisoners are multifaceted and modifiable. A comprehensive multidisciplinary control and preventive approach involving prisoners, health officials and prison authorities should be adopted. The team will implement screening for TB upon prison entry, isolation of suspected cases, routine cross-matching of incoming inmates with local TB registry, HIV counseling and testing of all patients diagnosed of PTB, educating jail staff on sign and symptoms of PTB and encouraging prisoners to quit smoking. Further studies on the role of BCG vaccination in adults, STI agent associated with PTB and molecular epidemiological studies to determine any epidemiological-linkage of tuberculosis spread amongst prisoners are warranted.

CHAPTER ONE

INTRODUCTION

1.1 Background information

Tuberculosis (TB) is a disease of antiquity, caused by *Mycobacterium tuberculosis* (MTB), which principally affects the lungs (Harries and Dye, 2006), but can spread to other parts of the body (Mary and Sandra, 2006).Tuberculosis is an airborne infectious disease that is preventable and curable. If TB disease is detected early and fully treated, people with the disease quickly become non-infectious and eventually cured. Multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), HIV-associated TB, and weak health systems are major challenges (Leopold *et al.*, 2003; Marcos *et al.*, 2001). Tuberculosis is one of the most common infectious diseases known to man (Dye *et al.*, 1999). The disease currently holds the seventh place in the global ranking of causes of death (Smith, 2004) with 99 % of deaths estimated to occur in developing countries. It is associated with poor socioeconomic development, in that 75 % of people with TB are within the economically productive age group of 15-54 years (Dye, 2006).

About 90% of those infected with *Mycobacterium tuberculosis* have asymptomatic, latent TB infection (sometimes called LTB), with only a 10% lifetime chance that a latent infection will progress to TB disease. An AIDS patient with latent TB has 10% chance per year of developing active TB (Onyebujoh and Graham, 2004). In 2000 an estimated 2 billion people (one in every three individuals in the world's population), were infected by the tubercle bacillus (Corbett *et al., 2003*), and are at risk of developing TB at some future period in their life-time (Chintu and Mwaba, 2005).TB

was declared an emergency in Africa in 2005 by 46 African Health Ministers (Anonymous, 2007a). Among the UN Millennium Development Goals, the five principal targets for global TB control are by 2005, to detect 70% of new smear-positive patients arising each year, and to successfully treat 85% of these patients; by 2015, to have halted and begun to reverse incidence; between 1990 and 2015, to half TB prevalence and death rates (Anonymous, 2008).

In Kenya, the National Leprosy and Tuberculosis Programme (NLTP) has the overall responsibility for tuberculosis and leprosy control and by 2005, the TB control focused on DOTS expansion. The total number of TB cases (all forms of tuberculosis) reported in 2005 was 108,401, representing a nine-fold increase compared to that reported in 1990 at 11,625 (MOH, 2005a).

1.2 Problem statement

Tuberculosis case rates are much higher in correctional populations than in the general population (Hammett *et al*.,2002;Hutton *et al.,* 1993) due to the overcrowding, closed living conditions, insufficient ventilation, generally low socioeconomic status, poor nutrition, and poor health of prison inmates (Aerts *et al.,* 2000). There is an increasing recognition that the high risk of MTB infection in prison settings poses a problem not only for those imprisoned but also for the wider society (Coninx *et al.,* 2000). Transmission of MTB in prisons is also a serious threat as most of the cases involve resistant strains (Campbell *et al.,* 1993). Jails can act as reservoirs of TB disease for inmates and staff, and for the community into which the inmates are released

(Pelletier *et al.*, 1993).An effective MTB infection control in prisons is necessary to protect the well-being of both prisoners and the wider community (Angie *et al.*, 2000). Knowledge of the epidemiology of tuberculosis in prisons, the need to use different measures from those in normal population settings, and understanding the principles of tuberculosis control are all necessary for governmental and other agencies to contribute to the implementation of effective tuberculosis control programmes in prisons (Coninx *et al.*, 2000).

1.3 Justification of the study

The HIV pandemic in Kenya has been associated with the re-emergence of TB. There is a need to re-examine the contribution of environmental and other host-related factors, especially in correctional institutions which acts as a reservoir for TB, in order to adjust and adapt appropriate TB control policies. Studies investigating the risk factors for TB have been conducted in a variety of settings, but very few of these studies have been done in Africa (Lienhardt, 2001).

Currently, there are no data or reports on factors associated with active PTB disease amongst prisoners in Kenya. Thus, this study aimed at establishing the factors associated with active PTB disease among prisoners at the Nakuru GK prison, in Kenya. The results of this study will be utilized in formulating recommendations for improving the living conditions in prisons and for better MTB control strategies in Kenyan prisons.

1.4 Objectives

1.4.1 General objective

The general objective of this study was to determine modifiable factors associated with active PTB disease amongst adult prisoners at Nakuru G.K Prison.

1.4.2 Specific objectives

1. To establish the risk factors associated with active PTB disease at Nakuru G.K Prison.
2. To establish protective factors associated with active PTB disease at Nakuru G.K Prison.

1.5 Hypothesis

1.5.1 Null hypothesis

There is an association between the host or environmental factors and active PTB disease amongst adult prisoners in Nakuru GK prison.

1.5.2. Alternate hypothesis

There is no association between the host or environmental factors and active PTB disease amongst adult prisoners in Nakuru GK prison.

CHAPTER TWO

LITERATURE REVIEW

2.1 Etiology of tuberculosis disease

Tuberculosis is a disease caused by *Mycobacterium tuberculosis* (*M.tuberculosis*) that adversely affects human health around the world (Elzinga *et al*., 2004). There are five closely related Mycobacteria groups in the *M. tuberculosis* complex: *M. tuberculosis, Mycobacterium bovis* (*M. bovis*), *Mycobacterium africanum* (*M. africanum*), *Mycobacterium microti* (*M. microti*), and *Mycobacterium canetti* (*M. canetti*) (Soolingen *et al*., 1997 and 1998).

The main host of *M. bovis* is cattle (*Bos taurus*) but it affects many other mammals including man. In man, it is the most frequent cause of zoonotic TB, i.e. TB transmitted from animals to humans, which is clinically indistinguishable from TB caused by *M. tuberculosis*. Before milk pasteurization, *M. bovis* was an important cause of human TB, especially intestinal TB in children. After the generalized adoption of pasteurization of milk and other dairy products, the occurrence of zoonotic TB dropped sharply (Angel and Maria, 2007).

Mycobacterium africanum is predominantly isolated in Africa and, in certain areas of the continent; it is thought to produce a significant proportion of the cases of PTB (Frothingham *et al*., 1999; Haas *et al*., 1997). However, *M. microti* has been recently identified as the causative agent of PTB in both immunocompromised and immunocompetent humans (Horstkotte *et al*., 2001).

2.2 Microbiology of causative agent of tuberculosis

Mycobacteria are Gram-positive, non-motile, pleomorphic rods, belonging to the family of Actinomycetales (Clark, 2008). It is an aerobic bacterium that divides every 16 to 20 hours, an extremely slow rate compared with other bacteria, which usually divide in less than an hour (Cox, 2004). *Mycobacterium tuberculosis* can withstand weak disinfectants and survive in a dry state for weeks. In nature, the bacterium can grow only within the cells of a host organism, but *M. tuberculosis* can be cultured *in vitro* (Parish and Stoker, 1999). It is commonly known as an 'acid-fast' bacillus because the lipid in its cell wall makes it resistant to discoloration with acid-alcohol (Puri and John, 1997).

Mycobacteria have very unusual cell wall. They contain considerable amounts of mycolic acid, a waxy substance that makes their cell wall difficult to stain using conventional stains (Heritage et *al*., 1996). They may however, be stained using Ziehl-Neelsen (Z-N) procedure. A heat-fixed film is prepared and flooded with strong carbol fuschsin solution. Starts to steam and kept steaming for 5 minutes. The heat allows the dye to penetrate through the waxy cell wall. The film is then washed with filtered water. Carbol fuschsin is a basic dye and reacts with acid to produce a yellowish-brown compound that may be leached easily from tissues.The leaching process is enhanced by alcohol. However, the waxy wall of mycobacterial protects the dye within their cells when exposed to a solution of 3% hydrochloric acid in 95% alcohol. When films are treated with acid alcohol, only Mycobacteria retain the carbol fuschsin and hence appear red. Methylene blue is generally used as a counter stain to colour other materials in the

film, although some prefer to use malachite green as a counter stain (Heritage et *al*., 1996).

2.3. Mode of infection and transmission of tuberculosis

Mycobacterium tuberculosis is spread by airborne particles, known as droplet nuclei. Droplet nuclei are produced when persons with pulmonary or laryngeal tuberculosis cough, sneeze, speak, or sing (Harries *et al*., 2004). They also may be produced by aerosol treatments, sputum induction, and aerosolization during bronchoscopy, and through manipulation of lesions or processing of tissue or secretions in the hospital or laboratory (Anonymous, 2000). The number of infectious droplets projected into the atmosphere by a patient is very high when coughing (3500) or sneezing (1 million).When they come into contact with the air, these droplets rapidly dry and become very light particles, still containing live bacilli, that remain suspended in the air. In an enclosed space, the droplets can remain suspended for a long time, and the bacilli remain alive for several hours in the dark: these are “infectious particles” ((Nadia and Enarson, 2003).Infection occurs when a person inhales aerosolized *M. tuberculosis* and the bacteria become established in the alveoli of the lungs and spread throughout the body (Carmine *et al.,* 1994).

Tuberculosis is a multifactorial disorder, in which environment interacts with host-related factors (Lienhardt *et al*., 2005). The development of tuberculosis in humans is a two-stage process in which a susceptible person exposed to an infectious case first becomes infected and second, after an interval of years or decades, may later develop the

disease, depending on a variety of factors. Since the acquisition of infection is often far removed from the development of disease and involves different physiologic mechanisms, the risk factors for infection are quite different from the risk factors for development of disease following infection (Comstock, 1975). Factors reported to influence the risk of mycobacterial infection include age, sex, overcrowding, socioeconomic conditions, urbanization, racial/ethnic group, and human immunodeficiency virus infection (Christian, 2001).

It has been suggested that genetic factors partly determine differences in host susceptibility to mycobacterial infection and that such factors might contribute to the pattern of clinical disease (Fine, 1981). The risk of exposure is associated with the frequency and duration of contact with an infectious case of TB. Exposure is very much linked to time spent with potentially infected individuals in confined and poorly ventilated spaces, overcrowded accommodation due to poverty or social norms of living together in extended family groups, working conditions and other social habits and behaviors, such as communal drug-taking. A higher risk of exposure to TB is also associated with urban areas where people are living, traveling and working in cramped conditions. TB is more prevalent in residential institutions such as prisons and hostels, where accommodation may be overcrowded. The higher the prevalence of the disease in a community, the greater the likelihood of contact with an infected person and the higher the risk of exposure to TB bacilli (Anonymous, 2004).

In general, people who become infected with MTB have approximately a 10% risk of developing active disease in their lifetime. This risk is greatest during the first

two years after infection and relates to the individual's health status, and most particularly to the status of the immune system. Human Immuno Deficiency Virus increases the risk of developing active TB once infected. World Health Organization estimated that one third of the approximately 40 million people living with HIV at the end of 2003 were to develop active TB (Haileyesus *et al.,* 2004). Other factors contributing to the risk of developing active disease, once the TB infection takes hold, are smoking (Tocque *et al.*, 2001), exposure to smoke from biomass stoves (Perez-Padilla *et al*., 2001) and Vitamin D deficiency (Wilkinson *et al*., 2000), and malnutrition often associated with poverty, alcohol and substance abuse, and other debilitating conditions (Crofton *et al.*, 1999).

Two main factors are the principal determinants of TB case fatality. First, the site and type of disease and second, the appropriateness and timeliness of the intervention and care provided. Inadequate treatment is likely to result in early death. Thirty to forty percent of untreated sputum-smear positive TB cases die within a year, and 50-60% will be dead within five years (Rieder, 1999). HIV infection, malnutrition and severe pulmonary disease are all associated with a greater risk of death from TB. Inadequate treatment for those suffering from MDR-TB also increases the risk of death (Anonymous, 2004).

Tuberculosis is classified as an opportunistic infection for person with Acquired ImmunoDeficiency Syndrome (AIDS). Human Immuno Deficiency Virus infection is a major risk factor for TB (MMWR, 2007). The association between HIV infection and tuberculosis stems from two distinct processes. In some cases, populations with latent

tuberculosis acquire HIV infection, which increases 100-fold the risk of reactivation of tuberculosis. In other cases, people with HIV-induced Immuno-suppression acquire new tuberculosis infections and are at extraordinarily high risk for active tuberculosis. This cycle of infection and disease is amplified by the interaction between patients with active tuberculosis and those with HIV infection in clinics, hospitals, and the broader community (Richard and Neil, 2008).Therefore, HIV infection is the greatest known risk factor for progression from latent TB infection to development of TB disease (MMWR, 2007). This risk has been shown to increase with declining CD4+ counts (Williams and Dye, 2003). Thus, the HIV pandemic presents a massive challenge to global TB control (Elizabeth *et al.,* 2003).

2.4 Pathology of tuberculosis

The pathogenicity of the MTB relies on its ability to survive destruction by the macrophages and to induce a delayed hypersensitivity reaction. The cell mediated or type IV hypersensitivity reaction to the MTB explains the massive tissue destruction so characteristic of the disease (Kavanagh, 2001). Two phases of this disease occur as a result of inhaling the tubercle bacillus. The location of the inflammatory foci and host response to the infection differ in these two phases (Margaret, 2008).

Primary infection occurs on first exposure to tubercle bacilli. Inhaled droplet nuclei are so small that they avoid the mucociliary defence of the bronchi and lodge in the terminal alveoli of the lungs. Infection begins with multiplication of the tubercle bacilli in the lungs. This is Ghon focus. Lymphatics drain the bacilli to the hilar lymph

nodes. The Ghon focus and related hilar lymphadenopathy form the primary complex. Bacilli may spread in the blood from the primary complex throughout the body (miliary TB). The immune response delayed hypersensitivity and cellular immunity develops about 4-6 weeks after the primary infection (Puri and John, 1997). The size of the infecting dose of bacilli, the strength of the immune response (Puri and John, 1997) and the virulence of the organism determine what happens next (Margaret, 2008). In most cases, the immune response stops the multiplication of bacilli (Puri and John, 1997) with resultant fibrosis and calcification of the Ghon complex (Margaret, 2008). However, a few dormant bacilli may persist. A positive tuberculin skin test would be the only evidence of infection (Puri and John, 1997) and the presence of the obsolete fibrocalcific Ghon complex (Margaret, 2008). The immune response in a few cases is not strong enough to prevent multiplication of bacilli, and disease occurs within a few months (Puri and John, 1997).

Secondary (reactivation) tuberculosis usually results from reactivation of dormant, endogenous tubercle bacilli in a sensitized patient who has had previous contact with the tubercle bacillus or by reinfection with exogenous bacilli (Sampura, 2007) or may follow a sub-clinical case of primary tuberculosis (Kavanagh, 2001). The cause of reactivation is presumed to be a decline in host immunocompetence. Granulomas form quickly and caseation is usually pronounced. The location of granulomas is typically in the apices of the lungs. The fibrotic reaction tends to confine the typical lesion, but concurrently there is an increased tendency to tissue destruction and cavitation. Cavitation favors proliferation of organism and spread to contacts.

Entrance into the lymphatics permits multiorgan dissemination. Hypersensitivity to the bacilli in the primary phase seems to enhance resistance and induces a more prompt response by activated macrophages and fibroblasts. It is the variable spectrum of the interaction of hypersensitivity and fibrotic reaction which determines the natural course of the disease, which ranges from cure through continuous progression, or multiple exacerbations to death (Margaret, 2008).

2.5 Diagnosis of tuberculosis disease

The diagnostic approach of TB disease includes four major steps mainly medical history, tuberculin skin test, chest x-ray, and bacteriologic examination. A medical history to establish possible contact of patient with a person with TB, symptoms of TB disease, previous TB infection or disease, or exposure to risk factors for developing TB disease, is established. Patients presenting symptoms of TB disease can be screened using a tuberculin skin test while a chest x-ray is used to rule out the possibility of PTB disease in a person who has a positive reaction to the tuberculin skin test. Other steps include bacteriologic examination of a sputum specimen from patients suspected of having PTB disease. Demonstration of acid-fast bacilli microscopically confirms the TB disease. A positive culture for MTB also confirms the diagnosis of TB disease. Together with culturing of specimen drug susceptibility test are performed to determine the appropriate drugs for use in treatment (Anonymous, 1997a). The most important symptoms in the selection of TB suspects in adults (over 15 years of age) are the following: productive cough of more than 3 weeks, or haemoptysis; and significant

weight loss. Patients with TB may also have other symptoms (which are more common, but less suggestive) such as chest pain, breathlessness, fever / night sweats, tiredness; and loss of appetite (Afranio and Fernando, 2007)

Most Mycobacteria grow at a relatively slow rate; therefore, the acid-fast smear plays an important role in the early diagnosis of mycobacterial infections. Microscopy is the oldest, easiest, most rapid, and inexpensive procedure that can be performed in the laboratory to detect the presence of acid-fast bacilli. Acid Fast Bacilli (AFB) smears require 10^5 AFB per ml of sputum for recognition by direct microscopy; culture detects as few as 10 to 100 colony forming units /ml of sputum (Provlab, 2008). Depending on the bacterial load, sensitivity of a single sputum smear is between 22% and 80%, but it can be improved if multiple sputum specimens are examined (Nolte and Metchock, 1995).

It has been suggested that primary MTB disease may not be recognized initially on chest radiographs from more than half of cases among hospitalized adults subsequently diagnosed with TB. Computerized tomography (CT) is more sensitive than chest radiography for detection of cavities, lymphadenopathy, miliary disease, bronchiectasis, bronchial stenosis, bronchopleural fistula, and pleural effusion (Gregory and Angeline, 2000).

In general, the sensitivity of culture is 80–85% with a specificity of approximately 98 % (Ichiyama *et al*., 1993). Liquid systems allow for rapid growth {detection of mycobacterial growth within 1–3 weeks compared with solid media, where growth takes 3–8 weeks} (Morgan *et al*., 1983).

The tuberculin skin test is currently the only widely used method for identifying infection with MTB in persons who do not have tuberculosis disease. Proper use of the tuberculin skin test requires a knowledge of the antigen used (tuberculin), the immunologic basis for the reaction to this antigen, the technique(s) of administering and reading the test, and the results of epidemiologic and clinical experience with the test (Anonymous, 2000).

Tuberculin skin test (TST) which is used for the detection of latent tuberculosis has many disadvantages such as false positivities due to cross reactions between environmental mycobacteria and BCG strain, false negativities due to immunosuppressant and malpractice, and also difficulties in application and evaluation. Recently new diagnostic tests which measure the production of interferon (IFN)-gamma in whole blood upon stimulation with specific ESAT-6 (Early Secretory Antigenic Target 6) antigen and CFP-10 (Culture Filtrate Protein 10) antigens of *Mycobacterium tuberculosis* has been introduced. Since most of the mycobacteria other than tuberculosis and BCG strain do not contain these antigens, the detection of IFN-gamma levels indicates the specific T-cell response against MTB (Oztürk *et al.*, 2007). The two commercially available tests are the T SPOT-TB assay, an enzyme-linked immunosorbent spot or ELISPOT test that uses peripheral blood mononuclear cells (Meier *et al*., 2005), and the QuantiFERON-TB Gold, an enzyme-linked immunosorbent assay (ELISA) that uses whole blood (Barnes, 2004).

Evidence indicates that QuantiFERON-TB Gold (QFT-G), a specific whole-blood interferon-gamma (IFN-gamma) based assay, can detect recent TB infections with

superior sensitivity and specificity (Mori *et al.*, 2007). Therefore, IFN-gamma assays tests can also be used to screen for latent and diagnosis of active TB and in vaccine studies as a marker of vaccine intake (Geiter, 2006).

Molecular typing methods have been utilized as an adjunct to classical epidemiological approach in studying TB transmission dynamics and enhancing understanding of the epidemiology of TB (Takashima and Iwamoto, 2006). In Japan, advances in the molecular epidemiology analysis of this disease have greatly improved TB prevention among epidemiologically linked patients (Takahashi, 2003) and helping in determining risk factors for tuberculosis infection (Kanduma *et al.*, 2003). Molecular techniques have provided quick, sensitive, and specific tests for MTB - such as polymerase chain reaction, DNA and RNA probes, and gamma interferon tests - but these are expensive and technically demanding (NICE, 2006). They are most useful in diagnosing multi-drug resistant organisms quickly and in differentiating MTB from other, non-infectious mycobacterial species (Ian and Oumou, 2006).

2.6 Tuberculosis prevention and control strategies

Tuberculosis can be controlled by promptly recognizing and treating people with the disease and ensuring that people with the disease complete their treatment. Lapse in treatment not only fails to cure the disease but contributes to the growth of drug resistance; identifying and treating people with early infection, to prevent them later developing the full disease; prevention through BCG immunization .BCG gives limited protection against TB so cannot, on its own, control the disease (Department of Health

England, 2004).

The World Health Organization (WHO) recommends the DOTS strategy for tuberculosis control which has been adopted by many National Tuberculosis Programmes (NTPs). An effective TB control programme depends upon laboratories providing accurate, reliable, and timely detection of TB cases (Anonymous, 2006a). Five components of the DOTS strategy are sustained political commitment; access to quality-assured sputum microscopy; standardized short-course chemotherapy for all cases of TB under proper case management conditions, including direct observation of treatment; uninterrupted supply of quality-assured drugs; recording and reporting system enabling outcome assessment of all patients and assessment of overall Programme performance (Engstrom, 2006). Although DOTS is regarded globally as the most cost-effective strategy for control of TB transmission, the strategy has failed to prevent rising tuberculosis incidence rates in Africa brought about by the HIV epidemic. However, rising incidence does not necessarily imply failure to control tuberculosis transmission, which is primarily driven by prevalent infectious disease (Elizabeth *et al*., 2007).

Without treatment within 5 years, 50% of PTB patients die from the disease, 25% of infected persons get cured by strong immune defense and remaining 25% remain ill with chronic infection (Harries *et al*., 2004). The selection of drugs to treat a patient to prevent the development of active tuberculosis or to treat active tuberculosis disease depends on a number of factors, including the health status of the patient, and the strain of MTB causing the infection. Some strains of MTB are resistant to the most commonly used drugs and require the use of other pharmaceuticals (Margarita *et al.*, 1992).

Usually, treatment is determined by-site of TB, sputum smear results, previous TB treatment, severity of TB, and age of patient amongst other factors. There are many different possible anti-TB treatment regimes. First line drugs include isoniazid, rifampicin, pyrazinamide, streptomycin, ethambutol and thioacetazone
(Harries *et al.,* 2004). The aims of treatment are; to cure the patient with TB; to prevent death from active TB or its late effects; to prevent relapse of TB; to decrease transmission of TB to others (Anonymous, 1997b); and to prevent the development of acquired drug resistance (MDHMH, 2007).

Tuberculosis treatment regimens must contain multiple drugs to which the organisms are susceptible. Treatment with a single drug can lead to the development of a bacterial population resistant to that drug. Likewise, the addition of a single drug to a failing antituberculosis regimen can lead to resistance to that drug. Each treatment regimen consists of an initial 2-month treatment phase followed by a continuation phase. The continuation phase is generally 4 months for the majority of patients. All TB drugs should be given together rather than in divided doses (Anonymous, 2006b).

The three main properties of antituberculosis drugs include bactericidal activity, sterilizing activity and the ability to prevent resistance. The essential antituberculosis drugs have these properties in different strengths. Isoniazid and rifampicin are the most powerful bactericidal drugs, active against all population of TB bacilli. Rifampicin is the most powerful sterilizing drug available, whereas pyrazinamide and streptomycin are bactericidal against certain population of TB bacilli. Streptomycin is bactericidal against rapidly multiplying TB bacilli. Ethambutol and thioacetazone are used in association

with more powerful drugs to prevent emergence of resistant bacilli (Leopold *et al.*, 2003).

In addition to enabling optimal patient management, knowing the HIV status (positive or negative) of TB patients helps public health agencies to identify HIV-infected contacts of TB patients. Highly active antiretroviral therapy (HAART) can reduce the progression to TB disease (Enrico *et al.*, 2005), TB relapse (Payam *et al.*, 2007), and death (Patrice *et al*., 2005). When taken according to medical prescription and advice, HAART controls HIV infection, prevents many of the life-threatening complications of AIDS and provides a powerful incentive for people to be counseled and HIV tested, interventions that are central to both treatment and prevention efforts (Harries, 2005). The strains of *Mycobacterium tuberculosis* resistant to anti-TB drugs have been recovered from both immunocompetent and immunocompromised patients worldwide. Multidrug-resistant *Mycobacterium tuberculosis* is an emerging problem of great importance to public health, with higher mortality rates than drug-sensitive TB, particularly in immunocompromised patients. MDR-TB patients require treatment with more toxic second line drugs and remain infectious for longer than patients infected with drug-sensitive strains, incurring higher costs due to prolonged hospitalization (Cohn et al., 1997).However, what is more disturbing is that since March 2006, the WHO has been reporting the first cases of extreme drug resistant (XDR) tuberculosis, which is characterized by resistance to the three main categories of medicines used to treat MDR tuberculosis and is associated with a very high mortality rate (Anonymous, 2007b).Multidrug-resistant tuberculosis (MDR TB) is a form of tuberculosis that is

resistant to two or more of the primary drugs (isoniazid and rifampicin) used for the treatment of tuberculosis. Extensively drug-resistant TB (XDR TB) is TB resistant to at least isoniazid and rifampicin among the first-line anti-TB drugs and among second-line drugs, is resistant to any fluoroquinolone and at least one of three injectable drugs.

Bacille Calmette - Guerin (BCG) vaccines are live vaccines derived from a strain of *Mycobacterium bovis* that was attenuated by Calmette and Guerin at the Pasteur Institute in Lille, France (Grange *et al*., 1983). Bacille Calmette - Guerin vaccine has displayed inconsistent efficacy in different trials conducted in various geographical regions. Nevertheless, it significantly reduces the risk of tuberculosis by 50% (Mauricio and Yolanda, 2004), risk of severe childhood tuberculosis by 70% (Vijaya *et al*., 2005) and provides protection for leprosy with the protection greatest in those receiving booster vaccinations before 15 years of age (Karonga Prevention Trial Group, 1996).

Interferon gamma is a licensed product for treating certain immune deficiency diseases, but its use in people with HIV is experimental. It is normally made by CD4 T cells (the cells which are depleted in people with AIDS), and it has antineoplastic effects and antiviral activity mediated by immunomodulatory effects. It is theorized that giving HIV-positive people co-infected with TB supplementary injections of interferon gamma may help boost their immune response (Auwal *et al.,* 2006).

2.7 Global impact of tuberculosis infection

Tuberculosis remains a worldwide problem despite well-documented and well-publicized methods of prevention and cure. Poverty and HIV infection have been

attributed as the main reason for its persistence (Ian and Oumou, 2006). Tuberculosis is the leading cause of mortality in adults due to an infectious agent and accounts for 26 % of all preventable adult deaths globally. According to the World Health Organization, 8 million cases of tuberculosis (TB) occur each year, resulting in 3 million deaths (Raviglione et al., 1995).

In developing countries an adult with TB loses on average three to four months of work time. This result in the loss of 20-30% of annual household income and, where infection results in death, an average of 15 years of income is lost at household level (Ahlburg, 2000). In addition to these devastating economic costs, TB imposes indirect negative consequences, including disruption of children learning because of their parents' tuberculosis, and women are abandoned by their families as a result of their disease ((Nadia and Enarson , 2003).

The economic burden of TB globally has been worked out based on 8.4 million new cases of TB annually, the bulk of victims being potential wage earners, and on assumption that there is a 30% decline in average productivity and the toll amounts to approximately $1 billion yearly. Two million annual deaths, with an average loss of 15 years' income, add an additional deficit of $11 billion. Every twelve months, then, TB causes somewhat near $12 billion to disappear from the global economy (Yong et *al*., 2007). Globally, the prevalence of infection with MTB is similar in males and females until adolescence, after which it is higher in males. These findings raise the possibility that cases of tuberculosis among women are being under-reported in developing regions (Holmes *et al.*, 1998).

2.8 Tuberculosis situation in Kenya

Kenya is ranked 10th out of the 22 high TB burdened countries in the world, based on estimated number of incident case (all forms) in 2005. The estimated case detection rate for Kenya is still about 50%, but with new data available concerning HIV in TB patients and improved monitoring and evaluation it should soon be possible to revise this estimate. Laboratory infrastructure and performance remain weak. The NLTP has started to implement new initiatives in Public-Private or Public-Public mix (PPM) and community involvement to improve the quality of TB control services and increase case-finding. Initiatives in TB/HIV were strengthened and by the end of 2006, collaborative TB/HIV activities were expanded to 70% of districts. Human Immuno Deficiency Virus (HIV) testing of TB patients increased rapidly, with 60% of all TB patients tested for HIV in the last quarter of 2006. To maintain these initiatives and to implement them more widely, the currently large funding gap for 2007 needs to be filled (Anonymous, 2007c).

Kenya is experiencing a generalized TB epidemic affecting the young economically productive age groups (15 - 44 years old). Males are 1.4 times more likely to have TB than females (MOH, 2005a). Apart from the HIV epidemic, poor socio-economic status leading to over crowded slums in the peri-urban areas coupled with poor nutrition and limited access to health services have been identified as contributing factors to the increasing TB burden. Current data indicate that TB cases occur mostly among slum dwellers in large cities (MOH, 2005a).

Tuberculosis is the leading cause of death among PLWAs (Godfrey- Faussett *et al.,* 2002). The epidemic in Kenya peaked in the late 1990s with an overall HIV prevalence of 10% in adults; this declined to 7% in 2003, and sentinel TB surveillance indicates that adult prevalence fell to 6.1% at the end of 2004 (NACC, 2005).

In the last 5 years the annual increase of notified TB case slowed down to an average of 11%. Case Notification Rates (CNR) increased from 53/100,000 for all forms of TB and 32/100,000 population for smear- positive PTB cases in 1990 to 324/100,000 population and 121/100,000, population respectively in 2005. Data coming through from the last half of the year indicates that the national average HIV prevalence in TB patients in 2005 was 57 % (MOH, 2005b). High-risk groups for MTB infection in Kenya, like other developing countries, may include people with human immunodeficiency virus (HIV)/AIDS, people with diabetes or cancer, the malnourished, those living with someone who has active TB, poor and indigent people, residents of homeless shelters, and present or former prisoners (Braun *et al.,* 1989). Whereas Human Immunodeficiency Virus (HIV) infection has clearly had a profound effect on TB epidemiology in general population, other potentially important risk factors have been somewhat neglected (Ernesto and Rodolfo, 2007).

2.9 Pulmonary tuberculosis situation in correctional institutions and prisons

A prison, penitentiary, or correctional facility is a place in which individuals are physically confined or interned and usually deprived of a range of personal freedoms. Prisons are conventionally institutions, which form part of the criminal justice system of

a country, such that imprisonment or incarceration is a legal penalty that may be imposed by the state for the commission of a crime. In popular parlance of many countries, the term jail (gaol) is considered synonymous with prison, although legally these are often distinct institutions: typically jails are intended to hold persons awaiting trials or serving sentences of less than one year, whereas prisons host prisoners serving longer sentences (Wikipedia, 2008). There are 9 million prisoners worldwide and there has been an increasing trend of prisoners in most countries over the last decade (Seena and Benning, 2006). They are settings in which TB transmission occurs, and TB rates in prisons are often five to 10 times higher than national rates (Maher *et al.*, 1998).

Several factors have been attributed with the high rate of TB in correctional and detention facilities. First, majority of those incarcerated are persons with high risk behaviors including illicit substances users such as drug abusers, persons of low socioeconomic status and with HIV infection. These persons often have not received standard public health interventions or non-emergency medical care before incarceration. Secondly, the physical structure of the facilities have also been shown to contributes to disease transmission in that facilities often provide close living quarters, have inadequate ventilation, and usually overcrowded (Jones *et al.,* 1999; Koo *et al.,* 1997; MacIntyre *et al.,* 1997 and White *et al.,* 2001). Thirdly, movement of inmates into and out of overcrowded and inadequately ventilated facilities, coupled with existing TB-related risk factors of the inmates, combine to make correctional and detention facilities a high-risk environment for the transmission of MTB and make implementation of TB-control measures particularly difficult (MacIntyre *et al.,* 1997).

Prisoners are also at risk of rapid progression to TB disease following recent infection or reactivation of latent infection as they also suffer from other (co-existing) pathology, particularly HIV and injection drug use, poor nutritional status, physical / emotional stresses(Angie *et al.,* 2000).

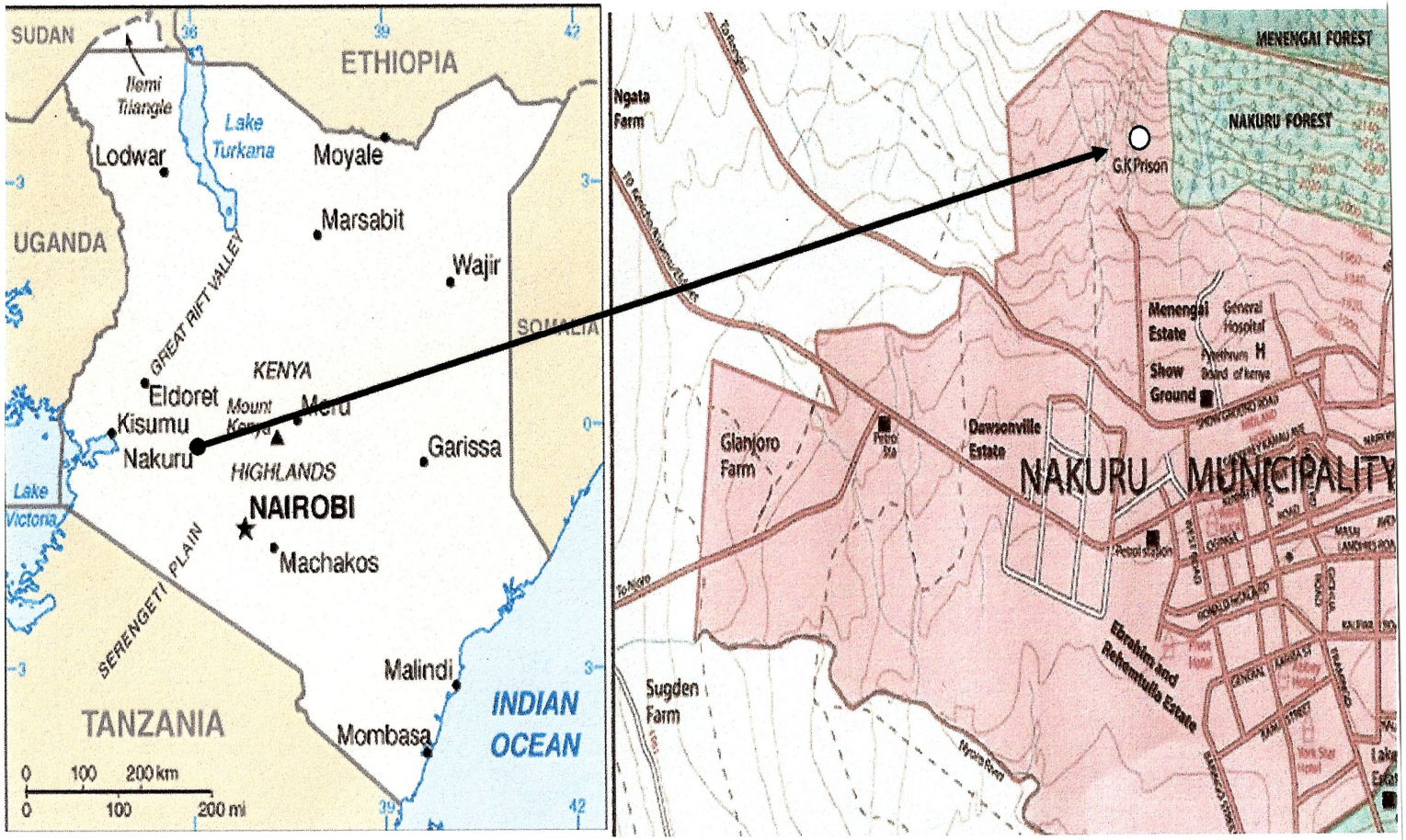
Other factors that have been associated with increased risk of development of active or latent PTB disease includes prisoner's age (>42 years), low educational level, average accommodation area of 60 ft^2 or less in prison barracks (Hamid *et al.,* 2003), a low BMI, a prison stay of $\leq$12 months, a history of previous incarceration (Noeske *et al*., 2006), male gender, absence of a BCG scar, anemia, HIV infection, history and treatment of worm infection, single marital status, family history of TB, smoking (with a dose–effect relationship) to be positively associated with PTB. These together with other risk factors make prisons condusive for TB epidemics which makes the disease not restricted to the confines of prisons (Angie *et al.,* 2000). Tuberculosis control can be particularly problematic in correctional and detention facilities (MacNeil *et al.,* 2005).

CHAPTER THREE

MATERIALS AND METHODS

3.1 Study design and site

This was a matched case control study by age and sex, conducted at the Nakuru G.K prison which has distinct and separate male and female wing. In Kenya, there are 93 penal institutions which handle 50,000-55,000 prisoners yearly and thus overcrowded by 294% (GOK, 2007). The Nakuru G.K prison was constructed to hold 800 prisoners and is located in Rift Valley province, about 5 km from Nakuru town central business area. Nakuru town is approximately 157 km from Nairobi, the capital city of Kenya **(Figure 1).** The choice of the study site was by convenient sampling due to the limited study resources



Source: Wikitravel.org Source: www.hassconsult.co.ke

Figure 1: Map showing location of Nakuru town in Kenya and Nakuru G.K prison within Nakuru Town

3.2 Study population

The target population was prisoners at the Nakuru GK prison Recruited into the study was done between 28th August 2007 and 12th December 2007. Adult prisoners above 16 years of age were legible for enrollment into the study. Both pre –trial and already sentenced prisoners were studied. An assumption was made that the Nakuru G.K prison was a reflection of other prison conditions under the government of Kenya.

3.2.1. Definition and inclusion criterion for study subjects

Cases were defined as "any adult prisoner who had at least two initial sputum smear examinations (direct smear microscopy) AFB+ and hence recruited to PTB WHO DOTS Programme" **(Appendix 1).** Cases were thus sought through retrospective review of the existing medical records of TB register at the prison health facility/clinic. Prisoners with no history of chronic cough who were not on TB medications and who had not been treated for TB in the previous 6 months.

Informed consent was sought before administration of questionnaire to the study subjects. A simple random sampling method was used to select controls using random numbers generated from SPSS Programme. The prison staff provided the sampling frame which consisted of the names of the inmates in the prison per day. Controls were matched to cases by a 5-year age group interval representing an age set and by sex/gender. A prisoner who did not consent to the study was replaced with the next consenting prisoner, who had similar selection status.

3.2.2 Exclusion criterion for study subjects

Any prisoner who was under 16 years of age or/and who had successfully completed treatment for TB, within the six (6) months, prior to the initiation of the study or/ and who self-reported having active PTB disease before incarceration i.e. community acquired PTB. Exclusion was done to minimize selection bias into my study.

3.3 Sample size determination

Fleiss formula (Fleiss, 1981) was used for sample size determination based on the following assumptions (**Appendix 2** for detailed symbol description):-

- The proportion of active PTB patients and controls exposed to host/environmental factors under study was 56% and 30% respectively
- Minimum Odds ratio worthy detecting by this study is 3.00.
- 2- tailed level of significance (**α**) = 5%
- Power of the study (**1-β**) = 80%, (**β**) = 0.20
- Sample is independently and randomly selected.

Fleiss formula

$$n_1 = \frac{\left[z_{\alpha/2} \sqrt{(r+1)\bar{p}\bar{q}} + z_{1-\beta} \sqrt{r p_1 q_1 + p_2 q_2} \right]^2}{r(p_1 - p_2)^2},$$

$$n_2 = r \times n_1 \quad \text{and} \quad p_1 = \frac{p_2(OR)}{1 + [p_2(OR - 1)]}$$

$$\bar{p} = \frac{p_1 + r \times p_2}{r + 1} \quad \text{and} \quad \bar{q} = 1 - \bar{p}$$

3.4. Data collection methods and instruments

A pre-tested structured questionnaire **(Appendix 3)** was used to collect data from each enrolled subject (cases and controls).

Typical BCG scar was checked on the upper outer part of the left forearm. Weight (in Kilograms) and height (in meters) measurements were taken. These were used to determine Body Mass Index (BMI) which was calculated as follows; Weight in kilograms divided by (height in meters) squared (Weight / $(\text{Height})^2$. The following cutoff points were considered: Underweight (below 18.5); Normal weight (18.5 to 24.9); Overweight (25 to 29.9); Obese (30 and above 40) (Anonymous, 2007d).

Interviewers were trained on data collection procedures using a pre-tested standard questionnaire, before the commencement of the study to ensure consistency in data collection. The interviewers were blinded in specific hypothesis being tested to minimize the possibility of interviewer's bias. At the end of each interview session, the chief supervisor cross-checked the questionnaires administered by interviewers, to ensure completeness and accuracy of data collected. Each active PTB case enrolled with its corresponding two (2) controls were thereafter assigned a similar unique number to be used in matched and multivariate analysis.

3.5 Ethical considerations

Enrolment into the study was voluntary. Each enrolled subject was informed of the study purpose and methods, as well as what action will be taken with the results. Legible controls found to have symptoms suggestive of PTB (i.e. chronic cough of $\geq$ 3

weeks, night sweats and chest pains) and any other incidental medical condition were forwarded to the local prison health facility for appropriate investigation, evaluation and treatment. Informed consent to participate in the study was sought and provided by the prisoner, in writing (**Appendix 4**, **and 5).** Anonymity was maintained by coding and using initials rather than using prisoners' name.

Approval from the appropriate ethical and review committees (JKUAT), Kenya Prison Service Authority and Ministry of Science and Technology, was sought and obtained, before starting the study **(Appendices 6 to 8)**. Information collected was held confidentially and findings will be shared with the relevant prison authorities and Ministry of Health (Kenya), NLTP and published in peer review journal.

3.6 Data handling and management

Data were coded during collection and Epi Info version 3.4.3. Statistical software (free software provided by WHO/CDC for developing countries) was used for data entry and analysis. Double data entry was done during the study period to minimize errors by identifying inconsistently entered data file and cleaned prior to analysis done. Each questionnaire was given a unique identifier to allow validation. To ensure confidentiality, the computer access was restricted by password protection.

3.7 Data analysis methods

A descriptive analysis was done based on frequency distribution of the selected socio-demographic characteristics. Dummy tables were used to direct the matched analysis. Matched analysis for factors associated with active PTB disease was performed, with measure of association being Adjusted (Mantel Hansel) Odds Ratio and

McNemars chi square test used for categorical variables (nominal data) at 95% Confidences Interval (CI) and alpha level of significance set at 0.05. An odds ratio (OR) of < “1” was taken to be protective while an odds ratio of > “1” was taken as a risk factor. An odds ratio of “1” indicated that there was no difference between cases and controls. Confidence interval was used to assess the variability of the odds ratio. A confidence interval which included 1 was interpreted to be not significant.

Using Statcalc in Epi-info, Chi square test for trend (Mantel Extension) with 1 degree of freedom (DF), was used to evaluate any statistically significance association in dose response involving number of cigarettes smoked per day, frequency of STI episodes, frequency of prison transfers, duration of incarceration (exposure variables) and their relationship with active PTB disease (outcome variable). A “2 by 2” table was used with DF calculated using “(row-1) (column-1)” formula. Crude odds ratio (COR) was calculated for separate exposure groups. Data for males and females were analyzed separately.

To identify complex interaction in this study, a pair of biologically sensible variables was entered in a conditional logistic model and unique number used as the matching variable. During each evaluation of complex interaction terms, an alpha level of 0.05 was used to determine the statistical significance of the interaction between the two variables and active PTB disease amongst the prisoners. A p-value ≤ 0.05 was considered significant interaction, while above 0.05 was considered an not significant statistically interaction within the selected variables

Conditional logistic regression was applied to calculate a MLE (OR) for the exposure variables while controlling simultaneously for multiple "potential" confounders. A stepwise conditional logistic regression with a backward elimination procedure was conducted to obtain a reduced model. The full model was fitted to include the entire biologically sensible exposure variable that had attained a p-value of ≤ 0.1 during the matched analysis. Variables were then removed one at a time (stepwise) as long as that p-value was >0.05, until all those remaining in the model contributed significantly to active PTB disease. The final model achieved, thus contained only statistically significant factors at an alpha level of 0.05. All the variables initially removed from the model were henceforth re-entered into the model for re-testing and subsequently removed if they did not contribute to improving the model.

3.8 Limitations of the study

1. Since age and sex were matched, these variables were not analyzed for association with the disease outcome of interest.

2. It was not possible to conduct the questionnaire interviews in strict privacy due to security reasons, and self-reported data, especially to sensitive questions (e.g. education level, employment status prior to incarceration, STI history, HIV knowledge and status may entail some response bias.

3. There was a potential selection bias during recruitment of study subjects with males being 135 (94%) and female being 9 (6%). This was related to low daily number of female inmates during the study period with daily average number of females being 172

(10%) compared with a daily average of males at 1,716. Low tuberculosis national notification rate amongst females likely compounded this bias. However, matching in design and analysis addressed this selection bias.

4. There was potential of mis-classification bias which may have occurred if recruited controls had already developed active PTB disease, which was at the sub-clinical stage or had not manifested to be detected by Z-N staining microscopy test. Attempts were made to address this by making sure that those recruited as controls were not exhibiting symptoms of active PTB disease.

5. Temporal relationship was not established in our study, between exposure variable under study and active PTB as both (exposure and outcome variables) had occurred by the time of initiating the study.

6. The impact of overcrowding and ventilation could not be assessed directly in this study because detailed environmental and structural assessment had not been conducted at Nakuru G.K prison prior to initiation of the study.

CHAPTER FOUR

RESULTS

4.1 Socio-demographic characteristics of the study subjects

One hundred and forty four inmates were recruited (48 cases and 96 age-sex matched controls) from Nakuru G.K prison during study period between August 2007 and December 2007. One hundred and thirty five (94%) of the study subjects were males. These subjects were selected from a pool of prisoners from Nakuru G.K prison which housed a daily average number of 1,716 male prisoners and 172 female prisoners. Seventy six of the study subjects had attained primary school education level and 65% (93) had been self employed prior to incarceration **(Table 1).** The ages of the study subjects ranged from 19 years to 70 years (Median age = 31 years). Eighty nine (62%) of the inmates recruited in the study had been incarcerated for a period of one year or less. The average duration of incarceration of the subjects enrolled in this study was 456 days for male and 422 days for female prisoners

Out of the 144 subjects, 55 (38%) were smokers and the commonly smoked cigarette brands were Supermatch by 34% followed by Sportsman 33% and Rooster 24% and others 9%. The mean number of cigarette sticks smoked per day was 10 (± 5), (range 2 -20). The proportion of smokers amongst the controls declined steadily as the number of cigarettes smoked per day increased. This decline was not observed amongst the cases who smoked **(Figure 2).**

Table 1. Selected socio - demographic characteristics of the enrolled study subjects

Characteristics of subjects	Frequency (N=144)	Percent (%)
1. Sex		
Male	135	94%
Female	9	6%
2. Age group in years		
16-25	39	27%
26-35	50	35%
36-45	42	29%
46-55	10	7%
>55	3	2%
3. Level of education		
None	19	13%
Primary	76	53%
Secondary	46	32%
Tertiary	3	2%
4. Employment status prior to Incarceration		
None	36	25%
Self-employed	93	65%
Formal employment	15	10%

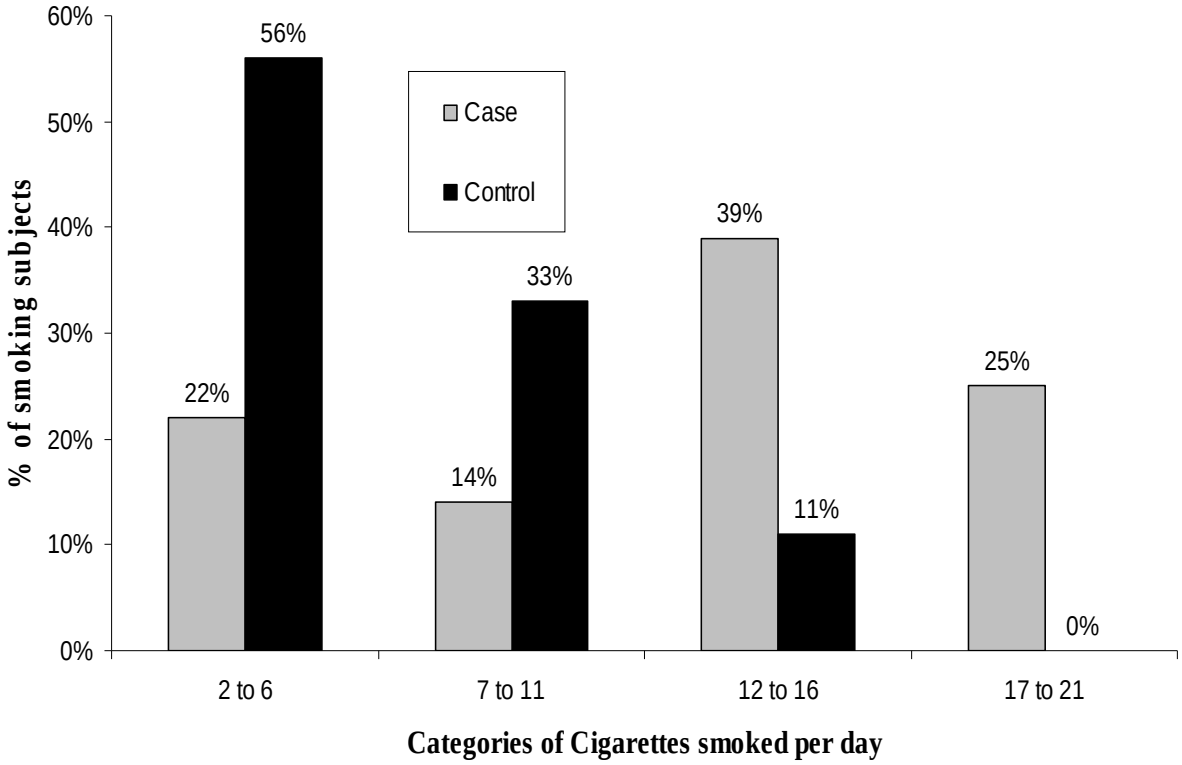


Figure 2. Distribution of smokers according to quantified categories of cigarettes smoked per day and by disease status

Approximately 80 % of the subjects enrolled in this study had normal BMI with less than 10% being underweight and approximately 14% being overweight **(Figure 3).** The BMI ranged from 15 to 29(mean 22± 3).

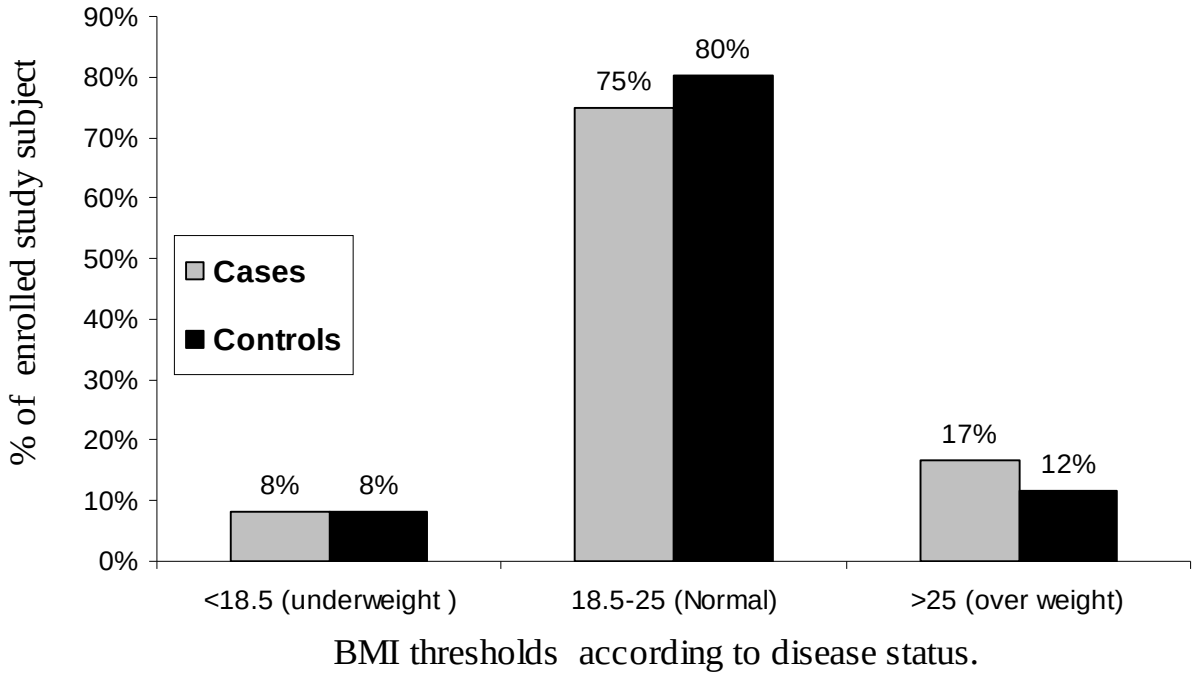


Figure 3. Distribution of enrolled study subjects according to categories of basal metabolic index thresholds and by disease status

4.2. Clinical presentation of enrolled pulmonary tuberculosis cases

A total of 48 cases in the study had a positive sputum smear examination and were in the PTB WHO DOTS Programme. Sixty seven percent (96) of the subjects admitted knowing their HIV status of which 36 (38%) were PTB cases and 60 (62%) were in the control group. Out of the 96 who knew their HIV status, 39 (41%) were HIV positive. Twenty seven (69%) of the 39 who were HIV positive, were PTB cases and 12 (31%) were controls. Ten (26%) of the HIV positive were on Antiretroviral Treatment (ART) treatment and nine of the ten (90%) patients on ART were PTB cases. However,

it was not established whether the ART had been initiated prior or during inmates' incarceration.

The most common symptoms reported by the 48 PTB cases as shown in **Figure 4** were night sweats 36 (75%) followed by chest pains 32 (67%).

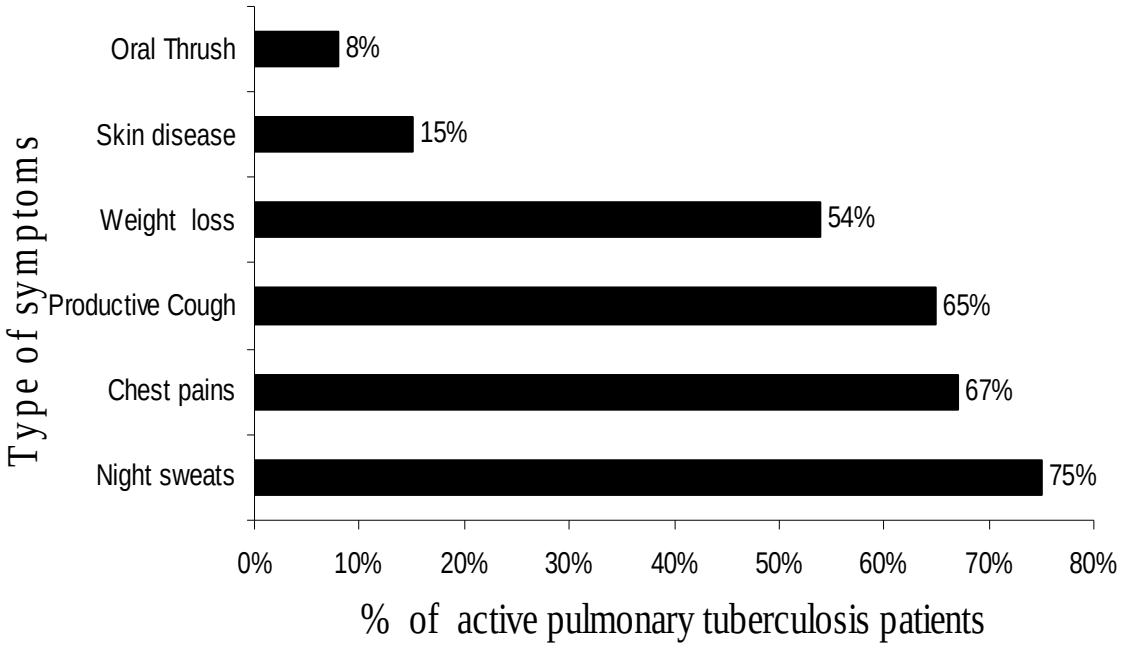


Figure 4. Distribution of enrolled active pulmonary tuberculosis patients according to the clinical symptoms

The median duration of anti-TB medication was 66 days (range 1- 150 days). There were 26 (54%) cases whose duration of incarceration was more than six months.

4.3. Matched Analysis results

In matched analysis the significant factors associated with active PTB disease at 5% significance level included being of positive HIV status which had OR of 9.4, history of prison transfer which had OR of 3.0, history of STI which had OR of 3.0, sharing towels and clothes with other inmates while in incarceration which had OR of

2.5,contact with PTB case which had OR of 9.0, alcohol consumption history which had OR of 4.5, smoking history which had OR of 3.0 and unemployment prior to incarceration which had OR of 6.0.While significant protective factor was the presence of BCG scar, which had OR of 0.2 **(Table 2).**

Table 2. Factors associated with active PTB disease at Nakuru G.K prison, 2007

	Totals			95% CI	
Exposure Variable	**No.**	**(%)**	**AOR**	***LL - *UL**	**P-Value**
1. Self reported HIV+	39	(27%)	9.40	3.2 - 27.09	<0.0001
2. Diabetic	5	(4%)	3.00	0.42 - 21.30	0.3768
3. Prison transfer	62	(43%)	2.60	1.32 - 5.40	0.0056
4. History of STI	49	(34%)	3.00	1.43 - 6.28	0.0034
5. Presence of BCG scar	93	(65%)	0.19	0.09 - 0.43	<0.0001
6. Sharing linen	42	(29%)	2.50	1.22 - 5.13	0.0164
7. PTB case contact	93	(65%)	9.25	2.90 - 29.46	<0.0001
8. Alcohol consumption	67	(47%)	4.50	1.98 - 10.21	<0.0001
9. History of smoking	55	(38%)	2.81	1.42 - 5.59	0.0014
10. Unemployment	36	(25%)	6.00	2.31 - 5.60	<0.0001
11. No formal education	19	(13%)	2.00	0.74 - 5.37	0.2650
12. Low BMI (<18.5)	11	(8%)	1.14	0.33 - 3.92	0.9110
13. Prison stay >3 months	97	(67%)	0.67	0.29 - 1.15	0.2293
14. Prison stay >6 months	81	(56%)	0.86	0.41 - 1.83	0.5613
15. Prison stay >12 months	55	(38%)	0.83	0.40-1.73	0.4984

NB: *LL = Lower limit *UL = Upper limit

4.4. Linear trends (χ^2 for trends) analysis results

The number of cigarettes smoked per day (P<0.0001), frequency of prison transfer (P<0.0001) and frequency of STI episode (P<0.0001), were all strongly associated with increased risk of active PTB disease amongst the male prisoners in this study. Each of the three tables below **(Table 3 to 5)**, shows increasing OR for the linear trend of the respective exposure factors.

Table 3. Dose – response relationship between quantities of cigarettes smoked per day and active pulmonary tuberculosis disease amongst male prisoner

	Smokers								**Non-smokers**	
	(2-6/day)		**(7-11/day)**		**(12-16/day)**		**(17-21/day)**		**Nil**	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Cases	06	12%	04	8%	11	23%	07	15%	20	42%
Controls	15	16%	09	9%	03	3%	0.0	0%	69	72%
Odds ratio	**1.29**		**1.52**		**13.14**		***N/A**		**1.00**	

p<0.0001 (χ^2 for linear trend = (34.95).

NB: *N/A indicates observation not included in OR calculation due to a zero OR denominator.

Table 4. Dose – response relationship between sexually transmitted infection episodes and active pulmonary tuberculosis disease amongst male prisoner

	Frequency of sexually transmitted infection episodes							
	(Once)		**(Twice)**		**(>Twice)**		**(Nil)**	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Cases	09	20%	08	18%	08	18%	20	44%
Controls	13	15%	06	7%	04	4%	67	74%
Odds ratio	**2.24**		**4.32**		***N/A**		**1.00**	

$p<0.0001$ (χ^2 for linear trend = (30.65).

Table 5. Dose – response relationship between prison transfers and active pulmonary tuberculosis disease amongst male prisoner

	Frequency of Prison Transfer							
	(Once)		**(Twice)**		**(>Twice)**		**(Nil)**	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Cases	05	11%	14	31%	09	20%	17	38%
Controls	20	22%	05	6%	05	5%	60	67%
Odds ratio	**0.88**		**9.11**		***N/A**		**1.00**	

$p<0.0001$ (χ^2 for linear trend = (44.39).

***NB:** N/A as in **Table 3**

4.5 Complex interaction terms analysis results

The association of complex interaction terms of biological sensible pairs with active PTB disease was evaluated by pairing alcohol consumption history and smoking history, contact with PTB case and sharing linen while in prison, positive HIV status and history of STI, no employment prior to incarceration and lack of formal education, low BMI score and history of diabetic, duration of incarceration and prison transfer history and also positive HIV status and low BMI score. No statistically significant complex interaction terms were identified as modifying the association between individual exposure variables and active PTB disease in this study **(Appendix 9).**

4.6 Multivariate analysis results

The model building procedure involved the nine variables found during the matched analysis to have a p-value of ≤ 0.1 being entered in conditional logistic regression model i.e. positive HIV status, history of prison transfer, history of STI, presence of BCG scar, sharing towels and clothing while in incarceration, contact with PTB case while in prison, alcohol consumption history, smoking history and unemployment prior to incarceration (**Appendix 10**).

From the "Best Final Model", five variables were independently associated with active PTB in our study. Presence of HIV infection was identified as the strongest factor associated with active PTB disease amongst prisoners at Nakuru GK prison. Other statistically significant risk factors at 0.05 alpha level of significance were, unemployment prior to incarceration, contact with PTB case during incarceration period and sharing towel/clothes with other inmates .While significant protective factor at 0.05 alpha level of significance during multivariate analysis was presence of BCG scar **(Table 6).**

Table 6. Final model of conditional logistic regression on factors associated with active pulmonary tuberculosis disease at Nakuru G.K prison.

Term or Variable characteristics	OR	95% CI		P-Value
		Lower Limit	Upper Limit	
1. Contact with PTB case	6.68	1.17	38.23	0.0329
2. Self – reported HIV+	10.75	2.42	47.77	0.0018
3. Unemployment	8.98	1.84	43.97	0.0067
4. Sharing clothes & towel (linen)	4.32	1.08	17.29	0.0386
5. Presence of BCG scar	0.17	0.05	0.60	0.0059

CHAPTER FIVE

DISCUSSION

Prisons are universally recognized as crucial settings for the prevention and control of MTB infection, which influences its spread among the general human population (Angie *et al.,* 2000; Coninx *et al.,* 2000; Hammet *et al.,* 1998; Hammett *et al.,* 2002; Saunders *et al.,* 2001).This case- control study aimed at determining the modifiable factors associated with active PTB disease in an urban prison in Kenya.

Matching was employed in the design phase to control for possible confounding effects of age and sex variables, reported in previously conducted studies on TB (Biber *et al.,*1999; Chan-Yeung *et al.,*2002; Wang *et al.,* 2005; Watkins and Plant, 2006). This is the first study to investigate factors associated with active PTB disease within a prison population in Kenya's correctional system.

In this study, 34% (49) of the study subjects had history of STI. There was a strong dose-response relationship as shown by the highly significant test for trend between the frequency of STI episodes and active PTB disease in Nakuru G.K prison. This finding supports a hypothesis raised by Nagelkerke *et al*. (2004) that in addition to HIV, unknown sexually transmitted infections also increases TB progression. The association between TB and sexual behavior has rarely been studied, except within the context of HIV infection. Recent evidence comes from a study on prison inmates in the United States in which inmates who reported a history of TB also reported higher sexual risk factors than those without such a history, although confounding by HIV infection cannot be entirely ruled out (Stephens *et al.,* 2003). Further studies need to be done to

corroborate these findings and determine which STI is related to TB progression and by which mechanism. Many prisoners usually contract sexually transmitted infections (STIs) outside of prisons and come from populations lacking access to reproductive and sexual health services. Unprotected sexual relation between men, are also more prevalent in prison than in the rest of society (Anonymous, 2007b). This might have increased the risk of transmission of STIs and HIV/AIDS amongst prisoners. Therefore, prevention, regular screening and treatment of STIs amongst prisoners would decrease risk of HIV/AIDS and by extension leads to reduction of TB incidence.

Since BCG vaccination is a part of the WHO recommended routine immunization programme for children in Kenya, the presence of a typical BCG vaccination scar on the outer upper part of the left forearm was taken as an evidence of previous BCG vaccination (Hamid *et al.*, 2003; Johnson *et al.*, 1995). In both matched and multivariate analysis this study demonstrated that presence of BCG scar was protectively associated with active PTB amongst adult prisoners confined at Nakuru G.K prison. These findings are contrary to other studies which reported a waning effect of BCG with age (Anuradha *et al.*, 2007; Britton and Palendira, 2003; Kaufmann, 2004) and absence of a relationship between BCG scar and protection against PTB in adults in Africa and India (Karonga Prevention Trial Group, 1996; Fine, 2001). The reasons for the contrast are unclear.

This study has shown that there is a strong dose-response relationship between the number of cigarettes smoked daily and having active pulmonary tuberculosis disease in Nakuru G.K prison. Our results are consistent with those reported in four different

community-based case-control studies carried out in Spain (Alcaide *et al*., 1996), India (Kolappan and Gopi, 2002), West Africa (Lienhardt *et al*., 2005) and Thailand (Ariyothai *et al*., 2004). However, this variable was not found to be statistically significantly associated with active PTB disease amongst prisoners in multivariate analysis after the control of multiple potential confounders which had not been addressed in the above previous studies. Several mechanisms have been advanced on how cigarette smoking is associated with increased risk of TB. Data from animal studies suggest involvement of Tumor Necrosis Factor (TNF) in host defence against TB (Vellore *et al.*, 2001). However, the exact mechanism in humans on the effect of cigarette smoking on the TNF activity and hence TB defence, is still poorly understood. Among the varied deleterious effects cigarette smoking has on pulmonary function, is the possible damage to the respiratory mucosa, thereby impairing host resistance to infection (Bieber and Kavanaugh, 2003).Smoking can facilitate the manifestation or detrimental effect of TB through a variety of mechanisms. First, because smokers tend to have a chronic cough which is also the hallmark symptom of TB, cough has in smokers reduced specificity and hence lower predictive value. Diagnosis of TB may then be delayed leading to a poor prognosis and possibly higher probability for relapse. Second, smoking is a cause for co-morbidities, such as chronic bronchitis, chronic airway obstruction, pulmonary emphysema as well as coronary heart disease, that may facilitate progression of TB-infection to disease, but also impair lung function in addition to that of TB alone leading to worse prognosis. Third, smoking causes iron overload of macrophages in pulmonary tissue which impairs cellular response to micro-organisms (Boelart *et al.*,

2003). An effective anti-smoking campaign boosted by the implementation of the recently enacted Tobacco Control Bill of September 2007 in Kenya, can have a positive outcome on reduction of TB incidence in prison. Patients with TB need and should receive counselling and assistance to stopping smoking.

Ninety-six (67%) of the study subjects (N = 144) admitted knowing their HIV status, 39 (41%) of them self-reported to be HIV positive. The HIV status could not be ascertained through review of medical records because the records were poorly maintained and incomplete. During matched analysis, being HIV positive by self-reporting was statistically significantly associated with active PTB disease at Nakuru G.K prison. This significance was maintained in multivariate analysis where it was identified as the strongest factor associated with active PTB disease. These results are comparable to those found in other studies where the estimated risk of clinical disease in HIV-infected persons was between 6 to 26 times higher than in non-HIV infected persons (Lienhardt and Rodriques, 1997). Therefore, data from this study supports the finding that TB and HIV epidemics are closely intertwined even in prison settings. Human Immuno Deficiency Virus suppresses host cell-mediated immunity (Broekmans, 1991) and worsens the tuberculosis situation by increasing reactivation of latent tuberculosis infection in dually infected persons as well as by favouring rapid progression of new infections in the HIV-infected (Narain *et al.*, 1992).In *vitro* studies have also shown that tuberculosis increases the ability of HIV to replicate by activating CD4+ T-lymphocytes and macrophages harboring latent HIV (Del Amo *et al.*, 1999). The onset of tuberculosis in HIV-infected patients' causes marked release of pro-

inflammatory cytokines that activate lymphocytes and macrophages. This results in an increased HIV viral load (Del Amo *et al.*, 1999). Lack of formal education, being diabetic and low BMI score were not statistically significantly associated with active PTB disease in this study. Conversely, other studies have reported a positive association of these factors and active PTB disease within different settings (Dong *et al.*, 2001; Noeske *et al.*, 2006; Shetty *et al.*, 2006; Stevenson *et al.*, 2007 and Toure *et al.*, 2007).Eliciting the correct response for level of education (being a sensitive question), during the study period was affected by response bias as it was not possible to conduct the questionnaire interviews in strict privacy due to security reasons. This could have affected any significant association expected from this variable in our study. Only 5 (4%) of the study subjects had diabetes disease and this small sample size amongst the diabetic patients affected the association and statistical significance of diabetes disease with active PTB disease in our study. Lack of a significant association of the low BMI value could be related to supplementary diet offered to any PTB patients within the prison system.

Forty seven percent of the enrolled study subjects had a history of alcohol consumption. In matched analysis, alcohol consumption was significantly associated with active PTB disease amongst prisoners at the Nakuru G.K prison but not in the multivariate analysis indicating that alcohol consumption was not an independent predictor of active PTB in this study. These results are contrary to those reported from other studies in Spain (Godoy *et al*., 2001 and 2004) and India (Kolappan *et al*., 2007) which found alcohol consumption to be an independent predictor of active PTB disease.

The significant association of alcohol consumption could have been affected by response bias, it being a sensitive question requiring strict privacy, not obtained due to security reasons.

In this study, lack of formal education and/or unemployment prior to incarceration, were taken as proxy for low SES. Twenty five percent of the study subjects had been unemployed prior to incarceration. In the matched analysis and multivariate analysis, unemployment was statistically significantly associated with having active PTB disease amongst prisoners admitted at the Nakuru G.K prison. The findings concur with other studies in Russia (Richard *et al*., 2006) and Estonia (Tekkel *et al.*, 2002) and reiterates that TB is a disease of the poor and prisoners are commonly derived from society of low SES. Elsewhere duration of incarceration has previously been associated with primary TB infection within the correctional facilities particularly with longer prison time or for members of the cohort of people who spend time in other high-risk areas, such as hospitals or homeless shelters, substance abuse, or other cumulative TB risk factors outside prison.

In this study, 45 % of prisoners had been in prison less than 200 days. This suggests that prison terms at the Nakuru G.K prison are rather short and may have had an effect on the significance of the association between duration of incarceration and active PTB cases observed. Incarceration duration of more than six months was found to be a risk factor for active TB in prisoners in Botswana, in a one-time survey in a prison system without regular screening at entry (Wang *et al.*, 2003) and in Cameroon a prison

stay of less than 12 months, and a history of previous incarceration was positively associated with PTB (Noeske *et al*., 2006).

This study found that 43% of the study subjects had experienced transfer within and outside the prison. There was a strong dose-response relationship between the frequency of prison transfer and active PTB disease at the Nakuru G.K prison. There were no significant complex interaction terms on active PTB disease by pairing duration of incarceration and frequency of prison transfer. Studies conducted in Pakistan's correctional facilities reported an association between history of prison transfer and latent PTB infection amongst prisoners (Hamid *et al*., 2003). However, further studies need to be done to corroborate these dose-response relationship findings. In this study, the statistical significance of history of prison transfers was found in matched analysis but was not retained during multivariate analysis.

In matched analysis, sharing linen was a statistical significant risk factor. The significance was retained in multivariate analysis. This indicates that sharing linen was independently associated with active PTB amongst prisoners at Nakuru G.K prison. Sharing linen indicates that unhygienic conditions occur in prisons. These findings show similarities to those of studies carried out in St. Petersburg remand prison in Russia (Lobacheva *et al*., 2007). However, this variable was not rated during the interview according to the frequency scale, in order to establish any dose-response relationship between frequency of sharing linen and active PTB disease amongst our study population.

A history of chronic cough of more than three weeks was used in this study as a proxy for contact with PTB case while in incarceration. Of the 144 study subjects, 65% admitted having been in contact with a person suffering with PTB while under incarceration. The PTB contact history was statistically significant during matched and subsequent multivariate analysis. This indicates that contact with PTB was independently associated with active PTB disease within the Nakuru G.K prison. This finding has been previously documented for a clinic based study conducted in Gambia (Philip *et al.*, 2006).Contact history indicates lack of isolation of patients with active PTB disease leading to transmission of infection to other inmates either before diagnosis is made or during the early treatment period when one is still infectious. Molecular epidemiological studies using genotyping techniques are needed to establish the strains of MTB circulating in prison and to identify whether there is an epidemiological-linkage in TB spread among prisoners.

Improving prison health brings with it so many opportunities (Gro and Jakob, 2001), for instance, imprisonment should be seen as an opportunity to tackle the health needs of prisoners, especially as many are drawn from a population on the margins of Kenya's society, often with little social support. For many convicts and detainees, imprisonment is one of a few opportunities to obtain much needed health care and counseling services. Hence, better understanding of TB in prison results in an overall benefit to both the inmates and the society and provides a means to strive toward the goal of TB elimination in Kenya.

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

1. Risk factors associated with active PTB disease were being self- reported HIV + status, sharing linen while still in prison, contact with PTB case while in incarceration and unemployment status prior to incarceration.

2. Evidence of previous vaccination was the only protective factor associated with active PTB disease in Nakuru G.K prison.

3. There was a strong dose-response relationship between the numbers of cigarettes smoked daily (host factor), frequency of STI episodes, frequency of prison transfer (environmental factors) and active PTB disease.

4. Based on my study finding (host and environmental factors are associated with active PTB disease among prisoners at Nakuru G.K prison.) I do not reject the Null hypothesis.

6.2 Recommendations

This study being the first to investigate factors associated with active PTB disease within a prison population in the Kenya's correctional system, will thus form a basis for other studies on factors associated with active PTB disease within other prisons in the Kenya's correctional system. A comprehensive multidisciplinary control and preventive approach should be adopted in order to reduce the risk associated with PTB control in prison. This should involve corroboration between prisoners, health officials and prison authorities to implement the following recommendation:-

1. Screening inmates for active tuberculosis at the time of admission to avoid introduction of infectious persons into the jail population. This should be followed by routine screening of inmates to identify PTB symptomatic inmates.

2. Isolation of suspected PTB cases pending prompt evaluation is needed.

3. Voluntary HIV counseling, testing, and referral should be routinely offered to all inmates diagnosed of PTB. HIV-positive inmates should be offered cotrimoxazole preventive therapy (CPT) and should be assessed for, and started on, antiretroviral therapy (ART) as soon as possible.

4. Cross matching of PTB registries between prisons facilities should be done regularly to identify the compliance or the defaulter pattern of inmates and those requiring follow-up.

5. Prison staff should be educated on signs and symptoms of PTB and encouraged to facilitate prompt evaluation of inmates suspected of having the disease.

6. Strict enforcement of no-smoking policy in jails needed and prisoners encouraged to quit smoking.

7. Further studies on the role of BCG vaccination in protection of adults against active PTB disease, association between frequency of STI episode and active PTB disease and identification of related causative agent of the STI, are necessary. Molecular epidemiological studies to identify the circulating TB strains in prison and to determine any epidemiological-linkage of TB spread amongst prisoners are also recommended.

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APPENDICES

Appendix 1. World Health Organization definitions of tuberculosis cases and treatment outcomes

A. DEFINITIONS OF TUBERCULOSIS CASES

Smear-positive pulmonary case: A patient with at least two initial sputum smear examinations (direct smear microscopy) AFB+; or one sputum examination AFB+ and radiographic abnormalities consistent with active pulmonary tuberculosis as determined by a clinician; or one sputum specimen AFB+ and culture positive for MTB.

Relapse case: A patient previously declared cured but with a new episode of bacteriologically positive (sputum smear or culture) tuberculosis.

B. DEFINITIONS OF TREATMENT OUTCOMES

(Expressed as a percentage of the number registered in the cohort)

Completed treatment: A patient who completed treatment but did not meet the criteria for cure or failure. This definition applies to pulmonary smear-positive and smear-negative patients and to patients with extrapulmonary disease.

Successfully treated: A patient who was cured or who completed treatment

(Anonymous, 2007c).

Appendix 2.Description of symbols used in the Fleiss formula for sample size calculation and their corresponding value

Description of Symbols in the formula	Value
Z - Score for two-tailed test based on α level ($z_{\alpha/2}$).....	1.96
Z - Score for one-tailed test based on β level ($z_{1-\beta}$).....	0.84
Ratio of controls: cases (r).....	2:1
Proportion of cases with exposure (P_1).....	56%
$1 - P_1$ (q_1)	44%
Proportion of controls with exposure (P_2).....	30%
$1 - P_2$ (q_2).....	70%
Number of cases (n_1).....	46
Number of controls (n_2).....	92
Total sample size ($n_1 + n_2$)	**138**

Appendix 3: Questionnaire of factors associated with active pulmonary disease amongst prisoners in Kenya, 2007

1a. Questionnaire Number ___ ___ ___ ___

1 b. Unique / Matching No. (For Supervisor) ___ ___ ___ ___

2. Date of interview (DD: MM: YR) ___ ___/___ ___/___ ___ ___ ___

3. Interviewer's code (initials) ___ ___ ___

Prison details

A). Name of prison _____

B). Current number of inmates in the prison ___ ___ ___ ____ ____ ___

C).Number of patients attended to by the health facility during last month?

___ ___ ___ ___

5. Personal details

5.1 Name of prisoner (initials) ___ ___ ___ ___

5.2 Sex/gender Male ☐ Female ☐

5.3 Status of subject: Case ☐ Control ☐

5.4 Date of birth (DD: MM: YR) ___ ___/___ ___/___ ___ ___ ___

5.5 Age in years ___ ___ ___

5.6 Date of incarceration (DD:MM:YR) ___ ___/___ ___/___ ___ ___ _

5.7 Duration of incarceration (in days)___ ___ ___ ___ ___

5.8 Department/ unit of incarceration _____

6. Clinical information

6.1 Presence of productive cough? Yes ☐ No ☐

6.2 Duration of Cough (in days) ___ ___ ___ ___

6.3 Do you have any of these symptoms

☐ Night Sweats

☐ Chest pains

☐ Weight loss

☐ Oral thrush

☐ Skin disease

6.4 Have you been taking any medication in the last one month?

No ☐ Yes ☐

6.5 If Yes to 6.4 which ones ?_____

6.6 What is the reason for taking the medication? _____

6.7 What is the duration of medication (in days)? ___ ____ ___ ___

7. Risk Factors information:

7.1 Level of education? None ☐ Primary ☐

Secondary ☐ Tertiary ☐

7.2 Employment status prior to Incarceration?

☐ Self Employed ☐ No employment ☐ Employed Formal

7.3 Do you Smoke? ☐ Yes ☐ No

If Yes

7.4 Name of commonly smoked brand? _____

7.5 Number of sticks per day? _____ ____ ____

7.6 Any history of alcohol intake? Yes ☐ No ☐

7.7 Number of people in the cell? ____ ____ ____ ____

7.8 What is the estimated size of the cell in M^2 ? ___ ____ ___

7.9 How many windows does the cell have? ____ ____ ____

7.10 Have you come in contact with somebody with chronic cough in your cell or the neighboring cell?

☐ Yes ☐ No

7.11 Do you share towels and clothing with other inmates? No ☐ Yes ☐

7.12 Height (in meters) ___ ____ ___ Weight (kg) ___ ___ ___

BMI (Kg/M^2) ___ ___

7.13 Presence of BCG scar Yes ☐ No ☐ Not checked ☐

7.14. How many times have you been moved from one prison to another since you were incarcerated? ___ ___ ____

7.15. Have you suffered from any STI? ☐ Yes ☐ No

7.16. If yes, how many times have you suffered f rom STI? ___ ___

7.17. Do you suffer from diabetes? Yes ☐ No ☐

7.18. Do you know your HIV status? Yes ☐ No ☐

7.19 If yes what is your HIV status?

Positive ☐ Negative ☐ Not willing to state ☐

8. Laboratory Information

	Date of Sputum collection	Laboratory result
Specimen 1		
Specimen 2		
Specimen 3		

Appendix 4. Consent seeking procedure

Factors associated with active pulmonary tuberculosis disease at Nakuru G.K prison

My name is _____from the Ministry of Health Kenya. I am involved in a study on the factors associated with tuberculosis in this prison. I am going to ask you questions on the conditions you experience in this prison as well as personal related question. I will also measure your height and weight and check for a vaccination scar on the upper part of your left arm.

Your name will not appear on the questionnaire and the information you give us will be handled with as much confidentiality as possible.

There are no individual benefits if you choose to participate in this study but the information we get from you will help us to come up with focused prevention strategies for tuberculosis in this prison as well as better living condition and improved health care. You will be informed your weight and height results. You are free to withdraw from this study at any time and you will not be penalized for withdrawing.

If you agree to be enrolled in this study, please fill the attached form as evidence of your voluntary participation.

Appendix 5: Consent form for PTB study in prison

Questionnaire no.____ ____ ____

I ……..do willingly wish to participate in the study on the risk factors associated with MTB infection in my prison having been full explained the process, methods and the intended use of the study results by the interviewer. I expect that the information gathered will be kept confidential and utilized for the explained intentions.

Signature ……

Date……

Appendix 6: Copy of letter from Permanent Secretary, Ministry of Science and Technology to conduct this study

REPUBLIC OF KENYA

MINISTRY OF SCIENCE & TECHNOLOGY

Telegrams: "SCIENCE TEC", Nairobi
Telephone: 02-318581
E-Mail:ps@scienceandtechnology.go.ke

JOGOO HOUSE "B"
HARAMBEE AVENUE,
P.O. Box 9583-00200
NAIROBI

When Replying please quote
Ref. MOST 13/001/ 37C 475/2

30th July 2007

Dr.Samuel Anyangu Amwayi
Jomo Kenyatta University
NAIROBI

Dear Sir

RE: RESEARCH AUTHORIZATION

Following your application for authority to carry out research on, ***'Modifiable Risk Factors Associated with Pulmonary Mycobacterium Tuberculosis (PTB) Infection at Nakuru GK Prison Kenya'***

I am pleased to inform you that you have been authorized to carry out research in Nakuru GK Prison for a period ending 30th November 2007.

You are advised to report to the Commissioner, Prisons Service before embarking on your research project.

On completion of your research, you are expected to submit two copies of your research report to this office.

Yours faithfully

pp **M. O. ONDIEKI**
FOR: PERMANENT SECRETARY

Copy to:

The Commissioner
Kenya Prisons Service
Nairobi

Appendix 7: Copy of letter requesting for research approval from Commissioner of Kenya Prison Service

DR. AMWAYI SAMUEL ANYANGU
P.0 B0X 688
NAKURU

31st July, 2007

TO:
The Commissioner,
Kenya Prison Service,
P.0 Box 30175
Nairobi.

Dear Sir,

RE: REQUEST FOR RESEARCH APPROVAL AT NAKURU G.K PRISON

I humbly request for permission to carry out research at Nakuru G.K. Prison from August to 30th November 2007, to identify modifiable risk factors associated with PTB Infection within the prison system in Kenya.

I am a medical doctor working with the Ministry of Health Kenya, currently pursuing a Master degree (Msc) in Applied Epidemiology at JKUAT.

The research project is part of fulfillment of the JKUAT requirements for the Masters degree in science in Applied Epidemiology. I intend to utilize the prison health facility at Nakuru for the recruitment of subjects into the study. Subjects will be prisoners seeking health services at the Nakuru G.K Prison health centre.

Please find attached a copy of the research authorization letter from the Permanent Secretary Ministry of Science and Technology.

Thanks in advance for your consideration.

Yours Faithfully,

31/07/2007

DR. AMWAYI SAMUEL ANYANGU
P/ N0. 99048427

Appendix 8: Copy of a letter from Commissioner of Kenya Prison Service to conduct this study at the Nakuru G.K prison

OFFICE OF THE VICE PRESIDENT AND MINISTRY OF HOME AFFAIRS
KENYA PRISONS SERVICE

Telegrams: "COMPRISONS" Nairobi
Telephone: +254 02 2722900-6
E-mail Comprisons@yahoo.com
When replying please quote
Ref. No. **36/1/VOL.XII/94**

PRISONS HEADQUARTERS
P.O.BOX 30175-00100
NAIROBI.
Date **13th August 2007**

Dr. Amwayi Samuel Anyangu,
P.O.BOX 688,
NAKURU.

RE: PERMISSION TO CARRY OUT RESEARCH IN NAKURU G.K PRISON.

Reference is made to your letter dated 31st July 2007 on the above subject.

I am pleased to inform you that the commissioner of prisons has approved your request to undertake research at Nakuru prison.

During that period, you will be expected to abide by the laid down prison rules and regulations. Upon completion of your study, you will be required to submit a copy of your report to this office.

By copy of this letter the officer in charge Nakuru prison is hereby requested to accord you any necessary assistance.

D.M Kingoo MBS SACP/A
FOR: COMMISSIONER OF PRISONS.

cc
The officer in charge
Nakuru Prison,
P.O. Box 14,
NAKURU.

The Provincial Prisons Commander
Rift Valley Province,
P.O. Box 651,
NYERI

Appendix 9: Complex interaction terms analysis results.

INTERACTION TERMS OF EXPOSURE VARIABLES	OR	95% CI *LL - *UL	P-Value
1. Alcohol consumption and smoking history			
Alcohol consumption	5.55	1.73 - 17.80	0.010
Smoking history	4.21	1.13 - 15.71	0.033
Alcohol consumption * Smoking history	0.37	0.07 - 1.90	0.232
2. Contact with PTUBERCULOSIS case and sharing linen			
Contact with PTB case	7.34	2.00 - 26.97	0.010
Sharing linen	2.25	0.34 - 15.03	0.403
Contact with PTB case * Sharing linen	1.26	0.15 - 10.75	0.834
3. Positive HIV status and STI history			
Positive HIV status	5.89	1.64 - 21.18	0.007
STI history	1.90	0.70 - 5.16	0.209
Positive HIV status * STI history	5.11	0.47 - 55.60	0.181
4. Lack of formal education and no employment			
Lack of formal education	1.18	0.22 - 6.35	0.845
No employment	4.91	1.79 - 13.49	0.002
Lack of formal education * No employment	1.49	0.16 - 13.56	0.726
5. Diabetes history and low BMI			
Diabetes history	2.73	0.20 - 33.00	0.429
Low BMI level	0.84	0.20 - 3.49	0.814
Diabetes history * Low BMI level	223452.81	0.00 >1.0E12	0.968

Appendix 9: Complex interaction terms analysis results (continued)

INTERACTION TERMS OF EXPOSURE VARIABLES	OR	95% CI *LL - *UL	P-Value
6. Duration of incarceration > 3months and history of prison transfer			
Duration of incarceration > 3months	0.64	0.22-1.86	0.408
Prison transfer history	4.27	1.19-15.34	0.026
Duration of incarceration > 3months*Prison transfer history	0.60	0.12-2.93	0.531
7. Duration of incarceration > 6 months and history of prison transfer			
Duration of incarceration > 6 Months	0.82	0.29 - 2.28	0.699
Prison transfer history	4.43	1.42 - 13.78	0.010
Duration of incarceration > 6 Months * Prison transfer history	0.53	0.12 - 2.39	0.408
8. Duration of incarceration > 12 months and history of prison transfer			
Duration of incarceration >1year	0.92	0.30 - 2.82	0.881
Prison transfer history	3.53	1.43 - 8.75	0.006
Duration of incarceration >1year * Prison transfer history	0.59	0.12 - 2.89	0.515
9. Positive HIV status and low BMI score			
Positive HIV Status	13.41	3.9 - 45.93	0.000
Low BMI level	1.59	0.22 - 11.72	0.650
Positive HIV Status * Low BMI level	0.19	0.01 - 6.17	0.348

NB: *LL = Lower limit * UL = Upper limit

Appendix 10: Conditional Logistic Regression Model building Process

Step 1

All variables with P≤0.1 were entered in the model with the resulting results.

Term	Odds Ratio	95%	C.I.	Coefficient	S. E.	Z-Statistic	P-Value
Alcohol history (Yes/No)	2.3568	0.4160	13.3533	0.8573	0.8850	0.9687	0.3327
Contact PTB Case (Yes/No)	6.3869	0.6725	60.6546	1.8542	1.1485	1.6145	0.1064
Knowing HIV Status+ (Yes/No)	26.8071	2.4198	296.9751	3.2887	1.2271	2.6801	0.0074
No Employment (Yes/No)	9.4881	1.4599	61.6637	2.2500	0.9549	2.3562	0.0185
Presence BCG Scar (Yes/No)	0.0938	0.0167	0.5254	-2.3669	0.8792	-2.6920	0.0071
Prison Transfer (Yes/No)	0.2165	0.0288	1.6279	-1.5301	1.0293	-1.4866	0.1371
Sharing clothes towel (Yes/No)	9.3594	1.2333	71.0249	2.2364	1.0340	2.1628	0.0306
Smoking history (Yes/No)	9.4376	1.0845	82.1319	2.2447	1.1039	2.0334	0.0420
STI history (Yes/No)	1.1464	0.2690	4.8856	0.1367	0.7396	0.1848	0.8534

Appendix 10: Conditional Logistic Regression Model building Process (continued)

Step 2

"History of STI" was removed from the model since it has the highest P- value. The remaining variables were entered in the model with the below results.

Term	Odds Ratio	95%	C.I.	Coefficient	S. E.	Z-Statistic	P-Value
Alcohol history (Yes/No)	2.3487	0.4084	13.5058	0.8539	0.8925	0.9567	0.3387
Contact PTB Case (Yes/No)	6.2896	0.6853	57.7245	1.8389	1.1310	1.6259	0.1040
Knowing HIV+ Status (Yes/No)	27.8760	2.6435	293.9556	3.3278	1.2019	2.7688	0.0056
No Employment (Yes/No)	9.9159	1.5805	62.2133	2.2941	0.9370	2.4485	0.0143
Presence BCG Scar (Yes/No)	0.0912	0.0166	0.5028	-2.3942	0.8707	-2.7496	0.0060
Prison Transfer (Yes/No)	0.2170	0.0290	1.6228	-1.5279	1.0266	-1.4883	0.1367
Sharing clothes towel (Yes/No)	9.3616	1.2452	70.3797	2.2366	1.0293	2.1730	0.0298
Smoking History (Yes/No)	9.3381	1.0993	79.3241	2.2341	1.0916	2.0467	0.0407

Appendix 10: Conditional Logistic Regression Model building Process (continued)

Step 3

"History of alcohol consumption" was removed from the model since it has the highest P- value. The remaining variables were entered in the model with the below results.

Term	Odds Ratio	95%	C.I.	Coefficient	S. E.	Z-Statistic	P-Value
Contact PTB Case (Yes/No)	6.4536	0.8113	51.3333	1.8646	1.0580	1.7624	0.0780
Knowing HIV+ Status (Yes/No)	28.5286	2.9003	280.6224	3.3509	1.1664	2.8729	0.0041
No Employment (Yes/No)	11.9883	1.9682	73.0216	2.4839	0.9219	2.6945	0.0071
Presence BCG Scar (Yes/No)	0.0852	0.0156	0.4660	-2.4629	0.8670	-2.8407	0.0045
Prison Transfer (Yes/No)	0.2630	0.0395	1.7504	-1.3357	0.9671	-1.3811	0.1672
Sharing clothes towel (Yes/No)	11.6349	1.5102	89.6384	2.4540	1.0417	2.3557	0.0185
Smoking History (Yes/No)	9.6946	1.3079	71.8571	2.2716	1.0220	2.2226	0.0262

Appendix 10: Conditional Logistic Regression Model building Process (continued)

Step 4

"History of prison transfer" was removed from the model since it has the highest P-value. The remaining variables were entered in the model with the below results.

Term	Odds Ratio	95%	C.I.	Coefficient	S. E.	Z-Statistic	P-Value
Contact PTB Case (Yes/No)	5.4039	1.0663	27.3855	1.6871	0.8280	2.0375	0.0416
Knowing HIV Status (Yes/No)	6.1864	1.2608	30.3536	1.8223	0.8115	2.2456	0.0247
No Employment (Yes/No)	16.1967	2.6811	97.8445	2.7848	0.9177	3.0347	0.0024
Presence BCG Scar (Yes/No)	0.1127	0.0305	0.4156	-2.1833	0.6659	-3.2785	0.0010
Sharing clothes towel (Yes/No)	4.9352	1.4755	16.5068	1.5964	0.6160	2.5915	0.0096
Smoking History (Yes/No)	2.7072	0.9072	8.0780	0.9959	0.5578	1.7855	0.0742

Appendix 10: Conditional Logistic Regression Model building Process (continued)

Step 5

"History of smoking" was removed from the model since it has the highest P- value. This become the "Final Best Model"

Term	Odds Ratio	95%	C.I.	Coefficient	S. E.	Z-Statistic	P-Value
Contact PTB Case (Yes/No)	6.6792	1.1669	38.2306	1.8990	0.8901	2.1334	0.0329
Knowing HIV+ Status (Yes/No)	10.7520	2.4198	47.7748	2.3751	0.7609	3.1213	0.0018
No Employment (Yes/No)	8.9842	1.8358	43.9667	2.1955	0.8102	2.7098	0.0067
Presence BCG Scar (Yes/No)	0.1657	0.0461	0.5957	-1.7978	0.6529	-2.7534	0.0059
Sharing clothes towel (Yes/No)	4.3211	1.0799	17.2914	1.4635	0.7075	2.0686	0.0386