

**NON-HEALTH SYSTEM RELATED FACTORS AFFECTING TUBERCULOSIS  
TREATMENT OUTCOMES: A CASE-CONTROL STUDY. UMGUNGUNDLOVU  
HEALTH DISTRICT**

**Submitted to**

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**MASTER OF PUBLIC HEALTH**

**By**

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## **ABSTRACT**

KwaZulu-Natal province records the highest number of tuberculosis cases diagnosed in the country, but less than 50% of these were cured in 2008, and fewer in those from rural areas and informal settlements where inadequate health care continues. HIV and AIDS associated tuberculosis frequently require labour-intensive methods of monitoring and combating for any success to be achieved. The socio-economic context wherein these diseases occur further limit their control.

The low proportion of tuberculosis patients currently with successful treatment outcomes in Umgungundlovu Health District makes essential an in-depth investigation to establish the factors that are associated with these poor outcomes.

This study investigates the factors affecting the current poor treatment outcomes in new patients with tuberculosis in a high disease burden district of KwaZulu-Natal in 2011.

### **Methods**

A retrospective case-control study was conducted comprising 300 adult cases of tuberculosis who failed to complete 6 months of ambulant therapy and 300 frequency matched controls who completed therapy. A random sample of 15 primary health care clinics was selected from where consecutive cases and controls were selected with probability proportional to the number of tuberculosis patients seen at the clinic. Data was extracted from patient records and interviews. Processed data was analysed to identify risk associations using multivariate logistic regression.

### **Results**

After adjusting for confounding statistically significant risk factors associated with poor tuberculosis treatment outcomes were unemployment (Odds Ratio (OR) 16.0; 95% CI: 6.7 to 37.8); living in a rural area (OR 14.3; 95% CI: 1.1 to 18), distance from home to clinic (OR 1.4; 95% CI: 1.3 to 1.6), living with HIV (OR 2.3; 95% CI: 1.1 to 4.7) and being very ill (OR 5.0; 95% CI: 2.1 to 11.9).

## **Discussion**

The principal findings are that non-adherence to TB treatment is significantly associated with a number of non-health systems issues. Determinants of poor TB treatment outcomes in patients receiving six-month ambulatory care are diverse and multifactorial. After adjusting for confounding variables, unemployment, distance from patient home to the clinic, living with HIV and being very ill during TB therapy remained significantly associated with a poor TB treatment outcome.

## **Conclusions**

Although determinants of poor tuberculosis treatment outcomes in patients receiving six-month ambulatory care are diverse and multifactorial, poor tuberculosis treatment outcomes are significantly associated with identifiable factors independent of the health system. Rigorous intervention strategies should prioritize at least these five major risk factors.

## **Recommendations**

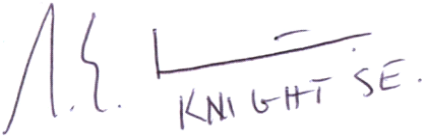
The TB control programme should go beyond the health systems issues to include inter-sectoral collaboration to address socio-economic and other non-health system barriers to adherence to TB treatment. Further research is recommended in this field.

## DECLARATION

I, Zanele Ndwandwe, declare that:

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Twelve field workers who collected data; and

Ms Gugu Mofokeng who assisted with capturing of data.

## **ABBREVIATIONS AND ACRONYMS**

ABET	Adult Basic Education and Training
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
CAM	Contemporary Alternative Medicine
CHC	Community Health Centre
CHW	Community Health Worker
CI	Confidence Interval
DHER	District Health Expenditure Review
DHIS	District Health Information System
DOT	Directly Observed Treatment
ETB	Extra-pulmonary tuberculosis
HIV	Human Immunodeficiency Virus
KM	Kilometres
KZN	Kwazulu-Natal Province
MDRTB	Multidrug Resistance Tuberculosis
PHC	Primary Health Care
TB	Tuberculosis
WHO	World Health Organisation

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# **1 CHAPTER 1: INTRODUCTION**

## **1.1.1 Introduction**

Tuberculosis (TB) has received heightened attention in the past two decades owing to its dramatic resurgence as a major public health threat in many low-income countries. South Africa experiences one of the worst TB epidemics in the world. The World Health Organization (WHO) ranked South Africa fourth among 22 severely affected TB countries in the world in 2008 (Stevens, 2008).

The above finding is confirmed in the Management Sciences for Health (2004) Annual Report which states that South Africa continues to endure one of the worst TB epidemics in the world. Factors such as poverty, the Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS) and attendant poor health infrastructure contributes to the high disease burden of TB and accentuates the low levels of cure achieved. Rural areas feature among the most severely afflicted (Management Sciences for Health, 2004). Such a finding is confirmed when the numerous challenges to access health care in rural areas are accounted for and taken into consideration.

## **1.1.2 Background**

### **1.1.2.1 Overview of Tuberculosis in South Africa**

The resurgence of pulmonary tuberculosis in South Africa, a development that is further exacerbated by the HIV and AIDS epidemic now poses as a major challenge to the relevance, appropriateness, and effectiveness of those current TB management programmes being implemented. It is thus essential that these TB programmes need to be re-evaluated, especially in relation to their applicability in rural areas (Dodor, 2004).

Nair *et al.* (2010) supports the contention that the observed rapid escalation of TB in sub-Saharan Africa reflects the increase in the prevalence of HIV infection in this

region. Approximately two million deaths from TB are recorded annually in sub-Saharan Africa (Nair *et al.*, 2010).

The burden of TB exerted upon the nation's health services is overwhelming. Despite South Africa's investment in TB control, progress toward reaching the programme objective has remained frustratingly slow and treatment success remains low compared with other African countries (USAID, 2006).

"The incidence of detected tuberculosis has tracked trends in the prevalence of HIV since 1994. Although the incidence of new cases of smear positive pulmonary TB has not increased as sharply, this is mainly due to the high rate of smear negative TB and late detection of TB, especially among newly infected people living with HIV, (meaning that people often present first with TB complications other than lung infection " ( Harrison, 2009).

KwaZulu-Natal (KZN) province records the highest number of TB cases in the country (Cullinan 2004). In 2002, 36% of those diagnosed with TB were cured. Two years later, there was an improvement with a figure of 49% being achieved; a statistic that still ranks far below the WHO target of curing 85% of cases (Cullinan, 2004). Currently, the TB cure rate in KZN is a mere 42% (Monticelli, 2008).

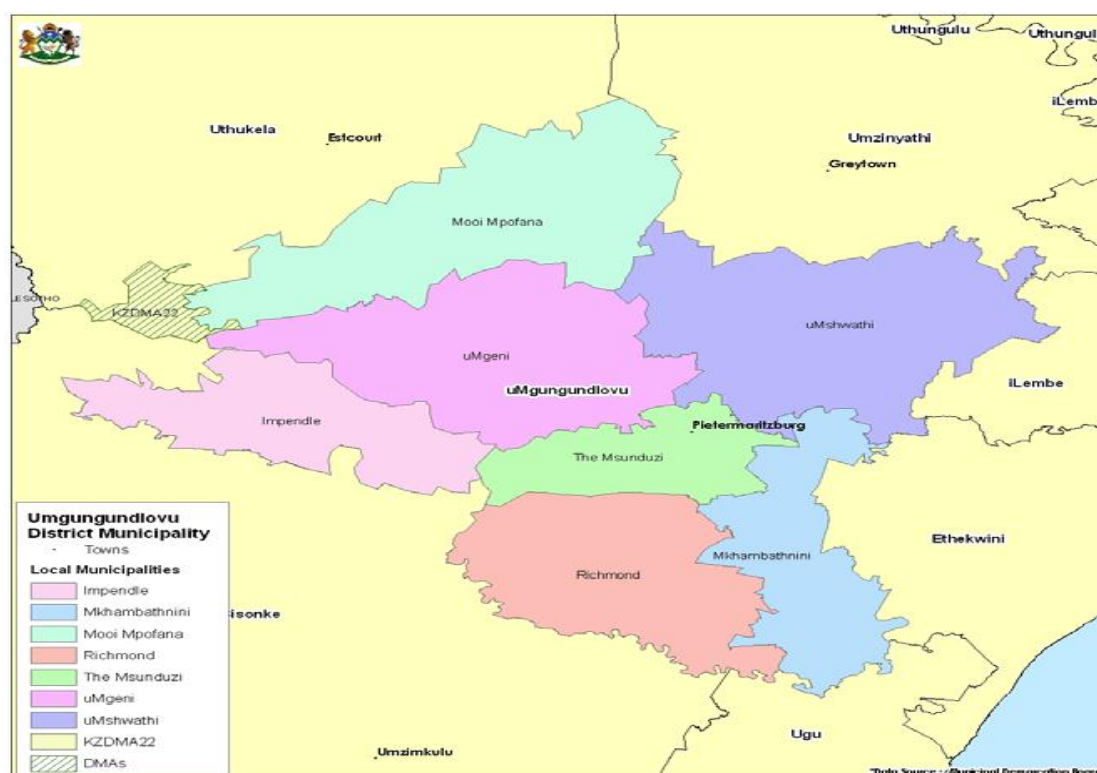
At least two million of 9.4 million KZN residents living mostly in rural areas and informal settlements continue to lack adequate health care in the most populous province of South Africa. The combined impact of epidemics such as HIV and AIDS and TB frequently require labour-intensive methods of monitoring and combating for any success to be achieved. In addition, the socio-economic context wherein these diseases occur further inhibits any discernible progress in their control being achieved (Cullinan, 2004).

Umgungundlovu Health District was declared a "TB Crisis Emergency Area" by the National Health Department due to the high incidence of the disease in 2006. The aforementioned region constitutes the district impacted by the second highest burden of TB in the province after Ethekwini Health District (National Department of Health 2006).

In uMgungundlovu only 35% of TB cases were cured in 2005. Currently the figure stands at 58%, a statistic, which remains below the specified 85% target (DHIS, 2010). The low proportion of TB patients currently being cured in Umgungundlovu Health District and recorded in recent history makes essential an in-depth investigation to establish the patient-related factors that contribute to the attainment of such undeniably inadequate TB treatment outcomes in the course of combating this scourge.

### 1.1.2.2 Overview of the Research Setting.

Umgungundlovu Health District is the second largest health district in KZN province with a population of 980 000 to 1 million. It has seven local municipalities. The majority of the population in Umgungundlovu Health District is African (83%) followed by Asian (9%), White (6%) and Coloured (2%). Females comprise 53% of the population (Tang, 2008).



**Figure 1: Map of Umgungundlovu Health District in 2006 District.**

*Source: Department of Local Government and Traditional Affairs, 2006).*

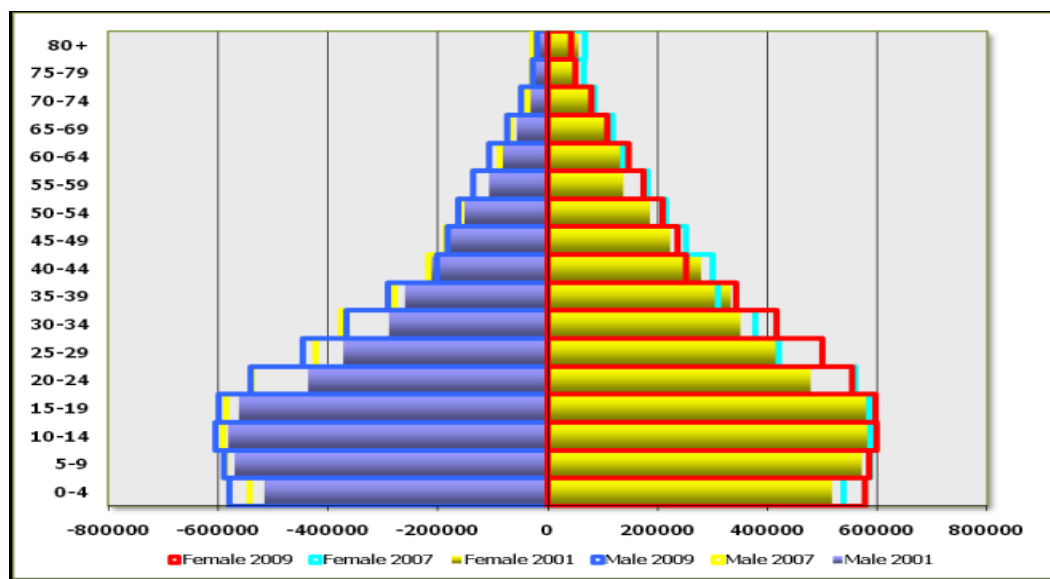
The map shows the distribution of seven local municipalities in Umgungundlovu Health District. In this study, data was disaggregated per municipality.

**Table 1: Distribution of Population per Local Municipality in Umgungundlovu Health District in 2006.**

<b>Municipality</b>	<b>Population</b>	<b>% Population</b>
<b>uMsunduzi</b>	568606	59
<b>UMshwathi</b>	93052	10
<b>uMngeni</b>	76354	8
<b>Mkhambathini</b>	69503	7
<b>Richmond</b>	63602	7
<b>Mooi Mpofana</b>	53435	8
<b>Impendle</b>	31757	8

*Source: Department of Local Government and Traditional Affairs, 2006.*

Over half of the population in Umgungundlovu Health District lives in Umsunduzi local municipality hence most of the study sites for this research were located in this municipality. The other local municipalities combined comprised nearly the same size of population. The number of households is estimated to be between 240 000 to 260 000. About 48% of the households (115 500) live in poverty (Umgungundlovu Municipality, 2006).



**Figure 2: Population Pyramid of KwaZulu-Natal Province in 2001**

*Source: Annual Report Department of Health KZN 2002*

The age-sex distribution in UMgungundlovu Health District is similar to that depicted in the population pyramid of KZN, which is typical of a developing or low income country. The target population for this study was adults between 18 and 70 years of age.

The budget allocation in 2009/10 financial year for Umgungundlovu Health District was approximately R1.6 billion, an amount required to cater for 8 hospitals and 42 clinics (District Health Expenditure Review, 2010).

### 1.1.3 Statement of the Problem

New adult TB patients on the six month first line TB treatment regimen have poor treatment outcomes, a factor which impacts adversely on the proportion of TB cases being cured in Umgungundlovu Health District.

### 1.1.4 Research Questions

- a. Why is the proportion of TB cases completing treatment low in new patients receiving TB treatment for six months in Umgungundlovu Health District?

- b. What are the non-health system related barriers to patient adherence to TB treatment in this area?

### **1.1.5 Purpose of the Research**

The purpose of the study was to investigate non-health system related factors that lead to poor TB treatment outcomes in Umgungundlovu Health District in 2010.

### **1.1.6 Specific Objectives of the Research**

The specific objectives of the study were:

- 1) To identify those non-health system factors that contribute to poor treatment outcomes in TB patients;
  - To describe the socio-demographic characteristics of these patients;
  - To assess patients' knowledge of and attitudes towards TB and TB treatment; and
- 2) To determine the extent of support received by patients on TB treatment;

### **1.1.7 Assumption Underlying the Study**

Non-health system factors contribute to successful or unsuccessful treatment outcomes in patients on ambulatory TB treatment, independently of the quality of the TB management programme.

This study will provide service providers and health planners with information that will assist in the re-design and improvement of the prevailing six-month ambulatory TB management services. It will further serve to allocate resources efficiently and equitably. It will also generate other useful research topics.

### **1.1.8 Operational Definitions Used in the Study**

New case:

A patient who has never had treatment for TB or who has taken anti-tuberculosis drugs for less than four weeks (WHO, 2003).

Treatment Outcome:



Treatment outcomes include bacteriological cure: patients with a positive smear or culture before treatment and negative bacteriological results at the end of TB therapy. It includes endpoints such as cure, treatment completion, treatment failure, default and interruption (WHO, 2003).

#### Bacteriological Cure:

Such a phenomenon concerns patients with a positive smear or culture before treatment and negative bacteriological results at the end of their therapy (WHO, 2003).

#### Treatment Completion:

Patients who complete treatment without bacteriological proof of cure or failure (WHO, 2003).

#### Treatment Defaulter:

The World Health Organization defines a TB treatment defaulter as a patient whose treatment was interrupted for two consecutive months or more (WHO, 2003).

#### Treatment Interruption:

A patient who interrupts treatment for two weeks or more, and returns to the health service with smear-positive sputum (sometimes smear negative but still with active TB, as judged on clinical and radiological assessment) (WHO, 2003).

#### Treatment Failure:

Patients who fail to achieve bacteriological conversion within five months after commencing treatment, which become smear or culture positive again during treatment after previous conversion, or who are identified with multi drug-resistant TB (WHO, 2003).

Adherence:

The extent to which a person's behaviour relating to the taking of medication, following a certain diet and/or success in executing lifestyle changes corresponds with agreed recommendations from a health care provider (WHO, 2003).

Multidrug Resistant Tuberculosis (MDR-TB)

It is defined as a specific form of TB that is resistant to the two most powerful first line anti TB antibiotic drugs, namely, isoniazid (INH) and rifampicin. MDRTB is a laboratory diagnosis of resistance of the *Mycobacterium tuberculosis* to INH and rifampicin (WHO, 2006).

### **1.1.9 Organisation of the Report**

This dissertation is divided into six chapters.

Chapter one provides an overview of TB treatment and cure in South Africa and in the Umgungundlovu Health District with special reference being devoted to non-health system related factors that contribute to successful or unsuccessful TB treatment outcomes. This chapter outlines the research setting, research questions, main objectives and purpose of the study. This chapter also provides definitions of concepts used in this research and report.

Chapter two outlines the body of knowledge related to TB treatment outcomes and highlights the particular risk factors associated with poor TB treatment outcomes. Information is derived from empirical research reported in the literature.

Chapter three describes the methods used in this research study. The study design, study population, data sources, sampling methods, variables and statistical analysis applied in this study are further explored in this chapter. The reliability and validity of the study and handling of bias and limitations are also described.

Chapter four focuses on the results of the research study. The overall study population concerns the cases that yielded poor TB treatment outcomes due to non-

adherence to TB treatment compared to controls that had successful outcomes. Risk factors associated with low TB cure are determined.

Chapter five outlines the findings of the study and discusses these results in relation to previous studies and importance of these results for South Africa.

Chapter six provides recommendations and conclusions based on the results of the study.

#### **1.1.10 Summary**

TB remains a major contributor to the burden of disease profile in South Africa and poor TB treatment outcomes continue to undermine all the efforts to achieve a cure of 85% of new TB cases, the target as set by WHO. There are numerous reasons for this and they include many non-health system related factors.

## **2 CHAPTER 2: LITERATURE REVIEW**

### **2.1 Introduction**

The current TB control programme has not been able to achieve an annual 85% cure rate in Umgungundlovu Health District in KZN province. The proportion of TB cases cured per annum has been as low as 29% in the past, and it is currently at 58% per annum. Such a figure is typical of many low income countries for new cases receiving ambulatory care, instead of hospitalization. The recommended treatment protocol for newly diagnosed ambulant TB cases involves six months of TB treatment.

There are many who barriers to successful TB treatment outcomes and many of these are non-health system factors. This is supported by Atkins (2011) who states that a recent systematic review indicated structural factors, patient-related factors, the social context and health service related factors as important factors influencing treatment adherence and successful TB treatment outcomes.

In this literature review the contribution of non-health system related factors described in the literature was assessed. This study assessed a number of these factors and their interrelatedness, thus contributing to a holistic picture of the problem.

### **2.2 Purpose of Literature Review**

The purpose of the literature review was to establish the current extent of knowledge and awareness regarding non-health system factors that contribute to TB treatment outcomes, in order to draw inferences from empirical research.

### **2.3 Scope of Literature Review**

Literature assessing factors related to poor TB treatment outcomes in new adult patients receiving six-month TB treatment were reviewed. The purpose thereof is to determine non-health system related risk factors associated with poor treatment outcomes.

### **2.3.1 Sources of Literature Reviewed**

The PubMed database was searched for studies pertaining to risk factors related to TB treatment outcomes between 1990 and 2011 in new adult patients on six-months of ambulant TB treatment. The following search terms were used to access citations related to risk factors: “TB treatment outcomes”, “factors associated with non-adherence to TB treatment”, “effectiveness of DOT support”, “TB and HIV”. Library sources were also used to retrieve information on what is already known about the topic. It was also undertaken to identify the most appropriate theoretical framework to support the basis for this study.

### **2.3.2 Literature Reviewed**

#### **2.3.2.1 Tuberculosis Diagnosis and Treatment**

According to the Health Systems Trust (2008), the annual cure rate for new smear positive patients is regarded as the key indicator to assess a TB programme in a high-burden country. South Africa is working towards achieving the accepted WHO target of curing 85% of new smear positive TB cases.

The process of TB diagnosis includes the following procedure: the patient presenting with both TB signs and symptoms is examined at a primary health care clinic and asked to supply a sputum sample on two consecutive days. These samples are forwarded to a laboratory and the results usually become available in less than 48 hours. Only one of the above needs to record a positive result to confirm TB infection. (Department of Health, 2001).

If the smear result is indeed positive, the patient will receive counselling and be advised on the inherent benefits of participation in the TB control programme. If both sputum samples are positive, TB treatment is given immediately. Furthermore, an X-ray may also be taken, but the sputum tests may be enough to confirm the diagnosis (Department of Health, 2001).

According to Schaaf *et al.* (2009), TB can only successfully be cured if the full course of treatment, encompassing as much as six months duration of TB therapy is

completed. They further state that interruption of treatment is likely to enhance the development of multi-drug resistance, creating further complications in treating the disease, and can indeed be fatal.

The classic presentation of TB is characterized by several weeks extending to a period of months of chronic cough, weight loss, fatigue, fevers, night sweats and haemoptysis. *“Fever is a classically diurnal with an afebrile period early in the morning and a gradual rising temperature throughout the day, and culminating in a fever peak in the afternoon or evening. Nighttime defervescence is often accompanied by diaphoresis leading to drenching night sweats”* (Schaaf *et al.*, 2009).

“Physical examination is usually non-specific. Classic findings are pallor, cachexia, tachycardia and post-tussive crackles over the affected lung Treatment occurs in two phases “(Schaaf *et al.*, 2009).The intensive phase involves the provision of four different drugs in tablet form for five days a week, for a period of two months. To facilitate the process of swallowing, the new combination drug *Rifafour* has been introduced (rifampicin, isoniazid, ethambutol and pyrazinamide) (Schaaf *et al.*, 2009).

The second phase is the continuation phase, where two drugs are supplied to the patient for five days a week for a period of four months. First-time TB patients must be treated for six months but for those on repeat treatment the duration of therapy is longer (Department of Health, 2011).

Short course chemotherapy of six months duration, including rifampicin, at least provided in the intensive phase, can achieve a cure rate of 97 to 99%, and a relapse in less than 6%.

Vasankari *et al.* (2007) recognized that early diagnosis of TB and then providing effective treatment constitutes the key elements involved in the reduction of transmission of infection and the final achievement of the goal of the elimination of TB. They emphasize that treatment outcome monitoring forms a core part of surveillance necessary to succeed in tuberculosis elimination.

TB drugs like any other medication have side effects, which can be very severe, and may cause patients to default treatment. Nausea was identified as one of the serious side effects of TB treatment that requires emergency attention (Solis, 2011).

Schoenstadt (2006) states that occasionally, the medication used to treat tuberculosis may cause side effects. Some side effects cause minor problems; others are much more serious. The latter author states that serious side effects from TB medication may include, but are not limited to lack of appetite, and symptoms of nausea and vomiting. In the study conducted by Elbireer *et al.* (2011) the side effects of treatment (OR 5.5; 95% CI: 2.3–13.6), was highlighted as a factor contributing to treatment default.

In another study conducted by Munro *et al.* (2007), it was highlighted that complex regimens with potentially severe side effects cause non-adherence and poor TB treatment outcomes. This is further supported by Awofeso (2006) who asserts that anti-tuberculosis medication side effects were also found to be significantly associated with defaulting.

### **2.3.2.2 Tuberculosis Treatment Outcome**

There is a consensus among authors that TB treatment outcomes include being cured, completion of treatment, treatment failure, default or death of the patient. In a study conducted on factors determining the outcome of treatment of adult smear-positive tuberculosis cases in Gambia in 1994 and 1995, data was analysed on 1357 patients and treatment outcome was recorded as the following: cured, completed treatment, failed, defaulted or died (Lienhardt *et al.*, 1998).

In another retrospective study that investigated factors associated with poor treatment outcome in the Southern Region of Ethiopia from 2002 to 2007 a sample of 6547 patients was categorized as having successful (cured or completed) or poor treatment outcome (failed treatment, defaulted or died) (Munoz-Sellart *et al.*, 2010).

Findings by JhaUm *et al.* (2006) findings were that amongst the large number of re-treatment patients in India, default occurs early and often. Atkins (2011) argues that

adherence to TB treatment is a complex issue and it is closely connected with larger societal and historical forces. He draws a conclusion that adherence is therefore related to social inequalities and their impact on health and health care.

Extensive research has been conducted on TB treatment outcomes. However, most studies have focused on health systems issues. Unfortunately, very little attention has been devoted to non-health system related factors contributing to treatment outcomes, yet there are three groups of non-health system constraints in the management of TB. These include: patient related factors, which concern the inability to access health services, a disadvantage which is likely to increase treatment interruption; lack of household income, lack of money for food and transport; and perceived social stigma. Other factors include contextual factors and health system factors (Naidoo, 2006).

This is supported by Amuha *et al.* (2009) who state that non-adherence to treatment is a problem in tuberculosis management, similar to that applicable to other long-term illnesses. They argue that a number of factors associated with non-adherence have been cited in the literature. These include health system, condition-related, patient-related, socioeconomic and therapy-related factors.

The key to an effective TB control programme involves ensuring adherence to therapy. Adherence increases the likelihood of successful TB treatment outcomes including cure and reduces the risk of drug resistance, and is determined by a multiplicity of both internal and external factors (Wilkinson, 1997).

#### **2.3.2.3 Tuberculosis Treatment Outcome, Sex Age and Socio- Economic Status**

Authors have different views about the sex of the patient and treatment outcome. A prospective study conducted in England found that the risk factors for poor treatment outcome included being a male (Ditah *et al.*, 2006). Whereas a retrospective study conducted in South Africa, found that the proportion of women (64%) who did not adhere to TB therapy was higher than for men (36%) (Mashimbye, 2009). Another South African based retrospective study showed that successful treatment outcomes



were significantly associated with male patients (Odour, 2006). Findings of a case-control study conducted by Jhaum *et al.* (2006) in India in 2006 revealed that defaulters were more likely to have been male (OR 1.4; 95% CI: 1.2-1.7). Findings of another retrospective study, which reviewed TB patient records in Effia-Nkwanta Regional Hospital in Ghana in 2001, revealed that default from treatment was also significantly associated with the male gender (Dodor, 2004).

In yet another study, multivariate analysis showed that the males were a predictor of a negative treatment outcome, after controlling for other significant socio-demographic and health related variables. (Bashour *et al.*, 2003). The findings of the study by Dooley *et al.* (2011) state that male sex, and substance use, appeared to be the principal risk factors for default.

Another interesting finding of a study conducted in Yemen, concerned the fact that the role of male relatives positively influences treatment outcomes for female patients (Date *et al.*, 2005). Such a fact highlights the complex role which a specific variable such as sex could of itself, form the framework for further research. The results of the study by Gupta *et al.* (2011) highlighted that PTB was significantly more common in male patients and unemployed people.

Age does not seem to affect TB treatment outcomes. Findings of a retrospective study conducted on adults infected with TB in the United States between 1993 and 2008, involving 250 784 participants, revealed that older patients who were on TB therapy, had similar treatment outcomes to those of younger adult TB patients (Pratt *et al.*, 2011). Age had no bearing on the treatment outcome. I

In a case-control study on new smear-positive pulmonary TB patients conducted by Pakasi *et al.* (2009) the prevalence of malnutrition and being unemployed were very high among TB cases. Socio-economic status also affects a person's access to effective healthcare in Ireland (Luddy, 2007). Socio-economic status would have a negative impact on the TB treatment outcomes, as those who are poor have less chances to adhere to TB therapy because of out of pocket expenses to cover transport and food.

Findings of a cohort study of 727 new TB cases between 2004 and 2009 conducted in Morocco revealed that a low income level remained significantly associated with treatment failure TB (OR 3.2; 95% CI: 1.1-9.3) (Tachfouti *et al.*, 2011).

Findings of a retrospective study conducted in Zambia in 2001 on 202 adult patients with pulmonary TB demonstrated that existing financial constraints and additional unrecognized patient costs, including special food expenditure, and travel distances served as barriers to a successful TB treatment outcome (Needham *et al.*, 2004).

A study conducted by Ogboi *et al.* (2010) revealed that most of the patients presenting with tuberculosis are in the economic productive age with unemployment and low literacy level being potent risk factors for tuberculosis.

In a case-control study on new smear-positive pulmonary TB patients findings showed that the prevalence of both malnutrition and being unemployed ranked very high among TB cases (Bumburidi *et al.*, 2006).

Findings in another study highlighted homelessness, migration, alcohol and drug abuse, previous incarceration, unemployment, and urban residence as risk factors that lead to poor treatment outcomes (Greene, 2004). The findings of the study by Muniyandi *et al.* (2008) also highlighted an association between TB and poverty, in terms of income, standard of living, house type and social class.

There is yet further evidence to support the notion that the patient's perspective, including socio-economic status and cultural environment, is an important consideration affecting the success of tuberculosis control programmes. Barriers to the completion of long-term treatment regimens include socioeconomic status, the health system and the condition itself (Garner *et al.*, 2007).

This is further supported by Hargreaves *et al.* (2011) who state that TB cases continue to cluster among disadvantaged groups such as the poor and the hungry. They further state that National TB incidence rates appear more closely correlated with social and economic determinants such as the human development index, access to water and sanitation (Hargreaves *et al.*, 2011).

A similar observation was made by Cosgrove (2007) who demonstrated that poverty has an important influence on health and despite continuing economic growth, poverty and health inequalities persist. Needham *et al.* (2003) state that within poor resource settings, patients face financial constraints specifically related to travel distances and transportation costs, which create a significant burden on patients.

Findings of a study conducted in South Africa also highlighted that deteriorating socio-economic conditions among already vulnerable populations is an important barrier to effective TB control (Weyer *et al.*, 2007). Day *et al.* (2009) refer to the accompanying social environment which includes housing conditions, and rural versus urban settings. They state that deprivation is, however, concentrated in specific areas within the country and is correlated with ill health. Poverty is reported as a contributor to non- adherence to TB treatment (Day *et al.*, 2007).

Sachdeva (2011) argues that it is not clear as to what extent these differences result from biological factors and socio-cultural contexts. The literature, however, suggests that an overemphasis of cultural difference without further exploration of other social dimensions of health care delivery can obscure a practical understanding of relevant factors related to treatment outcomes. These include the hidden costs of treatment, poor access to care, ethnic discrimination, and prior poor treatment furnished by the health system.

This argument is strengthened by a further study on adherence to tuberculosis treatment conducted in 2002 in India. Here, the argument is postulated that the reasons for default stem primarily from a poor correlation between patient and programme needs and priorities, and from characteristics of the disease and its treatment (Jaiswal *et al.*, 2003).

#### **2.3.2.4 Tuberculosis Treatment Outcome and Level of Education**

A meta-analysis of studies identified illiteracy as a confounding variable associated with treatment outcomes (Munro *et al.*, 2007). It can be asserted that lack of education does not hinder patients from receiving both a TB diagnosis and treatment. However, the traditional perceptions of illness may cause a longer

diagnostic delay among illiterate patients, as patients may perceive such illness as being of supernatural causation.

Cheng *et al.* (2005) showed that lack of education and distance from home to a township health centre were significantly associated with delay in seeking care from service providers. This is further demonstrated by a prospective cohort study conducted in South Africa, which found that illiterate patients were more likely to interrupt treatment (Mashimbye, 2009).

#### **2.3.2.5 Risky Social Behaviours: Alcohol, Smoking and Drug Abuse and Non-adherence to Tuberculosis Treatment**

Findings of a four year retrospective study that was conducted in Switzerland based on a computerised database and a review of medical records for 252 patients, revealed that alcohol abuse (OR 21; 95% CI: 2-288) and smoking were associated with unsatisfactory outcomes, and was also significantly associated with cavitary pulmonary TB (Kherad *et al.*, 2009).

Findings of a cross sectional study conducted on 153 268 TB cases from 1997 until 2006 in the United States showed that there was a significant association between drug and alcohol abuse and treatment failure (Oeltmann *et al.*, 2009). A retrospective study conducted in Kasturba Hospital in South India also highlights smoking and alcoholism as risk factors for poor TB treatment outcomes (Gupta *et al.*, 2011).

The study by Dujaili *et al.* (2007) further reaffirms that tobacco smoking is a predictor of poor TB treatment outcomes. The findings of the study by Kherad *et al.* (2009) confirm that smoking appears as a possible risk factor.

According to Gelmanova *et al.* (2007) in a multivariate model, substance abuse was identified as the only factor that was strongly associated with non-adherence with an odds ratio of 15 (95% CI: 4–70).

This is further supported by Creswell's (2011) findings that alcohol and injection drug use were the only independent risk factors for non-adherence and default that we identified. These findings echo those of numerous previous studies that found

substance abuse to be the single major factor associated most strongly with non-compliance with TB regimens and resulting poor TB treatment outcomes.

Dodor (2004) states that despite the clear need for new approaches to this problem, and to date there has been relatively little research on those treatment options for patients with chronic infectious diseases and who practise concomitant substance misuse.

### **2.3.2.6 Tuberculosis and HIV and AIDS**

The HIV epidemic has significantly increased the incidence of TB, in high prevalence and poor resource settings. “The concomitant epidemics of HIV and tuberculosis present a major public health problem in South Africa” (Abdool Karim *et al.*, 2007).

Findings of a meta-analysis conducted in 2006, which focused specifically on long-term adherence to TB treatment, revealed that TB and HIV present a particular challenge to adherence. Both are chronic infectious diseases that mainly affect the most vulnerable populations in terms of their being disadvantaged and the fact that they involve complex treatment regimens (Munro *et al.*, 2007).

A retrospective study conducted in KwaZulu-Natal, showed a high uptake of HIV testing for TB patients. The study reported HIV testing uptake on a monthly basis. More than 80% knew their HIV status (Wallrauch *et al.*, 2010). However in another cross-sectional study conducted in the Free State Province only a third (32%) of TB patients had not undertaken HIV testing, due to a combination of individual related factors, and also health systems limitations including non-offer of HIV testing (Kigozi *et al.*, 2011).

This outcome is echoed by the findings of the study conducted in Spain by Diez Ruiz-Navarro *et al.* (2005) who showed that the outcome for tuberculosis treatment greatly deteriorates in those living with HIV. Abdool Karim *et al.* (2004) argue that with the high rates of HIV co-infection (60%), the impact of HIV on outcomes of these patients is substantial.

This was also confirmed by Schaaf *et al.* (2009) who found that in southern African countries, where HIV prevalence is highest, more than half of new TB cases are living with HIV. In South Africa this was corroborated in a study that showed that HIV associated TB- co-infection was approximately 55% in 2002 (Gasa, 2009).

Heysell *et al.* (2010) contend that those living with HIV (PLHIV) are prone to malabsorption and are at higher risk for low drug levels. This is echoed by Nahid *et al.* (2007) who state that PLHIV- were significantly more likely to develop drug resistance (4.2% in HIV-infected versus 0.5% in HIV-uninfected) to rifampicin, and to experience adverse reactions to TB treatment regimens.

Findings of a retrospective study of 700 patients with TB, conducted in San Francisco from 1990 to 2001, revealed that TB relapses were found to be significantly higher in people living with HIV on a standard six-month therapy compared to those HIV-uninfected patients. According to the authors, the current TB treatment guidelines do not distinguish between those infected with HIV and those who are uninfected, in terms of the length of treatment. They argue that a standard six-month therapy may be insufficient to prevent relapse TB associated HIV (Nahid *et al.*, 2007).

Results of a South African based article review Naidoo *et al.* (2007) also showed that treatment interruption rates are much higher in patients living with HIV who have TB than HIV negative patients. This is likely due to the burden of co-infection.

Sebastino *et al.* (2009) state that the immune recovery associated with antiretroviral therapy (ART) results in dramatic clinical benefits. They still believed that using ART might not be appropriate during the first weeks of anti-TB therapy in HIV-infected patients due to immune reconstitution problems (Sebastino *et al.*, 2009).

Initiation of ART during anti-TB treatment can lead to immune reconstitution disease (IRD) manifested as worsening of symptoms and signs or appearance of new TB lesions. The majority of cases have been reported to occur within the first two months of ART (Schaaf *et al.* 2009).

On the contrary Lonnroth *et al.* (2009) state that ART reduces risk of poor TB treatment outcomes in patients living with HIV. This is further supported by Nahid (2007) who found that the use of ART during TB treatment was associated with a faster *Mycobacterium tuberculosis* negative culture conversion, and an improved survival.

### **2.3.2.7 Tuberculosis Treatment Outcome and Directly Observed Therapy**

Treatment success achieved in the 2005 Directly Observed Treatment (DOT) cohort yielded over two million patients scoring 84.7% success on average; close to the 85% target. Global targets for TB control refer to treatment success for new smear-positive cases treated under DOT (WHO, 2006).

In a study conducted by Dudley *et al.* (2011) in South Africa it is reported that community health worker support contributed to better TB control programme performance than an approach based exclusively on health facilities.

Findings of a study evaluating directly observed therapy for tuberculosis in KZN in 2009 revealed that districts that had received high DOT coverage had recorded better cure rates (Ntshanga *et al.*, 2009). The findings of a controlled trial on DOT, conducted in Thailand on 836 patients diagnosed in 1998, were in agreement with above findings (Kamolratanakul *et al.*, 1999).

According to a WHO report treatment success rates tend to be lower in patients without DOT support and those on self-administered therapy (SAT) than those for new cases treated under DOT (WHO 2008). This is echoed by Jasmer *et al.* (2004) who reported that levels of cure was significantly higher in those treated by DOT compared those on self-administered therapy. (98% vs. 89%,  $p < 0.002$ ).

Conversely the findings of the study conducted in South Africa by Zwarenstein (1998) suggest that treatment for tuberculosis was more successful among self-supervised patients (60% of patients) than among those on DOT (54% of patients).

Garner *et al.* (2007) argues that models that involve either family or community members provide an opportunity to tackle existing social and family barriers contributing to poor TB treatment outcomes, including encouraging family members to complete treatment. There was also a strong association between the frequency of DOT support and TB treatment outcome.

Hargreaves *et al.* (2011) confirm that DOT has significantly reduced TB morbidity and mortality, and remains one of the most cost-effective public health interventions ever implemented, although findings of a study conducted in Nepal indicated that community DOT and family-member DOT achieved success rates of 85% and 89% respectively (Newell *et al.*, 2006).

A cluster randomised trial conducted in Senegal found that decentralization of treatment and patient choice of DOT supporter led to improvement in patient outcomes compared to the usual TB control procedures (Thiam *et al.*, 2007). A South African based study also found that DOT was 2.8 times cheaper to deliver than the conventional treatment (Floyd *et al.*, 1997).

### **2.3.2.8 Multidrug Resistant Tuberculosis (MDRTB)**

A South African based case-control study has investigated both favourable and unfavourable outcomes, in order to compare determine which factors, lead to better adherence to MDR-TB treatment. The study conducted by Moodley *et al.* (2011) in KZN highlighted the fact that 20% of patients had cultures positive for MDRTB. Sturm (2010) states that, the number of MDR per 100 new cases is 14.8 in Umgungundlovu Health District.

Results of a systematic review indicate that TB treatment outcomes were substantially worse in the presence of initial drug resistance (Lew *et al.*, 2008). Consensus among authors is that the low levels of treatment success, has resulted in an increasing MDR-TB burden. The appearance and growth of resistance to anti-tuberculosis drugs threatens the success of the tuberculosis DOT programme and the ART distribution programme (Abdool- Karim *et al.*, 2009).



A retrospective 10 year review of patients diagnosed with MDR-TB conducted in Victoria found that the number of patients diagnosed with MDR-TB increased, and if sustained, the increase will have important implications for public health policy and planning (Lavender *et al.*, 2009). Brust *et al.* (2011), in another study, revealed that 80% of MDR-TB patients were HIV co-infected. Another study conducted by Kliiman *et al.* (2009) highlighted that one of the risk factors for poor treatment outcome in MDRTB was HIV infection.

#### **2.3.2.9 Knowledge, Beliefs and Practices of TB Patients**

The literature shows that patients' knowledge of TB has been assessed previously, including knowledge of signs and symptoms of TB, mode of transmission and TB drugs. Findings of a cross-sectional study conducted in Vietnam revealed that sex; occupation, economic status, education and sources of information were significantly associated with level of TB knowledge (Hoa *et al.*, 2009).

Previous studies have also investigated use of contemporary and alternative medicine during TB therapy. Findings of qualitative research conducted in Zambia highlighted that patients often consider the advice of respected individuals and use of herbal self-treatment of their symptoms. TB patients paid the equivalent of 10% of their monthly income for consultation with a traditional healer, while others tried self-medication with drugs from a local pharmacy (Needham *et al.*, 2003).

In sub-Saharan Africa, traditional healers outnumber medically qualified doctors eighty-to-one. It also remains a region in which most people turn first to traditional healers on becoming ill. Traditional healers also usually provide immediate treatment, whereas clinics may have lengthy waiting lists and eligibility criteria tests (Hsiao *et al.*, 2003).

A quarter of the patients in KwaZulu-Natal consulted a traditional healer sometime during their illness and once they knew they had TB. Sixteen per cent of the patients went to a traditional healer as their first choice of care. Of those who went to a traditional healer, 72% were male (Loveday *et al.*, 2007).

### **2.3.2.10 Conceptual Framework**

Bandura's Cognitive Social Learning Theoretical framework was used to explain adherence behavior in this study. Munro *et al.*, (2007) argue that theories play a role in the design of behavioural change interventions by promoting an understanding of adherence behaviour.

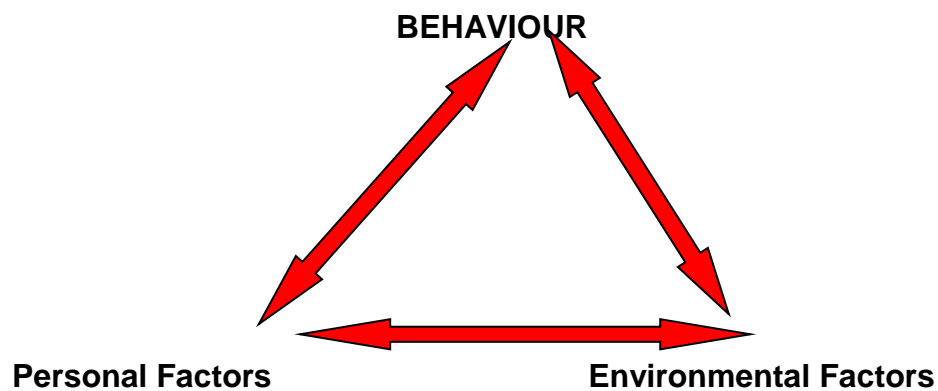
Bandura (1986) argues that human behaviour is learned observationally through a process of modeling. One forms an idea as to the means whereby new behaviours are developed, derived from observing other actors. Furthermore, such coded information serves as a guide for action (Bandura, 1986).

According to Bandura (1986), observational learning incorporates four components: attention, retention, motor and motivational processes that help to understand why individuals imitate socially desirable behaviour.

He further suggests that other factors involved herein are the influence of social groups, and the structural arrangement of human interactions. Retention processes deal with the ability to remember the observed model, as well as mentally organizing and rehearsing the particular behaviour concerned. Motor reproduction comes through trial and error, observation of behaviour or skill (Bandura, 1986).

The latter author states that motivational processes explain why people usually enact those behaviours that seem to be effective tools for other people. There exists a greater inclination to adopt modeled behaviour if it results in outcomes which are valued, rather than if it results in unrewarding or punishing effects (Bandura, 1986).

Bandura argues that people operate cognitively on their social experiences. These conditions then influence behaviour and development. The influences of behaviour, namely individual, cognitive, and environmental factors determines how people both interact and learn from each other. Human behaviour is explained as a dynamic and correlated interaction between the person and the environment (Bandura, 1986).



(Cognitive, affective, and biological events)

**Figure 3: Conceptual model**

*Source: Boeree & George, 2008*

One of the main tenets of Bandura's theory is that personality is an interaction between three factors: the environment, behaviour, and a person's psychological processes.

According to this particular theory, people are definitely not driven by inner forces nor are they automatically shaped and controlled by external stimuli. Such an argument is very relevant in relation to the investigation into contributory factors leading to TB treatment outcomes.

As a result the proposition demonstrates that internal motivation to adhere to treatment is not in itself a sufficient factor to produce a cure. Internal motivation in some patients may be sufficient. However, in others, it may well be overshadowed, or even eroded, by external circumstances and social contexts. It is on the basis of this theory that the study attempted to investigate those multiple factors that influence TB treatment outcomes.

The above notion is also supported by Benson's Behavioural model as cited by Bandura (1986). The assumption of this model is that human behaviour is a product of multiple dynamic factors that develop synergistically in combination with genetic,

psychological and environmental vulnerabilities. Predisposing factors include personality and coping style.

#### **2.3.2.11 Summary**

This chapter presented the findings of previous studies that have relevance and significance to the study that has been conducted. The common trend was that most of the studies were retrospective observational studies. This is similar to the research design used in this study and has sound scientific basis. It remains appropriate to highlight factors associated with poor TB treatment outcome. Similar non-health system related factors have been identified as affecting TB treatment outcomes, regardless of the country wherein the study was conducted.

Although the emphasis on the majority of the studies was on health systems performance in relation to TB treatment outcomes, some of the studies highlighted non-health system factors were identified in this particular study. These include significant association between low socio-economic status and non-adherence to TB treatment. Other factors include smoking, alcohol, and drug abuse. Other significant factors identified were HIV infection, MDR-TB and DOT support.

The limitation of these studies is the tendency that exists of investigating different factors in isolation, for example examining factors such as drug abuse, culture or poverty, independently of other variables. Such research might answer the question as to why some patients exposed to a similar social milieu can still be cured, whilst others are not. Further analysis will also be facilitated in understanding how these contributory variables interplay to result in either a favourable or an unfavourable outcome.

The study also draws from the theoretical framework as it has used Bandura's cognitive, social learning theoretical model to assess patient related factors that contribute to TB treatment outcome. Relevant terms were defined in this chapter.

### **3 CHAPTER 3: METHODS**

#### **3.1 Introduction**

The resurgence of TB combined with low levels of cure in Umgungundlovu Health District warrants an in-depth investigation into non-health system related factors that contribute to poor TB treatment outcomes. This study explored the following relevant issues: demographic characteristics, socio-economic status, harmful social behaviours, immunologic and pathological characteristics, DOT support programme, and the health seeking behaviour characteristics of new adult TB patients who have been exposed to six-month TB treatment.

In this chapter, the type of research undertaken and the study design are outlined. The chapter further describes the study population, sampling strategy, data sources, data management, statistical methods and analysis, as well as bias and limitations of the study design and findings.

#### **3.2 Type of Research**

This study was an epidemiological research study.

##### **3.2.1 Study Design**

An observational analytical study using a case-control design was used. This study design was appropriate for the primary objectives as it provided comprehensive data on the cases that had poor TB treatment outcomes and who had not completed six months of therapy in the six-month period, since their period was prolonged beyond six months because they had either interrupted or defaulted treatment, and returned to the health system for further management with or without smear positive result upon their return. According to WHO (2003) the endpoints of treatment outcome include cure, treatment completion, treatment failure, interruption or default. These cases that interrupted or defaulted TB treatment were judged to be having active TB clinically and by radiological examination. These were thereafter compared with those controls that had indeed had successful completed six months of treatment in the prescribed time.

The study quantified the extent of non-health system- related factors affecting poor TB treatment outcomes by investigating are factors that could contribute to this. The study will provide service providers and planners with information that will help them design TB control programmes and allocate resources efficiently (Katzenellenbogen *et al.*, 2002).

### **3.2.2 Study Setting**

The study was conducted in the primary health care facilities in Umgungundlovu Health District in KwaZulu-Natal.

### **3.2.3 Target Population**

The results of this study could be generalized to new adult TB patients who received six-month TB treatment in other districts in South Africa, which are similar to the Umgungundlovu Health District in KwaZulu-Natal.

### **3.2.4 Study Population**

The study population constituted the entire aggregate of TB patients both those who had completed their ambulatory TB therapy within the prescribed 6-month period. The accessible population for the study comprised those TB patients who were attending the local health facilities and were conforming to designated criteria as participants of the study.

#### **Inclusion criteria:**

The study included adult patients (18 years and above) who were diagnosed with pulmonary tuberculosis (PTB) in a health facility and, therefore, would have had the opportunity to complete a six-month course of TB treatment on an ambulatory basis. Patients who had completed six months of treatment within the time period constituted the controls.

The cases were those who had started treatment but had either interrupted or defaulted therapy and failed to complete six months of therapy within the time period

and were re-introduced back to the health system and therefore were unable to finish TB treatment within six months. Those who interrupted treatment had not taken TB treatment between two weeks to one month, and those who defaulted had not taken TB treatment for two consecutive months or more' Cases and controls were obtained from the local TB registers in the clinics of the same district population of UMgungundlovu Health District during the study period.

### **Exclusion criteria:**

Hospitalized TB patients were excluded from the study. Although this was a captive population, hospitalized patients were not representative of the reference population due to a number of factors. Hospitalized patients may not necessarily be residing in Umgungundlovu Health District because of the occurrence of a cross boundary flow of patients having been referred from EThekweni, Thukela, UMzinyathi and ILembe Districts. Many hospitalized patients may be more ill than those who are on ambulatory treatment, and the administration of TB treatment in a hospital is very different from what pertains in a clinic. Therefore, factors relating to completing therapy timeously would be different in hospitals, from those in primary health care settings.

### **3.2.5 Sampling**

### **3.2.6 Sampling Method**

Multistage sampling was conducted.

1. The first stage of sampling involved the selection of 15 out of a total of 42 clinics. Clinics were categorized as urban, semi-urban and rural. Urban clinics are those situated in a settlement that is legally proclaimed within a municipal or local authority boundary as urban, and they have formal, informal and other facilities built according to municipal by-laws. Semi-urban clinics are situated in an area that is not part of a legally proclaimed urban area, but adjoins it. Rural clinics are part of the area that falls outside of legally proclaimed urban areas, and include commercial farms, small settlements and rural villages (Census 96).

A proportional random sample of each category of clinic was selected so that there were a total of 15 clinics. This ensured a balance of urban, semi-urban and rural clinics. The study sites randomly selected were: Ashdown Clinic, Caluza Clinic, East Boom Community Health Center (CHC), Imbalenhle CHC, Gomane Clinic, Mafakathini Clinic, Mpumuza Clinic, Ndaleni Clinic, Ntembeni Clinic, Nxamalala Clinic, Pata Clinic, Richmond Clinic, Sondelani Clinic, Songonzima Clinic and Taylor's Clinic. Selecting 63% of the clinics (15) from a total of 42 clinics would allow for an adequate sample size required for the study, and it was based on the estimated population that is served by these clinics in Umgungundlovu Health District.

2. The second stage of sampling involved a probability proportional to size random sampling of TB patients and who were new smear positive cases, within those selected clinics. An unmatched control on a one to one basis was selected from each clinic register. The selection was done consecutively. Cases were selected first and the next immediate patient who completed treatment functioned as the control. The next person listed on the TB register who had not completed six months of therapy was selected as the next case until the required sample population was available.

### **3.2.7 Size of Sample**

A biostatistician was consulted before undertaking the study to give guidance as to sample size, and the power of the study. There was no existing data to calculate sample size. However, based on the assumptions and established trends that Umgungundlovu Health District has the second highest number of TB patients, and the fact that the proportion of cases cured is low. There were 3913 TB patients on the TB registers at the beginning of this study in the 15 selected clinics. The highest proportion was in bigger clinics that serve a larger population. The study size was set at 300 cases and 300 controls to control for at least 10 confounding factors.

The sample size calculations were based on a cure of 35% in Umgungundlovu Health District, and a minimum detectable odds ratio of 1.5. The power of the study



was 80% and the confidence interval 95% to ensure statistical and clinical significance.

The study thus comprised 600 participants; 300 cases, and 300 controls randomly selected from the facilities' TB registers. Cases involved those patients with new smear positive pulmonary tuberculosis commenced on the full six-month course of treatment, but who interrupted or defaulted their TB treatment and who failed to complete TB treatment in the prescribed 6-month treatment period. These patients were identified as cases when they presented back to the health system usually as a result of being tracked by the TB tracing teams. These patients would have had a chance to complete TB therapy in six months, however they had interrupted or defaulted which meant that had to re-enter the system, and thus prolong therapy beyond six months period.

The controls were identified at the point where they had completed six months of therapy within the time period without interrupting and defaulting and were sputum smear-negative at the end of the six-month treatment period.

### **3.2.8 Data Sources**

### **3.2.9 Measurement Instruments/ Data Collection Techniques**

The measurement instrument used was a structured questionnaire administered by 12 trained fieldworkers. The questionnaire covered a broad spectrum of areas and these included the demographics of the participants, their socio-economic status, risky behaviours like alcohol, smoking and drug abuse, DOT support, HIV status, physical condition during treatment as well as knowledge, attitudes and practices of TB and TB treatment. The questions were structured to determine non-health system factors associated with treatment outcome, which was either completion of treatment within six months, with a smear negative result or interruption or default resulting to failure to complete treatment within six months, and the reasons thereof.

Fieldworkers were trained by the researcher.

### 3.2.10 Data Abstraction

Patients themselves were the primary sources of data in this study. Data was obtained from them at the time that they completed the six months period when treatment was completed or should have been completed. However, clinic based TB registers were used to select patient samples as well as patient records, which were used to confirm susceptibility profiles and treatment outcomes.

Twelve field workers collected data by means of a structured questionnaire. Fieldworkers were trained to ask the questions in a uniform manner throughout, thus minimizing inter- and intra-investigator variation. Questions were administered in both English and *isiZulu* to cater for those participants who preferred to be asked in *isiZulu*. Interviews were conducted in the 15 selected clinic sites. Cases were presenting back to the health system on a continuous basis through the Defaulter Tracing Teams, and some came back on their own as their condition was getting worse. Data collection took place over a period of ten months.

Field workers were trained intensively to adhere to ethical procedure, especially relating to questions of anonymity and confidentiality, as well as concerning the rights of participants, data collection and handling. Supervision and periodic checks were performed by the principal investigator.

### 3.2.11 Data Handling

A quality check at the site was done by field workers with the assistance of operational managers of the study sites and errors were corrected on the document by the researcher.

Questionnaires with recorded responses from participants were checked for completeness. Data was recorded onto a data form, accompanied by the corresponding identification numbers for cases and controls. Quantitative data was first aggregated manually to screen for completeness of data and for identification of outliers. The hard copies of the questionnaires containing patients' responses and all data sheets were locked in a safe place to ensure confidentiality.

Data was entered electronically from the questionnaire onto a database (Dataset 1) Errors were corrected. Data was cleaned for missing data, inconsistency, and typographic error. Entered data was then summarize and prepared for analysis (Dataset 2)

Dataset 1 and Dataset 2 were validated by the data capturer and the researcher through the checking of source documents to ensure correct entry. Electronic data was safeguarded by using only one computer and the password was only known by the Principal Investigator.

### 3.2.12 **Variables**

Exposure variables fell into two categories as follows:

#### **Numerical Variables (Quantitative variables)**

- Discrete numerical variables. – Taxi fare
- Continuous numerical variables – Income
- Binary variables- Sex, marital status, employment status
- Ordinal variables, which follow a natural order - educational level completed: no education, / grades completed / Tertiary education etc.

Examples of variables that were measured included access to a health facility in terms of distance and financial access, access to TB therapy in terms of distance to the clinic, DOT support, level of knowledge of signs and symptoms and understanding of TB in terms of the information that is made available to the community through various sources and forms of media, mode of transmission, knowledge of drugs, adherence (obtained both from self-report of patients and TB register), socio economic status, and the perception of quality of care received from health care providers, including experiences of patients in a health facility during treatment.

### **3.2.13 Validity of Data Sources**

#### **3.2.13.1 Internal Validity**

The study was piloted at Edendale Hospital Gateway Clinic in Umgungundlovu Health District on a sample of 10 TB patients to ensure that what was being asked made sense <sup>1</sup>(Face validity). Content validity was also ensured by asking similar questions in different ways at different places in the questionnaire. The variables tested were constructed in a simple language. The questionnaire was also provided in *isiZulu*.<sup>2</sup>

### **3.2.14 Bias and Limitations**

#### **3.2.14.1 Selection Bias**

This was unlikely to be a problem in this study as clinics were randomly selected to be representative of all the clinics in the health district. Cases and controls were selected consecutively at the selected clinics. The controls were selected from the same population that produced the cases.

#### **3.2.14.2 Information Bias**

The interviewer, being aware of the identity of cases and controls, could have unconsciously probed further among cases, seeking a positive association. The interviewers were trained to avoid probing, and if not avoidable to be consistent in asking questions to all participants throughout the interview process.

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<sup>1</sup>The pilot study enabled the researcher to modify the questionnaire to ensure content validity

<sup>2</sup> The majority of patients who participated in the study were Africans, hence the importance of having a questionnaire in their own language.

Misclassification was minimized through the proper training of interviewers. Data was carefully checked for inaccuracies. Differential and non-differential misclassifications were reduced throughout all stages of the research. During sampling participants were categorized correctly into cases and controls. Completed questionnaires were numbered from one to 300 for each group and labeled as either cases or controls. Data entries on the spreadsheet were done according to the two groups, namely cases and controls, and data analysis was done to compare the two groups thus minimizing measurement error. Data presentation on tables clearly distinguished the two groups. To prevent these sources of bias, extensive training of data collectors was undertaken, and biostatistician was consulted.

#### **3.2.14.3 Recall Bias**

To avoid selective recall among both cases and controls, prompts were used during interviews to stimulate accurate recall. Prompts were only used in the aspect of knowledge of participants in relation to signs and symptoms of TB, mode of transmission and knowledge of TB drugs. Patients who had received treatment within only a few months prior to the study were selected.

#### **3.2.15 Social Desirability Bias**

The study might have contained information bias as study participants might have furnished information that would impress the researcher, and not the reality which prevails in real situations. Examples hereof involved responses concerning alcohol intake, substance abuse, smoking and the use of alternative medicine. To reduce this bias, respondents were assured of anonymity, and advised that their responses were most useful if they reflected the true situation.

#### **3.2.16 External Generalisability**

External validity refers to the extent to which the results of the study can be generalized to and across populations. The size of the sample was adequate to ensure an 80% power, and a 95% confidence limit.

Results of this study are generalisable to the TB patient population in rural areas of South Africa, because the study was conducted in public sector clinics, which is how TB care is delivered to most TB patients in South Africa.

### **3.2.17 Confounding Factors**

The fact that each independent variable may act as a confounder when assessing the effect of each independent variable on the dependent variable on univariate and bivariate analysis was considered. These confounders included sex, age, geographical area of residence, distance from home to the clinic, level of education, socio-economic status, HIV status, MDRTB, smoking, drug and alcohol abuse, DOT support and use of alternative medicine during TB treatment. Adjustment for confounding variables was achieved by using multivariate analysis to control for confounding effects.

### **3.2.18 Statistical Considerations**

### **3.2.19 Descriptive Methods**

Data were abstracted to Microsoft Access 2007 database, and thereafter imported into Microsoft Excel and SPSS version (PASW Statistics 18) for cleaning of data summarizing the data into basic frequency measures.

### **3.2.20 Analytical Methods**

Univariate, bivariate and multivariate analyses were conducted. Univariate analysis of socio-demographic variables, as well as of adherence and other outcomes were done in order to describe the data. Bivariate analyses were performed to test associations between TB outcomes and socio-demographic variables, and other independent variables using Chi square.

The significance level was set at  $p < 0.05$ . Odds ratios and 95% confidence intervals were calculated. A non-parametric (Mann-Whitney) test was used to analyse quantitative variables, which were not normally distributed as relates to distance from home to clinic and cost of a taxi fare between home and the clinic.

Multivariate analysis was performed to test the confounding effect of variables of interest, using cured/not cured of TB as the dependent variable. Standard logistic regression model incorporating an indicator variable in the model corresponding to each case- control set was used (Kirkwood, 2005).

Binary logistic regression analysis was performed in order to control for confounding while assessing the individual effects of the independent variables. For example, data was stratified by degree of urbanization (rural, semi- rural, urban), unemployed/employed, distance from home to clinic to calculate responses to TB treatment per each stratum of urbanization.

Those variables which were significantly associated with case/control status on bivariate analysis were entered into the model as independent variables. Backward stepwise selection was used to arrive at a final model.

Data was coded, captured and analysed using SPSS (PASW Statistics 18) under the guidance of the Statistician. Finally, the Database was then analysed, and the results presented in appropriate tables and figures.

### **3.2.21 Ethics**

The research protocol was approved by the University of KwaZulu Natal Biomedical Research Ethics Committee (BF 112/09) (Appendix A) before this study was conducted.

### **3.2.22 Permissions**

Permission was sought from the Head of the Department of Health, KZN in writing to conduct research in the Umgungundlovu Health District primary health facilities and was accordingly granted. Permission to undertake the study in Umgungundlovu Health District primary health care facilities was also sought from the District Manager, Mrs. NM Zuma-Mkhonza.

Written informed consent was obtained from the participants, in a language with which the participants felt comfortable using. Participants were assured that

withdrawal or refusal to participate in the study was not going to exert a negative impact upon them or compromise their health care.

Respondents were assured of confidentiality and anonymity. No respondent names, identity, or patient card numbers were collected in this study, and questionnaires were not made available to anyone, except the investigator and data capturers. Completed questionnaires were locked in a safe place to ensure confidentiality. Original questionnaires will be destroyed after a period of two years.

Results of this study will be communicated to the respondents by posting them on the clinic walls and in information brochures that will be distributed to the study sites. A copy of the report will be submitted to the Umgungundlovu Health District Manager. A copy of the dissertation will be made available to the KZN Provincial Department of Health. A report of this study will be submitted for publication to a peer review journal.

### **3.2.23 Pilot Study**

A pilot study was conducted at Edendale Hospital Gateway Clinic in Umgungundlovu Health District. It was a small-scale study using a sample of five patients for each group, (five cases and five controls). The group was similar to the target population to be studied. The purpose of the pilot study was to test the validity and reliability of the measurement instruments. Words, phrases, sentences or questions that were not clearly understood were recorded by the researcher. Refinements were made to the questionnaire based on the findings of the pilot study. Data from the pilot study were not included in the data analysis.

### **3.2.24 Summary**

This epidemiological study used an observational retrospective case-control design to measure the non-health system related risk factors associated with TB treatment outcomes. The purpose of the study was to investigate non-health system related factors that contribute to poor TB treatment outcomes in Umgungundlovu Health District. In this chapter the study population, study sampling methods, data sources, data processing and analysis, biases and limitations were described. The study was



conducted on new TB adult cases that had an opportunity to complete a standard 6-month TB treatment course. The data was collected from 15 randomly selected primary health care clinics in Umgungundlovu Health District .The study comprised of 300 cases and 300 controls. The primary source of data was patients themselves, data was collected by means of interview based on a structured questionnaire, and secondary sources were TB Registers and Patient-held TB Carrier Cards. Data was analysed on SPSS programme, and the results are presented in the next chapter.

## **4 CHAPTER 4: RESULTS**

### **4.1.1 Introduction**

The purpose of this retrospective case-control study was to measure non-health system -related risk factors that contribute to poor TB outcomes due to patients interrupting their therapy and not completing their treatment in the prescribed six-month period in the Umgungundlovu Health District in KwaZulu-Natal. The study population comprised of 600 new cases diagnosed with pulmonary TB (PTB) that were initiated on six month of TB treatment on ambulatory care and would have had a chance to complete treatment within six months. The cases were those who interrupted or defaulted treatment, but returned to the health system and thus not being able to complete TB therapy within six months. These were compared to controls that completed TB therapy within six months and were cured after six months of TB treatment on ambulatory care, based on a smear negative result. In this chapter the contribution of non-health system factors to TB treatment outcome are presented. According to WHO (2003) the end points of treatment outcome include cure, treatment completion, treatment failure, interruption and default. Socio-economic, demographic, setting and other non-health system characteristics of cases and controls were summarised in Tables 2 to 12.

### **4.1.2 Demographics**

The proportion of male cases who had poor outcomes (n=161, 54%), in the sample was slightly higher than that of female cases (who completed their therapy in six months and were cured) (n=139, 46%). There was however no statistically significant difference in sex among the cases and controls. There were 139 female cases (46%) and 138 female controls (46%), 161 male cases (54%) and 162 male controls (54%). Sex was not a risk factor for poor completion of TB treatment within six months in this study (p=0.935) (Table 2).

Two thirds of cases (n=180, 60%) were in the 18 to 30 year old age group. There was a higher proportion of younger patients who had poor outcomes. A one sample Chi-square test showed that this was statistically significant (p<0.05).

There was no significant difference in age between cases and controls ( $p=0.138$ ) overall. The categories of age group occur in the cases and controls with equal probabilities. However, the proportion of participants between age group 18 to 30 years in both cases and controls was much higher compared to other age groups (Table 2).

Two thirds of cases ( $n=188$ , 63%) and controls (207, 65%) were single ( $p<0.005$ ). There was no significant difference in relationship status between cases and controls ( $p=0.884$ ). The various categories of relationship status occurred with equal probabilities in both groups. Relationship status was not a risk factor for poor TB treatment completion in the prescribed time period.

A higher proportion of cases ( $n=54$ , 18%) had no education compared to controls ( $n=14$ , 5%). This was statistically significant ( $p<0.05$ ).

Only 27 cases (9%) had Matric compared to 105 (35%) of the controls. Only three cases (1%) had tertiary qualification compared to 42 controls (14%). A lower level of education is a risk factor for not completing TB therapy at within 6 months ( $p<0.05$ ) (Table 2).

#### **4.1.3 Socio-economics**

The majority of cases ( $n=274$ , 91%) were unemployed compared to 89 (30%) controls. There was a significant association between unemployment status and non-adherence to TB therapy. A low proportion of cases ( $n=15$ , 3%) reported being employed, whereas ( $n=190$ , 63%) controls reported being employed ( $p<0.05$ ) (Table 3).

The majority of cases ( $n=274$ , 91%) reported that they were earning less than R1000 per month compared to controls ( $n=90$ , 30%). The only source of income for cases was from temporary disability grants (social pensions). There was a statistical difference between cases and controls in terms of lower income bracket for cases. ( $p<0.05$ ). (Table 3) The majority of controls earned between R4000 and R5000 ( $n=77$ , 26%) compared to cases ( $n=7$ , 2%). Only ( $n=4$ , 1%) of cases reported

earnings above R5000, whereas controls were more likely to earn within this income bracket (n=80, 27%) There was a statistical difference between cases and controls in terms of higher income bracket for controls. ( $p<0.05$ ) (Table 3).

The majority of cases (n=232, 85%) reported going to bed hungry at least three times per week compared to controls (n=77, 26%) and more cases than controls (n=42, 14%) reported going to bed without any food three times a month compared to controls (n=6, 2%). The majority of controls (n=217, 72%) did not report any lack of food during TB therapy compared to 26 (9%) of cases.

There was a statistically significant association between lack of food not completing TB therapy within the six-month period ( $p<0.05$ ).

#### **4.1.4 Residential Area, Housing, Water Source and Sanitation**

The majority of cases (n=179, 60%) lived in a more rural area compared to controls (n=106, 35%). The majority of controls (n=185, 62%) lived in a township compared to cases who lived in the same setting (n=113, 37.6%). There was a significant difference between cases in terms of area of residence. Living in a rural area was significantly associated with non-completion of TB therapy ( $p<0.05$ ) (Table 4).

Less than half (n=127, 42%) of cases reported that they live in brick houses compared to controls (n=240, 80%) whereas the majority of cases (n=160, 53%) lived in mud houses compared to controls (n=49, 16%). There was a significant difference between cases controls with regard to type of housing they lived in ( $p<0.05$ ).

The majority of cases (n=242, 83%) drew water from a community tap compared to controls (n=176, 60%). A low proportion of cases (n= 49, 17%) had access to piped water compared to controls (n=117, 40%). There was a significant difference between adherers and non-adherers to prescribed therapy with regard to their source of water ( $p < 0.05$ ) (Table 4).

The majority of cases (n=294, 98%) reported using pit toilets for sanitation in their homes compared to 252 controls (84%) and only 6 (2%) of the cases used flushed

toilets in their homes compared to 47 controls (16%). This result was statistically significant ( $p < 0.05$ ).

#### **4.1.5 Alcohol, Drug Use and Smoking among Adult TB patients**

More of the cases ( $n=86$ , 38%) reported that they drank alcohol compared to 66 controls (24%), which showed a statistically significant difference ( $p=0.037$ ). Alcohol is a risk factor for not completing TB therapy within the six-month period.

The majority of cases ( $n=74$ , 29%) reported smoking compared to 66 controls (18%) ( $p=0.018$ ). Smoking is a risk factor for cases, as they did not complete continuous six months of TB therapy, by either interrupting or defaulting treatment.

More cases ( $n=39$ , 13%) reported using illicit drugs compared to only one of the controls (0.3%). Reported illicit drug usage is a risk factor for cases, as they did not complete continuous six months of TB therapy, by either interrupting or defaulting treatment.

#### **4.1.6 Directly Observed Therapy for Tuberculosis**

The majority of both cases ( $n=247$ , 82%) and controls ( $n=246$ , 82%) had equal access to DOT support ( $p=0.524$ ).

The majority of cases ( $n=200$ , 81%) had DOT supporters allocated by a health worker. Only 47, a low proportion of cases (19%) had DOT supporters of their own choice ( $p < 0.05$ ).

Most cases ( $n=159$ , 64%) had a Community Health Worker (CHW) as a DOT supporter compared to 26 controls (11%), whereas the majority of controls ( $n=189$ , 77%) had family members providing DOT support, and lower proportion ( $n=60$ , 24%) for cases supported by family members. This was statistically significant ( $p < 0.05$ ). There was no significant difference in the proportion of cases and controls who received DOT support from a friend, partner or pastor ( $p=0.500$ ).

The frequency of DOT support for the majority of controls (n=216, 90%) was daily, whereas 193 (80%) of cases had daily DOT support. A higher proportion of cases (n=33, 14%) had DOT support on a weekly basis compared to controls (n=17, 7%). A high proportion of cases (n=14, 6%) had only occasional DOT support compared to controls (n=7, 3%). Cases had far less daily contact with DOT supporters compared to controls who had contact with DOT support more frequently and regularly, which is statistically significant as a risk factor for not completing TB therapy within the six-month period either by interrupting or defaulting treatment, ( $p<0.05$ ) in this study.

There was equal proportion of patients who administered TB medication themselves (SAT) in both cases (n=54, 18%) and controls (n=55, 18%). There was no statistically significant difference in self-administered (SAT) TB treatment between cases and controls ( $p=0.500$ ) (Table 6).

#### **4.1.7 HIV and AIDS**

A statistically significant proportion of cases (n=132, 44%) reported that they were living with HIV compared to 74 controls (25%) ( $p<0.05$ ).

A higher proportion of cases living with HIV (n=39, 30%) were on ART compared to only nine (12%) of the 74 controls. More cases were on antiretroviral drugs than controls ( $p<0.05$ ).

#### **4.1.8 Severity of Illness of Adult TB Patients**

The majority of cases (n=297, 99%) remained AFB smear positive after two months of TB therapy. There was a highly statistically significant difference in smear conversion after two months on those taking regular TB treatment between cases and controls ( $p<0.05$ ).

The majority of the cases (n=297, 97%) had interrupted or defaulted treatment. Out of this total 236, (79%) interrupted their TB therapy for at least one month, while 60, (18%) defaulted TB therapy for two months and four (1%) defaulted TB therapy for three months. This is statistically significant ( $p<0.05$ ).

The majority of cases (n=295, 98%) stated lack of money as the reason for their non-adherence to TB therapy, and 186 (62%) of cases stated that both lack of money and ill health were reasons for non-adherence. Patients who defaulted TB therapy and remained smear positive after two months were tested for MDRTB as part of the standard TB management protocol. All the cases (n=300, 100%) were tested for MDRTB, and (14%) of those tested were found to be MDRTB positive ( $p<0.05$ ) (Table 8).

The most severe state of illness during TB therapy was observed and reported among cases. A high proportion of the cases (n=118, 39%) more often reported to be very ill during treatment than controls (n=41, 14%), as well as being fairly ill (n=180, 60%) compared to controls (98, 33%). This was statistically significant as one of the risk factors for non-adherence to TB therapy ( $p<0.005$ ). Just over half of the (n=161, 54%) controls reported being reasonably well during TB therapy compared to only (n=2, 0.6%) cases.

Cases were also more likely to have side effects to TB therapy compared to controls. (n=178, 59%) cases had side effects due to their TB therapy compared to controls (n=40, 13%). Nausea was the commonest side effect ( $p<0.05$ ). The majority of controls did not report any side effects to TB therapy (n=260, 87%), compared to (n=122, 41%) cases.

Both 16 (5.5%) cases and 16 (5.5%) controls had equally reported other physical illnesses other than TB whilst on TB therapy. The most common conditions were hypertension, diabetes mellitus and arthritis ( $p=0.500$ ) (Table 8).

#### **4.1.9 Other, Health Seeking Behaviour, Knowledge, Attitudes and Practices of Adult TB Patients**

More cases (n=63, 21%) reported using some form of alternative medicine whilst on TB therapy compared to controls (n=34, 11%). Controls were less likely to seek alternative medicine during the course of TB therapy. A report of having used an alternative practitioner was found to be a statistically significant risk factor not completing TB therapy within the six-month period ( $p<0.05$ ).

The type of practitioner that was consulted by 42 cases (14%) was a traditional healer compared to 21 controls (7%) This was followed by a diviner (*isangoma*) which was consulted by cases (n=14, 5%) compared to controls (n=4, 1%) This was statistically significant ( $p<0.05$ ) (Table 9).

Cases were less likely to consult a homeopath (n=4, 1%) compared to 8 controls (2%) The result was however not statistically significant ( $p=0.014$ ). Conversely cases were more likely to consult a faith healer (n=41, 14%) compared to controls (n=12, 4%) This was however not statistically significant. ( $p= 0.191$ ). Only (n=26, 9%) of cases who used alternative medicine reported that it was effective and only (n=21, 7) controls. Ten cases (3%) reported that alternative medicine relieved cough, compared to eight (2%) of the controls. Only (n=16, 5%) of cases reported that alternative medicine restored energy and only (12, 4%) of controls reported similar effect. This was statistically significant ( $p<0.05$ ).

Both cases and controls were less likely to report relief of night sweats from taking alternative medicine (n=5, 2%) cases and (n=7, 2%) as well as restoration of appetite respectively (n=1, 0.3%) and controls (n=2, 0.5) this was not statistically significant ( $p=0.500$ ).

On assessing knowledge levels, both 300 cases (100%) and 300 controls (100%) demonstrated adequate knowledge of at least four signs and symptoms of TB and mode of TB transmission without being prompted. There was no significant difference between cases and controls with regard to knowledge of signs and symptoms of TB as well as TB mode of transmission ( $p=0.500$ ).

Cases were less likely to know which TB drugs they were taking as only (n=15, 5%) of the 300 respondents knew the TB drugs they were taking without being prompted, whereas 285 (95%) of cases did not know the names of TB drugs even being prompted. This was statistically significant ( $p<0.05$ ). Cases demonstrated poorer knowledge of TB medication that they were taking compared to adherers.

Both cases (n=300,100%) and controls (n=300,100%) had reported that they received good care from the staff at the clinic from which they were collecting their



TB medication. There was no significant difference between cases and controls in terms of care received at the clinic ( $p=0.5$ ) (Table 9).

No stigmatisation against these TB sufferers was reported in the 300 cases (100%) and 300 controls (100%) ( $p=0.5$ ).

A slightly higher proportion of cases ( $n=100$ , 33%) reported that other family members staying with them were being treated for TB as well compared to controls ( $n= 87$ , 29%). However this was not statistically significant as a risk factor for non-adherence ( $p=0.15$ ).

### **Continuous Variables**

Continuous variables were computed using Mann-Whitney test. This was followed by comparison of means

#### **4.1.10 Distance to Clinic, in Kilometres and Taxi fare in Rands**

The median range for distance travelled by the majority of cases to the clinic was 16 km compared to a median of 4 km for controls. Cases were more likely to travel longer distances to the clinic compared to controls. There was a significant difference between cases and controls in terms of the distance travelled from home to the clinic ( $p<0.05$ ). There was strong association between non-adherence to TB treatment and distance from home to clinic and the cost of transport from home to clinic (Table 10).

The mean taxi fare was R14.00 for cases compared to R6.00 for controls from home to the clinic. Cases were more likely to spend more money on taxi fare due to the distance travelled compared to controls. This is a significant risk factor for not completing TB therapy within the six-month period ( $p<0.05$ ).

#### **4.1.11 Number of people in the household and number of sleeping rooms**

Although the median number of sleeping rooms in the household was the same in cases and controls, the distribution was wider in the cases, meaning that cases tended to have more people in the house than controls. The majority of cases shared

their homes with a median of 18 people, compared to the median of eight people for controls. Both the number of people and the number of rooms were measured. This was statistically significant ( $p < 0.05$ ).

**Table 2: Comparison of Sex, Age, Marital Status and Level of Education of Adult TB patients (Cases and Controls) in Umgungundlovu Health District, 2011.**

<b>Characteristic</b>		<b>Cases n *%</b>	<b>Controls n*%</b>	<b>P Value</b>
<b>Sex</b>	<b>Female</b>	139(46.4%)	138 (46.0%)	p=0.935
	<b>Male</b>	161(53.6%)	162 (54.0%)	
<b>Age (years.)</b>	<b>18-30</b>	180(60.0%)	179 (59.7%)	p=0.138
	<b>31- 40</b>	66 (22.0%)	70 (23.3%)	
	<b>41-50</b>	24 (8.0%)	26 (8.0%)	
	<b>51-60</b>	30 (10.0%)	25 (8.3%)	
<b>Relationship Status</b>	<b>Single</b>	188(62.0%)	207 (69.0%)	p=0.884
	<b>Married</b>	39 (13.9%)	34 (11.3%)	
	<b>Divorced</b>	9 (3.2%)	14 (4.6%)	
	<b>Widowed</b>	15 (5.0%)	15 (5.0%)	
	<b>Living with partner</b>	49 (17.5%)	30 (10.0%)	
<b>Level of education (completed)</b>	<b>None</b>	54 (20.0%)	14 (4.9%)	p<0.05
	<b>ABET</b>	18 (6.7%)	2 (0.6%)	p<0.05
	<b>Grade 1-5</b>	67 (24.8%)	37 (12.3%)	p<0.05
	<b>Grade 6-9</b>	131 (43.6%)	100 (33.3%)	p<0.05
	<b>Matric</b>	27 (9%)	105 (35.2%)	p<0.05
	<b>Tertiary</b>	3 (1.1%)	42 (14.2%)	p<0.05

**Table 3: Comparison of Employment Status, Income and Going to Bed without Food of Adult TB patients (Cases and Controls) in Umgungundlovu Health District, 2011.**

<b>Characteristic</b>		<b>Cases n*%</b>	<b>Controls n*%</b>	<b>P Value</b>
<b>Employment Status</b>	Unemployed	274 (91.3%)	89 (29.6%)	p<0.05
	Full Time	15 (5%)	190 (63.3%)	p<0.05
	Part Time	11 (3.6%)	21 (7.0%)	p<0.05
<b>Income – Rands / Month</b>	<1000	274 (91.3%)	90 (30.0%)	p<0.05
	1000-1999	2 (0.6%)	7 (2.3%)	p<0.05
	2000-2999	5 (1.6%)	17(5.6%)	p<0.05
	3000-3999	8 (2.6%)	29 9.6%)	p<0.05
	4000-4999	7 (2.3%)	77 (25.6%)	p<0.05
	>=5000	4 (1.3%)	80 (26.6%)	
<b>Going to bed without food</b>	Three times a week	232(84.6%	77 (25.6%)	p<0.05
<b>In a month</b>	Three times a month	42 (14.0%)	6 (2.0%)	p<0.05
	Not at all	26 (8.6%)	217 (72.3%)	p<0.05

**Table 4: Comparison of Residential Area, Housing, Water Source and Sanitation of Adult TB patients (Cases and Controls) in Umgungundlovu Health District, 2011.**

<b>Characteristic</b>		<b>Cases n*%</b>	<b>Controls n*%</b>	<b>P Value</b>
<b>Residential area</b>	Rural	179 (59.6%)	106 (35.3%)	p<0.05
	Township	113 (37.6%)	185(61.6%)	p<0.05
	Urban	7 (2.3% ) Out of 299	9 (3%) Out of 300	
<b>Housing</b>	Brick house	127(42.3%)	240 (80.0%)	p<0.05
	Mud house	160 (53.3%)	49 (16.3%)	p<0.05
	Other	13 (4.3)	11(3.6)	p=0.500
<b>Water source</b>	Community tap	242 (83.1%)	176 (60%)	p<0.05
	Piped water	49 (16.8%) Out of 291	117 (39.9%) Out of 293	p<0.05
<b>Sanitation</b>	Pit toilet	294 (98.0%)	252 (84.3%)	p<0.05
	Flush toilet	6 (2.0%)	48 (16 %)	p<0.05

**Table 5 Comparison of Alcohol, Smoking and Drug Use in Adult TB Patients (cases and controls) in Umgungundlovu Health District, 2011**

<i><b>Characteristic</b></i>	<i><b>Cases n*%</b></i>	<i><b>Controls n*%</b></i>	<i><b>P Value</b></i>
<b>Drinking Alcohol</b>	86 (37.7%)  Out of <b>228</b>	66 (23.9%)  Out of <b>276</b>	p=0.037
<b>Drug use</b>	39 (14.9%)  Out of <b>262</b>	1 (0.3%)	p<0.05
<b>Smoking</b>	74 (29.1%)  Out of <b>254</b>	52 (18.1%)  Out of <b>287</b>	p=0.018

**Table 6: Comparison of Directly Observed Therapy for Tuberculosis (Cases and Controls in Umgungundlovu Health District, 2011**

<b>Characteristic</b>		<b>Cases n*%</b>	<b>Controls n*%</b>	<b>P Value</b>
<b>Access to DOT Support</b>	Yes	247 (82.3%)	246 (82%)	p=0.542
<b>Health Worker Choice</b>		200 (80.9%)	30 (12.1%)	p<0.05
<b>Own Choice</b>		47 (19.0%)	216 (87.8%)	P<0.05
<b>Type of DOT</b>		<b>Out of 247</b>	<b>Out of 246</b>	
	CHW	159 (64.3%)	26 (10.5%)	p<0.05
	Family member	60 (24.2%)	189 (76.8%)	p<0.05
	Friend	22 (8.9%)	26 (10.5%)	p=.5
	Partner	3 (1.2%)	4 (1.6%)	p=.5
	Pastor	3 (1.2%)	1 (0.4%)	P=.5
		<b>Out of 247</b>	<b>Out of 246</b>	
<b>Frequency of DOT</b>	Daily	193 (80.4%)	216 (90%)	p<0.05
	Weekly	33 (13.7%)	17 (7.0%)	p<0.05
	Occasional	14(5.8%)	7 (2.9%)	p<0.05
		<b>Out of 240</b>	<b>Out of 240</b>	
<b>Self-administered treatment (SAT)</b>		54(18%)	55 (18 3 %%)	p=0.500

**Table 7: Comparison of HIV and AIDS among Adult TB patients (Cases and Controls) in Umgungundlovu Health District, 2011.**

<i><b>Characteristic</b></i>		<i><b>Cases n*%</b></i>	<i><b>Controls n*%</b></i>	<i><b>P Value</b></i>
<b>HIV positive</b>	Yes	132 (44%)	74 (24.6%)	p<0.05
<b>HIV + on ART</b>	Yes	39 (13%)	9 (3%)	p<0.05



**Table 8: Comparison of Severity of Illness of Adult TB patients (Cases and Controls) in Umgungundlovu Health District, 2011.**

<b>Characteristic</b>		<b>Cases <i>n</i>*%</b>	<b>Controls <i>n</i>*%</b>	<b><i>P</i> Value</b>
<b>Smear positive after two months</b>		296(99%)	0(0%)	p<0.05
<b>Number of months interrupted or defaulted</b>	1 Month	236 (78. 6%)	0 (0%)	p<0.05
	2 Months	60 (18%)	0 (0%)	p<0.05
	3 Months	4 (1.3%)	0 (0%)	p<0.05
<b>Reasons for defaulting</b>	No money	295 (98.3%)	0 (0%)	p<0.05
	Ill health	186 (63%)	0 (0%)	p<0.05
<b>Tested for MDRTB</b>		300 (100%)	0 (0%)	p<0.05
<b>MDRTB positive</b>		42 (14%)	0 (0%)	p<0.05
<b>Very ill</b>		118 (39.3%)	41 (13.6%)	p<0.05
<b>Fairly ill</b>		180 (60%)	98 (32.6%)	p<0.05
<b>Reasonably well</b>		2 (0.6%)	161(53.6%)	
<b>TB treatment side effects</b>		178 (59.3%)	40 (13.3%)	p<0.05
<b>Not at all</b>		122(40.6%)	260(86.6%)	
<b>Any other physical illness</b>		16 (5.3%)	16 (5.3%)	p=0.500

**Table 9: Comparison of Other, Health Seeking Behaviour, and Knowledge, Attitudes and Practices of Adult TB patients (Controls) in Umgungundlovu Health District, 2011.**

<i>Characteristic</i>		<i>Cases n*%</i>	<i>Controls n*%</i>		<i>P Value</i>
<b>Used alternative medicine</b>		63 (21%)	21(7%)		p<0.05
<b>Practitioner consulted</b>	Traditional healer	42 (14%)	11(3.6%)		p<0.05
	Diviner	14 (4.6%)	4 (1.3%)		p=0.01
	Homeopath	4 (1.3%)	8 (2.6%)		p=0.19
	Faith healer	41 (13.6%)	12 (4%)		P<0.05
<b>Effectiveness of alternative medicine</b>	Restored energy	16 (5.3%)	12 (4%)		
	Treated night sweats	5 (1.6%)	7 (2.3%)		p=0.5
	Restored appetite	1 (0.3%)	2 (0.6%)		p=0.5
		<b>6</b>	<b>9</b>		
<b>TB Knowledge:</b>	4 signs & symptoms- Prompted	300 (100%)	300 (100%)	0.000	p=0.5
	4 modes of TB transmission Prompted	300 (100%)	300 (100%)	0.000	p=0.5
	No Knowledge of TB drugs Prompted	285(95%)	252(84%)		p<0.05
<b>Other members treated</b>		100(33.3%)	87 (29%)		P=0.15

## Continuous Variables

Continuous variables were computed using Mann-Whitney test. This was followed by comparison of means

### Distance from Home to the Clinic and Transport Cost

**Table 10: : Comparison of Distance to Clinic, in Kilometres and Taxi fare in Rands for Adult TB patients (Cases and Controls) in Umgungundlovu Health District, 2011.**

Characteristic	Cases	Controls
Distance from Clinic (median in km; range)	16 (1-55)	4 (0-35)
Taxi fare to clinic (median in R, range)	14 (6-40)	8 (4-25)

**Table 11: Comparison of Number of people in the household and number of sleeping rooms for Adult TB patients (Cases and Controls) in Umgungundlovu Health District, 2011.**

Characteristic	Cases	Controls
Median number of people in the household (range)	1.924 (1-18)	1.574 (1-8)
Median number of sleeping rooms in the household(range)	1.074 (1-13)	.826 (1-5)

### Number of sleeping rooms and number of people in the household

The majority of cases share the sleeping rooms with a large number of people, median 18, whereas the median for controls is eight.

Although the median number of people in the household is the same in cases and controls, the distribution is wider in the cases, meaning cases tend to had more people in the house than controls. This is statistically significant ( $p < 0.05$ ).

## **Multivariate Analysis Results:**

### **Methodology:**

Binary logistic regression analysis was performed in order to control for confounding while assessing the individual effects of the independent variables. Those variables, which were significantly associated with case/control status on bivariate analysis, were entered into the model as independent variables. Backward stepwise selection was used to arrive at a final model.

Multivariate analysis was performed to test the confounding effect of variables of interest, using cured/not cured of TB as the dependent variable. Standard logistic regression model incorporating an indicator variable in the model corresponding to each case- control set was used .After 10 steps the variables remaining in the model were unemployment, distance from home to the clinic, living in a rural area, living with HIV and being very ill during TB therapy.

### **Employment:**

After adjusting for confounding variables using logistic regression, being unemployed versus full time employment was 16 times more likely in non-adherers sounded in the. Unemployment remained significantly associated with non-adherence to TB therapy in Umgungundlovu Health District (OR 16.0; 95% CI: 6.7 to 37.8;  $p < 0.005$ ).

### **Distance from Clinics:**

After controlling for confounding variables, distance from home to the clinic increased by one km, and the odds of being a case increased 1.5 times. Distance from home to the clinic is significantly associated with non-adherence to TB therapy (OR 1.4; 95% CI: 1.3 to 1.6;  $p < 0.005$ ).

### **Area:**

Those in rural areas were the most likely to be cases. Those in townships versus rural were (67.4%) less likely to be cases. After adjusting for confounding variables

living in a rural area remained significantly associated with non-adherence to TB therapy in Umgungundlovu Health District (OR 14.3; 95% CI: 1.1 to 18;  $p < 0.005$ ).

#### **HIV Status:**

After adjusting for confounding variables, TB patients who were living with HIV were 2.3 times more likely to be cases. Living with HIV remained significantly associated with non-adherence to TB therapy in Umgungundlovu Health District (OR 2.3; 95% CI: 1.1 to 4.7;  $p < 0.005$ ).

#### **Severity of Illness:**

After controlling for confounding variables, TB patients who reported being very ill during treatment phase were 5 times more likely to be cases. Being very ill during TB therapy remained significantly associated with non-adherence to TB therapy (OR - 5.0; 95% CI: 2.1 to 11.9;  $p < 0.005$ ).

**Table 12: Multivariate Analysis**

<b>Characteristics of Step 10</b>	<b>Difference</b>	<b>Significance</b>	<b>OR</b>	<b>95% Confidence Intervals</b>
<b>Not employed vs. Employed</b>	2	.00	16.0	6.8-37.9
<b>Full time vs. part time</b>	1	.47	1.7	0.4-7.9
<b>Distance to clinic</b>	1	.00	1.4	1.4-1.6
	1	.00	0.3	0.2-.663
<b>Township vs. Rural</b>	1	.00	14.3	1.1 -18
<b>Urban vs. rural</b>	1	.16	.2	0.03-1.9
	1	.02	2.3	
<b>HIV positive</b>				1.1-4.7
<b>Very ill whilst on treatment</b>	1	.00	5.0	2.1- 11.9

## **Summary**

This chapter presented results that showed statistical significance on a number of variables that are associated with TB treatment outcomes. On univariate and bivariate analysis, cases were more likely to interrupt or default TB treatment due to factors like their male gender, low level of education, low income, living in a mud house and sharing the house with a large number of people. Other factors highlighted were lack of food, lack of money, ill health, less frequent contact with DOT support, use of alternative medicine, alcohol, smoking and drug abuse. Multivariate analysis highlighted unemployment, living in a rural area, long distance from home to clinic, HIV infection and being very ill during treatment as risk factors associated with poor TB treatment outcomes.

## **CHAPTER 5: DISCUSSION**

### **Introduction**

In chapter five, the significant patient -related factors to TB treatment outcomes are discussed. This study has generated a number of significant and interesting findings, which allow a holistic picture of the predicament of patients with regard to adherence to TB treatment to be arrived at in Umgungundlovu Health District in 2010.

The aim of the study was to identify those patient-related factors, which contribute to successful or unsuccessful outcomes in patients who have had the opportunity to complete six months of TB treatment in Umgungundlovu Health District.

The hypothesis was that patient-related factors contribute to non-adherence to TB therapy not completing TB therapy within the six-month period in patients receiving ambulatory TB treatment, independent of the quality of the TB management programme. The present study involved a case control study including 600 participants: 300 cases and 300 controls. TB treatment constituted the exposure and the outcome which, was either interrupted, defaulted or cured.

The present study has found that a failure to achieve an 85% TB cure rate per annum in Umgungundlovu Health District, in which the study was conducted, is due to multiple factors. A number of patient related factors have been found to contribute to non-adherence to TB treatment. The findings of this study considered possible biases and limitations in terms of the study design, method of data collection and results obtained.

The format of the discussion is similar to the results and it is presented under the following 11 headings:

Sex, Age, Marital Status and Level of Education;

Employment Status, Income and Going to Bed without Food;

Residential Area, Housing, Water Source and Sanitation;

Alcohol, Drug Use and Smoking;

Directly Observed Treatment;

HIV and AIDS;

Severity of Illness;

Other Health Seeking Behaviour, Knowledge, Attitudes and Practices;

Distance to Clinic, in Kilometres and Taxi fare in Rands;

Number of People in the Household and Number of Sleeping Rooms; and

Major Risk Factors after controlling for confounders using logistic regression.

### **Sex, Age, Marital Status and Level of Education**

The demographic characteristics of this study population differ from other observational studies.

#### **Sex**

This case- control study found that there was no statistically significant association between sex and adherence to TB therapy, although the proportion of male was slightly higher than that of female cases in Umgungundlovu Health District (). Sex on its own is not a contributory factor to not completing TB therapy within the six-month period.

The results of this study corroborates the findings of a case control study conducted in China on 659 new smear positive TB cases in 2005 also revealed that being a male was not an independent risk factor associated with TB treatment default. (Xianqin *et al.*, 2009).

A similar finding was made in a-retrospective study conducted in Nigeria on 983 TB patients, which showed that there was no significant difference in default rate between male and female patients (15.3% versus 13.5%,  $p=0.432$ ) (Amoran *et al.*,



2011). Another retrospective review of records conducted in Nigeria also showed that there was no significant difference in default rate between male and female patients. Comparing the sex of compliant and non-compliant groups was not statistically significant ( $p>0.05$ ) (Erhabor *et al.*, 2000). Another retrospective study conducted in South Africa, found that the proportion of women (64%) who did not adhere to TB therapy was higher than for men (36%) (Mashimbye, 2009). Another South African based retrospective study showed that successful treatment outcomes were significantly associated with male patients (Odour, 2006).

Other studies elsewhere do not support this finding. A retrospective study conducted in India showed that treatment success rates were higher in women (89 %) than those in men (87%) and fewer women dropped out of TB treatment than men (4 % default rate for women and 6% default rate for men) (Sachdeva, 2011). Another retrospective study conducted in Ghana, which showed that default from treatment was significantly associated with the male sex (Dodor, 2004). A retrospective cohort study based in South Africa highlighted that women were more likely to complete treatment successfully (68%) compared to men (63%) (van der Walt *et al.*, 2002). This study found like other studies elsewhere found that sex was not a risk factor for non-adherence to TB therapy in Umgungundlovu Health District, although other studies had contrasting findings. This provides opportunity for further research.

## **Age**

This study demonstrated an equal proportional distribution of age between controls and cases. There was no statistically significant difference in age groups between cases and controls in this study. However it must be noted that half of participants who participated in the study were between the age group of 18-30 in Umgungundlovu Health District. This is an indication of TB burden among young adults in Umgungundlovu Health District. The findings of this study corroborate the results of a retrospective study conducted in United States from 1993-2008, which showed that older adults and younger completed therapy in a timely manner and treatment outcomes were similar between the two groups ( Pratt *et al.*, 2011).

The findings of this study are contrary to the findings of a retrospective study conducted in Ghana, which showed that patients in the 25-44 year age group and those put on the retreatment regimen demonstrate higher defaulter rates (Heysell *et al.*, 2010). Age was not associated with non-adherence to TB therapy in this study.

### **Level of education**

Controls had higher educational standards, compared to cases, and therefore were more likely to adhere to TB treatment. This is statistically significant ( $p < 0.05$ ). The chances of patients with higher education to comply with six month TB therapy are higher due to the fact that they are more enlightened about the implications of not completing TB therapy within the six-month period. The majority of them would be having jobs, and it would be critical for them to complete treatment. There is significant association between low education level among cases and treatment default ( $p < 0.05$ ). Patients with low levels of education might not understand fully the implications of non-adherence to treatment. The majority of them would be unemployed, and travelling to a health facility to collect TB medication this puts an extra financial burden on them.

The results of this study corroborate other observational studies. In a case-control study conducted in China low education level was one of the independent risk factors for non-cure (Xianqin *et al.*, 2010). This result also correlates with the findings of a retrospective study which highlighted that successful treatment outcomes were significantly associated with those whose highest education levels were tertiary and secondary (Odour, 2006).

In another retrospective study conducted in China on 190 new smear-positive TB patients, multivariate analysis using Cox Regression showed that lack of education was significantly associated with a delay in seeking care from service providers. (1.24; (5% CI 0.82-1.90) (Cheng *et al.*, 2005). A retrospective record review conducted in Nigeria on 694 case records revealed a statistically significant association between low literacy level and TB ( $p < 0.005$ ) (Ogboi *et al.*, 2010). Lack of

education and low level of education contributed significantly to non-adherence to TB therapy in this study.

### **Socio-economics: Employment Status**

This study demonstrated that the proportion of unemployed cases was higher compared to controls. Unemployment was a significant risk factor for treatment default ( $p < 0.05$ ). Multivariate analysis using logical regression showed that unemployed patients were 16 times more likely to default treatment than employed patients in Umgungundlovu Health District. Unemployed patients are worse off as they lack basic resources for day-to-day survival. They have no means of transport to get around, and they are mostly likely to default long-term TB treatment because of poverty, as they cannot afford out of pocket expenses related to their health care.

The findings of this study corroborate other observational studies elsewhere. Findings of a retrospective record review conducted in Nigeria on a 694 case records revealed that most of the patients presenting with tuberculosis are in the productive age with unemployment serving as potent risk factors for non-adherence to TB treatment in the study area ( $p < 0.05$ ) (Ogboi *et al.*, 2010).

A cohort study conducted in Morocco on 727 new TB cases also showed significant association between low income and treatment failure (OR 3.3, 95% CI: 1.1-9.3 (Dooley *et al* 2011). This finding also correlate to a retrospective study conducted in South Africa on 450 patients in 2006 which revealed that patients who were unemployed were more likely to be lost to follow up (Kharsany *et al.*, 2006).

Another retrospective cohort study conducted in South Africa on 400 participants demonstrated that unemployed people had 1.6 times higher risk of unsuccessful treatment outcome than employed people ( $p < 0.05$ ). The findings of this current study indicate that unemployment poses a burden on TB patients who have to be on six month therapy on the ambulatory basis.

### **Income per Month**

This study revealed that the majority of cases ( ) had no basic income and were dependent on temporary disability grants only. There was a significant association between lack of income and non-adherence to TB therapy ( $p < 0.05$ ). This is directly linked to unemployment. These patients cannot afford to meet the health care costs, due to other priorities, which include food and education for children.

The results of this study are comparable to the results of a prospective descriptive study conducted in Thailand, which highlighted illness-related costs of (15%). of the total annual household income. This affects patients with income below the poverty line, (Kamolratanakul *et al.*, 2009).

In line with the findings of this study though slightly lower was the results of a cross-sectional study conducted in Tanzania which showed that (21%) of patients did not have a defined income (van den Boogaard, 2009). Another retrospective study conducted in Morocco on 727 patients highlighted that low income remained significantly associated with treatment failure (OR 3.3, 95%CI 1.1-9.3) (Tachfouti *et al.*, 2011).

In this study the challenge of poverty, a factor which links directly to lower levels of education, unemployment, low income, poor living conditions, the distance to a clinic, and out of pocket expenses is evident. These are factors predisposing to non-adherence. Patients who live below the poverty line and who rely only on social grants for their sustenance are more likely to default on treatment than those who fare in a higher socio-economic category. The majority of TB patients rely on the disability grant which is less than R1000 for their survival. These patients are less likely to afford out of pocket expenses for six months duration of ambulatory care.

### **Going to Bed without Food**

This study showed that a high proportion of cases went to bed without food in most instances three times a week and on some occasions, less than three times a month

respectively in Umgungundlovu Health District compared to controls) respectively. This is another independent risk factor that is associated with low socio-economic status of the study population. This finding was statistically significant ( $p < 0.05$ ).

Although TB treatment is a free service, out of pocket expenses for travelling and food have a bearing on treatment adherence. Patients have no choice regarding the predicament they find themselves in, as they did not invite these circumstances upon themselves, however, such economic factors contribute to not completing TB therapy within the six-month period, and these factors are external to the health system. The results of this study agree with the previous research findings.

This is comparable to the findings of a case- control study conducted in Timor and Role Island, Indonesia, which enrolled 121 cases and 371 controls showed that 87% of patients had malnutrition compared to 33% among controls (Pakasi *et al.*, 2009). Results of systematic reviews conducted in 2008 show that poor nutrition at time of diagnosis worsens treatment outcomes (Lonnoroth *et al.*, 2009).

The findings of another case-control study (1055 cases and 2110 controls), conducted in South Africa in 2002 highlighted that cases were more likely than controls to report having to take TB treatment on an empty stomach (OR 1.6, 95% CI: 1.2-2.3) (van der Walt *et al.*, 2002). An article review also highlighted that when the food is not available patients may not take TB treatment (Naidoo *et al.*, 2007).

One of the objectives of the study was to assess the socio-demographic characteristics of the patients with poor TB treatment outcomes. The results of this study agree with the existing evidence from previous research, which highlight that poverty is an important influence on health, and despite continuing economic growth in South Africa, poverty and health inequalities persist. Lack of food is an independent risk factor to adherence to TB therapy in this study.

## **Residential Area**

This study found that a high proportion of cases (lived in rural areas,) Multivariate analysis showed a statistically significant association between living in a rural area and non- adherence to TB therapy (OR 14.3; 95% CI: 11 to 18).

This is a reflection of the geographical distribution of the population. There are seven sub districts in Umgungundlovu Health District. Only one sub district is classified as urban, and four of these are situated in deep rural regions. The study also found that adherence to anti- tuberculosis therapy remained a challenge amongst the rural population, particularly in terms of access to health centres. Living in a rural area, though not a patient's choice overburdens patients as they are in worse situations compared to those living in urban settings. The findings of this study corroborate other observational studies.

In an unmatched case- control study conducted in Uganda between March and May 2009 distance from home to clinic was identified as one of the factors associated with defaulting from TB treatment (OR 4.2; 2.2 - 8.0) (Elbireer *et al.*, 2011). In a retrospective study conducted in Ghana default from treatment was significantly associated with living in communities far from the treatment centre (Dodor *et al.*, 2004). In a study conducted in Ireland socio-economic status has also been found to greatly impact on a person's access to effective healthcare (Luddy, 2007).

The findings of a multi- faceted retrospective descriptive case study conducted at a Regional hospital and its three feeder clinics in Umgungundlovu Health District in 2007 highlighted that, the clinic was too far to reach and transport was either expensive or unavailable (Loveday *et al.*, 2007). The majority of the participants hailed from the poor rural settings in this study. The clinics in which the study was conducted are spread throughout these sub districts of Umgungundlovu Health District.

### **Type of house**

This study found that the proportion of cases who lived in a mud house was higher, compared to fewer controls. There is strong association between living in a mud house and treatment default ( $p < 0.05$ ). Living in a mud house is an indicator of low socio-economic status of the participants. This factor combined with other adverse factors such as unemployment and living in rural area, exacerbates the economic hardship that the patients face.

This finding is comparable to the results of a retrospective study conducted in Peru which demonstrated that substandard housing conditions (hazard ratio, 1.8; 95% CI, 1.1-3.1;  $p = 0.03$ ) predicted default from therapy in a multivariate analysis (Muniyandi *et al.*, 2008). They further highlight association between TB and poverty in terms of income, standard of living, house type and social class.

This finding is linked to low socio-economic status of the study population, which is an independent risk factor for non-adherence to TB therapy. This study did not investigate the conditions of the houses in which these patients dwell, but it could be assumed that the houses owned by non-adherers were in a poor state.

### **Water source**

This study found that the majority of patients were drawing water from community taps and the proportion was higher among cases compared to adherers (60%) in Umgungundlovu Health District. This study showed statistically significant association between poor access to water supply and treatment default. This is one of the independent factors that are indicative of low socio-economic factors ( $p < 0.05$ ).

The findings of this study are in line with the result of a case study conducted in Umgungundlovu District in 2010, which identified huge backlogs in the delivery of services such as water and electricity services (Makhathini, 2010). Poor access to water is one of the indicators of low socio-economic status, and therefore an independent risk factor for non-adherence to TB therapy.

## **Sanitation**

The present study revealed that a proportion of cases using pit toilets was much higher compared to controls. There was statistically significant association between using a pit toilet and non-adherence ( $p < 0.05$ ). This variable, combined with other factors predispose patients to extreme levels of poverty, which causes them not to adhere to TB therapy.

The findings of this study corroborate the results of a case study conducted in Umgungundlovu District in 2010, which identified huge backlogs in the delivery of services such as sanitation services (Makhathini, 2010). This is also one of the independent factors that determine the poverty levels of clients who default treatment in Umgungundlovu Health District.

## **Alcohol**

This study revealed that majority of the cases consumed alcohol whilst they were on TB therapy compared to controls in Umgungundlovu Health District., This was statistically significant ( $p = 0.03$ ). There is an association between drinking alcohol and treatment default. This is attributed to the fact that irresponsible drinking of alcohol will lead to persons not being responsible enough to take responsibility for their own health. It therefore becomes a challenge to even keep clinic appointments.

The findings of this study corroborate the results of a case-control study conducted in South Africa in 2002, which indicated that among those who used alcohol, cases (68%) reported heavier alcohol drinking than controls (41%), (van der Walt *et al.*, 2002). The findings of this study are in contrast with the results of a surveillance conducted in Kazakhstan during 1995 to 2002, which showed that unfavourable treatment outcome of new TB patients was associated with alcohol abuse (Bumburidi *et al.*, 2006).

Findings of a retrospective study conducted in Kasturba hospital showed that alcoholism is a risk factor although it is a lower proportion (13%) of TB patients that consume alcohol compared to this case-control study (Gupta *et al.*, 2011). In a



retrospective cohort study conducted in Tomsk on 237 adult patients, results showed that there existed no statistical significance between cases and alcohol dependence (95% CI 2.3-17.7) (Gelmanova *et al.*, 2007).

Results of systematic reviews conducted in 2008 showed that alcohol abuse increases the risk of TB about three- fold. This factor is due to the increased risk of a negative social mixing pattern and social drift (Munro *et al.*, 2008).

It is a logically deducted fact that if some of the money received by TB patients from a temporary disability grant of R750 a month was used to buy inter alia alcohol, such patients who consume alcohol will consequently be less likely to possess any money for transport. Such an impact will invariably lead to treatment default.

Lack of statistical significance of alcohol abuse between cases and controls in this study could be attributed to under reporting by study participants. Systematic studies using standardized and validated alcohol assessment instruments will be needed to ascertain the full impact of alcohol disorders on patients' ability to comply with TB treatment.

### **Smoking**

The present study showed that a quarter of cases ( ) were current smokers, the majority of whom were males, compared to a smaller proportion of controls. ). There was statistically significant difference between cases and controls ( $p=0.01$ ). This finding could be explained by the fact that patients were smokers even before they contracted TB. Smokers are more likely not to complete TB therapy within the six-month period than non-smokers are, particularly if they are poor. The little money they get might be used to feed their smoking habit than being spent on transport to collect TB medication from the clinic. The results of this study corroborate previous studies conducted in different settings.

In a cohort study conducted in Malaysia the rate of default was higher among regularly smoking TB patients compared to those who never smoked (12.8%; 35/274 vs. 2.0%; 5/250, respectively) (Dujaili *et al.*, 2010). After controlling for confounders,

including age, sex, alcohol use, Intravenous drug use (IVDU) and a history of chronic disease, ever smokers were three times more likely to default from treatment compared to never smokers.(3.24) Another study conducted in South India indicated that smoking was significantly associated with treatment failure (Gupta *et al.*, 2011). There could have been under reporting of smoking status by the participants in this study.

### **Drug Abuse**

This study showed that more cases who abused drugs whilst receiving TB treatment compared to controls in Umgungundlovu Health District. There is statistically significant association between drug usage and non-adherence to TB therapy ( $p < 0.05$ ). This percentage could be higher; the assumption is that a social desirability bias might have influenced the response of participants to this question, as it is a sensitive issue.

A most probable reason thereof can be ascribed to not answering truthfully. Drug abuse, a category which includes dagga, pills and most recently *whoonga* is rife especially in poor communities in UMgungundlovu Health District. The participants admitted using these substances. These patients are most likely to default treatment as getting drugs becomes their first priority than worrying about taking TB treatment. This irresponsible behavior contributes indirectly to non-adherence to TB therapy, as they lack money for other important things like travelling to the clinic to collect TB medication.

The findings are in agreement with other observational studies elsewhere. In a multivariate model, substance abuse was identified as the only factor that was strongly associated with non-adherence, an odds ratio of 15.6 (95% CI: 3.5–70.1) was obtained. Findings of a retrospective study conducted in Morocco on 291 patients identified male sex, as one of the principal risk factors for default (Dooley *et al.*, 2011).

This discovery is further supported by findings of the systematic review which state that alcohol and injection drug use were the only independent risk factors for non-adherence and default that we identified (Creswell, 2011).

Findings of a cross-sectional study conducted in the United States showed that odds of treatment failure were 2.4 times greater among those who reported substance abuse (Oeltmann *et al.*, 2009). These findings resound in those of numerous previous studies that had found substance abuse to serve as the single major factor associated most strongly with non-compliance with TB regimens.

Conversely the findings of a case- control study conducted in South Africa in 2002 indicated that only a small proportion of patients, both among cases (6%) and controls (4%) reported drug usage (van der Walt *et al.*, 2002).

## **Directly Observed Treatment**

### **Access to Directly Observed Treatment**

This study revealed that both cases and controls had equal access to DOT support. There was no statistically significant difference between the two groups ( $p=0.54$ ). Although both cases and controls had access to DOT, the major differences became manifest around the choice of DOT support and the frequency thereof.

The results of this study are comparable to the findings of a retrospective study conducted in KZN, South Africa to evaluate the DOT programme undertaken in EThekweni, UMgungundlovu, UMzinyathi and UThungulu districts showed that on average, priority facilities in districts that have high DOT coverage exhibited better cure rates compared with those that have low DOT coverage ( $p=0.04$ ) (Ntshanga *et al.*, 2009).

Conversely the findings of a cross sectional study conducted in Nigeria revealed that accessibility to DOT services was still suboptimal and it was worse among the rural dwellers, most of who are poor and living several kilometres from DOT service

centres (Fatiregun *et al.*, 2010). This study found that DOT coverage was good and is not centralized to health centres, but is more community based.

### **Choice of Directly Observed Treatment**

This study showed that the majority of TB patients) who made their own choice of DOT supporters had better treatment outcomes because of adherence to TB treatment, whereas cases had DOT supporters chosen by the health worker. There was statistical significance in terms of DOT supporters, (community health workers) that were allocated to the patient by the health worker, compared to the patient's own choice ( $p < 0.05$ ).

Patients who had chosen their own DOT supporters were more likely to have a successful TB treatment outcome because of adherence to treatment compared to those who did not make the choice. This could be attributed that these patients would choose people who are reliable and they have a trusting relationship with, instead of relying on strangers as DOT supporters.

This study demonstrated that approximately a higher proportion) of the cases had CHWs as DOT supporters, whereas the majority of the controls had family members as DOT supporters. Those who had family members as DOT supporters also demonstrated a better chance of completing treatment successfully within six months, .compared to cases. This was statistically significant ( $p < 0.05$ ).

The results of the present study corroborate the findings of a prospective cohort study conducted in Thailand which highlight the fact that the pattern of drug administration impacted on treatment success. Family-based DOT had the highest success rates compared with centre based DOT (OR 20.9, 95% CI 5.0-88.3) (Kamolratanakul *et al.*, 2009).

Conversely the findings of a retrospective cohort study conducted in KZN in 2008 demonstrated that TB patients who had workplace based DOT had the best treatment outcomes that were statistically significantly ( $p < 0.01$ ) better than family member supported DOT (Nair *et al.*, 2010). Yet another retrospective study

conducted in Cape Town, South Africa, demonstrated that community health worker support contributed to better TB control programme performance than an approach based exclusively on health facilities (Dudley *et al.*, 2011).

Findings of a cluster randomised controlled trial conducted in Nepal however found that community DOT support and family-member based DOT support achieved success rates of 85% and 89% respectively (Newell *et al.*, 2006).

Contrary to the above findings, the results of a retrospective cohort study conducted in Tomsk, Russia showed that despite the implementation of a DOT programme and the provision of extensive social services to patients undergoing TB therapy, non-adherence and default continued in a substantial proportion of those who initiated treatment (Gelmanova *et al.*, 2007).

Furthermore, findings of a multi- faceted retrospective descriptive case study conducted at a Regional hospital and its three feeder clinics in Umgungundlovu Health District in 2007 suggest that there were no systems for support, monitoring and evaluation of the treatment supporters and other cadres of workers, and there was no uniform system of training (Loveday *et al.*, 2007).

Findings of this current study, which showed better treatment support by family members compared to other forms, indicates diversity of opinion by researchers about which approach works best in different settings and situations among researchers. This opens another opportunity for further research.

### **Frequency of DOT support**

This study showed that ( cases had less frequent contact with DOT supporters ranging from weekly to once a month intervals respectively compared to controls These were more likely to interrupt or default compared to patients that had DOT support on daily basis for a high proportion of controls (compared to that of cases which proved to be very effective. This was statistically significant ( $p < 0.05$ ).

This study showed that those who received DOT support on a daily basis were able to complete treatment successfully, compared to those who had DOT support weekly

or occasionally. It is not feasible for CHWS to supervise treatment regularly as they are allocated a number of households to visit, and they only work 22 days a month. Although this factor is not the patients' choice, the situation they find themselves in contributes to non-adherence to TB therapy. Patients who have frequent DOT support stand a better chance of adhering to TB treatment, resulting to being cured within six months, whereas patients who have less frequent contact with DOT supporters are more likely to interrupt or default treatment.

A significant observation in support of this finding was made in the descriptive study conducted on 216 new adult TB patients in South Africa in 2006, whereby successful treatment outcomes were significantly associated with treatment supporters having fewer than 10 patients (Odour, 2006).

The less frequent coverage for cases that are mostly supported by CHWs could be attributed to shortage of DOT supporters. This study did not investigate the number of community DOT supporters allocated per clinic versus number of current TB patients in the register as well as their availability.

### **Self-Administered Therapy**

This study demonstrated that there was no significant difference in treatment outcomes on patients that are supervising their own treatment between cases and controls (and this was not statistically significant ( $p=0.500$ )). There was a smaller proportion in both groups who opted to administer their own treatment. This was probably determined by their own personal circumstances, whereby some of them live on their own and there is no support system around them.

Conversely the findings of an unblinded randomized controlled trial conducted in South Africa showed that treatment for tuberculosis was more successful among self-supervised patients (60% of patients) than among those on DOT (54% of patients, difference between groups 6%; 90% CI 5.1-17.0) (Zwarenstein, 1998).

The findings of another retrospective study conducted in the United States of America on 372 TB patients showed that patients treated by DOT at the start of

therapy (n=149) had a significantly higher cure rate compared with patients treated by SAT ( $p<0.002$ ) (Jasmer *et al.*, 2004).

The findings of this study indicate that the DOT programme can be beneficial if implemented correctly and with some degree of patient choice. It is for this reason that the Department of Health is currently reviewing the CHW policy with the view to replace Community health Workers with Community caregivers who will provide holistic care to communities instead of various groups undertaking different interventions in one household. The new strategy is being piloted at Umgungundlovu Health District in 2011. (Personal communication and involvement May 2011).

## **HIV and AIDS**

### **HIV Status**

This study showed that a higher proportion of cases had TB- HIV co-infection compared to fewer controls. There was a statistically significant association between people living with HIV-and unsuccessful TB treatment outcome, related to non-adherence to TB therapy ( $p<0.05$ ). These findings are lower than the current trends where TB co-infection is about 70% in South Africa. The burden of TB/HIV co-infection contributes to non-adherence to TB therapy, especially if it is coupled with poverty. If patients have no food to eat, they are less likely to adhere to TB treatment if they have to take it on an empty stomach as it causes more nausea and sometimes vomiting.

The result of this study corroborate the findings of a retrospective study conducted in California on 700 patients which revealed that 264 (38%) were HIV infected. Relapse rates were found to be significantly higher in HIV-infected patients compared with HIV-uninfected patients following a Rifamycin-based regimen. Furthermore, TB relapse rates were higher in HIV-infected patients who received intermittent or standard 6-month therapy when compared with those receiving daily or longer treatment (Nahid *et al.*, 2007).

The findings of this study are also slightly higher than the findings of another prospective study conducted in Cape Town, South Africa showed that 238 (25%) of patients enrolled for ART programme had prevalent TB (Lawn *et al.*, 2006).

A retrospective study conducted in South India on 207 patients showed that 10.6% of TB patients were living with HIV, which is even much lower than the finding of this study. It further highlights that relapse rates were found to be significantly higher in HIV-infected patients compared with HIV-uninfected patients following a Rifamycin-based regimen (Gupta *et al.*, 2011). Furthermore, TB relapse rates were higher in patients living with HIV who received intermittent or standard 6-month therapy when compared with those receiving daily or longer treatment (Nahid *et al.*, 2007).

Contrary to this finding, a prospective diagnostic study conducted in South Africa on 534 adult TB patients showed that 73% were living with HIV. Findings of a population based cross-sectional study conducted in South Africa showed that overall 55.3% of TB patients were also living with HIV. Female patients had significantly higher rates of HIV when compared to males. (62.2% versus 51.5%) (Shah *et al.*, 2011).

The findings of a multi-faceted retrospective descriptive case study conducted at a Regional hospital and its three feeder clinics in Umgungundlovu Health District in 2007, showed that there are increasing numbers of TB and HIV co-infected patients who have higher mortality and morbidity and are more difficult to diagnose and treat at a PHC level, due to smear-negative PTB, EPTB (Extra pulmonary TB) or MDRTB (Multidrug resistance) (Loveday *et al.*, 2007).

This outcome is echoed by the findings of a retrospective cohort study conducted in Spain in 1996-1997, which state that the outcome for tuberculosis treatment greatly deteriorates in HIV-positive patients (Diez Ruiz *et al.*, 2005).

This study demonstrated an association between HIV status and MDRTB, as well as the poor state of health occurring among cases. Findings of this study are comparable to a routine surveillance conducted in Virginia highlighted that those patients living with HIV are prone to malabsorption and are at higher risk for low drug levels (Heysell *et al.*, 2010).



The rate of TB and HIV co-infection among cases was found to be associated with a poor treatment outcome. The combination of these factors will inevitably negatively affect adherence to treatment resulting in poor treatment outcomes. Such a compromised situation is exacerbated by adverse socio-economic factors as described earlier.

## **Severity of Illness**

### **Treatment Default, Number of Months and Reasons**

This study found that a high proportion of the cases interrupted or defaulted treatment, and the majority of them had interrupted treatment for one month whilst others had defaulted treatment for two (19%) and three months (1.3%) respectively, and this was statistically significant ( $p < 0.05$ ). Overall default rate was found to be much higher in Umgungundlovu Health District than the WHO recommended rate of 3%.

The main reasons provided by participants in this study concerned were lack of money and illness, as well as risky behaviours, such as alcohol, drugs and smoking. Such a finding proves that there exists a strong correlation between socio-economic status and adherence to TB treatment. Poverty acts as a major barrier in accessing health care. Illness as a barrier could be attributed to TB and HIV co-infection, as 44% of cases had exhibited HIV co-infection.

The results of this study also agree with the findings of previous studies that non-adherence exerts certain important adverse effects on the outcomes of TB treatment. All poor outcomes occurred among patients who did not adhere to TB therapy. The results of this study showed a higher proportion of patients who defaulted compared to a retrospective study conducted in Ethiopia, which showed that 61% defaulted (Munoz-Sellart *et al.*, 2010). In a retrospective cohort study conducted in Nigeria the default rate was slightly lower (14.4%) (Ogboi *et al.*, 2010).

Results of an article review conducted in South Africa also highlight the fact that treatment adherence is also affected by beliefs concerning the origins of and

transmission means of TB and HIV (Naidoo *et al.*, 2007). This current study agrees with the findings of other researchers elsewhere. This study was a retrospective case-control, therefore cases were enrolled on the basis of not having completed treatment successfully hence the higher proportion of cases compared to other studies.

### **MDRTB Positive**

This study revealed that a proportion of cases were MDRTB positive in Umgungundlovu Health District, and this was statistically significant ( $p < 0.05$ ). These were included in the analysis as they had defaulted treatment at some stage during the six month period of TB therapy.

The proportion of MDRTB cases was slightly higher than (10.0%) on a retrospective study conducted in Peru ( Findings of an earlier study conducted in 1999 in South Africa showed that the prevalence of primary and acquired MDRTB was 1.8% and 4.1% respectively (Davies *et al.*, 1999).

Findings of a retrospective study conducted in Ghana suggest that these patients may harbour multiple different strains of Mycobacterium TB, some of which may indeed prove to be drug-resistant. In these mixed infections, standard short-course therapy may have unmasked the drug-resistant strain population by suppressing the previously dominant drug-sensitive strain (Dodor, 2004).

This study found the incidence rate of MDRTB slightly lower than the findings of a cross-sectional study that was conducted in KwaZulu Natal on 20858 patients, which showed that 20% of them had MDRTB (Moodley *et al.*, 2011). The results of surveillance conducted in rural South Africa from 2005 to 2006 found that the prevalence among patients with culture-confirmed tuberculosis was 39% for MDRTB (Ghandi *et al.*, 2006). However, the results of a retrospective study conducted in Umgungundlovu Health District which showed that the number of MDRTB case per 100 new cases was 14.8%, which is similar to the findings of this study (Sturm, 2010).

Findings of a retrospective observational study conducted in KZN, South Africa, in 2002-2003 revealed that 80% of MDRTB patients were HIV co-infected (Brust *et al.*, 2011). In another retrospective study conducted in rural KZN, South Africa the results showed that 78% of MDRTB cases were living with HIV.

In a retrospective cohort study conducted in California on 700 patients, 264 (38%) were HIV infected and were significantly more likely to develop drug resistance (4.2% in HIV-infected versus 0.5% in HIV-uninfected) to rifampicin, and to experience adverse reactions to TB regimens (Nahid *et al.*, 2007). This study did not assess the percentage of patients living with HIV who had MDRTB.

### **Physical Status during TB treatment**

This study found that a higher proportion of cases indicated that they remained very ill after being diagnosed with TB compared to controls. There is a statistically significant association between being very ill during TB therapy and non-adherence to TB therapy on multivariate analysis ( $p < 0.05$ ). Patients who were feeling ill during TB therapy were more likely to default treatment as they would perceive that the treatment is making them worse. Being very ill combined with poverty would cause patients to delay to seek health care intervention thus exacerbating the condition.

The findings of this study are comparable to other studies elsewhere. The findings of a multi-faceted retrospective descriptive case-control study conducted at a Regional hospital and its three feeder clinics in Umgungundlovu Health District in 2007, highlighted as one of the factors that respondents were either too sick to physically access the clinic (Loveday *et al.*, 2007). Another retrospective cohort study conducted in India on 980 patients showed that good health status was only perceived in less than 7% of patients. Physical condition was found to be an independent risk factor for non-adherence to TB therapy in this study.

### **TB treatment and side effects**

This study showed that a higher proportion of cases reported TB treatment side effects mainly nausea compared to controls. This result was statistically significant,

indicating association between treatment side effects and non-adherence to TB therapy ( $p < 0.05$ ). Participants who did not report side effects were most likely to adhere to therapy compared to those with side effects.

The results of this study are comparable to the findings of a case-control study in China which showed the presence of adverse effects during treatment on 46.5% cases (Xianqin *et al.*, 2010). This is lower than the findings of this study and even lower in the study conducted in Switzerland in 2009 using a retrospective review of medical records, which revealed that drug related side effects were noted in 75 cases (30%), however side effects severe enough to change or stop treatment were reported in only 38 cases (15%) (Kherad *et al.* 2009) compared to the study population in Umgungundlovu Health District.

In an unmatched case control study conducted in Uganda between March and May 2009 the side effects of treatment (OR 5.53; 2.25–13.61), was highlighted as a factor contributing to treatment default (Elbireer *et al.*, 2011). Results of a paper review conducted in South Africa highlighted that, complex regimens with potentially severe side effects cause non-adherence (Munro *et al.*, 2007).

This is further supported by results of a systematic review which state that anti-tuberculosis medication side effects were also found to be significantly associated with defaulting, and were responsible for termination of therapy in up to 23% of patients during the intensive phase (Awofeso, 2006). Treatment side effects were found to be an independent risk factor for non-adherence to TB therapy in this study.

### **Other, Health Seeking Behaviour, Knowledge, Attitudes and Practices**

All respondents felt that they experienced good treatment at the health facility and did not feel stigmatised because they had TB. Thus, it is unlikely that poor treatment at clinic level was the factor responsible for non-adherence. It is also unlikely that a social desirability bias prompted patients to minimise dissatisfaction with the health service because interviewers were not clinic staff.

It is, however, important to note that there were contrasting findings in a multi-faceted retrospective descriptive case study conducted at a Regional hospital and its three feeder clinics in Umgungundlovu Health District in 2007 as the perception among respondents was that they were stigmatised by some health workers and were not treated with respect (Loveday *et al.*, 2007).

### **Type of alternative medicine and practitioner consulted**

This study found that a significant proportion of cases resorted to alternative medicine and a traditional healer was most commonly consulted, followed by a diviner, compared to controls, and this was statistically significant ( $p < 0.05$ ). These practitioners are easily accessible compared to the health centres and their services are less onerous financially.

However, this practice could have contributed to a high defaulter rate, if patients had perceived that these alternative medicines were potentially helpful in alleviating certain symptoms. Other respondents (albeit a lesser percentage) consulted a homeopath, or a faith healer. These practitioners are probably not readily available or accessible in the area where the study was conducted. The findings of this study are supported by those of other researchers'.

The findings of a multi-faceted retrospective descriptive case study conducted at a Regional hospital and its three feeder clinics in Umgungundlovu Health District in 2007 highlighted the fact that a quarter of the patients had consulted a traditional healer on occasions during their illness, after their knowledge of their TB status. Sixteen per cent of the patients visited a traditional healer as their first choice of care. Of those in the latter category, (72%) were male (Loveday *et al.*, 2007). This study did not analyse the gender distribution of patients that use alternative medicine.

The findings of this study also corroborate the results of a case-control study conducted in South Africa in 2002, which indicated that cases (17%) were more likely than controls (7%) to report consulting a traditional healer during TB therapy (OR 2.8, 95% CI: 1,7-4.3) (van der Walt *et al.*, 2002).

Researchers further state that two thirds of the home remedies used originated from a chemist or supermarket and one third from a traditional healer/herbalist or traditional chemist. Sixteen per cent of the patient's interviewed consulted a traditional/spiritual healer. Fifteen per cent of the TB patients went to a spiritual/traditional healer. A quarter of the respondents visited a traditional healer/spiritual healer/ herbalist at some stage during their illness (i.e. either before or during). Use of alternative medicine during TB therapy was found to be an independent risk factor for adherence to TB therapy in this study.

### **Tuberculosis Knowledge**

This study found that all respondents from both groups , cases and controls knew at least 4 signs and symptoms of TB as well as the TB mode of transmission, and the majority indicated that the most reliable source of information were the health workers. There was no statistically significant difference between these groups in terms of knowledge of TB signs and symptoms as well as mode of transmission ( $p=0.500$ ). Prompts that were provided in the questionnaire would have contributed to high knowledge levels than when participants were unprompted.

This conclusion also bears testimony to the fact that a lot of groundwork has been covered in intensification of TB awareness in the community, which includes a TB blitz, which involves a community meeting hosted by health workers with various activities to raise TB awareness. Door to door campaigns, which include household visits and distribution of pamphlets, have been implemented in Umgungundlovu Health District on a continuous basis. (Umgungundlovu Health District Report 2010)

The results of this study are comparable to the findings of a multi- faceted retrospective descriptive case study conducted at a Regional hospital and its three feeder clinics in Umgungundlovu Health District in 2007, which showed that over 90% of the patients, were fully cognisant of the fact that TB was curable and taking medication was important. Patients, however, felt that information from health care providers remained the most trustworthy source of relevant and appropriate guidance (Loveday *et al.*, 2007).

A contrary conclusion was witnessed in a population based cross sectional study conducted in the rural community in Vietnam highlighting the fact that a large proportion of the general population possessed only a limited knowledge of TB, despite many years of health education (Hoa *et al.*, 2009). Such differences are significant as they provide an opportunity for further research.

This study however revealed that the knowledge of TB drugs was very poor among the majority of cases, even with prompting. There was a statistically significant association between non-adheres and lack of knowledge of TB drugs ( $p < 0.05$ ). It would appear that this is linked mainly to the low literacy levels of participants or their lack of interest in being fully informed of the medication they were receiving.

### **Distance to Clinic, in Kilometres and Taxi fare in Rands**

This study showed significant difference between cases and controls in terms of the distance travelled from home to the clinic in Umgungundlovu Health District ( $p < 0.05$ ). Cases had a median of 16 to 55 km to travel to the health facility and between R14 to R40 spent on travelling costs. This is linked to the socio-economic status and rural setting, and it contributes indirectly to non-adherence. Patients who are already poor are overburdened by the travelling costs to the clinics and are most likely to default treatment than those who have means. Although this factor is also not the patients' choice, it points to the external patient-related factors that the health system has no control of.

The findings of this study are comparable to a qualitative study conducted in Zambia on 202 adult patients with TB showed that within a poor resource setting, patients face financial constraints, specifically regarding travel distances and related transportation costs, factors which create a significant burden on patients (Needham *et al.*, 2004). Findings of this study are also in line with results of a retrospective study conducted in China on 190 new smear- positive TB patient showed that the distance from home to a Health Centre were significantly associated with a delay in seeking care from service provider (OR 1.04; 95% CI 0.64-1.28) (Cheng *et al.*, 2004).

In a retrospective study conducted in Ghana default from treatment was significantly associated with living in communities far from the treatment centre (Dodor, 2004). In a study conducted in Ireland socio-economic status has also been found to greatly impact on a person's access to effective healthcare (Luddy, 2007). Results of another systematic review conducted in Nigeria showed that accessibility to DOT is sub-optimal among rural dwellers, most of who are poor and live several kilometres from health centres (Amoran *et al.*, 2011). Long distance and transport costs were found to be independent risk factors for non-adherence to TB therapy in this study, as they both hinder access to health facilities.

### **Number of People in the Household and Number of Sleeping Rooms**

This study showed that a high proportion of cases shared the sleeping rooms with a large number of people, median 18, whereas the median for controls is 8 in Umgungundlovu Health District. This was statistically significant as one of the risk factors for treatment default ( $p < 0.05$ ).

This finding is linked to socio-economic status of the majority of TB patients who are burdened by poverty. Overcrowding itself is a risk factor for the spread of TB in one household. If they are more people infected in one family, it increases the chances of non-adherence to TB therapy because of the socio-economic conditions they find themselves in, which prevents them from keeping clinic appointments.

This finding is comparable to the findings of systematic reviews conducted in 2008 which showed that the risk of TB increased with lower socio-economic status as regards six indicators: crowding, education, income, poverty, public assistance and unemployment (Lonnoroth, 2011). Large numbers of people in one household is linked to the poor socio-economic status in this study. Poverty is an independent risk factor to adherence to TB therapy in Umgungundlovu Health District.

### **Major Risk Factors**

After controlling for confounding, five major risk factors associated with poor treatment outcomes were identified in Umgungundlovu Health District. These were



unemployment, living in a rural area, living far from the local clinic, being HIV infected, and being very ill while taking TB treatment.

## **Validity**

This section discusses internal validity of the study, which refers to whether the outcomes of this study are a function of the dependent and independent variables measured. The external validity section considered generalisability of the study findings to the population.

### **Internal Validity**

There were two data sources that were used to determine risk factors to poor TB outcomes with specific reference to treatment default. The primary source of data was TB patients themselves and some data like MDRTB status, treatment interruption; treatment default was extracted from the TB register and TB carrier cards.

Data that was supposed to be extracted from patients was missing in some instances from the questionnaires, but this not affect the measurement as it comprised of only two percent. Approximately four percent of the participants chose not to respond to certain questions. The questionnaire was quite long and some of the questions might have made respondents uncomfortable to respond to, especially if they are asked personal questions by strangers.

Responses on exposures like HIV infection, smoking, alcohol intake, drug use and alternative medicine were based on the truthfulness of each participant, there could have been under reporting. HIV status is not recorded in the patient cards and this was common practice in all clinics. This can be explained by the fact that all new TB patients are diagnosed, tested for HIV and initiated TB treatment at a hospital level and they are thereafter referred to their nearest clinics for follow up and collection of their treatment under the supervision of professional nurses.

Field workers themselves might have made an error in recording and missed some data. This could have been prevented if interviews were recorded by tape as well. It

would have been cumbersome to record 600 interviews, and participants were perhaps not going to respond freely knowing that they were being recorded.

### **External Validity**

Umgungundlovu Health District is the second most populous district in KZN province. The study population comprised 600 participants selected from only 15 out of 42 clinics. The results of this study are not generalisable to the TB patient population in South Africa. The results can be generalized to new TB patients who attend the clinics in rural clinics of South Africa as the sample size was adequate.

### **Bias and Limitations**

The bias and limitations of this study are discussed with regards to the design, data collection and the findings of the study.

Although this retrospective study demonstrates the significant risk factors associated with non-adherence to TB therapy in Umgungundlovu Health District, this study is not without limitations. The major limitation to this study was that it was conducted retrospectively, and it therefore relied on the truthfulness of the respondents and accuracy and completeness of data entered by 12 field workers on the questionnaires. Recall bias was a limitation in this study. Accuracy of data was dependent on how best the respondents were able to recall certain facts.

Another limitation of this study was the social desirability bias. It was not possible to ascertain accuracy of information on risk factors like alcohol intake, smoking and drug use, use of alternative medicine during TB therapy although study participants were assured of confidentiality and anonymity, and the fact that data was collected for research purposes only.

Funding for the study was a limitation. The initial proposed budget proved to be insufficient as the actual data collection only took place two years after the estimates were compiled, following the approval by the Ethics Committee. The major costs were around sustenance costs for the 12 field workers, which included transport and food. These costs were met by the researcher, including her own transport costs to

visit study sites to monitor data collection. The advantage was that other study sites were within reach and in close proximity to each other. There were no incentives for the study participants, which could have increased the budget demand. The costs of the research project were however curtailed by the fact that a case-control study is simple and cheap to administer. The statistical analysis of this study was conducted by the researcher under the supervision of a biostatistician at the University of KwaZulu-Natal.

## **Summary**

This chapter discussed the statistical significance of demographic and socio-economic factors, as well as health status and health seeking behaviour associated with unsuccessful TB treatment outcomes. Drug abuse was identified as being the only risky behaviour associated with poor treatment outcomes and one of the factors leading to non-adherence of TB treatment in Umgungundlovu Health District, while alcohol and smoking were not found to be independent risk factors.

The combination of these factors bore a casual relation to higher proportions of cases reporting that subjects were very ill during the TB treatment period. This contributed to treatment default and lack of money for transport to the clinic and impacted on the treatment outcomes. DOT support proved to be a limitation in terms of frequency. Cases were not able to receive daily DOT support compared to controls. This also affected adherence to treatment.

These patient-related factors indicate that the health system is faced with a huge challenge in TB control. The comparison with other study findings indicate that the challenges faced by the South African TB programmes are not unique, and that the recommendations and changes made to those programmes are as a result of their studies need to be taken into consideration locally. There is enough evidence to indicate that most of the factors highlighted are significantly associated with non-adherence to TB treatment including unemployment, living in a rural area, living far from the local clinic, being HIV infected, and being very ill while taking TB treatment

all of which need to be considered when developing policies and plans to improve treatment uptake.

## **5 CHAPTER: CONCLUSIONS AND RECOMMENDATIONS**

### **Introduction**

This study has demonstrated the following:

There are numerous patient related factors which have previously hindered the success of TB control programmes. These factors are of a complex and interrelated nature. The study assumed a holistic approach wherein it examined the multiple factors that interact upon each other to allow for either a successful or an unsuccessful outcome to be achieved. For example, in the low socio- economic group, the burden of TB may be high.

Such a factor, together with the high incidence of TB and HIV, may lead to an increased severity of illness. This may cause patients to seek alternative medicine as traditional healers are more accessible compared to the clinics which are situated far from where patients live in rural areas. Patients are more likely to consult such healers rather than attend the clinic. This phenomenon is likely to increase the defaulter rate and lead to a poor treatment outcome in Umgungundlovu Health District.

### **Conclusions**

The major risk factors associated with poor TB outcomes are unemployment, distance from home to clinic, living in rural areas, having TB and HIV co-infection and being very ill during treatment.



**Figure 3: Diagram of interrelatedness**

The diagram above illustrates the infinite interplay of multiple factors which influence each other.

The application of Bandura’s behavioural theory was appropriate in this study as the factors identified link to cognitive, social and environmental aspects. The aim and objectives of this study were achieved. The greatest benefit to patients is likely to come if many of these factors are addressed simultaneously, rather than addressing one at a time. Furthermore, it can be confidently asserted that the aim and objectives of this study were achieved. The study was adequately powered to ascertain the real differences.

## Recommendations

It is important to review the definition of treatment interruption and treatment default especially in the context where non-adherence to treatment remains a challenge. Introduction of new and quicker ways of TB diagnosis is vital to reduce costly trips to the health facility. The *Gene-Xpert* machine should be available in most populous districts like Umgungundlovu health district to facilitate quick diagnosis and initiation

of TB therapy, and to minimize number of trips to the health facility, which contributes to non-adherence.

District Intervention strategies should prioritize the five major risk factors that contribute to poor treatment outcome, which were identified in this study.

The current system of temporary social grants for TB patients needs to be reviewed jointly by the Department of Social Welfare and the Department of Health. These grants are meant to assist the poor to buy food and have money for transport to the health facility. However, the government retains no control on how this money is used by each individual.

Furthermore, interpersonal communication with family members, among other strategies, linking poor and vulnerable populations with social welfare schemes will prove a significant benefit and aid in achieving treatment outcomes. Vouchers should be introduced for patient transport and food. Such a development will eliminate the problem of non –adherence because of a lack of money and food. The Department of Social Welfare is currently issuing vouchers to deprived families usually to the value of R800 a month, as part of social relief. The recipients merely proceed with the voucher to selected supermarket for groceries.

These pro-poor strategies will go a long way to reducing the financial burden of patients on TB treatment. This will require that a full risk assessment be undertaken on each newly diagnosed TB patient so as to identify potential factors for non-adherence. This should be done in conjunction with individualized patient counseling, which must be followed by individualized plan of taking six month therapy. The DOT strategy needs to be reviewed and implemented based upon circumstances applying to each patient.

Incentives should be provided to patients that have adhered to the full course of treatment to encourage adherence. There exists an urgent need for health care providers to form a partnership with providers of alternative medicine.

Integration of HIV and AIDS, TB STI services should be implemented as a matter of urgency. Community based services should be strengthened through the new *Sukuma Sakhe* programme. Thus, one cadre of well-trained Community Care Givers will be introduced. It will be appropriate to initiate an SMS system for appointment reminders for patients who possess cell phones. This serves as one means of improving communication between health care providers and patients. Integration of TB in Education and care for HIV/AIDS (ITEACH) and Non- Governmental Organisation based at Edendale hospital has already introduced this form of communication for patients on ART.

Strengthening of PHC services from community level to clinics is imperative, as this remains the first point of contact with the patients, which is critical to ensure a proper assessment of risk factors that might lead to non-adherence to TB therapy. This effort will reduce the number of new TB patients that are lost in the health system, while they should still be receiving treatment. The issue of allocating health posts closer to where people predominantly live will improve access to some basic health care, and is a matter requiring urgent implementation by the Department of Health.

It is important to review a definition of interruption and default as the difference is merely technical. In reality if the patient interrupts treatment for one month that is already a precursor for treatment default. TB registers and patient cards ought mandatorily to include HIV information so as to ensure holistic care. Currently the TB referral form from the hospital to the clinic, and the patient TB card do not have space for the HIV status.

New cost effective Community based TB prevention strategies are critical to reduce the burden of TB. These may include anti-smoking, anti-alcohol and anti- substance abuse interventions, which should be incorporated into TB community education and community involvement, must be encouraged in fighting these social behaviours.

Community support groups for TB patients will most likely prove beneficial in encouraging compliance as is the case with patients on ART. Allocation of more resources to support the TB management programme is critical in order to improve



TB cure rate per annum. The 'opt' out choice of TB patients to health provider initiated HIV counseling and testing should be reviewed.

### **Recommendations for Further Study**

Although the study investigated multiple risk factors that are associated with poor treatment outcomes, it would be beneficial to assess each of these variables closely. The proposed areas of further study should include:

Investigation into the effectiveness of social grants; effectiveness of DOT; male patients and adherence to TB treatment; younger age group: 18-30 and adherence to treatment; TB and people living with HIV, patients lost to follow up; the burden of MDRTB; comparison between effectiveness of institutionalized and ambulatory TB control programme, smoking, alcohol and substance abuse as risk factors to adherence and use of alternative medicine and non-adherence to treatment.

### **Summary**

This chapter summarized risk factors associated with non-adherence to TB treatment and poor treatment outcomes for new TB cases, which have been exposed to TB treatment for six months. After adjusting, the major risk factors identified were unemployment, living in a rural area, distance from home to the clinic where TB medication is collected on monthly basis, HIV infection and being very ill during treatment.

Based on the results it was recommended that patient centred and community based interventions should be redesigned and implemented by health care providers in order to strengthen TB control programme in ambulatory care. Further research is also recommended, as the tendency in the previous studies has been to focus on individual risk factors that contribute to TB treatment outcomes, yet it is a number of factors that interplay to produce a poor outcome. They cannot be looked at in isolation.

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## APPENDIX A QUESTIONNAIRE A ( English version)

DATE OF INTERVIEW	-----
INTERVIEWER'S NAME	-----

**Respondent:** Any able and willing person above 18 who is a new case on TB treatment

**NB: ENSURE YOU HAVE A SIGNED CONSENT FORM BEFORE YOU BEGIN**

### QUESTIONS TO BE DIRECTED TO RESPONDENTS

Please Tick or circle relevant answer

#### PART 1: SOCIO-DEMOGRAPHIC CHARACTERISTICS

SEX	MALE	FEMALE				
AGE	18-30	31-40	41-50	51-60	61-70	Above 70

MARITAL STATUS: SINGLE/ MARRIED/DIVORCED/WIDOWED/LIVING WITH A PARTNER

CITIZENSHIP	SOUTH AFRICAN	OTHER-(Please specify) -----
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HIGHEST STANDARD OF EDUCATION

No education	ABET	Grade1-5	6- 9	MATRIC
Tertiary qualification				



EMPLOYMENT STATUS:

EMPLOYED IN FORMAL SECTOR / EMPLOYED IN INFORMAL SECTOR/  
UNEMPLOYED/ SELF- EMPLOYED/ HOUSEWIFE/ STUDENT

FULL TIME

PART TIME

OCCUPATION (IF EMPLOYED)

1. Managerial job -----

2. Administrative job -----

3. Mining and Mineral Industry -----

4. Education sector -----

5. Factory and textile industry -----

6. Health industry -----

MONTHLY INDIVIDUAL INCOME – (circle)

-99/ 100- 999 /1000-1999/ 2000- 2999/ 3000-3999/ 4000-4999/ 5000 and above

MONTHLY HOUSEHOLD INCOME- 0-99/ 100- 999 /1000-1999/ 2000- 2999/  
3000-3999/ 4000-4999/ 5000 and above

HOW much is spent on?

Food -----

Clothing -----

Education -----

Medical expenses -----

Other please specify-----

ARE YOU RECEIVING ANY SOCIAL GRANT? Yes/No

Please specify which one:

Child support

Old age pension

Disability grant

Other (please specify)

RESIDENCE – OWN HOUSE/RENTAL/ INFORMAL SETTLEMENT/OTHER

WHAT IS YOUR HOUSE BUILT? Brick/ Wood/Mud/Cardboard/Tin/Other

HOW MANY PEOPLE LIVE IN THE HOUSE? -----

HOW MANY SLEEPING ROOMS? -----

AREA- RURAL----- SEMI-URBAN----- URBAN-----

Access to water supply -	River	Piped water	Communal tap	Other (please specify)
--------------------------	-------	-------------	--------------	------------------------

Type of sewage system

None	Pit latrine	Flush toilet	Other (please specify)
------	-------------	--------------	------------------------

In the last six months Have you ever gone to bed without food; because you could not afford it?

OFTEN/SOMETIMES/NEVER

In the last six months Have your child/children gone to bed without food because you could not afford?

OFTEN/SOMETIMES/NEVER

Alcohol intake	Daily	Once a week	Once a month	Never
Current				

Consumption levels: Heavy/ moderate/ small amounts

Past alcohol intake Yes/No

Smoking            Yes/ No

current

No. of cigarettes per day?-----

Have you ever smoked in the past? Yes/No

Illegal Drug use        Often /   Occasionally/Never

Type of drugs    Injectable/ pill /dagga

Have you ever used drugs in the past? Yes/ No

Have you developed drug addiction?    Yes/No

How far is your nearest clinic in kilometres from your home?        -----

Do you usually walk to the clinic? YES/NO

If you use transport to get to the clinic what is the Mode of transport?    Own  
transport/ taxi/ bus/ other(please specify)-----

How much does it cost to get there and back?        -----

Is it expensive for you? Yes/No

Tick (✓)

Have ever been counselled for HIV

Have you ever been tested for HIV?

If yes what was the result?

Yes	No
-----	----

HIVPositive/ HIVNegative (circle one response)

Have you ever been put on long term antibiotics, such as bactrim/cotrimoxazole

Yes/No/ Not sure

If positive are you on ARV treatment yet? Yes/ No

Are you having any other physical illness?

Yes	No
-----	----

If yes what? .....

### How does someone get TB?

(Tick (✓) respondent's answer for UNPROMPTED)

RESPONSE	UNPROMPTED	PROMPTED
1.Germ in the air		YES/NO/Don't know
2.Living in a crowded house		YES/NO/Don't know
3.Staying in a dirty place		YES/NO/Don't know
4.Poisoning		YES/NO/Don't know
5.Eat/drink something		YES/NO/Don't know
6.Eating or drinking leftovers from sick person		YES/NO/Don't know
7.Spitting on the ground		YES/NO/Don't know
8.From another person who has TB		YES/NO/Don't know
9.Smoking		YES/NO/Don't know
10.Drinking alcohol		YES/NO/Don't know
11.Witchcraft/evil spirit/curse		YES/NO/Don't know
12. Other (specify)		

### How would you know if someone had TB?

(Tick (✓) respondent's answer for UNPROMPTED)

Signs and Symptoms	UNPROMPTED	PROMPTED
1.Cough> 2 weeks		Yes/No/Don't know
2.Coughing up blood		Yes/No/Don't know
3.Loss of appetite		Yes/No/Don't know
4.Night sweats		Yes/No/Don't know
5.Tired-no energy		Yes/No/Don't know
6.Chest pain		Yes/No/Don't know
7.Shortness of breath		Yes/No/Don't know
8.Fever and chills		Yes/No/Don't know
9.Other ( please specify) _____	→	

### How did you get this knowledge?

(Tick (✓))

Friend                    -----  
 School teacher        -----  
 Partner                   -----  
 Television              -----  
 Radio                     -----  
 Newspaper             -----  
 Pamphlet                -----  
 Health worker         -----

Other ( please specify)-----

Can TB be cured? (circle one response) Yes/ No/ Don't know

Do you know of anyone who has been cured of TB?

(circle one response) Yes/ No/ Don't know

The quality of care received at the clinic is good

(Tick (✓))

Yes	No	Neutral
-----	----	---------

Did you complete full TB treatment ( Six months)

(Please circle)

Yes/No

Is the evidence of completion of treatment on your TB card?

Yes/ No/ Don't know

What TB drugs were you taking?

(Tick (✓) respondent's answer for UNPROMPTED ( do not offer suggestions) for PROMPTED circle one option

NAME OF DRUG	UNPROMPTED	PROMPTED
RIFAFour	YES	Yes/ Do't know.
RIFINAH	YES	Yes/ Do't know.

Have you been told about the outcome of the treatment?

Yes /No

Are you cured from TB?

Yes / No

( Interviewer will confirm status from the card ot TB register)

What motivated you to finish the six month course of TB treatment?

1.Will to live	
2.Effectiveness of medication	
3.To retain my job	
4.Seeing others getting better	
5.Other (specify)	

Did you keep your card throughout the treatment period?

Yes/ No

Did you keep all your appointments during the course of treatment?

Yes /No

What was the smear results after two months?

Negative/ Positive/ Don't know

( Interviewer will confirm status from the card ot TB register)

If you were smear positive, were you tested for MDRTB ?

Yes/ No

What was the results?

Culture positive for MDR/ Not isolated/ Not sure

Were you ever hospitalised during the course of treatment?

Yes/No

Did they change your TB medication to a new one?

Yes/ No / Not sure

Did you have DOT support? Yes/No

If Yes Who is your DOT supporter?-----

(Tick (✓))

Family	Shop	Teacher	Community	Councilor
Pastor	Friend	Other (please specify---		

How was your DOT supporter allocated?

Allocated by health worker	Own choice
----------------------------	------------

Frequency of DOT support

Daily	Weekly	Occasionall	Never	Other (please
-------	--------	-------------	-------	---------------

Were you stigmatised for having TB?

Yes/No/Not sure (circle one response)

Did you have any side effects fro the treatment you were taking?

Yes /No

If Yes which ones? (UNPROMPTED RESPONSE)

(Tick (✓))

1.Nausea	
2.Vomiting	
3.Jaundice	
4.Painful joints	
5.Skin rash	



6.Painful feet	
7.Other (please specify)	

Did you ever have to interrupt treatment ?

☐ Yes

☐ No

If yes for how long?

-----

Reason for interruption

☐ No money

☐ No transport

☐ Ill health

☐ Other (Please specify)

Have you ever stopped taking treatment?

Yes/No

If yes for how long were you on treatment? Less than 1 month/ 1 month/ 2 months/ 3 months/ 4 months/ Other-----

Reasons for stopping

☐ Too many pills

☐ Got better

☐ No food

☐ Got worse

☐ No Money

☐ Relocated to another area

☐ Other

Did you use any alternative medicine together with TB treatment

☐ Yes

☐ No

If yes, who did you Consult? –Traditional Healer /Diviner / Faith healer/ Homeopath/ Other (please specify

-----

What did you use?

Tick (✓)

1.Oral mixture	
2.Emetic	
3.Steam inhalation	
4.Nasal spray	
5.Inhalant	
6.Enema	
7.Holy water	
8.Other (please specify)	

Did it work? Yes/ No/ Do't know

If Yes how did it work?

Tick (✓)

1.Relieved cough	
2.Restored anergy	
3.Treated night sweats	
4.Restored appetite	
5.Other (please specify)	

How was your health been during treatment?

Very well	Very ill	fairly ill	reasonably well
-----------	----------	------------	-----------------

Did you carry on work while having TB treatment?

1.All the time	
2.Sick leave	
3.Dismissed from work	
4.Stopped voluntarily	
5.Other (specify)	

Has anyone living with you in recently been treated for TB?

Yes/ No/ Don't know (circle)

THANK YOU FOR YOUR TIME AND PARTICIPATION

Signature of interviewer\_\_\_\_\_ Signature of  
Supervisor:\_\_\_\_\_

Date:\_\_\_\_\_

Date \_\_\_\_\_

## APPENDIX B CONSENT DOCUMENT (ENGLISH)

### THE CONTRIBUTION OF PATIENT-RELATED FACTORS TO IN THE TUBERCULOSIS TB TREATMENT OUTCOMES. A CASE-CONTROL STUDY-

#### UMGUNGUNDLOVU DISTRICT

#### Consent to Participate in Research

You have been asked to participate in a research study.

You have been informed about the study by Mrs. Z. Ndwandwe.

Where applicable: You have been informed about any available compensation or medical treatment if injury occurs as a result of study-related procedures;

You may contact Zanele Ndwandwe at 083 460 2593 any time if you have questions about the research or if you are injured as a result of the research.

You may contact the Medical Research Office at the Nelson R Mandela School of Medicine at 031-260 4604 if you have questions about your rights as a research subject.

Your participation in this research is voluntary, and you will not be penalized or lose benefits if you refuse to participate or decide to stop.

If you agree to participate, you will be given a signed copy of this document and the participant information sheet which is a written summary of the research.

**The research study, including the above information, has been described to me orally. I understand what my involvement in the study means and I voluntarily agree to participate.**

---

Signature of Participant

---

Date

---

Signature of Witness

---

Date



BIOMEDICAL RESEARCH ETHICS ADMINISTRATION  
Research Office, Westville Campus  
Govan Mbeki Building  
Private Bag X 54001  
Durban  
4000  
KwaZulu-Natal, SOUTH AFRICA  
Tel: 27 31 2604769 - Fax: 27 31 2604609  
Email: [BREC@ukzn.ac.za](mailto:BREC@ukzn.ac.za)  
Website: <http://research.ukzn.ac.za/ResearchEthics/BiomedicalResearchEthics.aspx>

16 March 2010

Mrs. ZS Ndwandwe  
c/o Department of Public Health  
Nelson R. Mandela School of Medicine  
University of KwaZulu- Natal  
e-mail: [zanele.ndwandwe@kznhealth.gov.za](mailto:zanele.ndwandwe@kznhealth.gov.za)

Dear Mrs Ndwandwe

**PROTOCOL: The contribution of Patient- related factors in the TB Treatment outcomes. Umgunundlovu District. A case-control study. REF: BF112/09.**

### PROVISIONAL APPROVAL

We wish to advise you that your letter dated 31 August 2009 in response to letter dated 27 July 2009 has been noted and reviewed by a sub-committee of the Biomedical Research Ethics Committee.

The study is given **PROVISIONAL APPROVAL** pending receipt of:

1. Permission from the managers of Umgunundlovu Health District Clinics.
2. Post Graduate Education Committee approval.

Please refer to attached document "Permission to Conduct a Research Study/Trial". This must be completed and submitted to the Hospital Manager for signature. For King Edward VIII Hospital (KEH) and Inkosi Albert Luthuli Central Hospital (IALCH) studies please submit the document **together with items 1 to 6 as outlined on the form.**

Once the document has been signed it should be returned to this office.

Only when full ethical approval is given, may the study begin. **Full ethics approval has not been given at this stage.**

**PLEASE NOTE:** Provisional approval is valid for 6 months only - should we not hear from you during this time - the study will be closed and reapplication will need to be made.

Your acceptance of this provisional approval denotes your compliance with South African National Research Ethics Guidelines (2004), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at <http://research.ukzn.ac.za/ResearchEthics11415.aspx>.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

Yours sincerely

  
Ms D Ramnarain

Senior Administrator: Biomedical Research Ethics

## APPENDIX 8

### PERMISSION TO CONDUCT A RESEARCH STUDY/TRIAL

This must be completed and submitted to the Medical Superintendent/s / Hospital Manager for signature.

For King Edward VIII Hospital (KEH) and Inkosi Albert Luthuli Central Hospital (IALCH) studies please submit together with the following:

- i) Two copies of the final, approved protocol
- ii) Letter giving provisional ethical approval
- iii) Details of other research presently being performed by yourself (individually or as a collaborator)
- iv) Details of any financial or human resource implications to King Edward VIII Hospital
- v) If a clinical trial, please produce proof of payment or intention thereof to KEH

Once the document has been signed it should be returned to this office so that full ethical approval can be granted.

To: District Manager

#### PROTOCOL

#### THE CONTRIBUTION OF PATIENT-RELATED FACTORS IN TUBERCULOSIS TREATMENT OUTCOMES. UMGUNGUNDLOVU DISTRICT- A CASE- CONTROL STUDY.

Permission is requested to conduct the above research study at the hospital/s indicated below:

Site 1 address: Investigator/

15 Clinics in Umgungundlovu Health District. Principal: Z.S.I Ndwandwe

Co-investigator: \_\_\_\_\_

Co-Investigator: \_\_\_\_\_

Signature of District Manager:

mm

Date: 21/04/2009

Site 2 address: Investigator/s

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

Principal: \_\_\_\_\_

Co-investigator: \_\_\_\_\_

Co-Investigator: \_\_\_\_\_

Signature of Hospital Manager :

\_\_\_\_\_ Date: \_\_\_\_\_

NB: Hospital Manager/s to send a copy of this document to Natalia.