**EPIDEMIOLOGICAL PROFILE OF TUBERCULOSIS IN SINAZONGWE DISTRICT**

**IN THE CONTEXT OF HIV/AIDS**

**BY**

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# DECLARATION

I James Lamon Mtalimanja hereby declare that this is my original work and has not been presented for any other award at the University of Zambia or any other University.

Signature of candidate      : ------------------------------

Date                        : -----------------------------

# CERTIFICATE OF APPROVAL

This dissertation submitted by **James Lamon Mtalimanja** is approved as partial fulfilment of the requirements for the award of the degree of Master of Science in One Health Analytical Epidemiology  by the University of Zambia.

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**ABSTRACT**

A retrospective cross-sectional study was conducted in Sinazongwe district located in the Zambezi valley region in Southern Province of Zambia to determine the prevalence of HIV among TB patients, examine trends and patterns of tuberculosis progression from 2007 to 2012 and compared treatment outcome of HIV positive and HIV negative TB patients.

A total of 484 TB patient clinical files from Sinazongwe Zonal Health Center (SZHC) were randomly selected for inclusion into the study. SPSS version 16.0 was used to analyse this data. Tuberculosis was more prevalent in males 52% (95% CI: 48.0 -56.9) than females 47.5% (95% CI: 43.1 -52.0). The mean prevalence of HIV among TB patients in the reference period was 62% (95% CI: 54.3 – 64.6). HIV was more prevalent among female TB patients at 52.7% (95% CI: 46.6 -58.9).  There was no statistically significant variations in the annual enrolment rate of new TB cases in the period under review ($\chi^2$=6.3 and p-value 0.076). HIV/AIDS accounted for about 15% of treatment outcomes of TB patients at SZHC ($F_{1, 298}$ =4.39, p < 0.037) by lowering cure rate (p = 0.023) whilst increasing death (p= 0.039) and defaulter rates (0.035).

 Human Immunodeficiency Virus (HIV) is a very important factor influencing tuberculosis treatment outcome at Sinazongwe Health Facility. The study concluded that high HIV prevalence among TB patients at this facility was the main reason for low TB cure rate, and high mortality rate with no statistical variations in the disease progression across the years. If the situation is not controlled, the trend of low cure rate and high mortality will be maintained resulting into undesirable treatment outcomes in this study population. Therefore, it is recommended that Ministry of Health should consider employing the rapid automated Nucleic Acid Amplification Test to improve diagnosis on TB among HIV patients and strength the Direct Observed Therapy through health education and sensitisation.

## DEDICATION

This work is dedicated to my loving parents and family. Without their prayers and support, this work would not have been accomplished.

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# LIST OF ABBREVIATIONS

**AFB**         Acid Fast Bacilli

**AIDS**        Acquired Immune Deficiency Syndrome

**ARVs**        Antiretroviral Therapy

**CDC**         Center for Disease Control and Prevention

**DOTS**        Directly Observation Treatment Short Course

**EPTB**        Extra Pulmonary Tuberculosis

**GDP**         Gross Domestic Product

**HAART**       Highly Active Antiretroviral Therapy

**HIV**         Human Immunodeficiency Virus

**MCH**         Maternity & Child Health

**MDG**         Millennium Development Goal

**MDR-TB**      Multi Drug-Resistant Tuberculosis

**MTC**         Mycobacterium tuberculosis complex

**NGO**         Non-Governmental Organization

**NRL**         National Reference Laboratory

**NTP**         National Tuberculosis Programme

**PTB**         Pulmonary Tuberculosis

**SZHC**        Sinazongwe Zonal Health Center

**TB**          Tuberculosis

**TDRC**        Tropical Diseases Research Centre

**UNDP**        United Nations Development Program

**UTH**         University Teaching Hospital

**VIF**         Variance Inflation Factor

**WHO**         World Health Organization

**ZN**          Ziehl–Neelsen

# CHAPTER ONE

## 1.0    INTRODUCTION

Tuberculosis is a chronic, progressive infectious bacterial disease that affects all species of mammals, both wild and domestic including humans. Human tuberculosis (TB) is mainly associated with infection by members of the *Mycobacterium tuberculosis* complex (MTC) which includes *Mycobacterium tuberculosis, Mycobacterium bovis, Mycobacterium africanum, Mycobacterium caprae, Mycobacterium microti, Mycobacterium pinnipedii and Mycobacterium canettii* (Malama et al., 2013). *Mycobacterium tuberculosis* is the common causative agent of human tuberculosis (TB). This bacterium mainly affects the lungs but may progress to other parts of the body such as the meninges, kidneys, bones and lymph (Brunner et al., 2009). According to World Health Organization (WHO, 2012a), tuberculosis that affects the lungs (lung parenchyma) is referred to as pulmonary tuberculosis (PTB) and is the most common form of tuberculosis whereas tuberculosis that affects other parts of the body other than lungs, such as pleura, lymph nodes, pericardium, spine, joints, abdomen or genito-urinary tract is called extra pulmonary tuberculosis (EPTB).

Human Immunodeficiency Virus (HIV) alone is a known cause of human mortality and when combined with TB becomes a lethal co-infection spreading very rapidly (Mulenga at el., 2010). HIV affects the immune system and increases the susceptibility for infection (CDC, 2011a). Studies have shown that one of the known powerful risk factor for TB epidemics is HIV (Kapata et al., 2013; USAID, 2012a). If an HIV patient has latent TB infection, it becomes active and there are more chances of relapse of TB in cured persons (WHO, 2012).  TB–HIV co-infection accounts for 13% of AIDS related death on the earth. Globally, about 8% of TB cases are attributed to HIV, while in Sub Saharan Africa this is estimated to be 40% (Ogunbodede, 2010;

Gutierrez, 2012). It has also been reported that the massive increase in the incidence of TB in Africa in last 20 years is due to the strong association between HIV and TB (CDC, 2010).

Research has further shown that from 2001 onwards, the global incidence of TB infection has declined by more than 25% but Sub-Saharan Africa's epidemic remains the largest in the world (UNAIDS, 2010). TB incidence in Sub-Saharan Africa has continued to be high due to high HIV prevalence (Panteix, 2012). The co-infection poses a serious challenge on the effectiveness of TB control strategies (Mulenga et al., 2010).

In 1993, World Health Organization (WHO) declared tuberculosis as a global health emergency. Among the infectious diseases, after HIV / AIDS, tuberculosis is the world second greatest cause of adult death being responsible for more than two million deaths per year (Kapata et al., 2011). WHO (2010), reported that globally, more than eight million people get active TB infection yearly, while out of these, two million die. It is further estimated that around fifteen million people are infected with TB annually around the globe. Tuberculosis is ranked 10th in the global burden of disease table of which about 95% of cases and 98% of tuberculosis related deaths are in developing countries (WHO, 2011). Tuberculosis is the leading cause of death due to a single infectious pathogen worldwide and is responsible for 26% of avoidable disease burden (World Bank, 2009).

In Zambia, a country with a population of thirteen million people, TB continues to be among the big public health problems (Mulenga et al. 2010b). In 2010, TB notification rates were reported at 365 per 100,000 populations for all ages (MoH, 2013). The disease varies among provinces, with the highest notifications being reported from Lusaka followed by Copperbelt and Southern Provinces (Anonymous, 2012). The country has 158 diagnostic facilities and 1800 treatment facilities and TB diagnosis in Zambia is mainly through microscopy (Kapata et al., 2011).

Sinazongwe district has a population of approximately 107, 695 people serviced by 2 TB diagnostic sites. In 2010, 141 cases of TB were notified of which 41% were smear positive for pulmonary tuberculosis while in 2011, 26% of the 140 notified cases were smear positive for pulmonary tuberculosis (Anonymous, 2011). Health Management Information System (HMIS, 2012) indicates that 95.7% (135/141) of the TB patients were reported to have undergone HIV testing of which 58.5% (79/135) tested positive for HIV in 2010 while in 2011 positivity reduced to 57.8% in the District.

## 1.1.0    Statement of the problem

The population of Sinazongwe district has been growing rapidly due to the influx of people (local and foreign investors, truck drivers, daily casual workers and contractors working for the coal mines and thermal power plant) as a result of increasing economic activities such as mining and fishing. As it is generally known that, the influx of people comes with numerous public health problems such mushrooming of shanty compounds, night clubs/bars leading to substance abuse, overcrowding, commercial sexual workers (prostitution) and all kinds of environmental pollution. These conditions are, in part, favorable as risk factors for rapid spread of infectious diseases such as HIV and TB (Henostroza et al., 2013).

The incidence of TB/HIV in Sinazongwe district has increased in the past few years (Anonymous, 2012). The number of patients started on Anti-Retroviral Therapy (ART) has been increasing since 2009 through 2011 with 18% increase between 2010 and 2011 (Anonymous, 2013). There is also a notable increase of 9.1% in the number of patients currently enrolled on ART between 2010 and 2011 with the majority of clients being females. Mortality, treatment failure and defaulter rates among TB patients have also been increasing in the recent past (HMIS, 2013; Justin et al., 2012). The reason for the observed increase is not well understood but could

be attributed to low treatment success below the WHO recommended target of 85% for all newly detected smear positive cases. However, data on treatment outcomes for TB patients (HIV positive and HIV negative) enrolled in the routine TB care program is limited in Sinazongwe. The absence of this information makes it difficult to plan for any effective mitigation measures.

### 1.2.0   Justification of the study

Since the introduction of TB diagnostics services in Sinazongwe district no study of this kind has been conducted to review trends and patterns of tuberculosis progression as well as treatment outcome of TB patients co-infected with HIV enrolled in the routine TB control program. This lack of information weakens the efforts to formulate strategies needed to combat the disease. Decisions on how to treat and control such public health problems are often based on available information. In the absence of sufficient information, the decision making process becomes very difficult. Retrospective cross-section studies usually provide a major tool to informed decision making.

In view of the public health threats associated with the influx of people due to increased social economic activities in the district (opening of two coal mines, opening of the thermal power plant, fishing and trend in livestock) there is need to carry out a study to determine the prevalence and trends of tuberculosis progression from 2007 to 2012 and determine how HIV has influenced TB treatment outcomes in the same reference period. This will involve identify factors that influence TB treatment outcomes and identifying mitigation measures that could be applied at various critical points of TB treatment and control. It is envisaged that once carried out, the report can be used as a basis for recommendations to the Government of Zambia (Ministry of Health), the scientific community, the private sector and other stakeholders.

**1.3.0    Research question**

What are the trends of TB in Sinazongwe district with reference to prevalence of HIV and treatment outcomes?

**1.4.0   Objectives**

**1.4.1   General Objective**

To conduct a trend analysis of tuberculosis in the context of HIV/AIDS in Sinazongwe district in the period 2007-2012

**1.4.2   Specific objectives**

1.  To determine the period prevalence of HIV among TB patients in Sinazongwe district between 2007 to 2012;

2.  To examine the trends of tuberculosis from 2007 to 2012;  and,

3.  Compare treatment outcomes of TB patients who are HIV positive against TB patients who are HIV negative.

# CHAPTER TWO

## 2.0    LITERATURE REVIEW

Tuberculosis remains a challenge to global public health.  It is one of the major causes of morbidity and mortality, and has proven to be particularly difficult to control in regions with a high prevalence of human immunodeficiency virus (HIV) infection (German, 2013). An estimated 1.3 million deaths due to TB occur annually among HIV-uninfected individuals, and an additional 0.5 million deaths occur among HIV-infected persons (WHO, 2012a). Of the estimated global burden of 9.3 million new TB cases in 2007, 1.37 million (14.8%) were associated with HIV infection and accounted for almost 25% of global AIDS-related mortality (WHO, 2012).

### 2.1.0    Biology of tuberculosis

Tuberculosis bacilli is a slow growing mycobacteria with a doubling time of 24 hours under optimal conditions (Delogu et al., 2013). A major feature of the bacilli is the peculiar cell wall structure that provides an exceptionally strong impermeable barrier to noxious compounds and drugs and that plays fundamental role in virulence (Blaser, 2010).

### 2.1.1    Causative agent of human tuberculosis

The genus *Mycobacterium* comprises more than 70 species. Many species of Mycobacteria occur in the environment and are rarely associated with disease in humans or animals (Jenkins et al., 2011). However, there is a number of species (members of the *Mycobacterium tuberculosis* complex) that are important pathogens of animals and humans (Malama et al., 2013).

Tuberculosis in bovines and many other animal species is primarily associated with infection with *Mycobacterium bovis* (CDC, 2011a). *Mycobacteria bovis* is most commonly found in cattle

and other animals such as African and American Buffalo (Syncerus caffer) and Elk (Cervus Canadensis). In people, *M. bovis* causes tuberculosis lesions that can affect the lungs, lymph nodes, and other parts of the body and are often indistinguishable from that caused by *M. tuberculosis* (CDC, 2009). In a recent study conducted in Zambia, eight isolates of *M. bovis* were recovered from adult human TB patients (aged: 20-65), six of these isolates were from the national survey and two from a survey conducted in Namwala rural district in Southern province (Malama et al., 2013). In Uganda, a prevalence of 7% *M. bovis* infections was reported in humans suffering from cervical lymphadenitis in a pastoral community in the Karamoja region (Oloya et al., 2008) while in Tanzania a prevalence of 16% was reported (Kazwala, 2001). However, as with *M. tuberculosis*, not everyone infected with *M. bovis* becomes sick (Russell, 2007). People who are infected but not sick have what is called latent TB infection (Food Safety Authority of Ireland, 2008).

*Mycobacteria africanum* is most commonly found in West African countries, causing up to a quarter of cases of tuberculosis in countries such as the Gambia (CDC, 2011a; Bouke et al., 2010). *Mycobacteria africanum* is not an infection of humans only but has also been isolated from cattle in Bangladeshi (Rahim et al., 2007). *Mycobacteria africanum* was first recognized as distinct sub-species of the *M. tuberculosis* complex (MTBC) in 1968 in Senegal (Florian et al., 2012). On the other hand, *Mycobacteria microti* is rare and is mostly seen in immunodeficient people, although the prevalence of this pathogen has possibly been significantly underestimated (Panteix et al., 2012).

### 2.1.2   Transmission

Tuberculosis is an airborne infection (WHO, 2004: Delogu et al., 2013). When an infectious person talks, coughs or sneezes, larger droplets settle and smaller droplets remain suspended in the air (Zumla et al., 2012). TB infection results mainly from inhalation of airborne particles

suspended in the air and are transferable from person to person (Basavanthappa, 2008). However, it is also vital to note that people can also get infected with *M. bovis* by eating or drinking contaminated, unpasteurized dairy products (Malama et al., 2013). Infection by *M. bovis* can also occur from direct contact with a wound, such as what might occur during slaughter or hunting, or by inhaling the bacteria in air exhaled by infected animals (CDC, 2011b). Direct transmission from animals to humans through the air is thought to be rare, but *M. bovis* can be spread directly from person to person when an infectious person coughs or sneezes (Anonymous, 2010).

*Mycobacterium africanum* can be spread through the airborne route from an infected individual with open cases of disease and also by consuming infected milk (Florian et al., 2012). It has also been reported that although transmission of *M. africanum* from host to host is a crucial element of the spread of the disease, the underlying biological mechanisms triggering transmission are elusive (Bouke et al., 2010). On the other hand, *M. microti* is associated with infection of rodents. Human tuberculosis caused by *Mycobacterium microti* is rare, but its prevalence and clinical significance may have been underestimated (Boschiroli, 2011). A study conducted by (Panteix et al., 2010) indicated that *M. microti* has a potential to cause clinical illness in immunocompetent patients.

### 2.1.3   Risk factors linked to Mycobacteria tuberculosis

According to WHO (2011), an individual risk of infection depends on the extent of exposure to tuberculosis and individual's susceptibility to infection. The risk of infection for a susceptible person is therefore high with prolonged indoor exposure during the stay in a small room together with a person with smear positive pulmonary tuberculosis coughing frequently (German et al., 2013). Infectious cough particles can stay in the air for prolonged periods of time or stay alive in dust (DOH, 2008). The risk of transmission of tuberculosis by a person with smear negative PTB is lower than that a person with smear positive PTB (CDC, 2010).

The risk of progression from infection to disease depends on the status of the immune system. The majority (90%) of people without HIV infection who are infected with tuberculosis do not develop tuberculosis since their immune system is often strong enough to prevent the development of disease (Mbembati, 2001). Most people infected with TB remain with so-called "dormant bacilli" that might develop into tuberculosis at a later stage (Hahns, 2011). The development of another disease or condition that suppresses an individual's immune system triggers the dormant bacilli to become metabolically active and causes the infection to progress to tuberculosis disease (CDC, 2011b).

Infection with HIV is currently the most common cause of immune suppression causing reactivation of tuberculosis in Sub-Saharan Africa (Kapata et al., 2011). People with Mycobacteria infection and HIV have up to 30-times higher risk of developing tuberculosis during their life than people without HIV infection (Mwaba et al., 2011) although other conditions like malnutrition, recurrent infections of any kind, diabetes mellitus can also cause reactivation of the TB infection (Van Grevel 2002; Kapata et al., 2011).

A number of factors have been associated with an individual's risk of infection. WHO (2010) highlighted the following:

(a) The extent of exposure to the infected airborne particles;

(b) Personal (genetic) susceptibility to the infection;

(c) Close contact with active TB patient;

(d) Immune compromised status, e.g. HIV;

(e) Substance abuse;

(f) Pre-existing medical conditions e.g. diabetes, chronic renal failure, etc.;

(g) Overcrowding and poor housing; and,

(h) Profession, e.g. healthcare workers

### 2.1.4 Pathophysiology of *Mycobacteria Tuberculosis*

When bacteria of the *Mycobacterium tuberculosis* complex gain access to tissues, they proliferate locally. Local proliferation of microorganisms at the site of access to the tissues is associated with an inflammatory response characterized by infiltration of tissue with macrophages and other cells of the immune system (Henao, 2013). Macrophages phagocytose the bacteria and following phagocytosis, macrophages present MTBC antigens to T-lymphocytes, which stimulate the development of an adaptive T-lymphocyte immune response over subsequent weeks (Brunner et al., 2009).

In the early stages of infection, before the adaptive immune response is fully developed, the macrophages are not capable of preventing proliferation of the microorganisms within the macrophage (Chisiza, 2010). During the period when the adaptive immune response is developing, the macrophages containing proliferating MTBC microorganisms migrate to the lymph nodes that drain the site of initial infection. From there, they are carried to the regional lymph nodes (Lopez et al., 2012)

It is however vital to note that from the regional lymph nodes, the microorganisms may gain access to the blood and can disseminate widely throughout the body. As the adaptive immune response develops, the stimulated T-lymphocytes interact with the macrophages to enhance the ability of macrophages to inactivate the microorganisms. As the cellular adaptive immune response develops, the cells involved form the characteristic histopathological feature, the granuloma (Russell, 2007).

The tubercle bacillus has special characteristics that makes it evade the immune response and thus survives in the body for a long time. Chan (1994) stated that, one of the major attributes of the bacilli that makes it evade the immune system is that the bacilli has the ability to hinder the

fusion between the phagosome and the lysosome, and thereby lives in the phagosome. *Mycobacteria tuberculosis* has the ability to produce excessive amounts of ammonia, which can concentrate up to 20mM (Henao, 2013). Production of ammonia leads to the evading of the fusion of the phagosome and lysosome by inhibiting the fusion itself, decreasing the effectiveness of lysosomal enzymes by increasing the pH (Chan, 1994). The bacteria also have the ability to stop maturation and acidification of phagosomes, thereby hindering the abilities of digestive enzymes (Van Crevel, 2002).

### 2.1.5   Symptoms of Tuberculosis

Common symptoms of TB include fever, cough (can be productive or nonproductive), night sweats, fatigue, weight loss and haemoptysis (Brunner et al., 2009). However, not all patients will present with the above signs and symptoms; any patient who presents with any of the above symptoms warrants further investigation for prompt commencement of TB treatment (Mulenga, 2010). On the other hand, extra-pulmonary TB often presents with the non-specific symptoms described above, such as fever, night sweats and weight loss as well as symptoms specific to the organ involved and these may include:  Abdominal TB  with effects like ascites, intestinal obstruction; TB meningitis associated with headache, neck stiffness, mononeuropathies, especially of the cranial nerves; Renal TB commonly associated with haematuria, proteinuria; Spinal TB associated with backache, deformity of spine (gibbus), neurological signs and Musculoskeletal System  associated with  pain and effusions (Pehme1, 2009).

### 2.1.6   Diagnosis of Tuberculosis

Tuberculosis is one of the deadliest public health threats today, but there still remains lack of effective diagnostic tools (WHO, 2010a). Traditionally, tuberculosis is mostly being diagnosed by a combination of chest X-rays, the staining of sputum with special dyes followed by microscopy, the growth of *Mycobacterium tuberculosis* in culture and the Mantoux test. These methods have problems of sensitivity, specificity and/or speed (WHO, 2012). In particular, the

sputum smear microscopy test does not work well in HIV-positive patients and children and relies on the expertise of the microscopist (CDC, 2012; Zumla, 2011; Kapata et al., 2011). The sensitivity of sputum smear microcopy in HIV infected individual's ranges from 43 to 51 because the HIV virus conceals the concentration of the bacilli in sputum (Smart, 2007). Sputum smear also cannot be used to determine drug susceptibility as such, drug susceptibility can only be diagnosed from the growth of *Mycobacterium tuberculosis* in culture which can take as long as 2 to 3 weeks for the results to be available (Merck, 2012).

The determination of drug susceptibility is particularly relevant because *Mycobacterium tuberculosis* becomes increasingly resistant to two of the major anti-tuberculosis drugs, isoniazide and rifampicin (Merck, 2012). This form of tuberculosis is called multi-drug-resistant tuberculosis (MDR-TB) and needs to be treated with different antibiotics. It is therefore relevant to detect cases of MDR-TB because these patients remain a source of infection even if treated in the standard manner (Kazwala, 2012).

In response to the challenges of TB diagnosis, World Health Organization in 2010 endorsed the Xpert MTB/RIF for use in TB endemic countries and declared it a major milestone for global TB diagnosis (Kapata et al., 2011). This followed 18 months of rigorous assessment of its field effectiveness in TB, MDR-TB and TB/HIV co-infection. This test, and others that are likely to follow, have the potential to revolutionize the diagnosis of TB (O'Grady et al., 2011). TB diagnosis in Zambia is mainly through microscopy. The country has 158 diagnostic facilities and 1800 treatment facilities. Sinazongwe contributes 2 diagnostic facilities and 14 treatment sites (MoH, 2013).

### 2.1.7 Conceptual framework for diagnosis of Tuberculosis/HIV

```
┌─────────────────────────────────────┐
│ TB Suspect:                          │
│ Coughing for 2-3 weeks or more       │
└─────────────────────────────────────┘
                  │
                  ▼
┌─────────────────────────────────────────────────┐
│ 3 Sputum Smear Examinations:                      │
│ Day 1-Spot Sputum, Day 2-Early Morning Sputum and │
│ Day 3-spot Sputum and HIV test if status is       │
│ unknown                                           │
└─────────────────────────────────────────────────┘
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┌──────────────┐                          ┌──────────────┐
│ AFB +++      │     Broad-spectrum       │ AFB - - -    │
│ AFB ++-      │     antibiotics for      └──────────────┘
│ AFB +--      │     7 days or
└──────────────┘

Re-examine → Improvement

No improvement

┌──────────────┐   ┌──────────────┐   ┌──────────────┐
│ AFB +++      │   │ Repeat sputum│   │ Order chest  │
│ AFB ++-      │   │ examination &│   │ X-ray        │
│ AFB+- -      │   │ HIV test if  │   └──────────────┘
└──────────────┘   └──────────────┘

┌──────────────────┐        ┌──────────────┐
│ AFB- - -         │        │ CXR not      │
│ CXR suggestive & │        │ Suggestive   │
│ M/Officer judgment│       └──────────────┘
└──────────────────┘

┌──────────────┐   ┌──────────────────┐   ┌──────────────────┐
│ Smear        │   │ Smear Negative or│   │ Non-Tuberculosis │
│ Positive TB  │◄──│ Extra-pulmonary  │──►└──────────────────┘
│ Initiate     │   │ TB Initiate TB   │
│ treatment    │   │ treatment with   │
│ with CPT     │   │ CPT              │
└──────────────┘   └──────────────────┘

**Figure 2.1**: Conceptual model illustrating the ideal procedure for diagnosing TB in the context of HIV

Whereas; (AFB) means Acid Fast Bacilli, (CXT) Co-trimoxazole or Septrin and (CRX) Chest X-ray

Figure 1 illustrates the ideal procedure for diagnosing TB in the context of HIV in Zambia. The figure also highlights possible stages where the bacilli can be detected or missed in the diagnosis process. It also emphasizes the importance of integrating HIV and tuberculosis intervention at the point of service delivery.

### 2.1.8  Prevention, treatment and control of Tuberculosis

According to WHO (2012), the only currently available vaccine for TB is Bacillus Calmette–Guérin (BCG) which, while it is effective against disseminated disease in childhood, confers inconsistent protection against contracting pulmonary TB. Nevertheless, it is the most widely used vaccine worldwide, with more than 90% of all children being vaccinated (Arbelaez, 2011). However, the immunity it induces decreases after about ten years (Chisiza, 2010).   As tuberculosis is uncommon in most of the western countries such as Canada, the United Kingdom, and the United States, BCG is only administered to people at high risk while in Zambia almost 98% of children receive the vaccine (Annynonmus, 2011b).

Since the World Health Organization (WHO) declaration in 1993 that TB was a global emergency, the directly observed therapy short-course (DOTS) strategy has been the key public health intervention that has been widely used to affect global TB control (Mwaba et al., 2012). The strategy focuses on TB case management of sputum smear-positive cases with use of short-course rifampicin- containing chemotherapy. Case finding is passive and facility based, with emphasis placed on case retention and the achievement of a high cure rate (National TB Control programme, 2008).

Tuberculosis is treated with antibiotics which kill the bacteria. However, effective TB treatment is difficult, due to the unusual structure and chemical composition of the mycobacterial cell wall, which hinders the entry of drugs and makes many antibiotics ineffective (Russell, 2007). The two antibiotics most commonly used worldwide, Zambia inclusive, are isoniazide and rifampicin, and treatments can be prolonged, taking several months.  Latent TB treatment usually employs a single antibiotic such as isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin while active TB disease is best treated with combinations of several antibiotics

such as isoniazid with rifampicin and pyrazinamide with ethambutol to reduce the risk of the bacteria developing antibiotic resistance (Blaser, 2010; Colijn, 2011). *M. bovis* is treated similarly to *M. tuberculosis*. In fact, healthcare providers might not know that a person *has M. bovis* instead of *M. tuberculosis*. *M. bovis* is usually resistant to one of the antibiotics, pyrazinamide, typically used to treat TB disease. However, resistance to just pyrazinamide does not usually cause problems with treatment, because TB disease is treated with a combination of several antibiotics (Asif and Singh, 2013).

### 2.1.9   Global trends of Tuberculosis

Tuberculosis has been known to man since the time of Hippocrates (Basavanthappa, 2008). Anti –tuberculosis medications were introduced in 1950's followed by vaccines. The introduced of drugs coupled with improved living standards, led to a noticeable decrease in and control of TB infection in the US and some developing countries (Henostroza et al., 2013). The successful implementation and progress of vaccine programmes throughout the world brought hope that TB would be eliminated (WHO, 2012). However, by the late 1980s there was a resurgence of TB due to the emerging HIV epidemic and multidrug resistant – TB (MDR-TB) (Zumla, 2012).

Studies have attributed the rapidly growing TB epidemic globally, and especially in Africa to increasing HIV co-infection rates. In 2011, there were an estimated 8.7 million new cases of TB globally (13% co-infected with HIV) (Mukadi, 2001); 79% of these HIV-positive TB cases were in the African region (Corbett, 2010). In the same period, approximately 1.4 million people died from TB, including almost one million deaths among HIV-negative individuals and 430 000 among people who were HIV-positive (Asif, 2013).

**2.1.10 Tuberculosis situation in Zambia**

Zambia is one of the countries in the world most affected by the dual TB and HIV epidemics. In 2008, Zambia reported 47,333 notifications which increased to 48, 591 in 2009 and a further increase to 48, 616 in 2010 (MoH, 2010). The majority of cases reported were in young adult population groups aged 15-45 years, the same age group affected by HIV/AIDS (Mwaba, 2013). In addition, (Kapata et al., 2011) reported that the rapid increase of tuberculosis in Zambia from 1985 onwards was mainly attributed to the HIV epidemic, though other factors like population growth, urban overcrowding and improved case detection have also contributed (Mulenga, 2010).

The hallmark of TB control in Zambia is early case detection and treatment which is promoted by Direct Observed Therapy (DOT) introduced in 2001 (Mwaba et al., 2012). By 2005, Zambia also implemented the WHO TB/HIV collaborative activities with the establishment of a TB/HIV co-coordinating body with representation from government, donors, NGOs and implementing partners. This body has worked closely with the Ministry of Health to implement activities designed to reduce the burden of HIV in patients with TB and to reduce the burden of TB in people living with HIV (National Tuberculosis Program, 2010; Mwaba et al., 2012).

In Zambia, TB diagnosis is mainly done by microscopy, using Ziehl–Neelsen (ZN) stains (Kapata et al., 2011). Culture and Drug Susceptibility Testing (DST) have been performed in Zambia since the late 1990s, although there are currently no reliable records and reports on this before the year 2000. Initially, routine culture and DST were only performed at the National Reference Laboratory (NRL), which catered for the whole country. The capacity to perform culture and DST gradually increased from one referral centre (NRL) to three by the year 2008, which included the University Teaching Hospital (UTH) and the Tropical Diseases Research Centre (TDRC).

The Health Management Information System (HMIS) has indicated that Southern Province is third from Lusaka and Copperbelt province with regards to TB notifications. In 2008, the province notified 391 cases per 100 000, followed by 376 in 2009 and 359 in 2010 (HMIS, 2010). In particular, Sinazongwe district of Southern Province notified 141 cases in 2010 of which 41% were smear positive for pulmonary tuberculosis while in 2011, 26% of the 140 notified cases were smear positive for pulmonary tuberculosis. Of all notified cases in 2010, 95.7% (135/141) were reported to have undergone HIV testing of which 58.5% (79/135) tested positive. At that time, all (79) positive cases were put on Cotrimoxazole (Septrin) medication and 43% (34/79) were put on ART. In 2011, all the notified patients were tested for HIV of which 57.8% tested positive and 46% were since initiated on ART (MOH, 2010).

## 2.2.0   Biology of Human Immunodeficiency Virus (HIV/AIDS)

Human Immunodeficiency Virus Infection / Acquired Immunodeficiency Syndrome (HIV/AIDS) is a disease of the human immune system caused by infection with Human Immunodeficiency Virus (HIV). Research indicates that HIV originated in West-Central Africa during the early twentieth century and was first recognized by the Centers for Disease Control and Prevention (CDC) in 1981 (Sharp and Hahn, 2011). Since its discovery, AIDS has caused millions of deaths and millions of people are living with the virus (HIV) globally. HIV/AIDS is considered a global pandemic (CDC, 2011).

## 2.2.1   Causative agent of HIV

HIV infection results from one of two similar retroviruses (HIV-1 and HIV-2) that are transmitted through body fluids (blood, seminal fluid and vaginal secretions). These viruses destroy CD4+ lymphocytes and impair cell-mediated immunity which increases the risk of certain infections and cancers (Basavanthappa, 2008).

### 2.2.2 Transmission

HIV may be transmitted through unsafe sex (mixing of body fluids). According to CDC (2013), the only certain body fluids; blood, semen (*cum*), pre-seminal fluid (*pre-cum*), rectal fluids, vaginal fluids, and breast milk from an HIV-infected person can transmit HIV. These fluids must come in contact with a mucous membrane or damaged tissue or be directly injected into the bloodstream (through a needle or other contaminated sharp objects) for transmission to possibly occur. Mucous membranes can be found inside the rectum, the vagina, the opening of the penis, and the mouth (Cheever, 2009).

### 2.2.3 Risk factors

The risk factors associated with HIV infection are unsafe sex, multiple sexual partners, substance abuse, poverty (multiple partners for financial gain), poor education (lack of knowledge) on the HIV epidemic and consequences thereof, and cultural factors (polygamous marriages, sexual cleansing, widow inheritance (Mwaba, 2010). The Zambia Sixth National Development Plan (SNDP), (2011), indicates that the prevalence rate of HIV and AIDS has slightly reduced and the treatment coverage of Anti-Retroviral Therapy (ART) increased significantly. A further reduction from 16.9 percent to 14.3 percent with gender variation (females 16.1% and males 12.3%) and geographical variation (urban areas 20% and rural 10%) was observed by the Zambia Demographic and Health Survey (ZDHS, 2013).

### 2.2.4 Pathophysiology

HIV is a retrovirus that carries its genetic material in the form of RNA. It attaches itself to the uninfected CD4 cell surface and fuses with the cell membrane (Lara, 2010). The viral core contents are emptied into the host cell (Chisiza, 2010). HIV's enzyme reverse transcriptase copies the genetic material from the RNA to a double stranded DNA. The double-stranded DNA merges with the cellular DNA (Provirus). The cell uses the provirus to make new viral proteins and viral RNA. These new viral proteins join the viral RNA and create new viral particles. New

viral particles bud from the cell and start the process all over (Russell, 2007; Brunner et al., 2009).

### 2.2.5 Clinical features of HIV/AIDS

The stages of HIV infection are acute infection (also known as primary infection), latency and AIDS. Acute infection lasts for several weeks and may include symptoms such as fever, swollen lymph nodes, inflammation of the throat, rash muscle pain, malaise and mouth and esophageal sores. The secondary stage can vary between two weeks and 20 years (Chisiza, 2010). During this phase of infection, HIV is active within lymph nodes which typically become persistently swollen in response to large amount of virus. And the final stage AIDS. The symptoms of AIDS are primarily the result of conditions that do not normally develop in individuals with healthy immune systems. Most of these are opportunistic infections caused by bacteria, fungi, parasites and virus (Mukadi et al., 2001).

### 2.2.6 Diagnosis

Most people infected with HIV develop specific antibodies (i.e. seroconvert) within three to twelve weeks of the initial infection (CDC, 2009). Diagnosis of primary HIV before seroconversion is done by measuring HIV-RNA or p24 antigen. The positive results obtained by antibody tests or PCR testing are confirmed either by a different antibody test or by polymerized chain reaction (PCR) (UNAIDS, 2013). Antibody tests in children younger than 18 months are typically inaccurate due to the continued presence of maternal antibodies, thus HIV infection can only be diagnosed by PCR testing for HIV RNA or DNA, or via testing for the p24 antigen (UNAIDS, 2013).

### 2.2.7 Prevention, treatment and control of HIV

There is currently no cure or effective HIV vaccine. Treatment consists of Highly Active Antiretroviral Therapy (HAART) which slows progression of the disease (CDC, 2011), and as of 2010 more than 6.6 million people were taking them in low and middle income countries (WHO, 2010). Treatment of HIV also includes preventive and active treatment of opportunistic infections.

### 2.2.8 Global HIV trends

HIV/AIDS is a global pandemic. As of 2012, approximately 35.3 million people had HIV worldwide with the number of new infections that year being about 2.3 million (UNAIDS reports, 2013). This is down from 3.1 million new infections in 2001. The report further established that of these, approximately 16.8 million are women and 3.4 million are less than 15 years old. Furthermore, it is estimated that HIV resulted in about 1.6 million deaths in 2012, down from a peak of 2.2 million in 2005 (UNAIDS, 2011a).

Sub-Saharan Africa is the region most affected. In 2010, an estimated 68% (22.9 million) of all HIV cases and 66% of all deaths (1.2 million) occurred in this region (UNAIDS, 2011b). This means that about 5% of the adult population is infected and it is believed to be the cause of 10% of all deaths in children (Chisiza, 2010).

Various studies have pointed out that Sub-Saharan Africa is still the largest contributor to the global HIV burden (Hahn, 2011). Lawn, et al. (2011) indicated that although the rate of new HIV infections has decreased, the total number of people living with HIV continues to rise in Sub-Saharan Africa. The HIV incidence appears to have peaked in the mid-1990s, with evidence of declines in incidence in several sub-Saharan countries. Between 2001 and 2009, the incidence of

HIV infection declined by more than 25% due to the introduction of Anti-Retroviral drugs although Southern Africa's epidemic remains the largest in the world (Ogunbodebe, 2010).

### 2.2.9  HIV/AIDS situation in Zambia

The Zambia Demographic and Health Survey 2007 which included HIV testing of over 10,000 women and men indicated that 14% of Zambians aged 15-49 are HIV-positive and the prevalence of the disease is higher among women than men in both urban and rural areas. The report further highlighted that overall, 16% of women and 12% of men are HIV-positive. HIV prevalence is twice as high in urban areas as in rural areas (20% versus 10%). Lusaka province recorded highest HIV prevalence of 21% followed by Central province at 18%, Copperbelt at 17% and Southern province at 15% while Northern and North Western provinces recorded the lowest HIV prevalence of 7% (ZDHS, 2007).

### 2.2.10  HIV/AIDS situation in Sinazongwe

Sinazongwe district has only two ART sites namely Sinazongwe Zonal Health center and Maamba Hospital. The number of patients started on ART has been increasing since 2009 through 2011 with 18% increase between 2010 and 2011 (Anonymous, 2013). There is also a notable increase of 9.1% in the number of patients currently enrolled on ART between 2010 and 2011 with the majority of clients being females.

### 2.3.0  TB/HIV co-infection

It is estimated that more than 65% of all TB patients in Africa are co-infected with HIV (Chisiza, 2010). TB is the leading cause of morbidity and mortality among HIV-infected patients (UNAIDS, 2011a). Despite the widespread availability of TB treatment, TB/HIV co-infected patients in Africa had an annual mortality rate of 25% to 40% before the introduction of ART therapy (Mukadi et al., 2001). This mortality was attributable to complications from

overwhelming TB disease as well as immunosuppressant from advanced HIV infection (Murray et al., 1993).

The emergence of human immunodeficiency virus (HIV) has exacerbated an already enormous number of cases of tuberculosis worldwide (UNAIDS, 2011a). Tuberculosis affects HIV positive individuals throughout all phases of HIV infection and is the leading killer of HIV positive people. Of the 9.4 million individuals with new cases of active TB each year, 1.4 million are HIV positive (Nakata et al., 1997). It is widely accepted that HIV causes a depletion of CD4 T-cells, which is likely to contribute to the susceptibility of co-infected persons to TB, as this T-cell subset is important in conferring human protection against TB (Manual for Infectious Disease control, 2009). However, HIV has effects on other cells, including macrophages, and influences cytokine production, which may also prevent a host from containing an initial or latent *Mycobacterium tuberculosis* infection (CDC, 2010).

### 2.3.1 TB/HIV treatment outcomes

Studies have indicated that treatment outcomes for TB patients who are HIV negative are better than those who are HIV positive (Mwaba, Chintu and Mwinga, 2008). A study done by Henostroza et al. (2013) in which the prevalence of TB and HIV co-infection among inmates in six prisons in Zambia was assessed revealed that TB prevalence was high in prisons with high HIV prevalence; and low in prisons with low HIV prevalence. Similarly, Sume et al. (2000) reported that TB patients co-infected with HIV were more likely to default from treatment compared to TB positive HIV negative patients OR 1.943, (95% CI: 1.150-3.285) and that the probability of dying whilst on treatment was high for TB patients co-infected with HIV OR 23.7, (95% CI: 2.9-194.3). Treatment failure was also observed to be high for HIV co-infected TB patients OR 0.40, (95% CI: 0.25-0.65) compared to HIV negative TB patients.

Furthermore, a study conducted in Karnataka, India by Shasti et al. (2013) with the objective of determining TB treatment outcomes among TB-HIV co-infected patients and compare the results with non-HIV tuberculosis indicated that of the 6,480 adult co-infected, a third occurred in women. Treatment success among co-infected patients not on ART (54%) were significantly lower compared to those already on ART (80%); death and default rates were higher in the non-ART group. Treatment success proportions (75%) for the co-infected patients were similar to those for 51,966 patients registered under the TB program. Death rates among co-infected patients (15%) were twice as high as for TB patients under the program, though default and failure rates were lower. Treatment success rates also varied according to sex. Females were reported to high treatment success rate than males (Ogunbodede, 2010).

## 3.0    MATERIALS AND METHODS

### 3.1.0   Study Area

The study was undertaken in Sinazongwe district which is situated in the Southeast of Southern Province and is one of the rural districts. The district is located in the Zambezi valley and extends from longitude $26^0$ 43' E to $27^0$ 45' E and latitude $16^0$ 50' S to $18^0$ 00' S (Action plan, 2012), and shares its borders with Choma district to the west, Gwembe district to the north and Kalomo district on the southwestern border.  Further-south, lays the national boundary with Zimbabwe through Lake Kariba. The district covers approximately 4200 square kilometers (Figure 3.1).
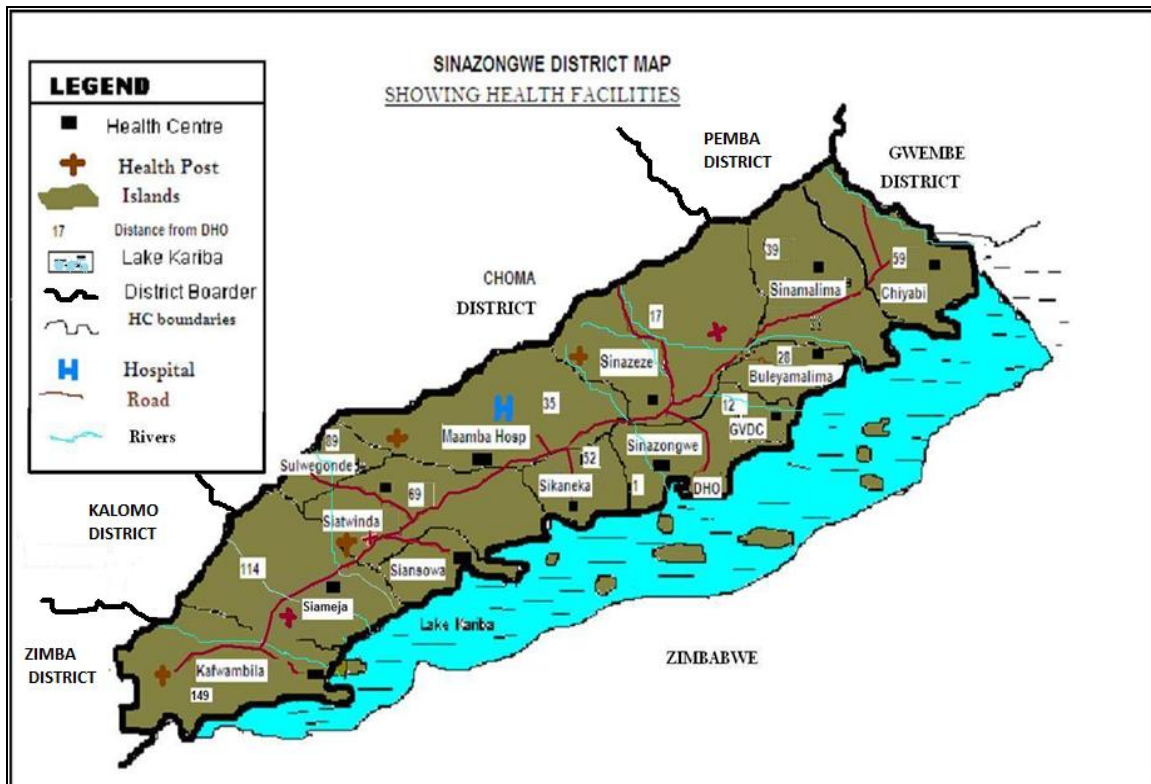


Figure 3.1: Map of Sinazongwe district showing administrative boundaries

The district has a population of 107,695 people with a growth rate of 2.5 per annum. Majority of the people are in the age group range of 15-45 years with a sex ratio of 49% males to 51% females (Action plan, 2012). Sinazongwe population is serviced by 12 primary health care facilities with only one first level hospital, two Tuberculosis diagnostic sites and 2 Antiretroviral Therapy (ART) sites. The district was selected as a study site due to its high contribution to TB notifications as well as high TB fatalities in Southern Province (Annual Statistical Bulletin, 2012). It is also one of the districts with a highest incidence of TB/HIV co-infection in the province (HMIS, 2012).

### 3.2.0   Study design

A retrospective cross-sectional study methodology was used in this study. A retrospective approach was preferred for this study because it is the most feasible and cost-effective way of managing a fairly large sample size sufficient to answer our research objectives.

### 3.3.0   External population

It was envisaged that the findings of the study would be extrapolated to all TB and HIV patients in Sinazongwe catchment area and other populations with similar demographic features.

### 3.4.0   Target population

The study targeted all TB and HIV patients at Sinazongwe Rural Health Center who were registered in the routine TB care between 2007 and 2012.

### 3.5.0   Study population

Being a retrospective cross-sectional study, the study did not have any direct interaction with patients; instead, patient files were reviewed to solicit pertinent information according to the research objectives. The study population included all patient files and charts registered at

Sinazongwe Zonal Health Centre in the routine TB programme and not the actual individuals. A total of 3,821 patient files were identified.

### 3.6.0 Sample

The sample population included the actual selected patient clinical files that participate in the study as determined using a set of carefully defined criteria prescribed below.

### 3.7.0 Inclusion criteria for selection of clinical files

Medical files of all adult patients (fifteen years and above) diagnosed with TB by symptoms, positive sputum smears, cultures and/or chest x-ray, entered into the TB register, and received treatment at Sinazongwe Zonal Health Centre at least 6 months prior to initiation of the study were included in the study. Only patients aged 15 years and older were considered for inclusion.

### 3.8.0 Exclusion criteria for ineligible clinical files

The study excluded medical files of patients aged less than fifteen years; medical files of patients with a known history of MDR-TB and medical files of patients who received treatment for more than one month at different facility outside Sinazongwe district and were then transferred to the study site to continue TB treatment.

### 3.9.0 Sampling procedures

Using tuberculosis suspects, diagnosis and treatment registers, individual patient clinical files for the period 2007 to 2012 were identified for Sinazongwe Zonal Health Centre (Total patient clinical files 3,821). Through the inclusion and exclusion criteria indicated above, 2,137 patient clinical files were eligible for inclusion in the study. Since the prevalence of TB for Sinazongwe is not known, an approximation of 50% was used. It was also planned that the prevalence estimated would be determined at 5% precision at a confidence of 95%. The researcher also assumed that the patient clinical files were drown from a normally distributed population.

The sample size was determined by the following formula;

$$n = \frac{Z^2 P (1-P)}{d^2}$$

Where:-

n   = required sample size

Z   = multiplier from normal distribution at 95% confidence level (1.96)

P   = estimated prevalence (0.5)

(1-P)   = the probability of having no disease (1-0.5)

d   = precision of estimation, 5% (0.05)

Thus, using this sample size determination procedure a sample of 384 was derived. Considering that this is the minimum sample size required, the researcher added 100 samples summing to make 484.

## 3.10.0  Data collection

A robust retrospective record review was accomplished by four (4) trained data collectors who were oriented in the data collection procedures. Patient's files, charts as well as registers were consciously reviewed to document pertinent patient level data such as age, sex, diagnosis, treatment history, HIV status and treatment outcomes onto a data summary sheet which acted as a questionnaire.  Each selected patient file had its own data summary sheet. *See appendix A.*

## 3.11.0  Data analysis

Data was cleaned and entered into the Statistical Package for Social Sciences (SPSS) version 16.0 where all the statistical analysis were performed including descriptive statistics to determine the mode, mean and median of key parameters.  Prevalence as opposed to incidence of HIV among TB patients was calculated. Chi-square test of association was computed to determine the relationship between independent and dependent categorical variables of interest while multiple linear regressions analysis was used to analyze the multiple effects of potential predictor

variables on the outcome (dependent) variables. Modeling the effects of HIV on each of the possible TB treatment outcomes was achieved using binary logistic regression analysis

Prior to the construction of the models, data was screened for possible confounders using the correlation matrix on the following predictor variables; sex of patients, weight, age, highest level of education, marital status, type of disease, TB treatment history and HIV status. Autocorrelation and normal probability plots were also produced.

### 3.12.0  Pilot test

Forty-eight (48) (10%) patient medical files were randomly selected to test the data collection and analysis procedures. The pilot was aimed at assessing the availability of data and evaluating face and content validity of the study.

### 3.13.0  Ethical and moral considerations

The study sought appropriate ethical approval from relevant authorities. Written permission was thus obtained from ERES CONVERGE IRB (reference number. 2014-Mar-001) and subsequent permissions from Sinazongwe District Medical Office and the health center in-charge at Sinazongwe Zonal Health Centre.  Being a retrospective study with no patient contact, data was collected from medical files and registers. Data collected was only identified by clinic and register numbers. No names of patients were collected and there was no link between numbers, clinic names and individual identifiable information. Since no patients was directly involved in the study, application for waiver of consent was sought and granted.

# CHAPTER FOUR

## 4.0     RESULTS

## 4.1     Background characteristics

A total of 484 TB patient files were randomly selected for inclusion into the study. The analysis of basic demographic and clinical characteristics of patients indicated that majority of TB cases registered at Sinazongwe Zonal Health Centre between 2007 and 2012 were 254 males, representing 52.5% (95%, CI: 48.0 – 56.9); and 230 females, representing 47.5% (95% CI: 43.7 – 52.0) of the sampled population. The mean age of males (38.9 years; 95%, CI: 36.3 – 41.4) was higher than that for females (35.4 years; 95%, CI: 32.8 - 38.0), p< 0.04 (Figure 4.1).


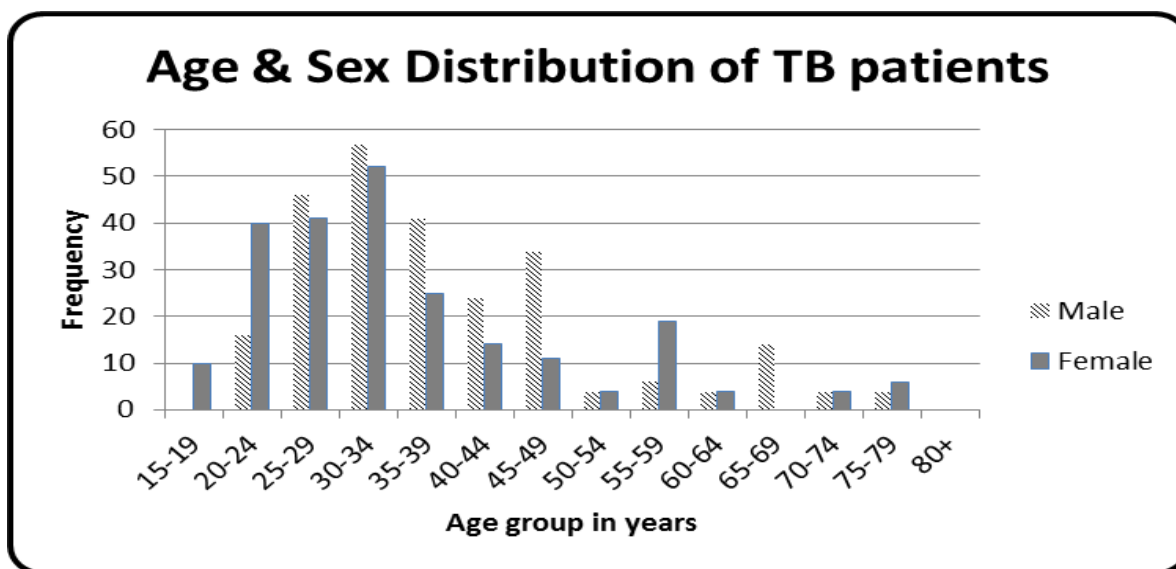
**Figure 4.1: Distribution of age of TB patients at Sinazongwe Zonal Health Centre (n=484) according to sex**

With regards to education, about 45% of the respondents did not state their level of education and amongst those who indicated that they had been to school, only 46.6% (125) (95%, CI; 40.6– 52.6)  reached primary level of education; 39.2% (105) (95%, CI; 33.3 – 45.0) reached secondary

school; and 14.18% (95%, CI; 10.3 – 18.8) had attained tertiary education. With respect to marital status, the study also reviewed that the majority of the TB patients at Sinazongwe Zonal Health Centre in the period under review were married followed by the singles (Figure 4.2).
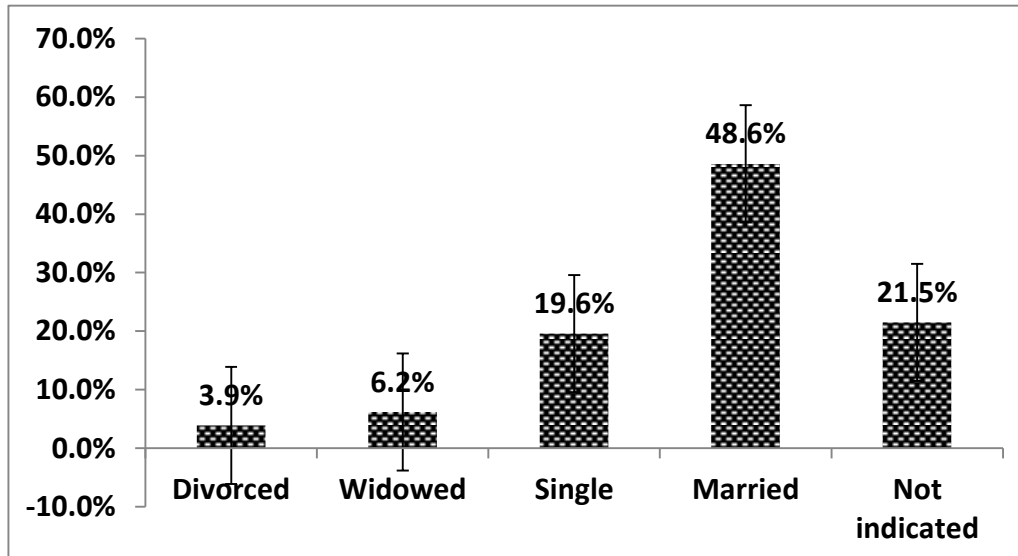


**Figure 4.2: Marital Status of TB patients at Sinazongwe Zonal Health Centre (2007-2012)**

It was also observed that over 79.8% (95% CI: 76.2 – 83.3) of TB patients at Sinazongwe Zonal Health Centre were diagnosed using sputum smear microscopy examinations followed by X-ray at 12.4% (95% CI: 9.5 – 15.3) and culture was the least at 7.8% (95% CI: 5.4 – 10.2). Further, it was observed that among the smear diagnosed patients, majority were males 57.2% (95%, CI; 52.3 – 62. 189) whereas among those diagnosed using X-ray and culture majority were females at 75% (95% CI: 64.0 – 86.0) and 52.6% (95% CI: 36.8 – 68.5), respectively.

Only 45.7% (95%, CI: 41.2 – 50.1) of TB patients knew their HIV status at TB registration and the majority of whom were males 58.8% (95% CI: 52.3 – 65.3). Those who did not know their HIV status at TB registration were further asked to consent for HIV testing and over 98% agreed to be screened and positivity rate was thus determined at 58.2% (95% CI: 52.2 – 64.2). Although most of the patients that tested positive for HIV were females at 61.5% (95% CI: 53.3 – 69.7)

(Table 4.1), Chi-square test for association indicated that there was no statistically significant association between the sex of the patients and their HIV status ($\alpha= 0.05$, $\chi^2$ 0.1895, $df_1$).

**Table 4.2: HIV testing results among TB patients at Sinazongwe Zonal Health Centre 2007-2012**

| HIV testing results | | | | | |
|---|---|---|---|---|---|
| Sex of patient | | | Test results | | Total |
| | | | Positive | Negative | |
| Male | | 2007 | 4 | 13 | 17 |
| | | 2008 | 10 | 11 | 21 |
| | Year of | 2009 | 13 | 8 | 21 |
| | registration | 2010 | 23 | 7 | 30 |
| | | 2011 | 8 | 2 | 10 |
| | | 2012 | 8 | 14 | 22 |
| | **Total male** | | **66** | **55** | **121** |
| Female | | 2007 | 10 | 16 | 26 |
| | | 2008 | 6 | 10 | 16 |
| | Year of | 2009 | 23 | 2 | 25 |
| | registration | 2010 | 14 | 4 | 18 |
| | | 2011 | 19 | 10 | 29 |
| | | 2012 | 11 | 10 | 21 |
| | **Total female** | | **83** | **52** | **135** |
| **Grand total (male and female)** | | | **149** | **107** | **256** |

Over, 38% of the TB patients registered at Sinazongwe Zonal Health Centre between 2007 and 2012 were managed on DOT plan administered by their relatives, 31% by Volunteers, and 30% by clinics and only 0.6% of the patients were left unmonitored (Table 4. 2). Chi-square test of association further demonstrated a statistically significant association between DOT plans used and TB treatment outcomes in the period under review ($\alpha= 0.05$, $\chi^2 =160.479$, $df_3$ $p>0.05$).

**Table 4.2: DOT Plan of TB patients at Sinazongwe Zonal Health Centre**

|  |  | Frequency | Percent | 95% CI |
|---|---|---|---|---|
| DOT Plan | Clinic | 146 | 30.2 | 26.1 – 34.3 |
|  | Volunteer | 151 | 31.2 | 27.1 – 35.3 |
|  | Relative | 184 | 8.0 | 33.7 – 42.3 |
|  | Not Observed | 3 | 0.6 | 00.0 – 1.32 |
|  | **Total** | **484** | **100** |  |

## 4.2    Trends and patterns of Tuberculosis

The study also highlighted that over 70% of the TB patients at Sinazongwe Zonal Health Centre

registered between 2007 and 2012 were new TB patients and about 23% were transferred in from

other facilities (Table 4.3).

**Table 4.3: TB treatment History at Sinazongwe Zonal Health Centre for 484 patients (2007-2012)**

|  |  | Patient's TB treatment history | | |
|---|---|---|---|---|
|  |  | **frequency** | **percent** | **95% CI** |
| Treatment history | New | 341 | 70.5 | (66.4 – 74.5) |
|  | Relapse | 18 | 3.7 | (2.0 – 5.4) |
|  | Trans-in | 109 | 22.5 | (18.8 – 26.2) |
|  | Treatment after failure | 12 | 2.5 | (1.1 – 3.9) |
|  | Treatment after default | 4 | 0.8 | (0.02 – 1.6) |
|  | **Total** | 484 | 100.0 |  |

**Table 4.4: TB treatment History per year at Sinazongwe Zonal Health Centre for 484 patients (2007-2012)**

| *Sex* | *Type of Patient* | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | New | Relapse | Trans-in | Failure | Default | Total |
| Male | Year of | 2007 | 24 | 0 | 7 | 0 | 0 | 31 |
| | registration | 2008 | 25 | 5 | 11 | 0 | 4 | 45 |
| | | 2009 | 30 | 0 | 5 | 4 | 1 | 39 |
| | | 2010 | 27 | 11 | 11 | 0 | 2 | 49 |
| | | 2011 | 19 | 2 | 13 | 3 | 1 | 38 |
| | | 2012 | 44 | 0 | 4 | 3 | 2 | 52 |
| | **Total male** | | **169** | **18** | **51** | **10** | **10** | **254** |
| Female | Year of | 2007 | 32 | 0 | 18 | 0 | 0 | 50 |
| | registration | 2008 | 21 | 0 | 14 | 0 | 0 | 35 |
| | | 2009 | 34 | 0 | 7 | 0 | 0 | 41 |
| | | 2010 | 31 | 0 | 1 | 0 | 0 | 32 |
| | | 2011 | 30 | 0 | 12 | 0 | 0 | 42 |
| | | 2012 | 24 | 0 | 6 | 0 | 0 | 30 |
| | **Total female** | | **172** | **0** | **58** | **0** | **0** | **230** |
| | **Grand total** (male & female) | | **341** | **18** | **109** | **10** | **10** | **484** |

A further analysis indicated that new TB infections were equally likely (50%) for both sexes ($\chi^2$= 0.0264, $\alpha$=0.05, $df_1$) and relapses, treatment after failure and treatment after default was high amongst the males whereas the rate of trans-in was high for females at 55.2% (Table 4.4). The table also shows numbers of new TB infections, relapses, transferred-in, re-treatment after failure and re-treatment after defaulting for the period 2007 to 2012.

Despite variations in the observed frequencies for TB treatment history, $\chi^2$ indicated that there was no statistically significant association in the enrolment rate of new TB cases in the period under review ($\chi^2$=6.3 and p-value 0.076).
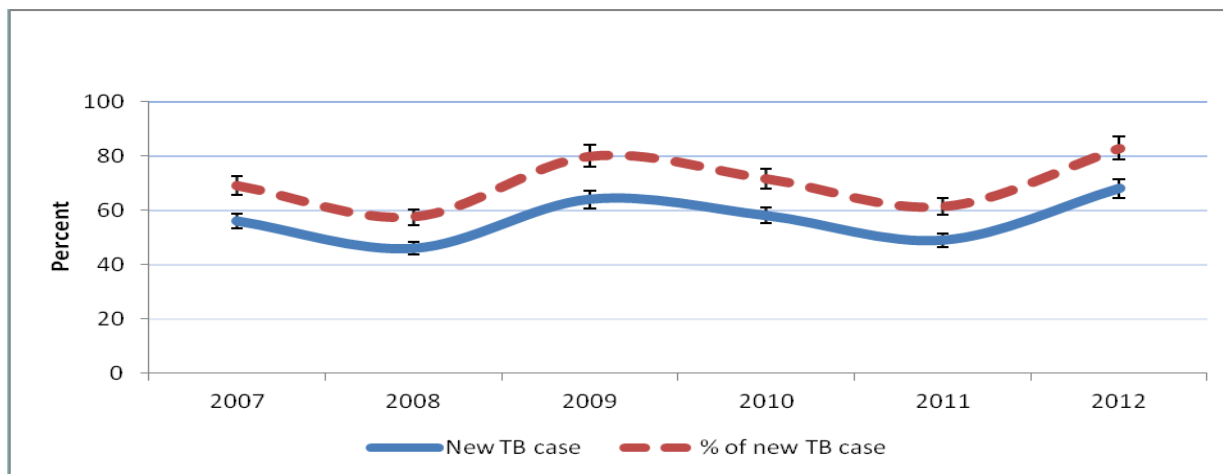


**Figure 4.3: Trends of New TB infections among TB patients at Sinazongwe Zonal Health Centre (n= 484) (2007-2012)**

The mean treatment success rate for the reference period was 67% with a maximum of 81% and minimum of 63% for 2009 and 2012, respectively. Deaths were high in 2010 and declined towards the end of the year as treatment completion rate started to increase.

## 4.3    Tuberculosis and Human Immunodeficiency Virus

Descriptive analysis indicated that about 84% (95% CI: 80.8 – 87.4) of the TB cases registered at Sinazongwe Zonal Health Centre were diagnosed as pulmonary tuberculosis and 16% (95% CI: 12.6 – 19. 2) as extra-pulmonary tuberculosis. The majority of the pulmonary cases were males at 55.3% (95%, CI: 50.4 – 60.1) while the majority of patients with extra-pulmonary TB were females at 62.4% (95% CI: 51.5 – 73.2). It was observed that females were more likely to get extra-pulmonary TB than their male counterparts OR 2.1 (95% CI: 1.6 – 2.7) and that HIV positive individuals had a higher risk of presenting extra-pulmonary TB than the pulmonary form, when compared to HIV negative patients OR 2.0 (95% CI: 1.6 – 2.5) (Table 4.5).

**Table 4.5: Type of tuberculosis by HIV status**

| *HIV status* | | Type of disease | | |
|---|---|---|---|---|
| | | **Pulmonary** | **Extra-Pulmonary** | **Total** |
| Male | Positive | 162 | 1 | 163 |
| | Negative | 54 | 32 | 88 |
| | Not tested | 2 | 0 | 2 |
| Female | Positive | 142 | 36 | 178 |
| | Negative | 32 | 19 | 52 |
| | Not tested | 1 | 0 | 1 |
| **Total** | | **396** | **88** | **484** |

Overall, the study indicated that the mean prevalence of HIV among TB patients in the reference period was 62% with the highest prevalence of 70% reported in 2009 and the lowest of 52% reported in 2007. However, the observed variations in the annual prevalence was not statistically significant ($\chi^2$=10.694, p-value 0.082) (Figure 4.4).
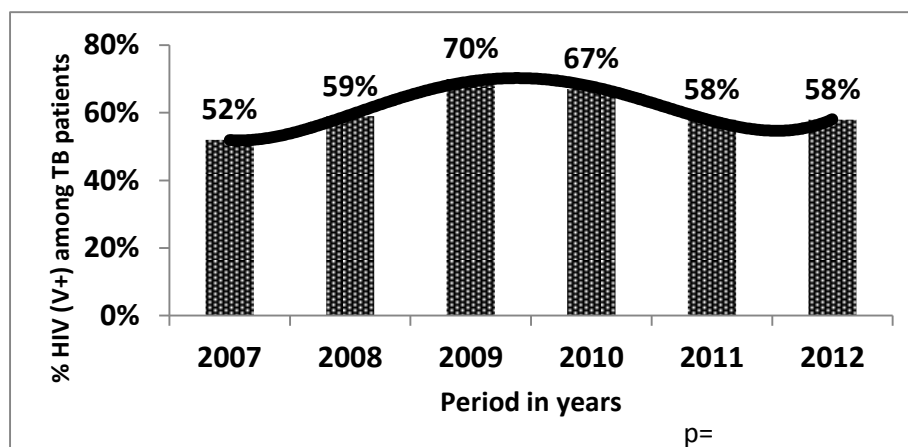


**Figure 4.4: Prevalence of HIV among TB patients at Sinazongwe Zonal Health Centre from 2007-2012 (n=484)**

## 4.4 Treatment outcomes for TB/HIV positive and TB/HIV negative patients

Out of the 484 investigated patients, only 35.3% (95% CI: 29.9 - 40.7) completed their TB treatment; 28.7% (95% CI: 24.5 − 34.8) were cured; 20% (95% CI: 15.5 − 24.5) died; 11.8% (95% CI: 7.8 − 14.9) transferred out; 2.1% (95% CI: 0.45 − 3.6) had treatment failure and defaulted. Table 4.6 below shows the treatment outcome of TB patients by age group.

**Table 4.6: TB patients' treatment outcome by age groups at SZHC 2007 - 2012 (n =484)**

| Age group | Cured M | Cured F | Died M | Died F | Completed M | Completed F | Trans-outs M | Trans-outs F | Failed M | Failed F | Defaulted M | Defaulted F |
|-----------|---|---|---|---|---|---|---|---|---|---|---|---|
| 15-19 | 0 | 3 | 0 | 3 | 0 | 7 | 0 | 0 | 0 | 0 | 1 | 0 |
| 20-24 | 6 | 2 | 7 | 14 | 3 | 17 | 0 | 9 | 0 | 0 | 2 | 0 |
| 25-29 | 11 | 11 | 3 | 9 | 18 | 11 | 3 | 10 | 3 | 0 | 2 | 0 |
| 30-34 | 16 | 13 | 13 | 7 | 20 | 16 | 5 | 4 | 1 | 0 | 1 | 0 |
| 35-39 | 15 | 4 | 7 | 0 | 6 | 12 | 1 | 0 | 2 | 0 | 2 | 0 |
| 40-44 | 18 | 12 | 3 | 6 | 7 | 7 | 4 | 0 | 3 | 0 | 1 | 0 |
| 45-49 | 7 | 4 | 9 | 1 | 11 | 3 | 12 | 0 | 1 | 0 | 1 | 0 |
| 50-54 | 0 | 4 | 2 | 3 | 0 | 3 | 0 | 1 | 0 | 0 | 0 | 0 |
| 55-59 | 0 | 3 | 3 | 0 | 2 | 11 | 0 | 3 | 0 | 0 | 0 | 0 |
| 60-64 | 4 | 0 | 1 | 0 | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 0 |
| 65-69 | 2 | 0 | 4 | 0 | 6 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| 70-74 | 0 | 0 | 0 | 1 | 0 | 3 | 2 | 0 | 0 | 0 | 0 | 0 |
| 75-79 | 4 | 0 | 1 | 0 | 1 | 6 | 0 | 0 | 0 | 0 | 0 | 0 |
| 80+ | 0 | 3 | 0 | 3 | 0 | 7 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total | 83 | 56 | 53 | 44 | 75 | 96 | 29 | 28 | 10 | 0 | 10 | 0 |

A further analysis reviewed that out of the 171 patients who completed treatment, 55.6% were females (95% CI: 48.1 − 63.0) and the rest were males, and 56.1% of the total number of patients who were cured were males (95% CI: 47.9 − 46.4). Deaths were high among the male patients 61.9% (95% CI: 58.2 − 63.4) compared with their females counterparts 38.1% (95% CI: 28.5 −

47.8). Females did not report any treatment failure or defaulters. However, with regards to age/treatment outcome, the cure rate was high between age group 25-29 and 40-44 for both males and females. Conversely, deaths were high between age group 20-24 and 55-59 for males and age group 15-19 and 50-54 for females. Tuberculosis treatment completion rates were also slightly statistically different between males and females of the same age group. In the age group 20-34 although females had a slight higher completion rate than males. However, the difference was not statistically significant at 95% confidence level interval ($p = 0.19$) and age group 35-49 males had better treatment outcome than females ($p=0.004$). It was further demonstrated that treatment completion rate for females were three times higher than of males in higher age groups (50 years and above) ($p < 0.003$).

A multiple regression model was setup to demonstrate if there was any significant difference between treatment outcomes of TB patients who are HIV positive and TB patients who are HIV negative. This model compared cure rates (favorable outcome) against all other outcomes (unfavorable outcomes). Prior to running the regression analysis model, the data set was screened for collinearity amongst predictor variables (sex of patients, weight, age and level of education, type of disease, type of patient, HIV status and marital status). The analysis reviewed that none of the predictor variables had their Variance Inflation Factor (VIF) nearing 5 as shown in Table 4.7. This outcome suggests that there was no multi-collinearity in our predictor dataset.

**Table 4.7: Testing for Collinearity among predictors on TB data collected at Sinazongwe Zonal Health Center 2007 - 2012**

|  | Collinearity Statistics | |
| --- | --- | --- |
| **Predictors** | **Beta** | **VIF** |
| Sex of patient | -0.067 | 1.189 |
| Weight of the patients | 0.040 | 1.062 |
| Age of patient | -0.193 | 1.143 |
| Level of education | -0.230 | 1.286 |
| Type of disease | -.312 | 1.042 |
| Type of Patient | -0.140 | 1.113 |
| HIV status | -0.127 | 1.083 |
| Marital Status of Patient | 0.036 | 1.390 |

Using Durbin – Watson statistics it was observed that there was no autocorrelation among the predictor variables (Durbin-Watson 2.173) at one percent level of significance. In addition, the normal probability plot produced a rough broken line especially in the middle and top right hand corner, where some of the data points look odd (Figure 4.6). This confirmed that the amount of correlation amongst the predictors was not significant.
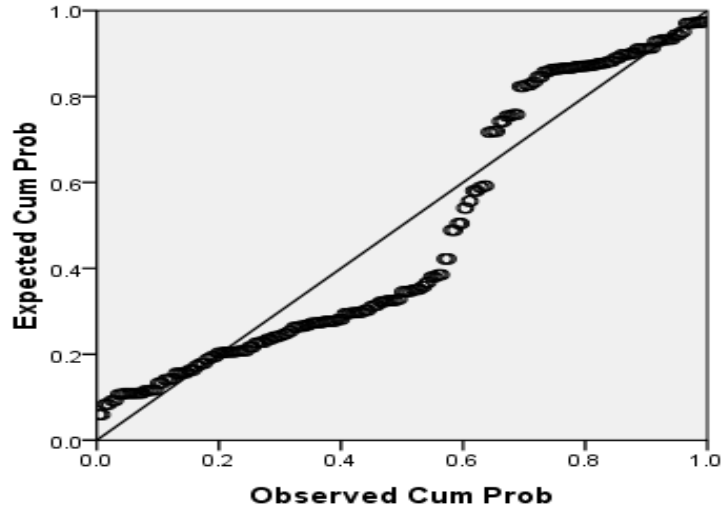
**Figure 4.5: Normal probability plot of regression standardized residues**
X-axes represent observed cumulative probabilities for treatment success whereas the y-axes represent the expected cumulative probabilities

With this justification, a multiple regression analysis model was set up to assess the statistical significance of HIV/AIDS in TB treatment. Using the enter method in SPSS version 16.0, a significant model emerged ($F_{8, 429}$ =11.688, p < 0.000, adjusted R square=0.164). Implying that education, type of TB, previous exposure and HIV status accounts for 16.4% of TB treatment outcome at this facility. Conversely, sex and marital status of patients were not significant in the model and hence excluded from the model (Tables 4.8).

**Table 4.8:  P-Value for significant predictors for TB treatment outcome at SZHC**

|  | t | Beta | LB | UB | P-value |
|---|---|---|---|---|---|
| Age of patient | -4.124 | -0.2 | -0.011 | -0.004 | **0.000** |
| Level of education | -4.646 | -0.2 | -0.069 | -0.028 | **0.000** |
| Type of disease | -6.979 | -0.3 | -0.525 | -0.294 | **0.000** |
| Treatment history | -3.034 | -0.1 | -0.113 | -0.024 | **0.003** |
| HIV status | -2.791 | -0.1 | -0.233 | -0.04 | **0.005** |

A second multiple linear regression model was setup to determine the association between treatment outcome (cured, died, completed, failed, defaulted and trans-outs) and HIV status (predictor variable). Using the stepwise method in SPSS version 16.0, a significant model emerged $F_{1, 298}$ =4.394, p < 0.037, adjusted R square=0.15) implying that about 15% of variations in treatment outcome (explanatory variable) is explained by HIV status at Sinazongwe Zonal Health Center p<0.05 (Table 4. 9).

**Table 4.9: Multiple regression analysis model for HIV status on TB treatment outcome**

| Model | | Sum of Squares | df | | Mean Square | | |
|---|---|---|---|---|---|---|---|
| F | Sig. | | | | | | |
| 1 | Regression | 2.719 | 1 | | 2.719 | 4.394 | .037[a] |
| | Residual | 184.427 | 298 | | 0.619 | | |
| | **Total** | **187.147** | **299** | | | | |

A predictive model was further constructed to show the influence of HIV status on each of the TB treatment outcomes. It was observed that HIV status is associated with TB cure rate p=0.023. Patient transfer out and defaulter rate is also influenced by HIV status although the association is not statistically significant (Table 4.10).

**Table 4.10: TB treatment outcome predictive model**

| Variables | Level | HIV positive | % HIV positive | P-value |
|---|---|---|---|---|
| Cure rate | Cured | 69 | 63.3 | 0.023 |
| | Not cured | 40 | | |
| Completion rate | Completed | 76 | 69.7 | 0.248 |
| | Not completed | 33 | | |
| Transferred | Not transferred out | 91 | 16.5 | 0.098 |
| | Transferred out | 18 | | |
| Defaulter rate | Not defaulted | 99 | 9.2 | 0.085 |
| | Defaulted | 10 | | |
| Failure rate | Not failed | 100 | 8.3 | 0.103 |
| | Failed | 9 | | |
| Died | Alive | 93 | 14.7 | 0.139 |
| | Died | 16 | | |

Using odds ratio as an approximation to the relative risk, it was observed that HIV status was cardinal in influencing treatment outcomes of TB/HIV co-infected patients at Sinazongwe Zonal Health Centre. Modeling using logistic regression analysis indicates that despite the influence of HIV on all treatment outcomes, it was observed that only cure rate was statistically associated with HIV status p = 0.026. Notably, HIV status also explains variation in treatment defaulter though not statistically significant (table 4.11).

**Table 4.11: Results of the logistic regression model**

| | Odds Ratio | P-value | 95% Confidence interval |
|---|---|---|---|
| Cure rate | 2.63 | 0.026 | 0.93 – 3.61 |
| Completion rate | 1.33 | 0.249 | 0.828 – 2.075 |
| Transferred out | 2.69 | 0.101 | 0.330 – 1.103 |
| Defaulter rate | 1.45 | 0.099 | 0.17 – 5.10 |
| Failure rate | 2.64 | 0.211 | 0.78 – 4.31 |
| Died | 2.159 | 0.142 | 0.864 – 2.786 |

# CHAPTER FIVE

## 5.0    DISCUSSION

### 5.1    Back ground characteristics

This study aimed to describe the epidemiological profile of tuberculosis in the context of HIV/AIDS for Sinazongwe district. This was achieved by determining the prevalence of HIV among TB patients, highlighting trend of disease progression from 2007 to 2012 and comparing treatment outcomes for TB patients known to be HIV positive and those known to be HIV negative.

It was observed that the majority of TB patients at Sinazongwe Zonal Health Centre were males (52%) and that tuberculosis was common among females aged twenty four to thirty six (24-36) years while in males the common age infected with the bacilli was between twenty eight to forty eight (28-48) years. The results obtained in this study regarding age and sex distribution of TB infected individuals are in line with what has been reported elsewhere as the age group most affected by tuberculosis and HIV/AIDS (ZDHS, 2007; Mwaba, 2008; Kapata, 2011). Interestingly, this result is in consistent with findings from other HIV/AIDS studies conducted in Zambia which showed high prevalence of HIV and TB among females in this age group (Mulenga et al., 2010; Bate et al., 2013; Henostroza et al., 2013).

In terms of marital status, the study revealed that most of TB patients in the routine TB programme at this facility were married. The other categories of the marital status (widowed, divorced, separated and singles) put together accounted only for 30%. The study observed that married individuals were the most affected group in the study population. This is in part due to the social economic activities associated with the residents of Sinazongwe as most people

involved in the fishing industry tend to leave their families (husbands, wives and children) for several days camping in the islands to drying or smoke fish for export to the Copperbelt, Livingstone and Lusaka where they camp again until all the fish is sold. A similar behavior was also observed among the drivers working at the coal mines. The married individuals are perceived to have increased pressure to fend for their families hence engaging into such high risk social economic activities. Although the observation was not statistically significant, such behavior is associated with high risk of exposure to TB and HIV (Mweemba et al., 2013; Needham, 1998).

With regards to education, the study established that most of the TB patients had a very` low level of education with only 39% reaching secondary level of education. Most patients had attended primary level of education, with more male patients in the majority. The education profile in this study was identical to that of general rural Zambia (anonymous 1999; MoH 2011). Although the study did not show any relationship between the individuals' level of education and TB infection rates, literature has indicated that there is a positive correlation between number of years spent in school and TB infections as it has been purported that increased schooling results into improved knowledge, decent work and work environment, improved health seeking behavior and improved housing conditions, nutrition and social wellbeing (Mulenga 2010; USAID, 2012).

## 5.2    Diagnosis and Testing

It was observed that the most popular TB diagnostic method at this facility was sputum smear microscopic examination. This diagnostic method accounts for about eighty percent (80%) of all TB diagnoses conducted in the period under review. The remaining twenty percent (20%) was shared between x-ray and culture.  Culture was the least, accounting for only eight percent

largely due to poor staffing levels, inadequate stocks of laboratory reagents and the length of time to grow *Mycobacterium tuberculosis* in culture (Merck, 2012). Although the use of smear microscopic examinations at this facility exemplifies the application of standard TB diagnosis and treatment guidelines recommended for rural health facilities in Zambia (MoH, 2013), the use of microcopy (sputum smear examination) comes with numerous challenges, especially in the light of high HIV prevalence and Multi Drug Resistant Tuberculosis MDR-TB (Med Res, 2013).

Sputum smear microscopy examination was also cited to have limitation in its performance; sensitivity is grossly compromised when the bacterial load is less than 10,000 organisms/ml sputum sample (Global Tuberculosis Control, 2010; WHO report, 2011). Current studies have also indicated that sputum smear microscopy has a poor track record in extra-pulmonary tuberculosis, paediatric tuberculosis and in patients co-infected with HIV and Tuberculosis (Biswas et al., 2012). Microscopic examination is also attributed to cause treatment defaulters and lost to follow up due to repeated requirement for sputum samples for subsequent examinations, as a result, patients do not come back for subsequent testing, collection of results and later for treatment largely due to long distances to health facilities (Med Res, 2013). It was also observed that staffing and lack of trained health personnel is a challenge in most of the TB diagnostic sites in the study community (anonymous, 2011b).

In view of these highlighted challenges, Zumla et al., (2012) and Kapata et al., (2011) observed that it is important to consider the use of the new rapid, automated Nucleic Acid Amplification Test, Xpert MTB/RIF) to revolutionarise TB diagnosis in Zambia. The use of this technology provides improved sensitivity and specificity especially in people living with HIV/AIDS with a detection rate of about 80% (95% CI: 67% - 88%) and increases case detection of TB by 45% when compared with microscopy (WHO, 2013). Unfortunately, Xpert MTB/RIF comes with its

own challenges such as running costs, dependence on electricity, demand for trained manpower, infrastructure and investment requirements that are often beyond the scope of most diagnostic facilities that offer TB diagnosis to communities, particularly in rural communities like the study site (Bate et al., 2012).

Tuberculosis treatment guidelines for Zambia allow patients to choose a DOT provider before being discharged (anonymous, 2013). This study has documented that the majority of the patients in Sinazongwe district are managed on the DOT plan administered by their relatives and only a minority, less than one percent (< 1%), were not supervised by anyone. The study also revealed that health care providers as well as community volunteers and families were playing a critical role in the management of TB cases at all levels of care. These findings indicate that health care workers at SZHC are in the right track as far as management of TB patients is concerned both in the community and at health facility level.

It is cardinal to note that DOT is an essential component of TB management as it allows relatives, friends, family members, community treatment supporters including health personnel (doctors, clinical officers, nurses and public health officers) to monitor patients more closely for adverse drug effects, prompt action and promoting drug adherence both in the continuation and the intensive phase of treatment (Ajzen, 1991). Kapata et al. (2011), also reported that DOTs ensures maximum adherence and prevention of default from treatment which is achieved through patient support groups, psychological counseling, family members and communities who provide health education, including stigma reduction (usually in the constitution phase whereas health care workers monitor patients in the intensive).

Monitoring for defaulters and treatment failures is very important in the management and control of tuberculosis as studies have indicated that MDR comes as a result of non-adherence to previous treatment protocols in form of treatment default and failure (Mwaba et al., 2010). Community tuberculosis treatment supports are playing a huge role in monitoring patients with regards to adherence to treatment, especially in the light of limited staff.

## 5.3    Trends of Tuberculosis

Overall, it was established that new tuberculosis infections accounted for over seventy percent of all diagnosed TB cases in each individual year (2007-2012) at this facility. This translates that tuberculosis is still a public health concern in the investigated community. It is almost certain that every community today has a working TB program characterized by various activities ranging from outreach sensitization programs to TB screening activities both at community and health facility level (anonymous, 2013b). On the contrary, despite the community and health facility level tuberculosis interventions, the study has indicated that the incidence of TB has not reduced in the period under review. This increase is in part due to increased case detection rate as a result of availability of logistics and increased community sensitization through community structures; and in part due to the influx of traders due to the dooming economic activities in the district (coal mines industry, fishing industry and construction works).

The study has further observed that in every one hundred TB patients, two to five relapses, one to four treatment failure and two defaulters were observed for each individual year in the period under study. These findings are very worrying especially in the light of MDR-TB as studies have demonstrated that increased number of relapses, treatment failure and high defaulter rates is a prerequisite for Multi-Drug Resistance Tuberculosis (MDR-TB) (Kapata et al., 2013).  It was

also observed that all the relapse, treatment failure and defaulters in this study were males. This finding though alarming, corroborates other findings drawn from different studies which concluded that treatment failure and defaulter rates are high among males mostly in the economically active age range 15-45 (ZDH, 2007; Jain et. al., 2013). Referring to the conclusions drawn elsewhere and also from this study, it can be explained that since Sinazongwe district is a trading centre for fish (Kariba breams and fresh water sardine) and coal mining (male dominated economic activities), it is expected that adherence to TB treatment is a challenge due to stringent working hours in the mines and the fishing industry (Odebiye, 1992).

## 5.4    Prevalence of HIV among TB patients

The study has revealed that over fifty four percent (54%) of the TB patients did not know their HIV status at TB enrollment. The year 2010 recorded the least number of patients who reported that they knew their HIV status at TB registration. Literature and expert opinion has documented the observed drop in the number of TB cases tested for HIV in 2010 as partly due to shortage of HIV test kits in most parts of the country as there was a national wide stock-out in this period (anonymous, 2010; District Action plan, 2011). Following the national guidelines for TB diagnosing and treatment in Zambia (Zambia National Tuberculosis Programme, 2010), all TB patients should be tested for HIV. As such, 98% of the two hundred and twenty three (223) patients who did not know their HIV status at entry into the TB programme were counseled and tested for HIV.

The study has thus reported that the overall HIV testing rate for TB patients in the routine TB programme at this facility is fairly good at 98% (95% CI: 97.7 – 99.2) when compared to most of the findings reported at 87.4% (Wesen, 2014) and 93% (USAID, 2012) for most of African

countries. Overall, the study indicated that the mean prevalence of HIV among TB patients in the reference period was sixty two percent with the highest prevalence of seventy percent reported in 2009 and the lowest of fifty two reported in 2007. Despite variations in the observed HIV prevalence rates among TB patients, these differences were not statistically significant ($\chi^2$ =10.694, p-value 0.082).

Similarly, although HIV positivity rate was observed to be relatively high among females mostly in 2009, 2010 and 2011 with the mean of 77.2% against the national figures reported at 70% in 2006 and 80% in 2008 (Mweemba et al., 2008), there was no significant statistical association between sex of the patients and their HIV status ($\chi^2$ 0.1895, $df_1$, p=0.1).

However, a positive association was observed between type of tuberculosis (pulmonary/extra-pulmonary) and HIV status (HIV positive/HIV negative). It was observed that HIV positive individuals had a higher risk of presenting extra-pulmonary TB than the pulmonary form, when compared to HIV negative patients OR 1.98 (95% CI: 1.6 – 2.5). It is widely observed that HIV causes a depletion of CD4 T cells, which is likely to contribute to the susceptibility of co-infected persons to TB, as this T cell subset is important in the control of TB. However, HIV has effects on other cells, including macrophages, and influences cytokine production, which may also prevent a host from containing an initial or latent Mycobacterium tuberculosis infection. Extra pulmonary tuberculosis does not usually manifest in individuals with a strong immune system but rather in people with a suppressed immune system. As observed by (Cheever, 2009) the weak immune system is a door way for extra pulmonary tuberculosis to reveal itself as the CD4 T cells are destroyed by the HIV virus. This explains why the study observed that the risk of getting extra pulmonary tuberculosis was high among HIV positive individuals than the HIV negative ones in the study population.

On the other hand, the study also aimed at defining the cure rate as a measure of progress in as far as implementation of the TB activities is concerned. Consequently, cure rate was defined as smear positive cases whose sputum was examined at the end of treatment and gave negative result expressed as a percentage of total new smear positive enrolled new TB cases (Ministry of Health, 2011). The results of this indicator showed that TB cure rate has steadily been increasing although the increase is statistically disturbing as they are far below the national standards of 85%. The overall cure rate for the country reported in 2011 stands at 82% with southern province leading at 87% (Annual statistical Bulletin, 2011). The increasing cure rate for TB patients in Sinazongwe is associated with increased surveillance through the weekly rapid surveillance system coupled with health promotion/health education in strategic places. Drug availability and monitoring of drug uptake using DOTs has also contributed greatly to the increasing cure rate. However, more needs to be done to further strengthen the surveillance system in order to reduce the number of patients lost to follow, defaulter and treatment failure,

## 5.5    Treatment outcomes for TB/HIV positive and TB/HIV negative

In order to compare between treatment outcome of TB patients who are HIV negative and those who are HIV positive, we produced two different regression models. The first model compared TB cure rates against all other outcomes, defined as unfavorable outcomes. It was observed that five out of eight predictors were statistically associated with TB cure rate; age of the patient $p=0.00$, level of education $p=0.00$, type of TB infection $p=0.00$, TB treatment history $p=0.00$ and HIV status $p=0.01$. These findings are consistent with what was observed by (Anonymous (1999; Kapata et al., 2011). Of a particular note, the study observed that control and treatment of

tuberculosis should be responsive to all age groups especially the age 15-49 years the same age group at risk of HIV.

Furthermore, health education messages should also be designed to appeal to all individuals most especially people with a low level of education as it was observed that the risk of not getting cured of TB increases with reduced level of education, whist that of being cured increases with increased level of education. Similar findings were also observed by (CDC, 2011b). The study also observed that TB patients with no history of previous TB exposure had a reduced risk of not being cured when compared with patients with history of previous exposure. This is in agreement with (López, 2010) and (USAID, 2011) who observed that people with history of previously exposure to TB have a tendency of discontinuing treatment which usually results into treatment failure. Consequently, the study observed that the status of being HIV positive or HIV negative is a very an important factor in TB favorable outcome.

Treatment outcome, just like human behavior, is inherently uneven to predict and therefore it is not always possible to produce totally accurate predictions thereof.  However, having more than one predictor variable is useful when predicting human behavior, as our actions, thoughts and emotions are all likely to be influenced by some combination of several factors (Ajzen, 1991). In this regard, multiple regression analysis models allowed the researcher to identify a set of predictor variables which together provide a meaningful influence on the dependent variable.

A second model was setup to determine the influence of HIV status on each of the individual treatment outcome. It was observed that although HIV influence cure rate among TB patients, the associating was not statistically significant implying that being HIV positive does not necessarily mean that one cannot be cured of TB. This finding favors what was reported by

(Harries et al., 2001) that prompt identification and initiation of TB/HIV co-infected patients into Antiretroviral Therapy (ART-care) has potential to improve TB cure rate by 65 percent, similarly, the study also observed that one's ability to complete TB treatment was not statistically associated with HIV status as the study indicated that the risk of treatment failure was equally likely among TB positive and TB negative patients in the study population. These findings are consistent with the finding of (Zumla, 2013) who observed that although the association between HIV/AIDS and TB cure rate is not statistically significant, HIV status is cardinal in the management of TB patients and later influencing treatment outcome thereof.

Of a particular note, the study observed that treatment failure, defaulter rate, transfer out and deaths were statistically associated with HIV status. It was observed that the risk of treatment failure was high among TB/HIV co-infected patients (OR; 2.6), whereas transfer out was (OR; 2.1), and death (OR; 1.88). Notably, it was established that most of TB patients avoid turning up for ARVs pick up at the ART clinic due to stigma associated with HIV hence the reason for high rate of transfer-outs, treatment failure and consequently deaths among TB/HIV co-infected patients in the study population. Therefore, there is need to employ sensitive health education services and strengthen the referral system from TB to ART and vise-vise whilst maximizing confidentiality of patients status.

# CHAPTER SIX

## 6.0    CONCLUSION AND RECOMMENDATIONS

### 6.1 Conclusion

The study has established that HIV prevalence among TB patients was high in Sinazongwe district. The high prevalence was observed in all individual years from 2007 to 2012 with the average of sixty two percent per year annum. There was no significant variation in the HIV prevalence's among TB patients across the year.

The trend of tuberculosis progression has remained constant in the reference period. The fact that disease progression has remained stable overtime deserves attention. These results indicate little progress in the implementation of TB/HIV collaborative activities at all levels of health care service provision.

HIV/AIDS is a very important factor influencing TB treatment outcomes at Sinazongwe Zonal Health Center. The study has demonstrated that the influence of HIV on TB treatment outcome has not changed over the years despite the availability of antiretroviral drugs. HIV/AIDS still accounts for about 15% of all treatment outcomes with the majority been unfavorable outcomes.

### 6.2 Recommendations

It is hoped that these results together with other studies will help highlight the TB situation in Sinazongwe District especially in the context of HIV/AIDS. In view of our findings, we recommend that:

- The Ministry of Health should consider employing the use of the more rapid diagnostic tests such as the rapid, automated Nucleic Acid Amplification Test, Xpert MTB/RIF) to improve TB diagnosis in Sinazongwe.

- Strengthen the TB surveillance system and community sensitization to reduce on the number of defaulters and treatment failure through DOTS.

- The district community medical office and all tuberculosis diagnostic sites should promote early diagnosis and detection of HIV among TB patients followed by prompt initiation into TB/HIV care programmes

- Strengthen TB/HIV collaborative activities

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# Appendices

## Appendix A1: TB questionnaire

**DATA SUMMARY SHEET (Form1)**

1. Name of data collector……………………………………………………………………………………

2. Name of health center in charge…………………………………………………………………………

3. Date of data collection………………………………………………………………………………….

| Demographic information | | | | | |
|---|---|---|---|---|---|
| 4.Gender | Male ☐ Female ☐ | 5. Weight | 1st weight ☐ | 2nd weight ☐ | 3rd weight ☐ |
| 6. Age | _____ Years | 7.Education | Primary ☐ | Secondary ☐ | Tertiary ☐ |
| 8.Village | …………………………… | | Any other ☐ | Not applicable (N/A) ☐ | |
| 9. Marital | Single ☐ , Married ☐ , Devoviced ☐ , Seperated ☐ , Widowed ☐ , N/A ☐ | | | | |

| Clinical diagnosis | | | |
|---|---|---|---|
| **10. Type of diagnosis Yes No** | **11. Diagnosis results** | **12. Disease type** | |
| Sputum smear ☐ ☐ | Positive ☐ Negative ☐ | Pulmonary TB ☐ | |
| Culture ☐ ☐ | Positive ☐ Negative ☐ | | |
| X-ray ☐ ☐ | Normal ☐ Abnormal ☐ | Other specify _____ | |

**23. Dot Plan**
Clinic ☐ ☐
Volunteer ☐ ☐
Relative ☐
Not observed ☐

**24. Dot Score**
Numerator _____
Denominator _____

| HIV testing and counseling | | HIV Care | |
|---|---|---|---|
| 13. | Known HIV+ at registration Yes ☐ No ☐ | 18. **ARV assessment** CD4 test done Yes ☐ No ☐ | |
| 14. | If No, Accepted TB registration Yes ☐ Not indicated ☐ | Viral Test Done ☐ No ☐ | |
| | | Any other assessment ☐ | |
| 15 | Date when HIV test was done _____ | 19 | CPT Started Yes ☐ No ☐ |
| 16. | CT Results P+ve ☐ N-ve ☐ | 20 | ARV Eligible Yes ☐ No ☐ |
| 17. | Post TC done Yes ☐ No ☐ | 21 | Date CPT started…………../………………./………… |
| | | 22 | ARV start date…………../………………./………… |

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## Appendix A2: HIV/AIDS questionnaire

**TB screening**

**DATA SUMMARY SHEET (Form2)**

1. Name of data collector……………………………………………………………………………………

2. Name of health center in charge…………………………………………………………………………

3. Date of data collection……………………….………………………………………………………..

| 10. ART patient known TB status at registration<br><br>Yes  ☐            No  ☐ | 11. **If No.** ART patient took TB test at registration<br><br>Yes ☐            No  ☐ |
|---|---|
| 12. Types of TB Diagnosis<br>Sputum        ☐<br>x-ray           ☐<br>culture         ☐ | 13. TB diagnosis results<br>Negative        ☐<br>Positive         ☐<br>Not indicated   ☐ |
| 14. Started TB treatment<br><br>     Yes ☐          No ☐ | 15. Date stated TB treatment<br><br>……………/…………………/………………… |