

PREVALENCE AND DETERMINANTS OF SPUTUM SMEAR NON-CONVERSION
IN SMEAR POSITIVE TUBERCULOSIS PATIENTS AT EPHRAIM MOGALE
MUNICIPALITY, LIMPOPO PROVINCE, SOUTH AFRICA

by

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DEDICATION

This dissertation is dedicated to the following people:

My husband: Ronald;

My children: Quintin and Yolanda;

My Parents: Johannes and Emily Maake;

My sister: Winnie Ledwaba: and

All my nieces

DECLARATION

I, -----Sylvia Radingoana declare that **PREVALENCE AND DETERMINANTS OF SPUTUM SMEAR NON-CONVERSION IN SMEAR POSITIVE TUBERCULOSIS PATIENTS AT EPHRAIM MOGALE MUNICIPALITY, LIMPOPO PROVINCE, SOUTH AFRICA** is my own work and that all the sources that I have used or quoted have been indicated and acknowledged by means of complete references and that this work has not been submitted before for any other degree at any other institution.

Sylvia Radingoana 14/08/2017

Full names Date

ACKNOWLEDGEMENTS

I would like to convey my greatest gratitude to the following people:

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- ❖ My beloved parents, Johannes and Emily Maake, for making my dreams come true.
- ❖ My sister, who was there for me when life was very trying
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ABSTRACT

Background

The present study presents data about the prevalence and determinants of sputum smear non-conversion in smear positive tuberculosis patients. Despite the intervention by the Sekhukhune District Department of Health through continual training and workshops of professional nurses in respect of the NTCP, there are still more challenges observed in terms of TB management.

Aim: To investigate the prevalence and determinants of sputum smear non-conversion in smear positive PTB patients after intensive phase of treatment.

Method: Quantitative, descriptive retrospective study of TB records was conducted. Data collection was done by extracting data from ETR.net and exporting it to excel. Data cleaning was done before analysis. Data analysis was done using the computer Statistical Package Software for Social research (SPSS) volume 23.1.

Findings: 834 TB patients' records were extracted from the ETR.net database. 34% of records were available at 2 – months; 57% of the patients were males; also, 81% of the patients were diagnosed/treated at PHC facilities; 52% of the patients were HIV positive; 69% percent of the patients who were smear positive grading p+++ failed to convert after two months.

In the univariate logistic regression patients with age 20 – 29 were observed to be 4.9 times likely (O.R. = 4.97) to be sputum positive (P = 0.142). Sputum grade 3(p+++) at the time of diagnosis was found to be significantly associated (P = 0.031) with sputum non – conversion after intensive phase of treatment. Conclusion: Two month sputum smear non-conversion is associated with pre-treatment sputum smear grading.

KEY CONCEPTS: Tuberculosis, Sputum grading, Intensive phase, Sputum smear conversions, Sputum smear positive pulmonary TB.

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DEFINITION OF CONCEPTS

Definition of concepts

The key concepts used will be defined as well.

Prevalence: Prevalence is defined as total number of cases of a disease in a given population at a specific time and it continues to mention that in epidemiology the number of all new and old cases of a disease or occurrence of an event during a particular period (Glaziou, Falzon, Floyd and Raviglione, 2013).

For the purpose of the study prevalence is the rate of smear conversion in patients with initial smear positive results after intensive phase of treatment.

Tuberculosis: tuberculosis refers to disease that occurs in someone infected with *Mycobacterium tuberculosis*. It is characterized by signs or symptoms of active disease might be Pulmonary Tuberculosis (PTB) or Extra –Pulmonary Tuberculosis (EXTB) (WHO, 2015).

Pulmonary Tuberculosis: Tuberculosis is an infection caused by bacteria called *Mycobacterium tuberculosis* and infects the lungs. In the study pulmonary tuberculosis means a serious infection of the lungs caused by the bacteria *Mycobacterium* (WHO, 2015).

Smear Positive Pulmonary Tuberculosis: (SPPTB): also defined as sputum fast acid bacilli positive pulmonary TB is the infectious form of TB and is mainly responsible for transmitting the disease. In the study SPPTB means TB that is AFB positive with grading (Scanty, P+, P++, P+++).

High bacillary load: Sputum AFB grading of P+++

Sputum smears non-conversion: Is defined by a positive smear results. In the study smear non-conversion is the persistent positive after intensive phase of treatment.

Pulmonary Tuberculosis Patient: is any person who diagnosed with TB and is seen at a health care facility.

Intensive phase of treatment: Initial phase of TB treatment whereby a combination of four different drugs is used and lasts for two months. For the purpose of the study intensive phase of Tuberculosis treatment is when a patient is initiated on TB treatment until two months of treatment.

Continuation phase of treatment: Phase of treatment starting after intensive phase lasting for four months characterised by combination of two drugs

Drug resistance tuberculosis: In the study drug resistance tuberculosis will mean when normal combination of treatment used for tuberculosis is not able to cure Tuberculosis.

Directly-Observed Treatment, Short Course (DOTS): Is the name given to the Tuberculosis control strategy recommended by WHO (Sharma, Lynrah, Sharma and Lyngdoh, 2013)

In the study DOTS will be defined as treatment support for TB patients for the duration of treatment

LIST OF ABBREVIATIONS

AFB: Acid –Fast Bacilli

AIDS: Acquired Immunodeficiency Syndrome

DOTS: Directly Observed Therapy Short course

DR-TB: Drug-Resistant Tuberculosis

ETR.Net: Electronic TB Register

HIV: Human Immunodeficiency Virus

IPT: Isoniazid Preventative Therapy

MDG: Millennium Developmental Goals

MDR-TB: Multi-Drug Resistant Tuberculosis

MTB/RIF: Xpert Mycobacterium/Rifampicin

NIMART: Nurse Initiated Management of Anti-Retroviral Therapy

PHC: Primary Health Care

SPPTB: Smear Positive Pulmonary Tuberculosis

SPSS: Statistical Package Software for Social Research

TB: Tuberculosis

TIER.Net: Three Interlinked Electronic Register

TFT: Training For Transformation

WHO: World Health Organization

XDR-TB: Extensively Drug-Resistant Tuberculosis

CHAPTER 1

1.1. INTRODUCTION AND BACKGROUND TO THE STUDY

Tuberculosis(TB) is a serious lung infection causing public health concern as it contributes to morbidity and high mortality rate globally alongside with HIV(Su,Feng,Chiu,Huang and Lee, 2011).TB is ranked as a leading cause of death in the world, especially in countries of low socio-economic status. Globally, 9.6 million TB cases were notified in 2014(World Health Organisation (WHO), 2015) where more men (5.4 million) are diagnosed with TB compared to 3.2 million women and contributes more to the burden of TB (Baker, Harries, Jean, Hart, Kapur, Lönnroth, Ottoman, Goonesekera and Murray, 2011).

Reports show that TB incidence has decreased by an average of 1.5% per year, and TB-related mortality having decreased by 47% since 1990 (Linzamo, 2011, WHO, 2015).A patient diagnosed with Pulmonary Tuberculosis (PTB) who is untreated is likely to infect 10–15 patients each year (Jayakody,Harries,Malharta,deAlwis,Samaraweera and Palewatta,2013). Despite the decrease in TB mortality in 2014, 1.5 million people died of TB included in the statistics were 890 000 men, 480 000 women and 140 000 children (WHO, 2015). Despite the association of TB and HIV, the statistics shows a high number of TB-related mortality among HIV negative patients estimated to be 1.1 million as compared to 0.4 million deaths in HIV positive patients (WHO, 2015).

Countries that are reported to have the highest number of incident cases include Indonesia, China, Nigeria, Pakistan and South Africa (Mabunda, Ramalivhana and Dambisya, 2014; WHO, 2015).Studies that look at TB infection in the context of reducing infectiousness in Africa have highlighted poverty as one of the drivers of this epidemic (Kuaban, Bame, Mouangue, Djella and Yomgni, 2009; Tweya,

Feldacker, Phiri, BenSmith, Tweya, Feldacker, Phiri, BenSmith, Fener, Jahn, Kalulu, Weigel, Kamba, Banda, Egger and Keiser, 2013).

The decrease in mortality is the result of effective diagnosis and treatment. Sputum smear conversion is part of monitoring effectiveness of treatment and reduction of infectiousness thereby decreasing the burden of disease (Jayakody, *et al* 2013). Studies have highlighted that delay in sputum conversion to negative increases the rate of relapse 5 – 6 times and also leads to emergence of resistant TB (Linzamo, 2011).

South Africa has one of the biggest TB epidemics in the world ranked 3rd highest after India and China. In 2014, 450 000 new cases of TB were reported of which 61% were co-infected with HIV (WHO, 2015). Incidence of PTB in South Africa was 234.2 per 100 000 in 2012 (Kigozi, Chikobvu, Heunis and van der Merwe, 2014). The TB epidemic is driven by social conditions, economic conditions, environmental conditions, HIV epidemic and inadequate management of TB programme (Sekotlong, 2014). Despite the burden of TB being so high there are only few studies which looked at smear pulmonary TB in order to assess factors contributing to smear non-conversion (Tiwari, Kumar and Kapoor, 2012; Kigozi *et al*, 2014).

Limpopo is one of the poorest and under-resourced provinces in South Africa, with about 80% of the households living below the poverty line, the highest rate in South Africa. Limpopo is the lowest in terms of PTB incidence with 354 per 100 000 cases in 2013. (Massyn, 2015) With this number of infectious patient within the community, there is a need for effective management of the patients (Gafar, 2013). The treatment outcome for Limpopo is very poor, considering that it has

the lowest PTB incidence, in terms of the cure rate Limpopo was at 74% as compared to the South African TB control programme target of 80% and WHO target of 85%. Remaining positive is a problem as it is directly related to remaining infectious (Department of Health, 2014; Sivhaga, Hlabano and Odhiambo, 2012; Acquah, Quaye, Walana, Vicar and Osei, 2015).

Treatment for TB is aimed at cure, decrease of transmission, decrease of deaths and prevention of acquired drug resistance Tuberculosis. Management of TB patients is reliant on the smear microscopy results (Salam, Rehman, Munir, Iqbal, Aasim and Saeed, 2016). Patient are diagnosed using genexpert and once tested positive an initial smear microscopy smear is collected for grading (Heunis, Kigozi, van der Merwe, Chikobvu and Beyers, 2014). The smear microscopy assist with the classification of patients whether patient is classified as smear positive pulmonary TB or smear negative pulmonary TB (Yellapa, Kandpal, Lall and Tabassium, 2016).

The grading is used to measure the infectiousness of the patient which guides the management of contacts. The grading is also used to monitor progress of patients on TB treatment. During treatment sputum samples are sent periodically to the laboratory to check treatment efficacy. The most widely accepted measure of treatment response in patients with pulmonary TB is the disappearance of acid-fast bacilli (AFB) from sputum smear (Yellapa et al, 2016). The TB treatment guideline provides guidance on when to collect sputum and how to manage patients following the sputum results (Department of Health, 2014).

After two months of treatment most patient with smear positive TB will convert to negative but presence of multiple cavities in the lungs, bacillary load, diabetes mellitus and tobacco smoking slows the sputum smear conversion time.

Smear conversion after intensive phase of treatment guides management of TB patients and is a predictor of cure at the end of TB treatment (Kayigamba, Bakker, Mugisha, Gasana and van der Loeff, 2012; Acquah *et al*, 2015).

Studies have shown that a considerable number of patients remains smear positive after two months of treatment and persistent positivity is related to poor treatment outcomes at the end of treatment (Kigozi *et al*, 2014). Other studies measuring associations between sex and two months sputum smear non-conversion have produced contradicting findings however longer delays before care seeking for TB in South Africa by males have been reported (Heunis *et al*, 2014). Delayed treatment onset is associated with higher bacillary load at diagnosis, which in turn is related to higher sputum non-conversion. (Heunis *et al*, 2014) These patients who still remain smear-positive after intensive phase of tuberculosis treatment may contribute to the transmission of TB to their family members and healthcare workers.

Limpopo province with sputum conversion rate of 59% is ranked fifth in South Africa. Studies to determine the prevalence and determinants of sputum positive TB were done in other countries like Sri Lanka, USA and Morocco and other provinces in South Africa like the Free State (Tweya *et al*, 2013, Bouti, Aharmim, Marc, Soualhi, Zahraoui, Benamor, Bourkadi and Iraqi, 2013). Sekhukhune district has 5 sub-districts which are Ephraim Mogale, Elias Motswaledi, Fetakgomo, Makhuduthamaga and Greater Tubatse (Mashishi, 2015). Literature on the prevalence and determinants of smear-positive Tuberculosis in Sekhukhune District is not available. The study will draw on different approaches to study the prevalence and determinants of smear positive TB after intensive phase of treatment.

1.2. RESEARCH PROBLEM

The prevalence of TB patients who remain positive after intensive phase of treatment is an indicator of management of patients and a predictor for the treatment outcome. An increased number of TB patients are associated with low smear conversion rates. Despite good adherence and treatment support 25% of initially smear positive patients remain positive after intensive phase of treatment (Visser, Stead, Walzl, Warren, Schomaker, Grewa, Swart and Maartens, 2012).

Previous studies have associated TB sputum smear non-conversion with age, sputum smear grading, HIV and sex (Kigozi *et al*, 2014). Studies that look at prevalence of smear positive tuberculosis and determinants after intensive phase of treatment were mostly done in African countries and there is less literature available in South Africa (Senkoro, Mfinanga and Mørkve, 2010, Kayigamba *et al*, 2012). Little is known about determinants of smear conversion in the South African context.

1.3. PURPOSE OF THE STUDY

The aim of the study is to investigate the prevalence and determinants of sputum smear non-conversion of smear positive PTB patients after intensive phase of treatment.

1.4. RESEARCH OBJECTIVES

- ❖ To determine the demographics of all TB patients in Ephraim Mogale
- ❖ To determine the proportion of patients remaining positive after intensive phase
- ❖ To identify the determinants of smear non-conversion in TB patients with smear positive pulmonary Tuberculosis after intensive phase of treatment.

1.5. RESEARCH QUESTIONS

- ❖ What are the demographic characteristics of patients who remain positive?
- ❖ What is the proportion of smear positive TB patients who remain smear positive after intensive phase of treatment?
- ❖ What are the determinants of smear non-conversion after intensive phase of treatment?

1.6. RESEARCH METHODOLOGY

1.6.1. Study setting

This study was conducted in Sekhukhune District, Limpopo, Ephraim Mogale local municipality, 38 km from Marble hall town in Limpopo province. Ephraim Mogale sub-district including all PHC facilities. To be discussed in detail in Chapter 3.

1.6.2. Research design

This study was a quantitative descriptive retrospective study of TB records for the period January 2014 to December 2015. This method is considered suitable because there is limited literature about the prevalence and determinants sputum smear non-conversion following intensive phase of treatment in Limpopo. The research design will be discussed in detail in chapter 3.

1.6.3. Study population

Population also known as unit of analysis is defined as a group of people, documents, events or specimens the research is interested in collecting information or data from (Botma, Greef, Mulaudzi and Wright, 2010). A population is further described as the total number of units or characteristics of the participants who will be included in the study.

The study used records of Pulmonary Tuberculosis (PTB) patients with an initial sputum smear positive results who have completed intensive phase of treatment for the period between January 2014 and December 2015. Total of 834 TB records were used.

1.6.4. Sampling and sample size

The process of selecting part of the population that will represent the accessible population is called sampling (Botma *et al.*, 2010). The sampling method that was used for the study was non-probability purposive sampling following convenient sampling method because the researcher was able to determine the most typical characteristics of the participants that should be included (Botma *et al.*, 2010). The sample size was records of all Tuberculosis patient registered on the TIER.net in Ephraim Mogale for the period January 2014 until December 2015 which included 279 smear positive TB records.

1.6.5. Inclusion criteria

Records of all TB patients enrolled at the facility for the period 2014- 2015 who have an initial or pre-treatment smear positive result and have completed intensive phase of treatment were eligible for inclusion in the sample.

1.6.6. Exclusion criteria

Records of TB patients who died before treatment and those with initial or Pre-treatment sputum smear result that was negative were excluded from the sample. Patients, who were transferred out, died or lost to follow-up before end of intensive phase, were also excluded.

1.6.7. Data collection

Data collection was done by extracting data from ETR.net and exporting it to excel. Data cleaning was done before analysis. Data collection will be discussed in details in chapter 3.

1.6.8. Data analysis

Data analysis is defined as a process whereby the researcher inspects and understands the meaning of the data (Blandford, 2013)).Data analysis was done using the computer Statistical Package Software for Social research (SPSS) volume 23.1 assisted by the university statistician and supervisor. Statistical techniques that were used for data analysis will be discussed in detail in chapter 3.

1.6.9. Reliability and validity

The ETR.Net is software designated for the capturing of TB patient information directly from standardized paper registers. At facility level, TB patients' clinical information is collated onto standardized paper TB registers by the TB nurse.

1.6.9.1. Reliability

Reliability is the consistency and dependability of a research instrument in measuring a variable, equivalence and internal consistency (Brink, van der Walt

and van Rensburg, 2012). A format was followed guiding on what variables to compare. Table 1.1 below shows variables selected.

Table 1.1.Variables for association

Variables of interest	
Independent variables	Dependent variables
Age	Smear conversion at two months
Gender	
HIV Status	
ART initiation	
Smear grading	
Local area	

1.6.9.2. Validity

Validity is the ability of an instrument to measure the variable that it is intended to measure (Brink *et al.*, 2012).The variables that were measured were according to the format developed.

1.6.10. Pilot study

Pilot study is a small scale preliminary study conducted in order to evaluate feasibility, time, cost, adverse events, and effect size (statistical variability) in an attempt to predict an appropriate sample size and improve upon the study design prior to performance of a full scale research project (Hulley 2007).For the purpose of the study the pilot study was not done as secondary data was used for the study.

1.6.11. Bias

Bias is an influence that produces an error or distortion, which can affect the quality of evidence in both quantitative and qualitative studies (Brink *et al.*, 2012).Potential bias in this study, could be due to sampling where records of TB

patients not diagnosed with PTB are included and was minimized by using standard guidelines to categorize patients.

Potential bias in this study could be due to sampling where records of TB patients not diagnosed with PTB are included and was minimized by using standard guidelines to categorize patients.

Implementation of the International Statistical Classification of Disease and Related Health Problems, 10th Revision (ICD-10) coding system presents challenges for using administrative data (Toson, Harvey and Close, 2015). ICD 10 coding was used to categorize patients only ICD 10 code 15.0 was used as it is patients with initial sputum smear that is positive.

1.7. ETHICAL CONSIDERATIONS

Is an accumulation of values and principles that address questions of what is good or bad in human affairs? Ethics searches for reasons for acting or refraining from acting; for approving or not approving conduct; for believing or denying something about virtuous or vicious conduct or good or evil rules (Stommel and Wills, 2004).

TB records are confidential records and should be stored in a secure area with limited access, and consider stripping them of identifying information, if feasible. For the study the names of the patients were removed from the excel spread sheet in order to keep the data anonymous. The paper based registers from the facility was used in a way that it was protected from tearing and no food or eating was allowed during handling of records.

1.7.1. Seeking permission

Proposal was forwarded to the University of Limpopo public health unit. Permission to conduct the study was obtained from the Turfloop Research Ethics Committee (TREC) and the Limpopo Provincial Research Committee.

Approval to collect data was obtained from the Limpopo department of Health. Consent from patients is not needed as no patient will be involved only files will be used. The information shared was kept confidential and no names were mentioned.

1.7.2. Confidentiality

Confidentiality was maintained at all times during the study. Names of participants were not mentioned. Records extracted from TIER.net were kept with the researcher and only shared with the supervisor and statistician (National Health Amendment Act, 2013).

1.7.3. Harm

The study was conducted in such a way that embarrassment, physical and psychological harm to the patients was avoided by protecting the records.

1.8. SIGNIFICANCE OF THE STUDY

The results of this study are hoped to assist with recommendations to the Department of Health TB control programme when developing guidelines for management of TB. Consideration should be made for consideration of determinants of sputum smear non-conversion when developing treatment programs. The significance of the study for the patients is that more support should be given to patient with high sputum smear grading as non-conversion is very high. Patient education should be strengthened in order to improve monitoring of TB patient through smear collection.

1.9. CHAPTER DIVISION FOR THE STUDY IS AS FOLLOWS

Chapter 1: Introduction & background / orientation to the study

Chapter 2: Literature review

Chapter 3: Research Methodology

Chapter 4: Presentation and interpretation of findings

Chapter 5: Summary, recommendations and conclusion

1.10. CONCLUSION

Chapter 1 presented an overview of the study and chapter 2 will focus on the national and international literature related to smear non-conversion in smear positive PTB patients.

CHAPTER 2

LITERATURE REVIEW

2.1. INTRODUCTION

Chapter 1 was an overview of the study. Chapter 2 will look at literature regarding smear conversion in TB patients and determinants of smear non conversion will be described. Literature review will look at TB diagnosis, treatment, management of patients on treatment and drug resistance TB

2.2. DIAGNOSIS OF TB

Tuberculosis is a serious infectious disease of the lungs and is mainly responsible for transmitting the disease. Two types of TB are known which are Pulmonary TB and Extra-Pulmonary TB. Pulmonary TB because it is infectious more efforts to monitor the patients is needed to decrease transmission. According to Department of Health (2014) the primary infection occurs on first exposure to tubercle bacilli, the inhaled droplet nuclei containing bacilli lodge in the terminal alveoli of the lungs.

For a person to develop TB the risk is increased by bacillary load, close contact with the index patient and duration of antitubercular treatment. Signs of Tuberculosis include cough for more than 2 weeks (24 hours in patients with HIV), unintended weight loss, night sweats, and fever. The use of Xpert to diagnose TB has improved detection of TB (Jayakody *et al* 2013, Moóre, Anyalechi, van der Walt, Smith, Erasmus, Lancaster, Morris, Ndjeka, Ershova, Ismail, Burton and Menzies, 2015). The standard procedure is collection of Gene Xpert for all people with symptoms of TB for diagnosis if positive; sputum specimen for microscopy is collected (Department of Health, 2014).AFB grading measures the infectiousness

Table 2.1. TB treatment regimen and phases

Pre treatment weight	Initial phase 2 months	Continuation phase 4 months	
		7 days a week	7 days a week
	RHZE 150/75/400/25	RH 150/75	RH 300/150
30 - 37 kg	2 Tablets	2 Tablets	
38 - 54 kg	3 Tablets	3 Tablets	
55 - 70 kg	4 Tablets		2
≥ 71 kg	5 Tablets		2

During the intensive phase patients are treated with a combination of 4 drugs which are Rifampicin, Isoniazid, Pyrazinamide and Ethambutol. The intensive phase of treatment is aimed at killing the bacteria. The continuation phase comprises of a combination of two drugs Rifampicin and Isoniazid (Ukwaja, Oshi, Oshi and Alobu, 2014).

Not all TB patients get the same treatment but treatment depends on whether a person is diagnosed with drug sensitive TB, drug resistant TB (MDR or XDR), also duration may be different depending on the site. Studies have shown that without treatment about two-thirds of patients will die within 5 to 8 years (Mabitsela, 2012).

2.4. MONITORING OF PATIENTS ON TREATMENT

2.4.1. Directly Observed Treatment Short-course (DOTS)

The DOTS strategy was developed following the declaration of TB as a global emergency in 1993 by WHO (Maimela, 2009). The five point strategies is implemented to combat the increasing incidence of the disease, also aimed at achieving the desired control objectives of reducing mortality and morbidity, reduce transmission and decrease the emergence of drug resistance TB (Maimela, 2009; Sharma *et al*, 2013).

The strategy has been adopted by many countries as an effort to improve treatment adherence and assist in monitoring of patients on treatment. Patients most often preferred family members as treatment supporters, whereas health

workers favour trained volunteers as DOT supporter (Parikh, Nataraj, Kanade, Khatri and Mehta, 2012). Studies have identified several factors that affect DOTS which include poverty, food shortage, cultural beliefs and side effects of medication. Poverty is associated with poor treatment outcomes as patients who receives disability grants prefers to remain uncured for the continuation of the grant (Mabunda & Bradley,2011).Smear conversion rate is an indicator that measures the effectiveness of the DOTS strategy (Tiwari *et al*,2011).

2.4.2. Sputum smear conversion

Sputum smear conversion is an effective predictor of the effectiveness of treatment and guides management of patients. Patient on treatment should be monitored bacteriologically. Sputum is to be collected for AFB at 7 weeks and at 23 weeks. Study done in Rwanda assessing the Rwandan control programme found that factors related to sputum smear conversion includes higher pre-treatment sputum grade, extensive disease involvement. Some studies also found that age and male sex were related to failure to convert (Kayigamba *et al.*, 2012, Sarkar and Seshadri, 2014). Knowing possible causes of sputum smear non-conversion is important in guiding the TB program as interventions can be tailored specifically to address the causes.

Two months sputum smear conversion is an important indicator for progress of TB treatment. The results of sputum smear at the end of intensive phase gives guidance to clinicians on whether the patient should be switched to continuation phase or intensive phase should be extended for another month (Lukoye, Adatu, Musisi, Kasule and Were, 2013).

Socio-economic status have been found to be a factor that has an impact on adherence to treatment with influence on treatment outcome (Sukumani, Lebeso, Khoza and Risenga ,2012).Cavitatory disease, high pre-treatment smear grade or a past history of TB are among other determinants of smear conversion at two months. Failure to convert at the end of intensive phase of treatment is a predictor for treatment failure. This patients need to be monitored closely in order to assist

in treatment adherence (Jeremia, PrayGod, Faurholt, Jepsen, Rangey, Anderson, Grewal, Friis, 2013, Parikh *et al*, 2012, Perfura-Yone, Kengne and Kuaban, 2014).

AFB is used to predict outcome of care during treatment of SPPTB patients. Studies have shown that above 5% to 30% of patients with 1st episode remains positive after two months of treatment and continue to contribute to the spread of the disease. Other factors found to be associated with sputum non-conversion include sputum grading of AFB 3+(in the study will be referred to as P+++), diabetes mellitus has also been linked to poor outcomes on TB. Patient who do not convert after two months on treatment have a one month extension of intensive phase with poor treatment outcomes. (Tiwari *et al*, 2011; Bouti *et al*, 2013; Tweya *et al*, 2013).

In order to ensure that each patient with TB symptoms and TB cases receives appropriate treatment it is very important to monitor patients on treatment. Early detection of patients with an increased risk of poor outcomes together with interventions such as treatment modification could reduce the burden tuberculosis (Kigozi *et al*, 2014).

According to (Su *et al.*, 2011) sputum acid-fast bacilli (AFB) smears serve as important indicators of treatment response for a patient to progress to continuation phase after two months of treatment the results of the AFB should be negative. There is also the importance of the AFB being collected according to the guidelines. WHO recommends the use of sputum conversion rates at two months as a useful indicator for TB control programs in monitoring TB program performance, also as a trigger for rigorous assessment of patients with smears that remain positive (Kayigamba *et al* , 2012). Patient education regarding importance of treatment adherence, sputum collection, the role of the sputum in TB management is essential in TB management.

The use of sputum examination in determining transition of patients to continuation phase as a criterion is not efficient (Su *et al*, 2011). Patient who improve bacteriologically but clinically still looks sick are also assessed using the

same criteria (Su *et al*, 2011).Pefura-Yone *et al* (2014) describe the criteria that are used in developing countries whereby transition to continuation phase of TB treatment is based on direct sputum examination for the presence of acid – fast – bacilli. Susceptibility to anti– TB drugs is not used as routine test due to resource constraints in developing countries (Pefura-Yone *et al*, 2014).

Early collection, non-collection and late collection of sputum can result in low smear conversion rate and may impact negatively on management of TB patients (Kayigamba , Bakker , Mugisha , De Naeyer , Gasana , Cobelens , van der Loeff, 2013).Proper management of TB is aimed at improving patient's lives and prevention of drug resistant TB (Department of health, 2014).The sputum smear completion rate is important in identifying the prevalence of smear positive patients after two months of treatment (Pefura-Yone *et al*, 2014).

Studies have shown that there is a high association between smear grading that is high and smear conversion at two months. Management of patient who remain positive after two months of treatment is important as a this patients continues to be infectious as they remain infectious for longer periods. Studies in Saudi Arabia and Burkina Faso have shown consistence in their findings that older TB patients are at a high risk of non-conversion (Kigozi *et al*, 2014).

2.5. DRUG RESISTANT TB

The most serious aspect of the TB epidemic is the emergence of drug resistance TB (DR-TB) in South Africa (Lukoye *et al*, 2013, Maurya, Kant, Kushwaha & Nag, 2011). According to National Department of Health (2013) DR-TB is a man-made problem which is largely due to human error in management of drug supply, patient management, prescription of chemotherapy and patient adherence (Baker *et al*, 2011). Currently two forms of drug resistant TB are known which is MDR-TB and XDR-TB.According to WHO (2014) there were 480 000 new cases of Multi Drug Resistant Tuberculosis (MDR-TB) nationwide.MDR-TB is resistance to two essential anti-TB drugs Isoniazid and Rifampicin,XDR-TB is resistance to Isoniazid, Rifampicin and most potent second line drugs(Lukoye *et al*,2013).

The study found out that over half of the patients with positive smears after the intensive phase of treatment have positive cultures for Mycobacterium Tuberculosis (culture non-converters), this patients remain contagious and might be having MDR-TB as the study suggest. Study revealed that about 1200 patients with TB in Cameroon remain contagious after completing intensive phase of treatment. Sub-Saharan Africa has a high prevalence of MDR-TB and contributes largely to the global epidemic. Strategies to reduce MDR-TB should be intensified in an effort to reduce global prevalence (Migliori, Dheda, Centis, Mwaba, Bates, O'Grady, Hoelscher and Zumla, 2010)

World Health Organization (2014) reports shows that South Africa has the most XDR-TB cases in the world and annual notifications have increased from 467 in 2009 to 1596 in 2012 with about 10% of MDR-TB cases having XDR-TB (Migliori *et al*, 2010).The numbers of MDR-TB and XDR-TB have increased due to the concurrent HIV epidemic and inadequate management of TB.Previous studies have grouped determinants of smear non-conversion into clinical, biological and sociological so as to guide treatment plans.

According to Tudor (2015) the South African drug resistant tuberculosis management guidelines as cited recommend that patients with drug-resistance tuberculosis (DR-TB) receive counselling to encourage optimal adherence to the lengthy, toxic, multidrug treatment regimens. Counselling should be started whilst patient is still on intensive phase of treatment in order to encourage adherence and prevent DR-TB (Tudor, 2015).Strengthening of existing TB control including DOT, re-enforcement of guidelines in routine Drug Sensitivity Testing (DST) monitoring of previously treated patients.

TB treatment is long-term and requires lots of efforts to improve treatment outcomes by understanding factors contributing to poor adherence (Xu, Lu, Zhou, Zhu, Shen and Wang, 2009). If poor adherence issues are not addressed there is a high possibility of patients remaining smear-positive after intensive phase of treatment (Xu *et al.*, 2009). In order to identify the factors leading to poor adherence firstly it is important to know how many patients did not convert and

then we can start unpacking factors that led to this problem (non-conversion) (Pefura-Yone *et al.*,2014).

2.6. CONCLUSION

Chapter 2 provided a review of literature pertaining to TB diagnosis, TB treatment, monitoring of patients on treatment and drug resistant TB management. The literature review described TB as a serious lung infection which has two types which are Pulmonary Tuberculosis and Extra- Pulmonary tuberculosis.

The aims of TB treatment are to cure, decrease transmission of TB to other patients and prevention of acquired drug resistance TB. Literature review revealed that factors related to smear conversion includes higher pre-treatment sputum grading, extensive disease involvement and gender. In chapter 3 the research methodology will be described.

CHAPTER 3

RESEARCH METHODOLOGY

3.1. INTRODUCTION

The literature review related to prevalence and determinants of sputum smear non conversion smear positive Pulmonary Tuberculosis (PTB) was discussed in Chapter 2. The focus of Chapter 3 is to describe the research methods and design used to determine the prevalence and determinants of smear non-conversion in Ephraim Mogale Municipality. The research methodology will be discussed in terms of research setting, research design, sampling, data collection and data analysis.

3.2. STUDY DESIGN AND APPROACH

A quantitative descriptive survey was used to conduct this study. A quantitative research determines causality among variables (Schneider, Whitehead and Eliot, 2007). According to Burns and Grove (2005), a descriptive design may be used for the purpose of developing theory, identifying problems in relation to the current practice, justifying current practice, making judgement, and determining what other researchers in similar situations are doing.

This study was a quantitative descriptive retrospective study of TB records for the period January 2014 to December 2015. According to Botma, Greef, Mulaudzi and Wright (2010), quantitative research is an essential tool for generating knowledge and for providing evidence for practice, education and management. Research frequently investigates questions developed during quantitative research or generates questions that should be explored qualitatively.

Retrospective record review was conducted on routine data recorded on ETR.Net for all smear positive TB patients (Coggin, 2016). Clinical record review is the use of previously recorded data for answering clinical queries. Records review is easy to use and uses less resources provided data is recoded correctly (Kigozi *et al* 2014, Sarkar and Seshadri, 2016). This method is considered suitable because there is limited literature about the prevalence and determinants sputum smear non-conversion following intensive phase of treatment in Limpopo.

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3.3. STUDY SETTING

The study was conducted in Sekhukhune District which is one of the five districts in Limpopo and has six sub–districts which are Ephraim Mogale, Elias Motswaledi, Fetakgomo, GreaterTubatse, Makhuduthamaga and Fetakgomo. Sekhukhune is a category C municipality which was developed in December 2000 and covers 13264 square kilometres (A complete guide to municipalities in South Africa, 2016). Only 5% of the Sekhukhune population lives in urban area. Main urban centres are Groblersdal, Marblehall, Burgersfort, Jane Furse, Ohrigstad,

Steelpoort and Driekop. A map of Sekhukhune district showing local municipalities is attached as figure 3.1



Figure 3.1. Map of Sekhukhune District showing local municipalities.

Ephraim Mogale municipality has one hospital which is situated at Tsimanyane village and 13 Primary Health Care (PHC) clinics. Matlala Provincial, situated at Tsimanyane, is the only hospital in the municipal area. There are also 2 health centres and 11 clinics. (Sekhukhune District Municipality, 2016) The TB data that was used for the study was generated from the PHC facilities using the paper-based TB registers. Individual patient records are taken from standard manual facility TB register and entered into a district-based data entry programme.

DOTS support is provided by health care workers around the Ephraim Mogale municipality and they are attached to the 13 PHC facilities. There are a number of DOTS support strategy available which are facility DOTS, family DOTS and community based DOTS. Due to the stigma attached to TB patients choose to have family DOTS supporters.

It is one of the poorest districts in the country, characterized by poor infrastructure and lack of safe water supply. Some 33% of the population still depends on natural water supply and 7% have no formal means of sanitation. The unemployment rate is at 61.6% which is very high (Health Systems Trust, 2016).

Bapedi traditional healers play a vital role in the primary health care of rural inhabitants in the Limpopo Province, South Africa. Due to high levels of poverty traditional medicines are considered essential for the physical and mental welfare of especially rural black households in South Africa, with more than 60% of all healing taking place outside the formal western-styled medical system. A considerable number of health-related problems, treated by Bapedi traditional healers in the poor rural areas of the Limpopo Province strengthen the fact that traditional medicine and traditional health practitioners represent the first line of healthcare for the majority of people in this province (Semenya and Potgieter, 2014).

3.4. STUDY POPULATION

McMillan and Schumacher (2010) describe a population as a group of elements or cases (whether individuals, objects, or events) that conform to specific criteria and to which it is intended to generalise the results of the research.

The study used records of Pulmonary Tuberculosis (PTB) patients registered on ETR.net for the period January 2014 and December 2015. The total numbers of records available were 834 TB records.

3.5. SAMPLING

The process of selecting part of the population that will represent the accessible population is called sampling (Botma *et al.*, 2010). The sampling method that was used for the study was non-probability purposive sampling following convenient sampling method because the researcher was able to determine the most typical characteristics of the participants that should be included (Botma *et al.*, 2010). The sampling method used as discussed in Chapter 1 was convenient sampling. Sample size included all TB records with initial smear positive results which had 279 records.

Inclusion criteria

Records of all TB patients enrolled on the ETR.net for the period 2014- 2015 who had an initial or pre-treatment smear positive result and have completed intensive phase of treatment were eligible for inclusion in the sample.

Exclusion criteria

Records of TB patients who died before treatment and those with initial or Pre-treatment sputum smear result that was negative were excluded from the sample. Patients, who were transferred out, died or lost to follow-up before end of intensive phase, were also excluded.

Records of patients who died before two months, those not evaluated after two months and those with missing data were excluded from the sample.

3.5.1. Ethical issues related to sampling

Due to confidentiality in safe keeping of patients records the records were exported only if they complied with the variables that were needed for the study. Secondary data is a challenge as some of the records were incomplete and as such could not be used.

3.6. DATA COLLECTION

Data collection will be described in terms of data collection procedure and data collection process.

3.6.1. Data collection procedure

Retrospective record review was conducted on routine data recorded on ETR.Net for all smear positive TB patients (Coggin, 2016). Clinical record review is the use of previously recorded data for answering clinical queries. Records review is easy to use and uses less resources provided data is recoded correctly (Kigozi *et al* 2014, Sarkar and Seshadri, 2016).

Data collection was done at sub-district office in Matlala hospital with the assistance of the sub-district TB co-ordinator and sub-district TB data-capture. Data was extracted from ETR.net and exported to excel sheet and thereafter copied to the researcher's storage device for safe keeping. The data was validated by checking the paper-based registers from the facility to identify mistakes in capturing.

Variables that were collected included:

Independent variables

Age and gender of the patient

Dependent variables

The dependent variables were determinants of smear non-conversion such as HIV status, antiretroviral treatment, co-trimoxazole prophylaxis, pre-treatment sputum smear grading and TB disease classification.

3.6.2. Data collection process

The data collection process started with an appointment after approval was granted from the Department of Health. The researcher made an appointment with the sub-district co-ordinator to discuss the details of the study and to submit the approval and proposal. The appointment was scheduled for 2 weeks after the meeting as there was a TB workshop. The data collection was done on the 26th July 2016. The sub-district computer was used which is located in the coordinator's office. The meeting in progress notice was placed on the door to prevent disturbances.

3.6.3. Ethical considerations related to data collection

The data capture was the person responsible for exporting the data and it was kept confidential between the researcher, coordinator and supervisors.

3.7. DATA ANALYSIS

Following the collection of data, the researcher has the task of describing and summarizing the data through the process called descriptive statistics. Descriptive statistics will be used as they convert and condense the collection of data into an organized, visual presentation. Data analysis was done using SPSS as follows.

3.7.1. Frequency distributions

The analysis involved descriptive analysis whereby frequency distribution of variables was determined to display distributions of the study participants in relation to the outcome measure which is smear non conversion. The mean and median was also used.

3.7.2. T-test

The independent t-test was used for variables having two categories as it assessed whether the means of two groups were statistically significant. This test

was performed at the 95% confidence level. The p-value of less than 0.05 in the study results was used for statistical significant difference in means between the categories which were investigated.

3.7.3. Categorical data

The grouping of variables to describe categories of individuals was used in the form of cross-tabulation, which explained the relationship between two or more categorical variables. Pearson chi-square was used to appraise the data for independence.

3.7.4. Logistic regression

In order to analyze the association of socio-demographic characteristics and smear non conversion, a framework of multiplicative model with the more obvious effect measure of odds ratio with an associated confidence interval was used (Greasley, 2008).

3.7.5. Odds ratios

The odds and relative odds (odds ratios) were calculated as these are used as useful ways of using the information in cross tabulations where one dimension of the table will be an outcome of interest (whether 2x2 tables or more complicated). This help to determine the odds of the probability of a TB patient not smear converting. Furthermore the data will be presented in a form of Charts, Graphs and Tables.

3.8. INTERNAL AND EXTERNAL VALIDITY OF THE STUDY

The information on the paper registers is then validated by the local area TB coordinator monthly. A copy of the validated information is then sent to be captured on the ETR.Net at the sub-district level. Once data is captured in the ETR.Net, it is available on a server and can be accessed at both the district and provincial levels (Kigozi *et al*, 2014).

The following measures were taken to ensure validity of the study

Cooperation of the TB coordinator ensured access to the records on ETR.net.

The selection of variables to be studied ensured that correct data was collected.

The findings of the research is applicable only to the study population due to the convenient sampling method it cannot be generalized.

3.9. CONCLUSION

Chapter 3 described the research methodology of the study and Chapter 4 will elaborate on the results of the study. Chapter 3 discussed the research methodology used in the study. Chapter 4 presents and describes the data collected through record reviews.

CHAPTER 4

PRESENTATION AND INTERPRETATION OF THE RESULTS

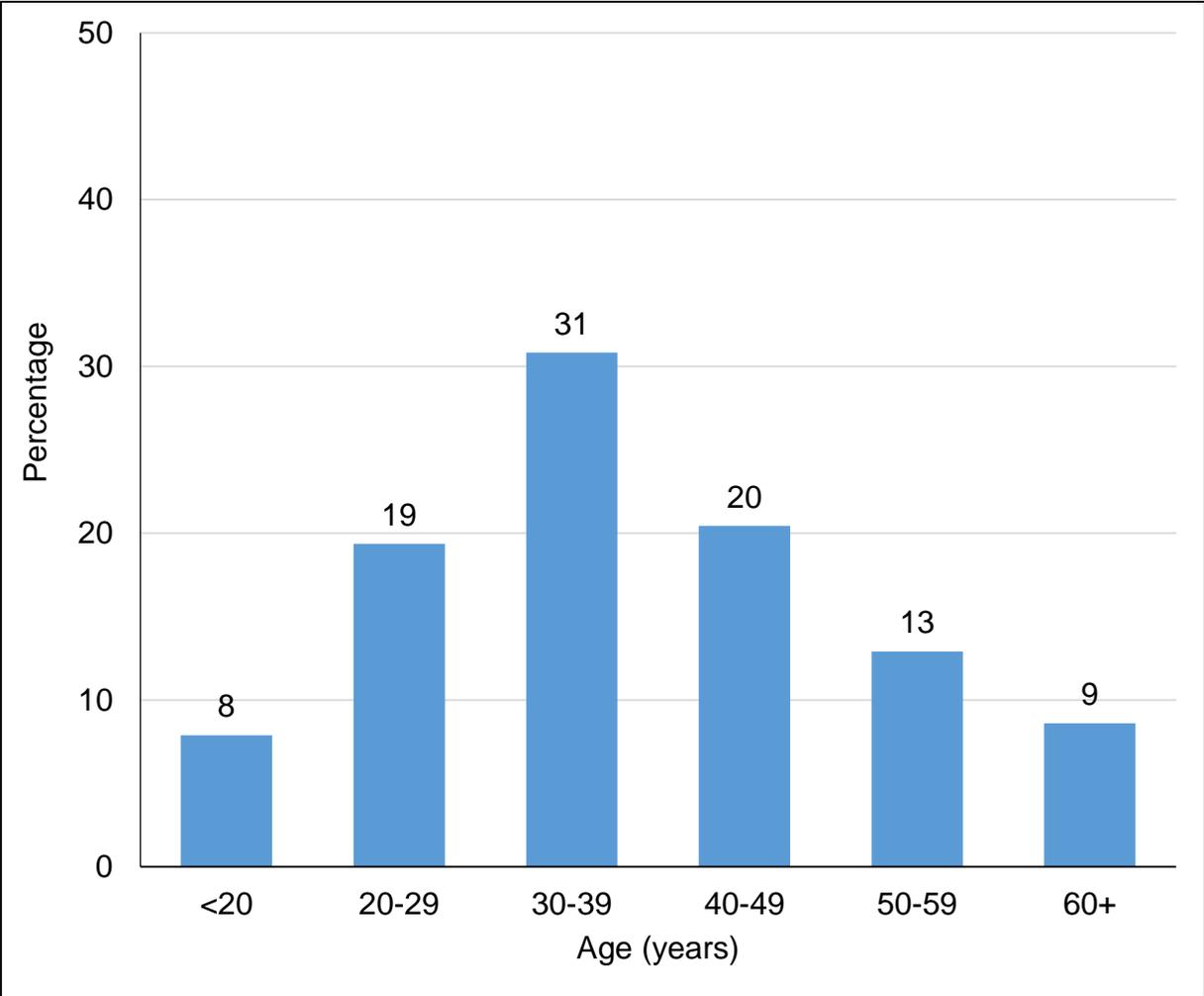
4.1. INTRODUCTION

Chapter 3 discussed the research methodology used in the study. Chapter 4 presents and describes the data collected through record reviews. The data is presented in the form of text, tables, figures and graphs. In this chapter the results of the study are presented focusing on socio - demographic characteristics of the participants, prevalence of PTB and smear conversion and lastly the determinants of smear conversion.

Demographic information of the study participants

A total of 834 TB patient records were extracted from the ETR.Net database and only 34% (279/834) of the records were available at 2-month. The age of this patients range from 14 to 83 years with average age of 38.8 ± 13.9 years. The age distribution of the participants is shown in Figure 1. Approximately 31% of the TB patients were in the age group 30 – 39 years and only few patients were in age groups less than 20 years and above 60 years at 8% and 9% respectively.

Figure 4.1: Age distribution of TB patients



As illustrated in figure 4.2 below, majority of the TB patient's records reviewed were males (57%).

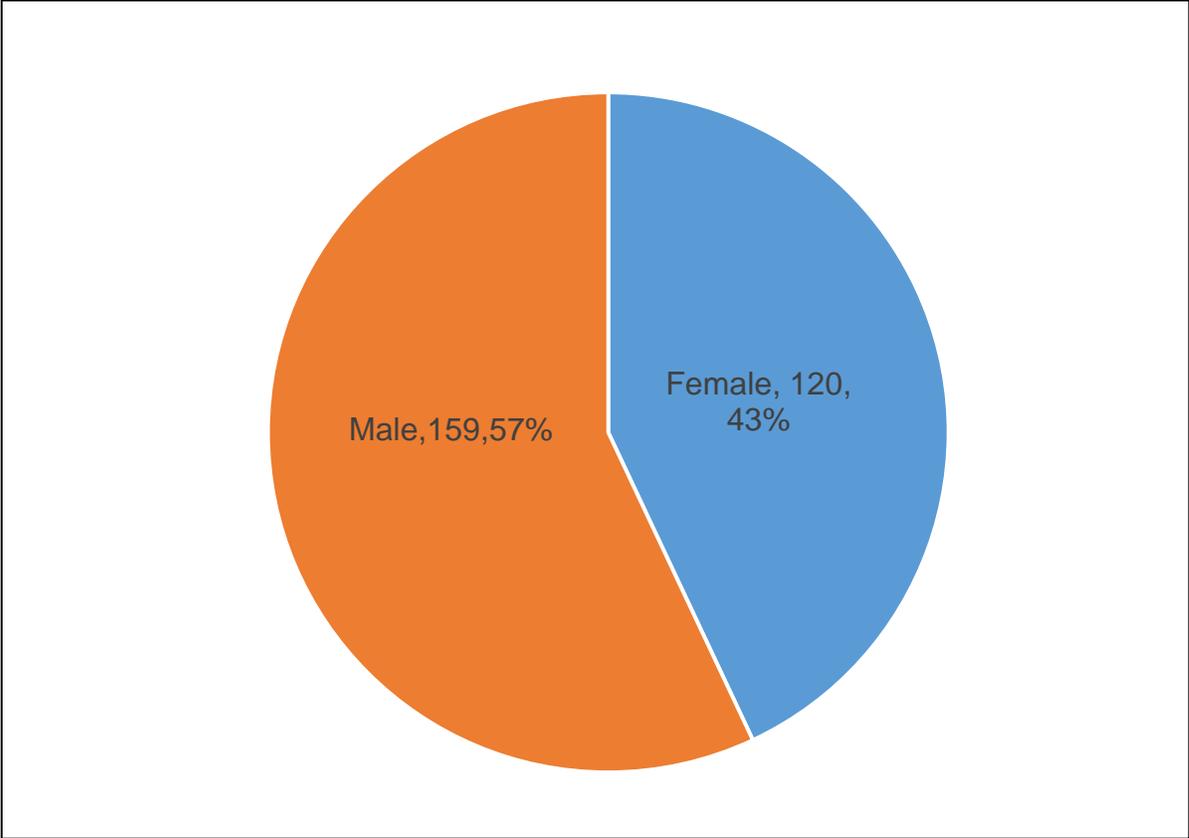


Figure 4.2: Gender Distribution of TB patient records reviewed

The facility where the TB patient were mostly tested and/or treated was primary health care been a clinic at 81% as compared to Hospital

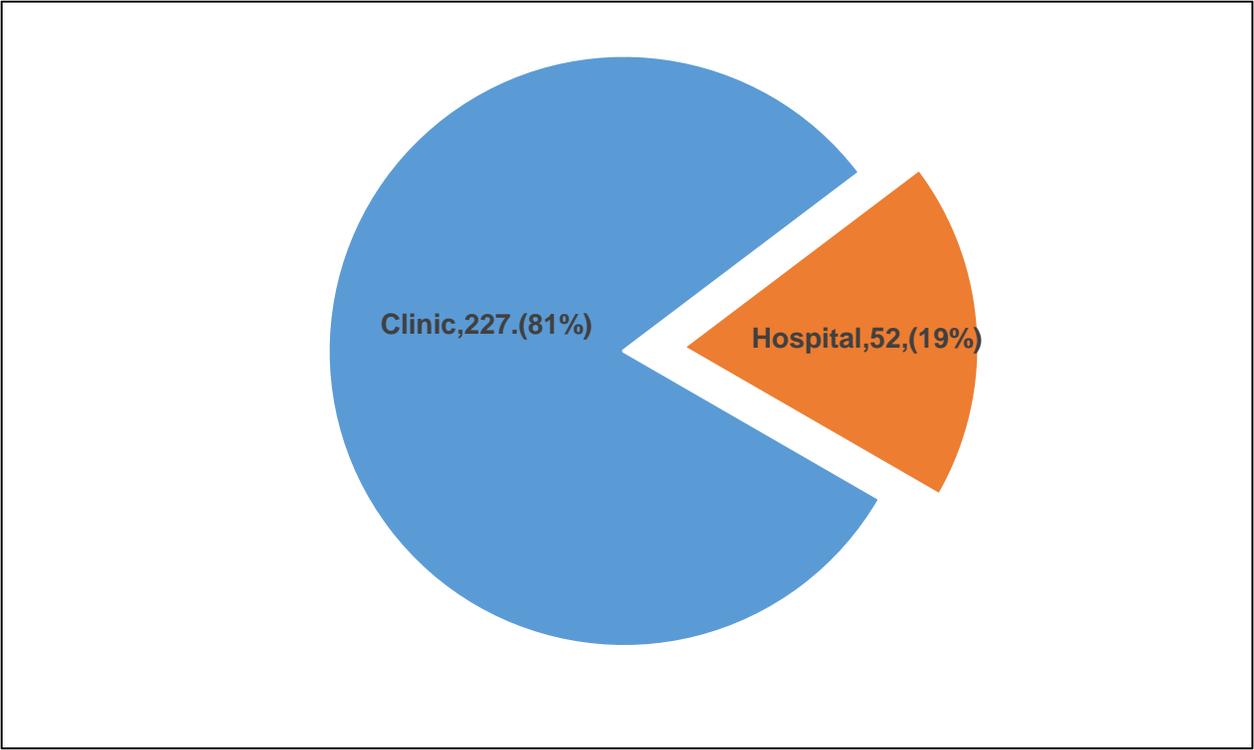


Figure 4.3: Facility for treatment of TB patient records reviewed

Prevalence and associate factors for HIV

Table 4.1 below presents the prevalence of HIV and the current study findings show that more than half (52%) of the patients were HIV positive. There were only 3 records with unknown HIV status and approximately 94% of the HIV positive patients were on ART programme.

Table 4.1: Association between HIV status and selected demographics of TB patient records reviewed

	N=279	HIV +ve (n=146)	HIV -ve (n=130)	HIV status unknown (n=3)	p-values
Age (years)					
<40	162(58%)	81(56%)	80(62%)	1(33%)	0.407
≥40	117(42%)	65(45%)	50(38%)	2(67%)	
Gender					
Female	120(43%)	80(55%)	39(30%)	1(33%)	<0.001*
Male	159(57%)	66(45%)	91(70%)	2(67%)	
Smear conversion					
Converted	144(52%)	67(46%)	76(59%)	1(33%)	0.112
Not converted	36(12%)	18(12%)	18(14%)	-	
Not evaluated	99(36%)	61(42%)	36(28%)	2(67%)	

* indicates level of significance at 95% CI

The association between HIV status and selected demographic variables as presented in Table 4.1 above, shows that patients younger than 40 years were more (58%) and having high co-infection rate but with no statistical significance from ages above 40 years. Gender was significantly associated with HIV/TB co-infection as more females were co-infected (67%) than males (37%) with *p-value*

<0.001. The TB smear conversion rate was not statistically different between the HIV positive and HIV negative TB patients.

The association between HIV status and the smear conversions stratified by level of health facility treatment as presented in Table 2 below, shows that approximately 65% of patients seen at the hospital tested HIV positive (34/52) vs. 49% of those seen at the clinic (112/227). Approximately 21% of the TB patients were not evaluated at clinic level as compared to 98% at hospital level with statistical significance of <0.001.

Table 4.2: Association between HIV status and smear conversion of TB patient records reviewed by facility level

	N=279	Clinic(n=227)	Hospital(n=52)	p-values
HIV status				
HIV +ve	146(52%)	112(49%)	34(65%)	0.006*
HIV -ve	130(47%)	114(50%)	16(31%)	
HIV status unknown	3(1%)	1(1%)	2(4%)	
Smear conversion				
Converted	144(52%)	144(63%)	-	<0.001*
Not converted	36(13%)	35(15%)	1(2%)	
Not evaluated	99(36%)	48(21%)	51(98%)	

* indicates level of significance at 95% CI

As illustrated in table 4.3 below, of the people who converted 63% are younger than 40 years. The conversion rate of those under 40 for whom an outcome is known is $90/(90+54) = 82\%$ and for all under 40 years is $90/(90+54+52) = 56\%$. More males (56%) had converted at end of intensive phase as compared to females at 44%. TB patients who had a smear grading of P+++ had a statistically significant high smear conversion rate, followed by P+, P++ and scanty at 48%, 27%, 19% and 6% respectively. The non-conversion rate was also significantly high in the patients with smear grading of P+++ followed by P+ and P++ at 69%, 17% and 14% respectively.

Table 4.3: Proportion of patients remaining positive after intensive phase (% in column)

	Smear conversion (%)			p-values
	Converted	Not Converted	Not evaluated	
Age (years)				
<40	90(63%)	20(56%)	52(53%)	0.286
≥40	54(38%)	16(44%)	47(48%)	
Gender				
Female	64(44%)	14(39%)	42(42%)	0.825
Male	80(56%)	22(61%)	57(58%)	
Grading				
Scanty	9(6%)	-	9(9%)	0.021*
P+	39(27%)	6(17%)	18(18%)	
P++	27(19%)	5(14%)	30(30%)	
P+++	69(48%)	25(69%)	42(42%)	

* indicates level of significance at 95% CI

Table 4.4: Univariate logistic model

	Odds 95% CI	p-values
Age		
<20	Ref	
20-29	4.97(0.58;42.32)	0.142
30-39	2.49(0.29;21.66)	0.409
40-49	4.46(0.49;40.19)	0.183
50+	3.93(0.45;34.12)	0.213
Gender		
Male	Ref	
Female	0.79(0.38;1.68)	0.548
HIV status		
Negative	Ref	
Positive	1.13(0.55;2.36)	0.735
Grading		
Scanty and P+	Ref	
P++	1.48(0.41;5.31)	0.546
P+++	2.89(1.11;7.60)	0.031

Univariate logistic regression was applied to evaluate the risk contributed by age, gender, HIV status and sputum grading on the sputum conversions at the end of the 2 months of treatment as shown in table 4.4 above. Patients with ages 20 - 29 years and 40 – 49 years were observed to be 4.9(O.R. = 4.97, 95% C.I. = 0.58–42.32) and 4.5 (O.R. = 4.46, 95% C.I. = 0.49–40.19) times more likely to have sputum conversion (P= 0.142) and (P= 0.183) respectively although not statistically significant.

Females were found to be 0.8 times less likely to have sputum conversion but it was not statistically significant. HIV positive patients were found to be 1.1 times more likely to have sputum conversion but was not statistically significant. The odds associated with higher sputum grading at the time of diagnosis and sputum conversion were 1.48 (95% C.I. = 0.41–5.31) and 2.89(95% C.I. = 1.11 –7.60) for P2+ and P3+ respectively. Sputum grade P3+ at the time of diagnosis was found

to be significantly associated ($P= 0.031$) with sputum conversion at the end of 2 months of follow-up of treatment.

4.2. CONCLUSION

Chapter 4 presented data analysis and interpretation of results. Chapter 5 will be about the discussion, recommendations, limitations and conclusion of the study.

CHAPTER 5

DISCUSSIONS, RECOMMENDATIONS, LIMITATIONS AND CONCLUSION

5.1. Introduction

The previous chapter presented data analysis and interpretation of results. Chapter 3 and chapter 4 discussed the research methodology that was followed when conducting this study and analysis, whilst this chapter focuses on discussion of findings and literature control to support study findings. LoBiondo-Wood and Haber (2010) described the purpose of literature control as a method of clarifying the findings and putting them into context. These findings emerged during data analysis of quantitative data analysis method. The following findings are categorized in order to discuss, conclude and recommend and address all the objectives set out in chapter 1. Chapter 5 will be discussion, recommendation, limitations and conclusion of the study.

5.2. Discussion

This is the first study in Ephraim Mogale Municipality of Greater Sekhukhune District in Limpopo Province to assess the prevalence and determinants of smear non-conversion in TB patients with smear positive pulmonary Tuberculosis after intensive phase of treatment. The discussion will be presented according to the study objectives

5.2.1. Objective 1: To determine the demographic characteristics of TB patients with smear collected at 2 months

The results of the current study revealed that the most of patients were less than 40 years of age. Furthermore, this study also showed a high number of TB cases among the economically productive age groups which is concurrent with other studies (Ukwaja, *et al.*, 2014). Massyn, (2015) however, found a relative differences in number of TB cases according to different age groups. The findings of the study are similar to the findings of studies done in India and Cameroon (Gafar, 2013 and Kayigamba *et al*, 2013) by age groups distributions. The findings

of the current study are also consistent with a study conducted in the Free State Province which shows that the most of TB patients were less than 40yrs of age Kigozi *et al*, 2014).

Other countries also show that the incidence of TB was highest among the 20-54 years age group. According to Jetan, Jamaiah and Jamaiah (2010) in their study in Malaysia, age group mostly affected was 21-40 years old (n=49; 37%). Studies show that, generally, more than 90% of all TB cases are found in adults aged 25-64 and older (Liao, Hsieh, Huang, Cheng, Lin, Chio and Ling, 2012; Majraand Acharya (2007; Cavalini (2010)).

According to Khan, Aslam, Hussain, Naz, Rana, Ahmad, Ali and Ahmad (2013), the occurrence of TB is low until young adulthood, and after that, it increases sharply. In their study, Khan *et al.*, found similar results where they reported that half of TB patients were 21–45 years of age compared to any other age group. These finding indicate that the people of this age group were more at risk to the disease than other age groups; therefore there is a need for more prevention strategies and awareness campaigns about the dangers of TB and how to prevent spread of this infectious disease. A high number of TB cases in this age group in the current study may be attributed to the fact that this age group is sexually active with a high prevalence of HIV, and TB is an opportunistic infection that attacks individuals when their immune system is compromised (Mabitsela, 2012; Ashezua, Akinwande, Abdulrahman, Olayiwola and Kuta, 2015).

In the current study, there were more TB cases in males than female patients and this finding is similar to other studies (Abdallah and Ali 2012;Zaman, 2010;Nhamoyende and Leslie,2014;Rhines,2013).In an epidemiological study conducted by Vora,Gandhi,Vasava,Ganava and Amin(2016) in India it was also found that more TB cases were in males than females In most studies including study done in Bangladesh(Hossain,2014) and another study done in West Africa(Mota *et al* ,2012) TB cases were reported to be more in males than females which according to Nhamoyebonde and Leslie (2014). An interesting factor is that the female population in South Africa is higher than the male population but the

TB incidence is high in males which signifies two major, but not mutually exclusive explanations that have been put forward to explain gender difference in infectious diseases patterns which are the behavioural and the physiological variations (Dorhoi, Iannaccone, Farinacci, Faé, Schreider, Moura-Alves, Nouailles, Mollenkopf, Oberbeck-Müller, Jörgand Heinemann, 2013). The behavioural hypothesis relates primarily to sex - specific exposure to infection, while the physiological hypothesis posits that biological differences between the sexes render one more susceptible to a given disease (Guerra – Silveira and Abad – Franch, 2013). Study done in Kwazulu – Natal shows that more males are infected with TB as compared to females (Narasimhan, Wood, Macintyre and Mathai, 2013).

Tuberculosis (TB) is one of the alarming diseases in the Limpopo Province (Sekotlong, 2014). The findings shows that the majority of the patients were from Primary Health Care (PHC) facilities as compared to hospital in this province. The results shows that TB patients who were diagnosed or treated at hospital were not evaluated (98%) and no reason could be attributed to this findings more research is needed.

Health seeking behaviours have been strongly correlated with socio-economic status, distance from health facility, and cultural norms according to ethnic and religious factions, making patients delay treatment unless symptoms become severe. Limpopo is one of the poorest provinces of South Africa, with relatively poor infrastructure and public services, including health (Mabunda, Ramalivhana and Dambisya, 2014).

HIV status and ART Initiation

The results of the study revealed that more than half of the patients were HIV positive and of those who were HIV positive nearly all patients were initiated on ART. The results of the study further revealed that more than 90% of HIV and TB co-infected patients were initiated on ART. This shows the good results of a well implemented ART programme in rural areas as South Africa is taking the lead in

improving the lives of HIV positive patients by scaling up of ART. The current study is supported by findings from another study conducted by Blanc, Sok, Laureillard, Borand and Rekacewicz *et al*(2011) stating that patients initiated early on had a significantly higher rate of survival than did those who were initiated late on ART (Blanc *et al.*, 2011).

The study also revealed that more than half of HIV positive patients were less than 40 years of age. A well implemented ART programme is more likely to benefit the HIV infected individuals by reducing the likelihood of tuberculosis incidence although this effect may be less pronounced over time as ART increases life expectancy and may, thus, increase the cumulative lifetime risk of tuberculosis (Dodd, Knight, Lawn, Corbett and White, 2013). Therefore, the majority of the HIV positive TB patients less than 40 years who are on ART in the current study might have an increased life expectancy.

The current study findings further revealed that there were more females than males amongst the HIV positive TB patients. This concurs with study conducted by Perumal, Padayatchi, Naidoo and Knight (2014) which revealed that HIV-infected people globally are women, in sub-Saharan Africa alone, 60% are women, and in South Africa >70% aged 20–30 years are women (Perumal *et al*, 2014). Despite the high prevalence of HIV infection among South African women in this age group, however, incidence of tuberculosis remains higher in men (Perumal *et al*, 2014), which is similar to our findings.

In 2014, the average HIV co-infection rate was 56.5% for the whole country, South Africa (Perumal *et al*, 2014). However, in the study done in Durban, South Africa, co-infection rates as high as 78.2% and 79.2% were reported in females aged 25 to 34 and 35 to 44 years old respectively. In males, the highest co-infection rate reported was 70.8%, in those between 35 and 44 years old (Massyn, Day, Peer, Padarath, Barron and English, 2014). Studies show that TB is more common in young adults due to the high epidemic of HIV in this age group, which predisposes them to opportunistic infections like active TB disease later if their immune system becomes weak, such as individuals with diabetes

or those who are infected with HIV (Ashezua, Akinwande, Abdulrahman, Olayiwola and Kuta, 2015).

5.2.2. Objective 2: To determine the proportion of patients remaining positive after intensive phase

Smear conversion

The study analysis of 180 PTB cases with documented smear results at the end of the intensive phase of treatment, between 2014 and 2015, showed that the overall sputum smear non-conversion rates of PTB cases were 20%. This translates into smear conversion rates of 80%, which is significantly higher than the South African national average of 66.7% but below NTCP's target of 85 % for the performance of TB control program at provincial and district levels (Massyn, 2015). However, it is worth noting that this data only represent one-third (33%) of PTB cases that were recorded in ETR.Net database. Consequently, the researcher cannot rule out that missing data in the ETR.net database may have impacted the calculated smear conversion rate in Ephraim Mogale sub - District.

Greater Sekhukhune District is reported to be amongst the worst performing districts in Limpopo Province with regard to TB treatment outcomes and has also high percentage of TB cases which are not evaluated at the end of intensive phase of treatment (Massyn *et al*, 2014). Therefore, the results of the current study are expected as the researcher found that approximately 36% of TB cases were not-evaluated. The research findings of 80% conversion rates are below the other reported studies. Sputum smear of one hundred fifty-eight patients (83.6%) converted at the end of intensive phase in study done in Iran (Behnaz, Mohammadzadeh and Mohammadzade, 2015).The conversion rate reported from a study done in India at the end of intensive phase was 84% (Bawri, Ali, Phukan, Tayal and Baruwa, 2008).Another study from Portugal reported conversion rate of 88.5 %(Mota, Carvalho, Valente, Braga and Duarte, 2012).

It has been known that the proportion of smear positive patients at the end of the intensive phase is a predictor of treatment success. Limpopo Province has witnessed poor Tb cure rates in 2012 and 2013 wherein Sekhukhune district is amongst the 3 districts (Vhembe, Waterberg and Sekhukhune) with declining cure rates. (Massyn *et al*, 2015) The cure rates in these districts, Vhembe, Sekhukhune and Waterberg declined from 77.5%, 73.2% and 68.8% in 2012 to 47.9%, 58.8% and 64.9% respectively in 2013(Massyn *et al* 2015).

The current study revealed that smear non- conversion after intensive phase of treatment is at 20%. This said, the study findings are comparable to prior studies conducted in Cameroon and Burkina Faso (Mlotshwa, Abraham, Beery, Williams, Smit, Uys, Reddy and Medina-Marino, 2016; Endris, Moges, Belyhun, Woldehana, Esmael and Unakal, 2014).Studies done in sputum smear/culture` conversion at the end of the second month of anti-TB treatment has been considered as an important indicator for the success of TB treatment (Nandawula, 2013).

Smear grading

The current study findings showed that half of the patients had smear grading of p+++ and this is in contrast with study done in Cameroon which shows a high percentage (97%) of TB patients having smear grading of p+++ (Djouma, Ngomba, Epee and Noubom, 2015).This finding could be attributed to delay in patients presenting at a health facility. In a study conducted in Limpopo Province, it was found that patients present late at a health facility mainly because a number of patients consult a traditional healer as a first choice for both physical and mental ailments and diviners being the most popular type of healers (Semenya and Potgieter, 2014). This could be also the case in this rural area of Sekhukhune district.

The study showed that patients with high bacillary load (p+++) had highest non-conversion rates. Having a high baseline grade of smear positivity was associated with failure to smear convert, a finding consistent with other reports and this

probably signifies high initial bacterial loads which take longer to clear during the initial phase of treatment.

5.2.3. Objective 3: To identify the determinants of smear non-conversion in TB patients with smear positive pulmonary Tuberculosis after intensive phase of treatment.

Smear non-conversion at the end of 2- or 3-month intensive phase of treatment is widely considered a poor predictor of treatment outcome (Mahtab, 2015). Thus, understanding factors that affect smear non-conversion is essential to improve TB cure rate and the success of TB control program. Previous studies have found that age, male gender, smoking, alcohol abuse, diabetes, high pre-treatment smear grading, HIV status, lung cavitations, anaemia, previous history of TB treatment, poor quality of anti-TB drugs, suboptimal dosage of anti-TB drugs and presence of TB drug resistant strain to be significant factors affecting TB smear non-conversion at the end of intensive phase of treatment (Sawadogo, Tint, Tshimanga, Kounza and Ouedraogo, 2015;Mota *et al*,2015;Jayakody *et al*,2014).

Results of the recent study showed no significant association between age, gender and HIV status. These findings are not consistent with studies conducted among TB patients in Saudi Arabia and Morocco which shows older TB patients showing high risk for non-conversion (Bouti *et al.*, 2013). Patients who had a pre-treatment smear grade p+++ were 2.9 times more likely not to convert at $p<0.050$ which is consistent with findings from Parikh *et al.*, (2012).

The results of the study showed high non-conversion rates in males although not statistically significant. The lack of smear conversion at the end of an intensive phase treatment with male gender has been associated with alcohol consumption and smoking habits (Muttath, Andrews and Prabhu 2017). However, in the recent study we could not establish this association as this data is not routinely collected in the South African electronic TB register. The study was unable to determine

any significant association between genders and smear conversion at two months. This data extend and confirms the finding of Heunis *et al.*, (2013) in Free State Province, South Africa, who reported a gradual decline in gender related trends of 2-month smear non-conversion in new smear positive PTB cases from 2003 to 2009.

The overall 2-month sputum smear non-conversion rate was higher in males than females; however, the present study did not ascertain the reasons for this difference. A study among TB patients in India (Vasudeven, Jayakumar and Gnanasekaran, 2014) established that women were significantly more likely to access health facilities compared to males and were also more likely to adhere to treatment. Another Indian study (Yellapa *et al*, 2016) found that males were less likely to be diagnosed early with TB, and further suggested that sputum non-conversion could be attributed to alcohol consumption and smoking habits. This might indicate a need to direct alternative TB control measures such as community-based intensified case finding at males.

In the recent study, we identified high pre-treatment smear grading to be independently and significantly associated with smear non-conversion at the end of intensive phase treatment. The findings of the study are similar to those reported in studies done in India and Portugal (Mota *et al*, 2012), which showed an association of higher pre-treatment grading with the lack of smear conversion at the end of intensive phase of treatment.

This is further corroborated by the retrospective cohort study conducted in Free State Province, South Africa, which showed that pre-treatment smear grading and TB disease classification were significantly associated with failure to smear convert at the end of intensive phase of treatment (Kigozi *et al*, 2014). More recently, Djouma *et al.*, (2015) showed that high pre-treatment smear grading and years of treatment (2009 to 2012) were independently associated with delayed smear conversion in a retrospective cohort study in Cameroon.

Pulmonary TB cases with baseline smear of p+++ in new and retreatment cases of TB were 5 and 6 times more likely not to smear convert at end of intensive phase of treatment. High bacillary load at the start of treatment could possibly reflect the presence of lung cavitations and thus severity of disease, which has been shown to be associated with TB treatment failure and relapse, and the development of TB drug resistance (Tiwari, Kumar and Kapoor, 2011). Moreover, there is a direct association between the presence of lung cavitations in TB patients and high bacillary load in their sputum. The odds of being sputum positive after 2 months of treatment was observed to be significantly high (OR = 2.89; 95% C.I. = 1.11–7.60; $P = 0.031$) for sputum grade 3+ at the time of diagnosis. Studies done in India and Pakistan are congruent to the present study (Yellapa *et al* 2016; Salam *et al* 2016).

In line with research conducted in other settings patients with severe pre-treatment sputum smear grading had a higher risk for two-month sputum smear non-conversion than those with scanty grading. The study is congruent with study done in Nigeria (Nwokeukwu, Awujo and Ukeagba, 2013). As shown in a Saudi Arabian study by Chaudry *et al* (2015), 3 patients with a high pre-treatment sputum smear grading not only showed poor sputum conversion at the end of the intensive treatment phase, but were also more likely to exhibit poor treatment outcomes including lower cure rate, and higher failure and death rates, than patients with a scanty grading.

5.3. Conclusions

Findings support the researcher's hypothesis that two month sputum smear non-conversion is associated with patient demographics, including pre-treatment sputum smear grading. Significant associations were thus established. The study provides program managers with evidence to support the development of more tailored care.

Patients who have had high pre-treatment smear grading were more likely not to smear convert at the end of intensive phase of treatment. The findings highlight

an urgent need in the district TB control program to explore strategies that will mitigate the risk of non-conversion and inform implementation of interventions to maximize indicators for TB treatment success rate.

From this study we conclude that the factors affecting sputum conversion in pulmonary tuberculosis is high bacillary load (p+++)¹ in sputum.

5.4. Recommendations

More studies need to be done in Limpopo to investigate reasons for a high number of patients not evaluated after intensive phase of treatment and smear non - conversion. The findings of the study highlight the need for more aggressive and cost-effective strategies to reduce smear non-conversion rates at the end of intensive phase of treatment. The first step towards improving smear conversion after intensive phase is to minimize the number of patients that are not evaluated. The study findings also highlight the need for better surveillance and data collection on TB indicators.

Health workers need ongoing training on implementation of TB guideline. Educate patients on importance of smear collection after intensive phase of TB treatment. Develop strategies that will remind health workers when to smear collection after intensive phase of treatment.

Further research is needed to ascertain the association of other factors like diabetes, smoking, substance abuse and body weight with 2-month sputum smear non-conversion, particularly with regard to male TB patients.

5.5. Limitations of the study

The results should be viewed in light of the following limitations: initial sputum was not collected for 26% of the cases, smear conversion outcomes were not available for 36% of cases, although the total number of cases included in the study was still reasonably large. Other possible factors affecting sputum conversion like diabetes, smoking, substance abuse and body weight at initiation of treatment could not be adjusted for as this data is not routinely collected.

Specifically, the use of retrospective routinely collected data in the electronic TB register excludes the collection of other potential risk factors.

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DATA COLLECTION SHEET

Table 1.1.Variables for association

Variables of interest	
Independent variables	Dependent variables
Age	Smear conversion at two months
Gender	
HIV Status	
ART initiation	
Smear grading	
Local area	

BUDGET

Below is the overall budget of items and logistics which were essential, particularly in collecting data and also ensuring this research program gets finalized. The budget is estimation since no quotations were done.

Item	Cost per item	Total cost
Stationery	5 reams @ R189.00 Printer & 1 Catridge	R189.00 R1999
Data bundles	500MB @ R4,23 per MB	R2,118.64
Transport	100km @ R3,15/km	R5000,00
Food		R600
Binding of final documents		R1500
Publication		R13 000
Total		R24,406.64

TIMELINE

Timeline stipulate an overview of the overall plan on each specific step of the study from the beginning to the final product. It also helps when evaluating the progress and feasibility of the study project.

2016/2017

No	Item	M a r 2 0 1 6	M a y 2 0 1 6	J u n 2 0 1 6	S e p 2 0 1 6	N o v 2 0 1 6	F e b 2 0 1 7	M a r 2 0 1 7	A p r 2 0 1 7	M a y 2 0 1 7	J u n e 2 0 1 7
1.	Submission of research proposal	X									
2.	Acquisition of ethical clearance letter from University		X								
3.	Acquisition of approval letter from DOH			X							
4.	Data collection				X						
5.	Data analysis					X	X				
6.	Report writing						X	X	X		
7.	Submission of document for correction							X	X		
8.	Submission of final document									X	
9.	End of project										X

ANNEXURE A: LETTER SEEKING CONSENT TO CONDUCT RESEARCH

The Director

Department of Health

Limpopo Provincial Government

18 College Street

Polokwane

Request to conduct research in Primary health care clinics

Dear sir/madam

My name is Sylvia Radingoana, and I am a master of Public health student at the University of Limpopo. Together with my supervisor Doctor Ramalivhana and my co-supervisor Professor Linda Skaal request permission to conduct research.

The research I wish to conduct for my master's dissertation involves the prevalence of smear positive TB after intensive phase of treatment in Ephraim Mogale sub-district. I am hereby seeking approval to use the patients' records at the facility through a questionnaire. I have provided you with copies of my research proposal which includes the questionnaire to be used in the research process.

Upon completion of the study, the Department of Health will be provided with a copy of the research report.

If you require any information please do contact me on the cell phone number 0827756305, email: sylviaradingoana.sr@gmail.com.

Yours sincerely

Sylvia Radingoana

University of Limpopo

ANNEXURE B: FACULTY APPROVAL OF PROPOSAL



University of Limpopo
Faculty of Health Sciences
Executive Dean
 Private Bag X1106, Sovenga, 0727, South Africa
 Tel: (015) 268 2149, Fax: (015) 268 2685, Email:noncebamk@ul.ac.za

DATE: 11 April 2016

NAME OF STUDENT: RADINGOANA S
STUDENT NUMBER: 201511362
DEPARTMENT: Public Health
SCHOOL: Health Care Science
QUALIFICATION – MPH

Dear Student

FACULTY APPROVAL OF PROPOSAL (PROPOSAL NO. FHDC2016/8)

I have pleasure in informing you that your Masters in Public Health proposal served at the Faculty Higher Degrees Meeting on the 11 April 2016 and your title was approved as follows:

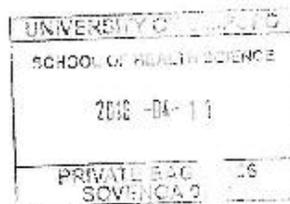
TITLE: PREVELANCE AND DETERMINATION OF SPUTUM SMEAR NON-CONVERSION IN SMEAR POSITIVE TUBERCULOSIS PATIENTS IN EPHRAIM MOGALE MUNICIPALITY, LIMPOPO PROVINCE, SOUTH AFRICA.

Note the following:

Ethical Clearance	Tick One
Requires no ethical clearance Proceed with the study	<input type="checkbox"/>
Requires ethical clearance (TREC) (apply online) Proceed with the study only after receipt of ethical clearance certificate	<input checked="" type="checkbox"/>

Yours faithfully

Prof NP Mbanjo-Kekana
Executive Dean: Faculty of Health Sciences
CC: Supervisor: Dr NJ Ramalivhana



Co-supervisor: Prof L Skeal

Finding solutions for Africa

ANNEXURE C: TREC CLEARANCE CERTIFICATE



University of Limpopo
Department of Research Administration and Development
Private Bag X1106, Sovenga, 0727, South Africa
Tel: (015) 268 2212, Fax: (015) 268 2306, Email:noko.monene@ul.ac.za

TURFLOOP RESEARCH ETHICS COMMITTEE CLEARANCE CERTIFICATE

MEETING: 05 May 2016

PROJECT NUMBER: TREC/39/2016: PG

PROJECT:

Title: Prevalence and determination of sputum smear non-conversion in Smear positive tuberculosis patients in Ephraim Mogale Municipality, Limpopo Province, South Africa

Researcher: Ms S Radingoana
Supervisor: Dr NJ Ramalivhana

Co-Supervisor: Prof L Skaal

Department: Medical Sciences, Public Health and Health Promotion

Faculty: Health Sciences

Degree: Masters in Public Health



PROF. TAB MASHEGO

CHAIRPERSON: TURFLOOP RESEARCH ETHICS COMMITTEE

The Turfloop Research Ethics Committee (TREC) is registered with the National Health Research Ethics Council. Registration Number: REC-0310111-031.

Note:

- i) Should any departure be contemplated from the research procedure as approved, the researcher(s) must re-submit the protocol to the committee.
- ii) The budget for the research will be considered separately from the protocol.
PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.

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ANNEXURE D: DEPARTMENT OF HEALTH APPROVAL LETTER



LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF HEALTH

Enquiries: Latif Shamila (015 293 6650)

Ref:4/2/2

Radingoana S
University Of Limpopo
Private Bag X1106
Sovenga
0727

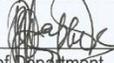
Greetings,

RE: Prevalence and determination of sputum smear non-conversion in smear positive tuberculosis patients in Ephriam Mogale Municipality, Limpopo Province, South Africa

The above matter refers.

1. Permission to conduct the above mentioned study is hereby granted.
2. Kindly be informed that:-
 - Research must be loaded on the NHRD site (<http://nhrd.hst.org.za>) by the researcher.
 - Further arrangement should be made with the targeted institutions, after consultation with the District Executive Manager.
 - In the course of your study there should be no action that disrupts the services.
 - After completion of the study, it is mandatory that the findings should be submitted to the Department to serve as a resource.
 - The researcher should be prepared to assist in the interpretation and implementation of the study recommendation where possible.
 - The above approval is valid for a 3 year period.
 - If the proposal has been amended, a new approval should be sought from the Department of Health.
 - Kindly note, that the Department can withdraw the approval at any time.

Your cooperation will be highly appreciated.



Head of Department

15/06/2016

Date

18 College Street, Polokwane, 0700, Private Bag x9302, POLOLKWANE, 0700
Tel: (015) 293 6000, Fax: (015) 293 6211/20 Website: <http://www.limpopo.gov.za>

The heartland of Southern Africa – development is about people