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RISK FACTORS OF UNSUCCESSFUL TUBERCULOSIS TREATMENT OUTCOMES AMONG TUBERCULOSIS PATIENTS IN SELECTED PROVINCES OF ZIMBABWE, 2013

By

Letitsia Mupanguri (1206016)

1206016@students.wits.ac.za

A research study submitted to the Faculty of Health Sciences, University of the Witwatersrand in partial fulfilment of the requirements for the Degree of Master of Science in Epidemiology in the field of Implementation Science.

Supervisor: Dr Juliana Kagura

Co-Supervisor: Dr Douglas James Momberg

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Declaration

I Letitsia Mupanguri declare that this research report is my own, unaided work. It is being submitted for the Master of Science degree in Epidemiology in the field of Implementation Science at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

Signature

28___day of__January__2022 in Johannesburg, South Africa

To my child

Shoana Tadisa Kufirwa

Born

14 May 2021

Abstract

Background: Zimbabwe remains one of the most tuberculosis (TB) burdened countries globally especially in Matebeleland province despite evidence-based treatment interventions. Factors associated with unsuccessful TB treatment outcomes are not fully understood therefore the aim of this study was to examine the prevalence and factors associated with unsuccessful TB treatment outcome of patients who started TB treatment between January and December 2013 in selected Southern Provinces of Zimbabwe.

Methods: This cross-sectional study used secondary data from medical records of 1971 of TB patients who started TB treatment between 1 January and 31 December 2013 from Bulawayo, Matebeleland North and Matebeleland South provinces. The outcome variable and main exposures were obtained from TB registers. Descriptive analyses were used to ascertain the prevalence of unsuccessful TB treatment outcomes. Multivariable logistic regression was used to identify factors associated with unsuccessful TB treatment outcome while adjusting for potential confounders.

Results: The study sample comprised of 1968 TB patients with 45.3% females who had the outcome data. The prevalence of unsuccessful TB outcome was found to be 551 (28.0 %) (CI: 26.0; 30.0) with 430 (78.0%) deaths, 77 (14.0 %) lost to follow up, 31 (5.7%) treatment failures and 13 (2.4%) not evaluated. The odds of having an unsuccessful TB outcome among retreatment cases was 1.63 (AOR: 1.63; CI: 1.21 ;2.21). HIV positive patients were 1.82 times (AOR: 1.82; CI: 1.39; 2.41) more likely to have unsuccessful TB treatment than those who were HIV negative. Other factors such as age (AOR: 1.01; CI: 1.00; 1.02), accessing TB treatment at a polyclinic (AOR: 0.53; CI: 0.38; 0.77), ART use (AOR: 0.08; CI: 0.05; 1.35), and CD4 count less than between 351-500 cells/mm3 (AOR: 0.20; CI: 0.04; 0.91) were associated with unsuccessful TB treatment outcome.

Conclusion: Death and lost to follow up were the most prevalent adverse treatment outcome**.** Factors such as age, HIV status, facility where treatment was accessed, Tb classification, ART use and timing were found to be associated with unsuccessful TB treatment. TB programs should intensify follow up of TB patients to ensure adherence and completion of treatment, especially HIV coinfected patients to avoid adverse treatment outcomes such as death and defaulters.

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Nomenclature

AOR	Adjusted odds ratio
ART	Anti-Retroviral Treatment
CD4	Cluster of differentiation 4
CI	Confidence interval
CPT	Co-trimoxazole preventive therapy
DOT	Directly observed treatment.
EPTB	Extra Pulmonary TB
HIV	Human Immunodeficiency Virus
HRQoL	Health-related quality of life
LMIC	Low and middle-income countries
MDR-TB	Multi-drug resistance Tuberculosis
MOHCC	Ministry of Health and Child Care
OR	Odds ratio
PTB+	Pulmonary TB positive
PTB-	Pulmonary TB negative
TB	Tuberculosis
WHO	World Health Organisation

CHAPTER 1

1 INTRODUCTION

1.1 Background

Tuberculosis (TB) continues to be a global threat and leading single infectious disease agent cause of deaths. The World Health Organisation (WHO) reported that more than a quarter of the population in the world have the bacteria but only 5-15% will fall sick with the infection, with TB accounting for 1.5 million deaths globally (1). Among all the TB cases in 2018, 24% were found in the African region and 11% of the incident TB cases are Human Immunodeficiency Virus (HIV) positive (2). However, in 2016, Africa and South East Asia regions had 82% of TB deaths among HIV-negative people, with 85% of deaths both from HIV-negative and -positive people (3).

The African region still carries a higher TB burden which has spiralled out of control. Possible causes are due to high levels of poverty which may lead to poor living conditions, insufficient access to TB drugs, underfunding of TB national programs, and the government not adhering to TB policies (4). HIV is known as the powerful factor that increases not only the risk of TB but also the progression of latent tuberculosis to the disease (1). These factors have exacerbated the transmission of TB in low- and middle-income countries (LMIC). The top 30 most TB affected countries accounted for 87% of all incident TB cases and this included India, Myanmar, Cambodia, South Africa, Namibia, Nigeria, Mozambique, and Zimbabwe.

The global TB strategy is to increase the TB treatment success rate (percentage of successfully treated TB patients) to 90 % by end of 2035 (2). According to the WHO, the 90% success rate is obtained through case finding, early diagnosis , correct medication and the directly observed (5).1n 2017, the WHO reported the treatment success rate in of 85% worldwide and the estimated incident cases of 34% were either not diagnosed, untreated or unreported (1). TB treatment outcomes includes cure, treatment completed, failed, died, lost to follow up and not evaluated (2). Unsuccessful TB treatment outcomes can cause catastrophic impacts on both individual and the community and can lead to increased morbidity and mortality. Inadequate TB treatment may cause multi-drug resistant TB which

may result in deaths (2).Therefore adequate treatment of TB and patient support is necessary to decrease unfavourable TB treatment outcomes. Identifying factors associated with unsuccessful TB treatment outcome helps in augmenting the implementation of interventions curtailing anti-tuberculosis drug resistance as well as stopping the tuberculosis transmission chain.

1.2 Contextual background

Zimbabwe is known to be a high TB burden country. According to WHO, Zimbabwe is the 17th of the 30 most TB burdened countries globally, with an incidence of 210 per 100 000 TB cases in 2018 (1). In 2015, the country had 242 per 100 000 incidence cases of TB (6). Zimbabwe carried out a national TB prevalence survey in 2014 and the survey showed that the prevalence of TB among all age groups was 292 per 100,000 population (6). This survey showed that TB treatment success rate was 81 % which was below the global recommended rate. The HIV-TB guideline in Zimbabwe, reported that the TB epidemic in the country is exacerbated by high prevalence of HIV, with 80% of the TB cases also being HIV-positive (7). The provinces of Bulawayo, Matebeleland South, Matebeleland North, and Bulawayo recorded the largest prevalence of HIV of 21%, 18%, and 19% respectively which was higher than the national HIV prevalence at 15.2% (8). Due to the dual epidemics in the country, TB treatment outcomes remains unfavourable.

Zimbabwe has managed to adopt strategies related to TB diagnosis, treatment and care such as using mobile truck for active screening, using standardised anti-TB regime regardless of HIV status, and using the Directly Observed Treatment (DOT) strategy (6). Despite all this, the TB treatment coverage in 2017 was 71% showing 30% of undiagnosed or unregistered patients causing ongoing TB transmission in the community (9). The country still faces huge difference in the treatment outcomes in different provinces in the country.

Higher TB related deaths in the provinces of Bulawayo, Matebeleland South and Matebeleland North has been observed in recent years (10). According to the National strategic plan, the proportion of TB related deaths in 2014 was highest in three provinces with Matebeleland North having 19%, Matebeleland South with 19%, Bulawayo with 15% (6). In 2013 alone, these three provinces had TB mortality rate of 16% which was higher than the country mortality rate of 10% (10). Therefore, this study will examine factors associated

with unsuccessful TB treatment outcome in the three provinces and give recommendations for action and inform policy changes.

1.3 Literature Review

This literature analysis will review the prevalence and the risk factors associated with unsuccessful TB treatment outcome. The literature review was guided by the conceptual framework that was adopted from socio-ecological framework and the health system construct (fig 1).

1.3.1 Prevalence of unsuccessful TB treatment outcomes

Recently LMICs have been reported to have a higher burden of TB related deaths (11). Different studies reported the prevalence of unsuccessful tuberculosis treatment outcome West Ethiopia (17.5%), Central Africa (27.6%), and India (14%) (12). In Asia, where TB is also common, the frequency of unsuccessful TB treatment outcomes in Cambodia, China, and Viet Nam was 10.1%, 3.0% and 9.1% respectively, where Viet Nam reported more treatment failures cases and Cambodia reported default and deaths as most frequent (13). These prevalence were lower than in other study settings, such as Malaysia that reported 19.3% of unsuccessful treatment outcomes of TB with deaths and lost to follow up as the most adverse outcome (10.2% and 5.3% respectively) and India with 55% of patients who did not finish treatment (14).

A meta-analysis study reported that in Africa, Sub-Saharan Africa in particular experienced a decline in TB treatment success rate in 2019 (15). A study in South Africa showed the TB unsuccessful TB treatment prevalence was 24.5%, 15.3% and 25.6 % among patients who were HIV positive, HIV negative and unknown HIV status respectively (16). Zambia had 43% of unsuccessful TB treatment outcome and the most adverse treatment outcomes were 29% not evaluated and 5 % deaths (17).In 2014, a study done in Zimbabwe reported that the prevalence of TB related deaths among the elderly (≥60) was 25% (18).

Unsuccessful TB outcomes can cause multi-drug resistant TB which is a risk to TB patients and also to their close contacts (19). Several studies showed that defaulting from treatment leads to prolonged infection which may cause resistant to antibiotics which can lead to multidrug-resistant TB (MDR-TB) or even worse outcomes (20,21). These studies also found

that people with MDR-TB have higher chances to default treatment, or even die compared to those without and high prevalence of MDR-TB is usually among patients with retreatment TB. Studies in Sub-Saharan African have shown that treatment of MDR is still minimum and complex in the region, creating a missed opportunity for successful TB treatment outcomes (22,23).

1.3.2 Risk factors of unsuccessful TB treatment outcome

Patient related factors

These are factors identified within an individual that can influence treatment patterns (24). The patient related factors include age, gender, knowledge, attitudes, and biomedical related factors.

Age

Age breakdown comparisons of TB treatment outcomes helps in informing TB age-specific interventions (18). Studies conducted in Africa and Asia showed that as age increases there is higher chances for all forms of unsuccessful treatment success (18,25). In Zimbabwe, a study showed that unsuccessful TB treatment outcomes such as death increased with increased age especially in people aged 60 years or more (18). This study found that the poor treatment outcomes in this age group were due to comorbidities causing high drug effects such as drug resistance and recurrent TB infection. In contrast, another study reported that younger adults (20-24years) and younger adolescents (10-14years) are had the worst TB treatment outcomes (26). The study depicts that these younger patients on TB treatment are likely to default from TB treatment due to increased drug abuse, alcoholism, and psychological effects of transitioning from teenage hood to adulthood.

Sex

Factors such as sex can influence TB treatment responses and there may be sex specific factors that influence treatment. A study in South Africa showed females were 93% less prone to unsuccessful treatment outcomes than their male counterparts (27). Similar studies suggested the possible reasons may be that males are more exposed to TB infection than women due to behavioural factors such as smoking, different occupation such as working in mines (17). However, other studies found that females who have TB have poorer treatment outcomes than males because of the higher co-infection of HIV-TB in this sex group (28,29).

These studies reported that higher co-infection among females was due to socio-cultural factors such as violence against women, lack of empowerment and no education which largely affect women in low- and middle-income countries. The different societal roles and occupation of males and females may not only affect their vulnerability to TB but also accessibility to care which influence treatment outcome. The contradictions in literature give opportunity for studies on sex disparities on TB treatment outcomes in a local context.

Knowledge of TB

Knowledge on TB is a predictor that undermines or encourages health-seeking behaviour such as late or early seeking treatment. Limited information about TB and its treatment causes unfavourable TB treatment outcome such treatment failure (12). A study done in Ethiopia found that treatment of TB patients is interrupted by lack of health education of the disease and information on importance of treatment completion (30). This study showed that patients with limited knowledge about the disease were 5 more times at risk of non-adherence to treatment compared to those with enough knowledge. A study in South Africa found that patients with TB were not given enough information of their TB medication due to task shifting, where the nurses believe that it was the doctors duty to inform the patient about their treatment (31). This study also reported that health workers did not have time to give patients comprehensive health education due to overload of work. These findings show that lack of knowledge of the disease may be due to poor communication breakdowns between providers and patients limited health literacy.

Biomedical related factors

TB diagnosis and TB category

A study conducted in Zimbabwe reported that lost to follow up was most found among patients with confirmed smear positive than those who were clinically diagnosed (10). Although studies showed that those with Extra Pulmonary TB (EPTB) patients usually have unsuccessful TB treatment outcomes than Pulmonary TB positive patients (PTB+). Another study in Ethiopia reported that most patients with a past record of TB or re-treatment cases have low treatment success that those with PTB+ (32). Even those with sputum smear negative diagnosed are at greater risk of unsuccessful treatment outcome (33). A study that was done in Gauteng Province in South Africa showed there was higher treatment default in retreatment cases than those with new cases(34). The study also found retreatment TB to be significantly associated with death and lost to follow up than the new cases. In countries with

high HIV endemic, retreatment TB after completion of treatment is mainly caused by the increase of HIV infection (10).

Co-morbidities affecting treatment outcomes.

HIV and Anti-retroviral Treatment (ART)

Co-infection of HIV and TB decreases the chance of successful TB treatment outcomes. Several studies in Africa have shown that patients who are HIV-positive are more prone to death and failure of TB treatment completion than those who are HIV negative (34–36).This evidence shows that unsuccessful TB treatment is highly driven by the HIV epidemic. HIV affects the immune system and increases vulnerability to infections; however, ARV can help reduce mortality and morbidity among these patients (16). A study that was done in Zimbabwe showed an increased risk of 2.60 of unfavourable treatment outcomes among TB patients who were co-infected with HIV and not on ART (37). A time series study which was conducted in Namibia showed that the completion and cure rates of TB increased significantly with increase of anti-retroviral treatment (ART) coverage although the treatment success rate was stagnant at 85% (38). It is known that co-trimoxazole preventive therapy (CPT) and ART increases chances of successful TB treatment but a study in South Africa reported that CPT alone without ART was not sufficient to cause successful TB treatment outcome (16). It also found that only 60% of people were on ART in 2011 which further exacerbated the poor treatment success rate. From these studies it is evident that even though co-infection of TB and HIV hinders successful TB treatment outcomes, initiating TB patients on ART can help attain favourable treatment outcomes.

Diabetes

People living with diabetes are two or three times at risk of falling sick with TB compared to those people with no diabetes (39). A study that was done in Zimbabwe showed that 8.5% of TB patients had diabetes, which was four times higher than what was reported in the general adult population (18). A meta-analysis study reported the prevalence of 15%, 11% and 10% of diabetes among TB patients in Nigeria, Tanzania and Ethiopia respectively, which further complicates TB treatment outcomes in these countries (40). Furthermore, two systematic reviews from 2011 and 2019 have shown that patients with diabetes mellitus are prone to adverse TB treatment outcome such as relapsing, failure and deaths as a combined outcome (39,41). Both studies showed that diabetes was associated with delayed culture conversion time and can be worsened by abuse of cigarette smoking, alcohol.

Community, Societal factors

These factors include the individual social support system such as families, peers and health care providers that affect treatment patterns (24). These include factors such as, stigma and discrimination and social support and patient and health provider communication and these can influence TB treatment patterns. These factors tend to promote or undermine TB treatment.

Social support system

Social support such as emotional support, companionship and financial support plays an important role in encouraging patients to complete their treatment(42). Patients who are on TB treatment need support as they face psychological distress which can cause poor adherence and treatment outcomes. In South Africa, a study conducted showed that TB patients with no family or community support failed to continue their treatment (31). Having no contacts during TB treatment was one of the predictive factors of unsuccessful treatment outcome (33). A local study from Zimbabwe reported that TB patients with adequate social support had better health-related quality of life (HRQoL) (43).

Provider-patient communication

TB patients disengage in treatment due to failure of health care providers to effectively listen and respond to misconceptions of TB and its treatment (44). Good communication between patient and health care provider can initiate or help patients complete their TB treatment. Another study reported that in South Africa health workers barely have time to give patients comprehensive health education due overwhelming workload (17).This study also emphasised that poor communication among the hospital staff caused poor coordinated patient care which may result in treatment failure.

Stigma and discrimination

Stigma and discrimination among people with TB affect their adherence to treatment (31). A study depicted that some caregivers and members of community are reluctant to interact or socialise with the TB patients due to fear of exposure to disease which negatively affect the TB patients' social relationships and treatment (31). Stigma and myths can cause depression,

low self-efficacy and a low emotional wellbeing of patients which instils fear to seek treatment (43).

Structural factors

These are broader social, economic, and political factors that can have an impact on treatment patterns of patients (24). These include policies and poverty.

Policies

Policies and interventions that ensures treatment completion are necessary to achieve the require cure rate of TB and different TB strategies apply to different setting in the world. Countries have comprehensive national strategic plans that prioritise interventions based on contexts and their capacity (5). Due to the double burden of HIV/TB co-infection, Zimbabwe developed national guidelines that strengthen the integration of HIV/TB services such as HIV testing, counselling, starting ART, and providing Isoniazid Preventive Therapy (IPT) to patient living with HIV (6). In South Africa, the National TB programme incorporated the DOT strategy and decentralise it to communities where community health workers supervise the TB patients at home (45).

Poverty

Poverty is a strong factor that affect access to TB treatment. Although TB drugs are free in most countries there is financial strain that comes with TB illness and its treatment. A study in Zimbabwe found that TB treatment costs were increased by follow-up visits to collect TB medication (43).In South Africa most of the patients diagnosed with TB were coming from poor communities with extreme poverty which can negatively affect their opportunities to seek care at specialized TB hospitals (31).

Health system factors

Health Facility type

The study in Lusaka showed that those who sought treatment at a referral hospital were likely to have better TB treatment outcomes compared to those who sought at an urban or peri-urban clinic (46). Another study in Uganda, reported that the patients at a private health facility had lower chances of finishing TB sputum smear monitoring used to monitor TB treatment response and identify early TB treatment defaulters (47). It reported that patients

who are treated at a peri urban or regional referral hospital had better chances of finishing sputum smear monitoring. Treatment of TB at a public hospital is better due to better health care services such as skilled personnel, enough medication and supplies as compared to the private institutions (47).

Service delivery

South Africa and India are well known to have made strides to control TB although analysis of patient cascade showed that the missed patients were not missing but are active in the health system that is failing to manage them appropriately (48). Another study from South Africa reported that among patients with TB symptoms only 8% of these patients were screened for TB (49). These results reflect a weak health system showing a missed opportunity in the health system to detect and monitor TB cases resulting in increased risk of unsuccessful treatment outcomes.

DOT as the model of treatment delivery

Between 2000 and 2018, 58 million people were saved through highly effective tuberculosis (TB) treatment through DOT (1). The TB cure rate in low- and middle-income (LMIC) countries is still below 50% and they can only achieve the cure rate above 90% if DOTs is done with intensive supervision (11). Most countries such as Namibia, Zimbabwe and Nigeria have also adopted the DOT as a patient-centred management strategy of TB (7,29,38).This strategy is to observe TB patients as they ingest each dose of their TB medication, increasing chances of completion of the medication. A systematic review showed that daily DOT improves TB cure by 15% comparing to self-administered treatments especially when the self-administered patients visit the clinic once month (50).However, the DOT strategy in LMICs have been compromised by inconclusive smear results (false negatives), and poor treatment outcomes such as poor adherence and failure to treatment and no monitoring of bacteriological endpoints (51,52). Several studies have shown that delay in implementing the DOTS can cause poor treatment outcomes such as deaths, defaulter and treatment failure (29,38).As evident from these studies, the TB treatment coverage and care are still suboptimal strategy in LMICs creating a higher burden of untreated TB, slowing down the attempt to reach the success TB treatment target set.

Although there is growing evidence of literature that mainly focused on risk factors associated with TB unsuccessful treatment outcomes, these pieces of evidence show no clear

factors that are major contributors of unsuccessful TB treatment outcomes in different countries. The contradicting findings in literature creates opportunity for further studies on the factors associated with unsuccessful TB treatment outcomes.

1.4 Conceptual framework

The conceptual framework used in this study was used to guide the literature review. It was built using constructs of the socio-ecological framework and health system construct. The socio-ecological framework is a theory-based framework used to understand multifaceted factors that influence treatment patterns (24) .This framework showed that the outcome can be influenced by several factors such as individual, interpersonal, organisational factors and health system. These factors can cause either cause late or early initiation TB treatment, and non-adherence or adherence to treatment which may determine treatment outcomes.

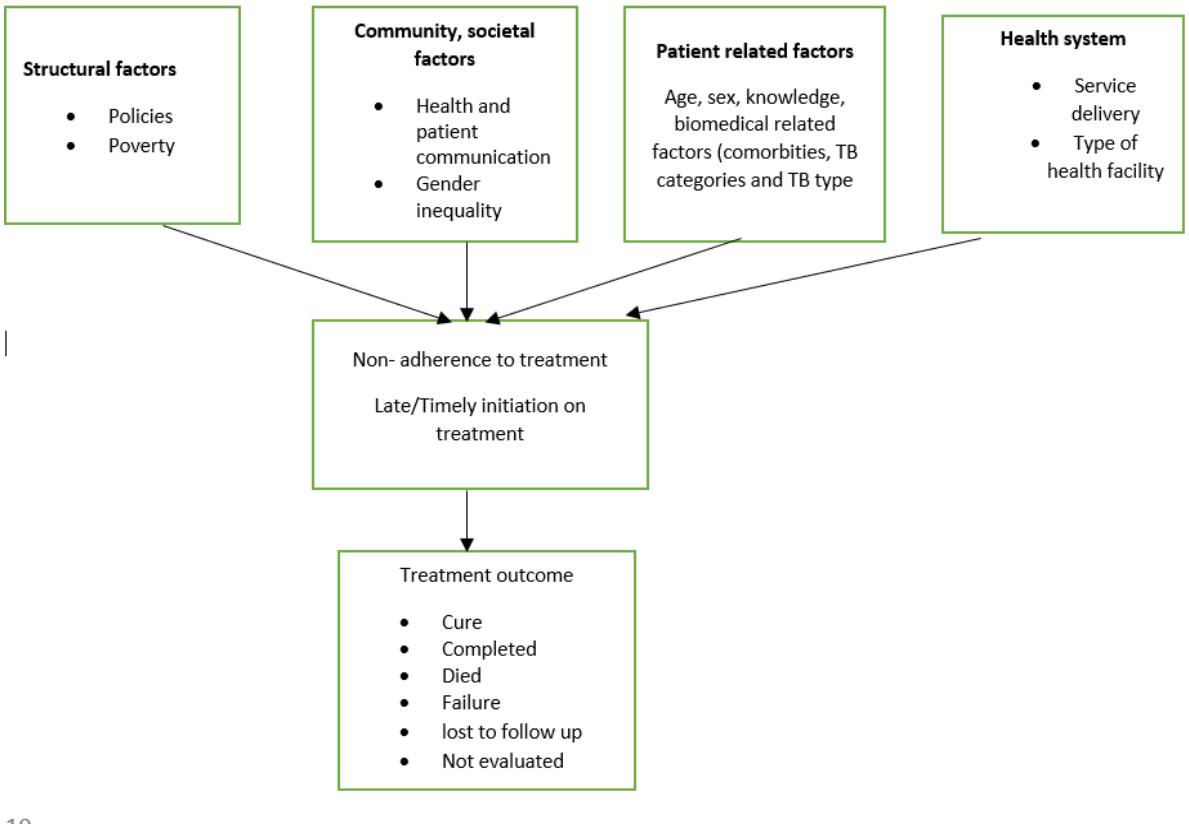

Figure 1: Conceptual framework showing factors associated with TB treatment outcomes

1.5 Problem Statement

The Southern region of Zimbabwe has reported poor TB treatment outcomes in recent years. In Bulawayo, TB related deaths increased 18 fold from 1988 to 2008 (53). In 2011, a study that was done in Matebeleland North reported 15% of TB related deaths, 8% TB treatment failures and 11% were lost to follow up (54) .The national programme data showed the provinces of Bulawayo, Matabeleland North and Matabeleland South in Zimbabwe as having highest TB case fatalities of 14%,16% and 18% respectively in 2013 (10).

This is a drawback to the country's fight against this 'old' disease, causing failure to reach the WHO optimum recommendation of the TB treatment success rate. In 2015, Zimbabwe reported a TB treatment rate of 81% which was far from the recommended rate of 90% (6). In 2017 a cohort study done in Zimbabwe showed 18.9% of lost to follow up of diagnosed TB patients resulting in treatment success of 59.9% (55).

1.6 Justification

Although in recent years, studies in different countries have focused on risk factors associated with unsuccessful TB treatment outcomes, they have shown to differ in predictive factors according to local context of the study population. There are no clear factors causing unsuccessful TB treatment outcomes in these countries. In attempt to achieve the global recommended TB treatment target, it is important to identify factors causing poor TB treatment outcomes in local context.

The primary study that was done in the southern region of Zimbabwe investigated factors associated with TB mortality, but it did not focus on risk factors of treatment outcomes such as death, failure, default and not evaluated combined. It is therefore compelling to investigate risk factors associated with these unsuccessful TB treatment outcomes in high TB transmission zones such as the southern region of Zimbabwe for better management of the disease and design of appropriate population or community strategies that reduces the disease.

1.7 Research question aims and objectives.

1.7.1 Research question

What are the risk factors associated with unsuccessful TB treatment outcomes among TB patients in three provinces of Bulawayo, Matebeleland North and Matebeleland South in Zimbabwe?

1.7.2 Aim

To examine the risk factors of unsuccessful TB treatment outcomes among TB patients who started treatment between January-December 2013 in Provinces of Matebeleland South, Matebeleland North and Bulawayo.

1.7.3 Objectives

1. To assess the prevalence of unsuccessful TB treatment outcomes of patients who started TB treatment between January and December 2013 in three provinces of Zimbabwe.

2. To identify the risk factors associated with unsuccessful TB treatment outcomes among these patients.

CHAPTER TWO

2. METHODOLOGY

2.1 Study setting

This study is a secondary study that used data from the primary study.

2.1.1 Primary study

The study was a retrospective cohort study that used routine data collected on TB patients who started TB treatment between January to December 2013 and followed through to their end of TB treatment outcomes i.e., 6 months after the commencement of TB treatment. This study selected three districts with the highest TB mortality from each three provinces of Bulawayo, Matabeleland North, and Matabeleland South.

2.1.2 Secondary study

Study design

This secondary study is a cross-sectional study. It used data that was collected at the end of TB treatment of study patients.

Study population.

This study includes nine districts altogether, three from each of the provinces of Bulawayo, Matabeleland North, and Matabeleland South. Districts such as Mzilikazi, Nkulumane and Emakhandeni were selected in Bulawayo Province. In Matebeleland North Province, Nkayi, Bubi, and Tshololotsho districts were selected, and lastly districts of Umzingwane, Matobo, and Bulilima were from Matebeleland South. Health facilities from these districts that offered TB services were included. The study population was TB patients from these nine districts who started TB treatment between 1 January and 31 December 2013.

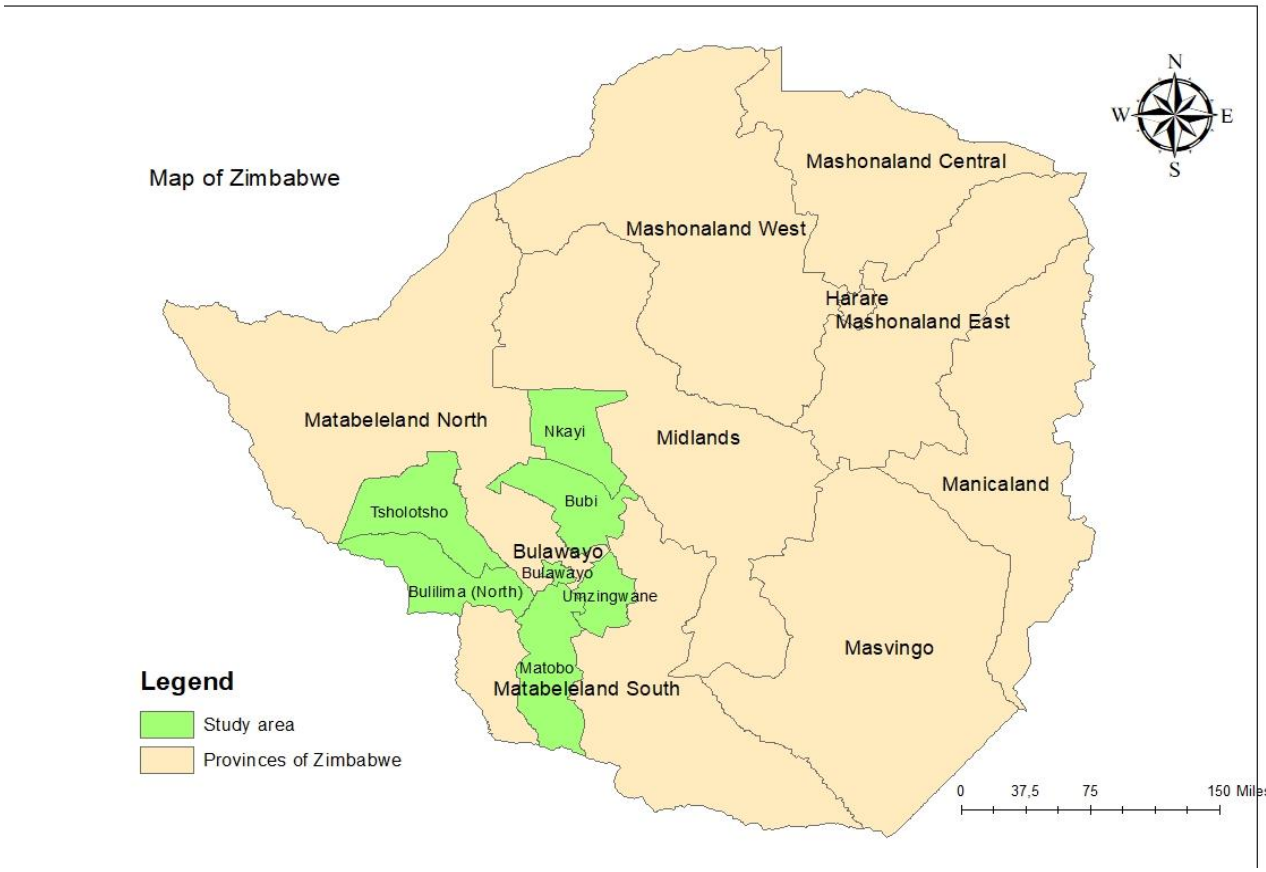

Figure 2: Thematic map of Zimbabwe made in ARC GIS showing study area

2.2 Study sample

This secondary study used a sample of 1971 of registered TB patients between January and December 2013 in the nine districts.

2.3 Inclusion criteria

All TB patients who initiated and completed treatment between 1 January to 31 of December 2013.

2.4 Exclusion criteria

Positive TB patients who initiated treatment between 1 January to 31 December but were still on treatment after 6 months of commencement of TB treatment.

2.5 Data Collection

Secondary data was obtained from the principal investigator of the primary study through email. The primary data was collected from routine TB registers in health facilities.

2.6 Measures

2.6.1 Outcome

The outcome variable is the unsuccessful TB treatment, which is defined as cases who had died during treatment, defaulted, failed treatment, and not evaluated.

The WHO classified TB treatment outcomes into two, successful outcomes and unsuccessful outcome (1). Successful treatment is when patients on TB treatment are cured and completed treatment.

Cured is when there is a confirmed negative smear or culture test in the last month of treatment

Completed treatment is when sputum smear or culture is negative in the last month of treatment and no evidence of failure.

Deaths, treatment failure, lost to follow up and not evaluated were defined as unsuccessful treatment outcomes (5,56).

Deaths: Any deaths of a patient before starting treatment or during TB treatment.

Failure: Patients with a TB positive results diagnosed through smear or GeneXpert at five months or more during treatment.

Lost to follow up: Patients with interrupted treatment for two or more consecutive months during treatment. In this study lost to follow up referred to defaulters.

Not evaluated: This includes patients whom the treatment outcome is not known and this also includes patients who transferred to a facility in another district to continue treatment but treatment outcome is still unknown at the reporting unit (1).

2.6.2 Exposure

The exposures included categorical variables and continuous variables.

Categorical variables

Sex, HIV-status, Duration on ART (in months, ART regimen, Comorbidities, CD4 count (cells/mL), Travelled, or resided outside the country before TB treatment, Type of health facility, TB category, HIV status, ART status, Type of retreatment TB.

Continuous variables

Age in years.

2.7 Data Management

De-identified secondary data in electronic form was sought from the person responsible for the primary study. Data was kept on the computer and synchronised to One Drive with a secured password. Data quality checks for completeness were done before analysis and for each variable, missing values were coded as missing and used in analysis. Variable such as CD4 was categorised according to the WHO clinical stages of HIV. STATA (version 16.1) was used as the software package for analysis.

2.8 Data Analysis Plan

Objective 1

- Descriptive statistical analysis

For background characteristics, descriptive analysis of the demographics and clinical characteristics was conducted. Categorical variables were stratified by TB outcomes and were presented as frequencies and proportions with their respective 95% confidence intervals (CIs). The Pearson's chi square test was used to show association of categorical variables and the outcome and fishers test was used for variables with frequency less than 5. For continuous variables' medians and interquartile ranges were recorded. Prevalence of unsuccessful TB outcome are presented as frequencies and proportions.

Objective 2

- Logistic regression analysis

To find the risk factors associated with unsuccessful TB outcome logistic regression models were constructed using the bivariate and multivariable logistic model. All variables were fit in the bivariate logistic regression model. Only variables with p-value less than 0.25 from the bivariate model were then fit in the multivariable logistic regression. The models were tested for goodness of fit using the Hosmer- Lemeshow and collinearity was tested using the tolerance method. Variables that included such as HIV status, TB classification, and category of TB were run while adjusting for age and health care facility. Variables such as ART use recorded, ART initiation in relation to start of TB treatment, and CD4 cell count at ART initiation were limited to those who were HIV positive. After testing for collinearity using the tolerance method multivariable logistic regression models were run separately adjusting for

confounders. Adjusted odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) was estimated for significant variables ($p < 0.05$) in the multivariable logistic regression model.

2.9 Ethical issues

A written permission to use the secondary data was sought from the Principal Investigator of the primary study at the Ministry of Health and Child Care (MOHCC) in Harare, Zimbabwe. The primary study MRCZ reference number is MRCZ/A/1994 and the union Ethics Advisory Group (EAG) reference number is 70/15. Ethical approval to do the secondary study was sought from the Human Research Ethics Committee (Medical), University of Witwatersrand, with certificate number M210137.

CHAPTER 3

3 RESULTS

This chapter describes the findings of this study which includes characteristics of study participants, prevalence, and risk factors of unsuccessful TB treatment outcomes of enrolled TB patients in Southern region of Zimbabwe.

3.1. Study characteristics of enrolled TB patients

A total of 1971 registered TB patients were enrolled in the study and 1968 patients were initially analysed. 3 participants were excluded from analysis because they were still on treatment. Among the enrolled TB patients in the Southern province 2013, patients who had unsuccessful treatment outcome were 551 (28.0 %) (CI: 26.0; 30.0) with 430 (78.0%) deaths, 77 (14.0 %) lost to follow up, 31 (5.7%) treatment failures and 13 (2.4%) not evaluated.

Information on the demographics and clinical characteristics of these patients was stratified according to the TB treatment status as shown in Table 1. In terms of the demographics characteristics, the median age of patients with unsuccessful TB outcome was 36years with an inter-quartile range (IQR) of 29-45years.The proportion of males was higher (55.9%) among the patients with unsuccessful outcome, compared to males with successful outcome (54.0%). For the women, the proportion was higher in those with successful TB outcomes (45.7%). Among those with unsuccessful outcome, majority (48.3%) accessed their TB treatment at rural health clinic, while the minority (8.6%) accessed treatment at polyclinic. Of all the patients who travelled out of Zimbabwe a proportion of 3.2% had successful outcome and 2.9% had unsuccessful outcome.

Clinical records of the patients showed that more than half of the participants (84.0%) were newly TB diagnosed. The majority (7.3%) of patients with retreatment TB had an unsuccessful outcome and 4.3% had successful treatment outcome. However, smear positive pulmonary TB patients, 32.1% had successful treatment outcome and 26.78% had unsuccessful treatment outcome. The proportion of extra pulmonary TB among those with unsuccessful treatment outcome was 9.7%. With regards to HIV status of those with unsuccessful treatment outcome, 84.0% were HIV positive and 14.8% were HIV negative and 1.3% had unknown status. Of those who were not on ART a higher proportion 24.3% were among patients who had unsuccessful outcome as compared to those with successful

outcome 2.1%. Majority of the patients (43.9%) were more than 3 months on ART prior to starting TB treatment. For those patients that started ART within 2 weeks after commencing TB treatment, the majority (42.2%) had successful treatment outcome while minority (28.7%) had unsuccessful treatment outcome. Patients with unsuccessful treatment outcomes remained constantly higher (14.2%) among those whose CD4 count was less than 350 as compared to those whose CD4 count was between 500 and 1800cell/mm².

Table 1: Demographic and clinical characteristics stratified by TB treatment status of enrolled TB patients in the Southern province 2013.

Characteristics	**TB treatment outcome status**		**Total (N)**	**Proportion% (95% CI)**
	Successful n (%)	**Unsuccessful n (%)**		
Age (years)				
Median (IQR)	34 (27-43)	36 (29-45)	1964	
Sex				
Male	767 (54.0)	307(55.9)	889	54.7(52.5-56.9)
Female	648 (45.7)	241(43.9)	1074	45.3 (43.1-47.5)
Missing	4 (0.3)	1 (0.2)	5	
Type of health facility where treatment was accessed				
Rural health clinic	656 (46.2)	265(48.3)	921	46.9(44.7-49.1)
Mission/rural hospital	240(16.9)	101(18.4)	341	17.4 (15.7-19.1)
Polyclinic	219(15.4)	47(8.6)	266	13.5(12.1-15.1)
District/provincial hospital	300(21.1)	134(24.4)	434	22.(20.4-24.1)
Missing	4 (0.3)	2(0.4)	6	
History of travel outside Zimbabwe				
Yes	45(3.2)	16(2.9)	61	3.2 (2.5-4.1)
No	1 374(96.8)	533(97.1)	1907	96.8(95.9-97.5)
TB category				
New	1220 (86.0)	433(78.9)	1653	83.9 (82.1-85.4))
Retreatment	198(14.0)	115(21.0)	313	15.9 (14.4-17.6)
Missing	1(0.1)	1(50.2)	2	
TB classification				
PTB +	456(32.1)	147(26.8)	603	30.7 (28.7-32.7)
PTB -	527(37.1)	193(35.2)	720	36.6 (34.5-38.9)
EPTB	174(12.3)	53(9.7)	227	11.5(10.2-13.0)
PTB unknown	61(4.3)	40(7.3)	101	5.1(4.2-6.2)

Retreatment TB	198(13.9)	115 (21.0)	313	16.0(14.4-17.7)
New, missing	2 (0.1)	0 (0.0)	2	
Missing	1 (0.1)	1 (0.2)	2	
HIV status				
Negative	337(23.8)	81(14.8)	418	21.3(19.6-23.1)
Positive	1075(75.8)	461(84.0)	1536	78.0(76.1-79.8)
Unknown	7(0.5)	7(1.3)	14	0.7 (0.42-1.12)
ART use for those HIV positive				
No	29 (2.1)	112(24.3)	141	9.1 (7.8-10.6)
Yes	1046(97.3)	349(75.7)	1395	90.9 (89.4-92.2)
ART timing				
>3 months pre-TB treatment	309(29.5)	103(29.5)	412	29.4(27.1-31.9)
0-3 months pre-TB treatment	109(10.4)	63(18.1)	172	12.3(10.7-14.1)
<2 weeks post-TB treatment	442(42.2)	100(28.7)	542	38.8(36.3-41.4)
2-8 weeks post TB treatment	11(1.1)	4(1.2)	15	1.1(0.6-1.7)
ART timing unknown	177(16.9)	79(22.6)	256	18.4(16.4-20.5)
CD4 count				
≤350(Advanced immunosuppression)	246(22.8)	65(14.2)	311	20.3 (18.3-22.4)
351-500(Mild immunosuppression)	26(2.4)	2(0.4)	28	1.8(71.3-2.6)
501-1800 (Not significant immunosuppression)	30(2.8)	5(1.1)	35	2.2 (1.6-3.2)
Missing	775(72.0)	387(84.3)	1162	75.6 (73.4-77.7

Abbreviations: IQR (inter-quartile range), CI (confidence interval), PTB+ (smear positive pulmonary tuberculosis), PTB- (smear negative pulmonary tuberculosis), PTBNT (pulmonary TB not tested)

The association between unsuccessful treatment outcome and the independent variables was tested using the chi-square test. There were significant association between unsuccessful treatment outcome and factors such as age, type of health facility, CD4 count, ART timing, ART use, HIV status, TB classification, TB category ($p<0.05$) (see Appendix 2).

3.2 Factors associated with unsuccessful TB outcomes among TB patients in 2013.

The crude and adjusted odds ratio and their 95% confidence interval were used to identify the characteristics that are associated with TB unsuccessful outcome (Table 2).

Bivariate logistic results for factors associated with unsuccessful TB treatment outcome.

The relationship between the dependent variable and each independent variable was examined using the Bi-variate analysis.

Variables such as age, type of health facility where TB treatment was accessed, TB classification, TB category, HIV status, CD4 count, ART use and ART timing had p-values less than 0.25 (Table 2).

Multivariable analysis of factors associated with unsuccessful TB outcome.

The adjusted odds ratio of the multivariable analysis and their CI of factors associated with unsuccessful TB treatment are shown in table 2. Among all the models, Model 1 was the best model with a higher R squared than the other models.

Based on the first model of the multivariable logistic regression, age was one of the predictors of higher unsuccessful outcome (AOR: 1.01; CI: 1.00; 1.02). In all three models, accessing TB treatment at a polyclinic was almost 50% less likely to have unsuccessful treatment outcome (AOR: 0.53; CI:0.38; 0.77, 1st model) indicating that those who accessed treatment at other health care facility other than the polyclinic were at more risk of having unsuccessful outcome. According to first model, other factors that were significantly associated with unsuccessful outcome were: patients with pulmonary TB unknown, and patients who had retreatment TB were 1.63 times more likely to have unsuccessful TB outcome times (AOR: 1.63; CI: 1.21; 2.21). Patients with HIV status which was unknown were 3.78 times (AOR: 3.78; CI: 1.26; 11.37) more likely to have unsuccessful treatment outcome while those who were HIV positive were 1.82 times (AOR: 1.82; CI: 1.39; 2.41) more likely to have unsuccessful TB treatment than those who were HIV negative. The second model showed that patients who had CD4 count which was between 351-500 cells/mm3 had 20% less chances of having unsuccessful treatment outcome (AOR: 0.20; CI: 0.04; 0.91) than those with less than 350 cells/mm3. The second model showed that being on ART (AOR: 0.08; CI: 0.05; 1.35) was associated with a lower likelihood of unsuccessful TB treatment outcome. From model 3, starting ART within 0-3 months prior to TB treatment is 2.07 times the odds of having unsuccessful treatment outcome (AOR: 2.07; CI: 1.38; 3.09).

Table 2 : Bivariate and multivariable logistic regression analysis of factors associated with unsuccessful TB outcome among enrolled TB patients in the Southern province 2013.

Variables	Total (N)	Unsuccessful TB treatment outcome n (%)	Bivariate Logistic regression		Multivariable Logistic regression					
					Model 1 (n= 1,968)		Model 2 (n= 1536)		Model 3 n= 1536	
			Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value	Adjusted OR (95% CI)	Pvalue
Age (years)	1964	548	1.01 (1.00 - 1.02)	0.004	1.00 (0.99-1.01)	0.002	1.00 (0.99-1.01)	0.519	1.00 (0.99-1.01)	0.305
Type of health facility where treatment was accessed										
Rural health clinic	921	265 (28,77)	1.00		1.00		1.00		1.00	
Mission/rural hospital	341	101 (29.62)	1.04 (0.79 - 1.37)	0.769	1.05 (0.79-1.39)	0.713	0.98 (0.70-1.39)	0.948	0.96 (0.68-1.36)	0.824
Polyclinic	266	47 (17.67)	0.53 (0.38 - 0.75)	0.001	0.54 (0.38-0.77)	0.001	0.54 (0.36-0.81)	0.003	0.58 (0.38-0.88)	0.011
District/provincial hospital	434	134 (30.88)	1.05 (0.86 - 1.42)	0.697	1.06 (0.82-1.36)	0.617	0.86 (0.63-1.16)	0.321	0.78 (0.57-1.08)	0.138
TB Category										
New	1653	433 (26.19)	1.00		_	_	1.00		_	_
Retreatment	313	115 (36.74)	1.64 (1.27 - 2.11)	0.000	_	_	1.74 (1.29-2.36)	0.000	1.84 (1.34-2.53)	0.000
Missing			2.82 (0.18 -45-14)	0.464	_	_	2.89 (0.18-46.54)	0.454	4.19 (0.26-6.66)	0.312
TB class										
PTB +	603	147 (24.38)	1.00		1.00		_	_	_	_
PTB -	720	193 (26.81)	1.14 (0.89 - 1.46)	0.314	1.01 (0.78-1.30)	0.966	_	_	_	_
EPTB	227	53 (23.35)	0.94 (0.66 - 1.35)	0.757	0.97 (0.67-1.39)	0.851	_	_	_	_
PTB unknown	101	40 (39.60)	2.03 (1.31 - 3.16)	0.002	2.13 (1.35-3.40)	0.001	_	_	_	_
Retreatment TB	313	115 (36.74)	1.80 (1.34 - 2.42)	0.000	1.63 (1.21-2.21)	0.002	_	_	_	_

HIV status										
Negative	418	81 (19.38)	1.00		1.00		_	_	_	_
Positive	1536	461 (30.01)	1.78 (1.37 - 2.33)	0.000	1.82 (1.39-2.41)	0.000	_	_	_	_
Unknown	14	7(50)	4.16 (1.42 - 12.19)	0.009	3.78 (1.26-11.37)	0.018	_	_	_	_
CD4 count										
≤350(Advanced immunosuppression)	311	65 (20.90)	1.00		_	_	1.00		_	_
351-500(Mild immunosuppression)	28	2(7.14)	0.29 (0.07 - 1.26)	0.099	_	_	0.20 (0.04-0.91)	0.037	_	_
501-1800 (Not significant immunosuppression)	35	5 (14.29)	0.63 (0.24 - 1.69)	0.359	_	_	0.62 (0.23-1.68)	0.345	_	_
Not recorded	1162	387 (33.30)	1.89 (1.40 - 2.55)	0.000	_	_	1.44 (1.05-1.99)	0.021		
ART use for those HIV positive										
No	141	112 (79.43)	1.00		_	_	1.00		_	_
Yes	1395	349(25.02)	0.09 (0.06 - 0.13)	0.000	_	_	0.08 (0.05-1.35))	0.000	_	_
ART timing										
>3 months pre-TB treatment	412	103(25.00)	1.00		_	_	_	_	1.00	
0-3 months pre-TB treatment	172	63 (36.63)	1.73 (1.18 - 2.54)	0.005	_	_	_	_	2.07 (1.38-3.09)	0.000
<2 weeks post-TB treatment	542	100 (18.45)	0.68 (0.50 - 0.93)	0.015	_	_	_	_	0.77 (0.56-1.07)	0.118
2-8 weeks post TB treatment	15	4 (26.67)	1.09 (0.34 - 3.50)	0.884	_	_	_	_	1.29 (0.39-4.20)	0.670
ART timing unknown	256	79 (30.86)	1.34 (0.95 - 1.89)	0.099	_	_	_	_	1.46 (1.02-2.10)	0.039

Model 1 Assessing for TB classification and HIV status adjusting for age and health care level.
Model 2 Assessing CD4 cell count and ART use adjusting for age, health care level and TB category.
Model 3 Assessing for timing for ART uptake, adjusting for age, health care level and TB category.

CHAPTER 4

4 DISCUSSION

This chapter elaborates and discusses the significance and implication of the research findings of this study with reference to published data.

This study was a secondary data analyses from a retrospective study that was conducted in the Southern province of Zimbabwe in 2013 which showed more than double of TB mortality rate in the province than the mortality of the national. We examined the prevalence and factors associated with unsuccessful TB outcome of patients in the southern province of Zimbabwe in 2013. Findings of this study showed that the patients with unsuccessful TB treatment outcome was 28%. Factors such as age, accessing TB treatment at the polyclinic, retreatment TB, pulmonary TB not detected, HIV status, CD4 which was between 351-500, ART use and starting ART within 0-3 months and timing unknown were found to be associated with unsuccessful TB treatment outcome in this study.

The prevalence of unsuccessful TB treatment outcome in this study was 28% with death and lost to follow up being the major unsuccessful TB treatment outcomes. Literature has shown that the TB treatment outcome is a significant indicator that evaluates the performance of TB programmes (2), and this high prevalence causes the success rate to fall below the 90 % WHO recommended success rate. The prevalence of this study is comparable with a study that was done in South Africa that showed 30% of the TB patients who had defaulted, failed treatment and died as their outcome (57). Similarly other studies showed that among the TB treatment outcomes, death and defaulter were the main unsuccessful TB outcome (32,36). Our study had a higher prevalence than that found in Malaysia (19.3%) with death and lost to follow being the most adverse outcome (14).

Despite the WHO recommended cure rate, these studies have proven that substantial shortfalls in TB treatment success are common in LMICS. This unsuccessful treatment outcomes provides opportunity for development of resistant TB which is an expensive and difficult disease to treat. In Zimbabwe, TB diagnostic services and free drugs are free to all persons (1). However, this study showed strong evidence that other predictive factors such as type of health facility, TB type, retreatment cases can cause unsuccessful TB treatment outcome. Although structural and interpersonal factors were not explored in this study,

literature has shown that they can cause non-adherence to treatment. Therefore, it is important to explore underlying factors such as structural factors that causes unfavourable TB treatment in further studies.

Sex disparities in TB treatment outcome has always been poorly understood in literature. This study showed that nearly 60% of males had unsuccessful treatment outcomes which echoes with a study that found that males had more unsuccessful TB outcomes than women (46). Evidence has shown that women adhere to treatment once enrolled in treatment than men resulting in better treatment outcomes among women. This statement is supported by a study that found a higher default rate among males compared to females (58). However, this study hypothesised no association between sex and unsuccessful TB treatment outcome, contrary to other studies that found sex to be one of the risk factors of unsuccessful TB treatment outcome (14,59). Although our study did not find any significant association of sex, it supports facts that women adhere to treatment better than men, but other issues such as sex inequities may influence their uptake of medication or access to health care services. It is important for programs put into consideration the sex disparities on access to treatment and more focus should also be put on men to improve their treatment outcomes.

This study showed that as age increases the higher risk of unsuccessful TB treatment, similar to many studies (20,27,46). These findings are similar to a local study done in Zimbabwe that showed that unfavourable TB outcome such as death increases proportionally with age (18). These studies compliment the fact that as one grows older the immune deteriorates and are more vulnerable to increased co-infections which may cause poor treatment outcomes.

Most studies found smear positive sputum and smear negative sputum test to be associated with unsuccessful TB outcome (18,28), a finding as opposed to our study. The difference may be attributed to difference in analysis. However, our results showed association between TB retreatment patients to be at more risk of unsuccessful TB outcome compared to new patients which is coherent with many studies (14,33). Most retreatment patients have history of poor adherence to treatment, more rates of lost to follow and higher drug resistance resulting in poor treatment outcomes.

Evidence have shown that health system factors such as type of health facility was associated with treatment outcome(32). Our study found that patients from a polyclinic had lower

chances of having unsuccessful outcome than those accessing at rural health clinic. Our study showed different results from a study that found referral hospitals have better chances of unsuccessful TB outcome (60). This relationship of facility setting, and treatment outcomes may be due to variations of workloads and the number of patients accessing treatment and the different care received at different facilities. In Zimbabwe, health care workers in polyclinics have higher donor funded retention allowances than those working in hospitals or rural clinics (60). Due to these reasons, it is possible that patients receiving treatment at polyclinic have successful treatment.

HIV is well known to be the major drive for the growth of TB epidemic, it is not surprising that this study found being HIV positive to be associated with unsuccessful TB outcome. This finding echo other studies in Africa have found that TB patients who are HIV positive are more at risk of unfavourable TB treatment outcome (16,46,59,61). Due to the realisation of this dual burden, Zimbabwe integrated the TB and HIV services where all presumptive TB patients in Zimbabwe are tested for HIV. While there is effort in Zimbabwe to integrate TB/HIV services our results have showed that not all TB patients had known HIV status which is a cause of concern. This may be due data management issues where HIV status is not recorded due to workloads of health care workers. Furthermore, our study showed patients who were on ART and early initiation on ART had better treatment outcome than those who were not on ART which is consistent with other studies (46,62). Being on ART results in 64–95 % reduction of risk of deaths among TB patient if initiated early(63).
Our study showed that half of TB/HIV coinfected patients had no CD4 count recorded even though in Zimbabwe, all HIV positive patients can start ART irrespective of CD4 count.

This current study used secondary data thus it was limited on the variables which were recorded. Some of the important variables were not recorded such MDR, educational level, that could have been of importance in the study. Although this study can determine correlation between two or more variables it cannot determine causation.

Despite this fact, this study adds on to the factors associated with unsuccessful TB treatment outcomes.

4.1 Recommendations & Conclusion

Although death was the most adverse treatment outcome, the higher proportion of defaulters is also alarming. Defaulting from treatment means a patient can be infectious for a longer time and spreads the diseases to others especially those infected with HIV, supressing the efforts to fight these two old diseases. Due to these serious consequences, it is important to ensure that there is standardized intense follow up of co-infected TB/HIV patients so that there are retained in care. Intense follow up of patients creates opportunities for continuous monitoring and fighting the dual burden of HIV.

Adherence and treatment completion are essential for improving tuberculosis control; therefore, it is important to address the underlying factors causing defaulting from treatment such as services delivery at health facilities and social support that encourages compliance to treatment. The study confirmed that age, HIV status, facility where treatment was accessed, Tb classification, ART use and timing was associated with adverse treatment outcomes, hence it urges the importance of TB programs to focus on predictors causing these treatment outcomes to ensure adherence among the patients. Although there is integration of HIV/TB services in all health facilities in Zimbabwe, strategies to strengthen supervision and support of patients should be put in place in these health facilities.

Due to globalisation, were many infectious diseases such as TB, coronavirus and many others can spread so easily, with older population at more risk of deaths, it is important for put strategies that encourages countries to have close collaboration that ensures continuity care of HIV/TB patients.

- To ensure continuity of care among TB patients, programs should intensify case identification and follow up by training community health workers for TB case identification especially among those living with HIV. The community health workers should be part of DOTs strategy.
- National TB programs should focus more on vulnerable population, especially the elderly, and HIV coinfected patients.
- TB programs should put in place strategies that encourage earlier diagnosis and better follow-up for TB patients.

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Appendices

Appendix 1: Plagiarism Declaration

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I Letitsia Mupanguri (1206016) am a student registered for the degree of MSc Epidemiology in Implementation Science in the academic year 2021.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: Mupanguri Date: 28 January 2022

Appendix 2: Chi-square test showing association of predictors with unsuccessful treatment outcome

Characteristics	Unsuccessful TB treatment n (%)	x^2 value	P value
Sex			
Male	307(28.56)	0.53	0.468
Female	241(27.05)		
Type of health facility where treatment was accessed			
Rural health clinic	265(28.77)	16.61	0.001
Mission/rural hospital	101(29.62)		
Polyclinic	47(17.67)		
District/provincial hospital	134(30.88)		
History of travel outside Zimbabwe			
Yes	16(26.23)	0.087	0.77
No	533(27.95)		
TB category			
New	433(26.19)	15.03	0.001
Retreatment	115(36.74)		
TB classification			
PTB +	147(24.38)		
PTB -	193(26.81)	26.31	0.000
EPTB	53(23.35)		
PTB unknown	40(39.60)		
Retreatment TB	115 (36.74)		
HIV status			
Negative	81(19.38)		
Positive	461(30.01)	21.90	0.000
Unknown	11(50.00)		
ART use for those HIV positive			
No	112(79.43)		
Yes	349(25.02)	180.512	0.000
ART timing			
>3 months pre-TB treatment	103(25)		

0-3 months pre-TB treatment	63(36.84)	29.90	0.000
<2 weeks post-TB treatment	100(18.45)		
2-8 weeks post TB treatment	4(26.67)		
ART timing unknown	79(30.86)		
CD4 count			
≤350(Advanced immunosuppression)	65(20.90)		
351-500(Mild immunosuppression)	2(7.14)	29.44	0.000
501-1800 (Not significant immunosuppression)	5(14.29)		
Not recorded	387(33.30)		

Appendix 3: Ethics clearance certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Miss Letitsia Mupanguri

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M210137

NAME: (Principal Investigator)	Miss Letitsia Mupanguri
DEPARTMENT:	School of Public Health
PROJECT TITLE:	Risk Factors of unsuccessful tuberculosis treatment outcomes among tuberculosis patients in selected provinces of Zimbabwe, 2013
DATE CONSIDERED:	29/01/2021
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr J. Kagura and Dr D.J Momberg
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	16/03/2021

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193. University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report.** The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **January** and will therefore be due in the month of **January** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature _____ Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

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