EFFECTS OF TREATMENT COMPLIANCE ON TREATMENT OUTCOMES FOR PULMONARY TUBERCULOSIS PATIENTS ON DIRECTLY OBSERVED TREATMENT-SHORT COURSE IN WINDHOEK DISTRICT, NAMIBIA

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A mini-thesis submitted in partial fulfilment of the requirements for the degree of Master in Public Health at the School of Public Health, University of the Western Cape

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DECLARATION

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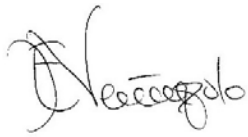

10 November 2015

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Signature **Date**

DEDICATION

This study is dedicated to my late father, Lukas ya Ndeshiilile Shaama, Tate, I am sure you are proud of this wherever you are!

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KEYWORDS

Tuberculosis (TB)

TB treatment

TB treatment compliance

TB treatment adherence

TB treatment outcomes

Directly Observed Treatment-Short Course (DOTS)

Factors influencing compliance

Treatment success

Poor treatment outcomes

Drug resistance

ABBREVIATIONS

ART	Antiretroviral treatment
CB-DOT	Community-Based Directly Observed Treatment
CNR	Case Notification Rate
DOTS	Directly Observed Treatment-Short Course
DOT	Directly Observed Treatment
HIV	Human Immunodeficiency Virus
MDR-TB	Multiple Drug-Resistant Tuberculosis
MoHSS	Ministry of Health and Social Services
NSA	Namibia Statistics Agency
TB	Tuberculosis
PTB	Pulmonary Tuberculosis
WHO	World Health Organization
XDR-TB	Extensively Drug-Resistant Tuberculosis

DEFINITION OF KEY TERMS

Compliance

Compliance is defined as the extent to which patient's "behaviour coincides with medical advice on how to take tuberculosis treatment" (Pandit & Chaudhary 2006:241). Although compliance and adherence have been used interchangeably, looking at the definition of adherence which is generally defined as the "the extent to which a patient follows the prescribed treatment regimen" (Farmer, 1999: 1074), the study has taken an approach of using the term compliance. In this study, compliance aims at looking at the actual percentages of the prescribed medications taken, factors involved in treatment taking that influence the actual taking of medications and the effectiveness of medications which is determined by treatment outcomes. This is considered different from adherence that generally assess whether the treatment regimen was followed and if medications were collected without further assessment on whether the medication was actually taken or not or whether it was effective.

Cured

Smear positive patient converted to smear negative in the last month of treatment and on at least one previous occasion (WHO, 2007).

Defaulter

A defaulter refers to a patient who interrupted TB treatment for two consecutive months during their treatment period (WHO, 2007).

Died (TB mortality)

These are the patients who died for any reason during the course of treatment (WHO; 2007).

DOTS supporter

A person who observes TB patients swallowing the medicines (WHO; 2007).

Transferred out

Patients who are transferred to another facility and whose treatment outcome is unknown (WHO; 2007).

Treatment completed

These are patients who have completed 6 months of treatment but who does not have a negative smear or culture results in the last month of treatment and on at least one previous occasion (WHO, 2007).

Treatment failure

A patient who is sputum smear positive at five months or at the end of 6 months treatment

(WHO; 2007).

Treatment outcomes

According to the WHO (2007), treatment outcomes are described as the end product of TB treatment. The following outcomes are possible: patients who are cured; completed treatment; died (TB mortality); failed treatment; defaulter and those who are successfully treated.

Treatment success

These are patients who are cured and have completed their 6 months of treatment (WHO, 2007).

Treatment success rate

This is defined as the proportion of TB patients who have been successfully cured and those who completed treatment over a specified period of time (WHO, 2007).

Tuberculosis

Tuberculosis (TB) as defined by the World Health Organization (WHO) (2011) is an infectious disease which is caused by the bacillus *Mycobacterium tuberculosis* that mainly affects the lungs PTB (pulmonary tuberculosis) although it also affects other sites of the body (extra pulmonary tuberculosis).

Multi-drug resistant TB

A type of TB which is considered resistant to at least isoniazid and rifampicin (Newell et al., 2006).

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ABSTRACT

Tuberculosis (TB) is a major health problem worldwide, with an estimated 9 million new cases accounting for an estimated 1.5 million deaths in 2012. Non-compliance with TB treatment has become a major barrier to achieving global TB control targets. Namibia is one of the worst affected countries in Africa with a high case notification rate (CNR) of all forms of TB and relatively low treatment success rate compared to the WHO targets.

The study aimed at investigating TB treatment compliance and measuring its association to patient characteristics and treatment outcomes, in determining the effects of compliance on treatment outcomes in Windhoek District. This information is crucial for TB programme management and development of targeted strategies.

A quantitative observational analytic study using a retrospective cohort design was adopted. New adult Pulmonary Tuberculosis (PTB) patients treated under DOTS in Windhoek District between 1st January 2013 and 31st December 2013 were included in the study based on specified criteria. Data was collected from the patients TB treatment cards using an extraction tool. Selection and information bias was eliminated by using clearly defined inclusion and exclusion criteria using a pre-tested standardised tool. Statistical analysis using descriptive and analytic statistics was done using Epi Info 7 to determine compliance, treatment outcomes and to measure the associations.

Overall treatment compliance (89%), initial phase compliance (97.2%) and continuation phase compliance (88.1%) were reported in the study. Age (OR=4.3 95% CI (1.72 – 9.90), p-value=<0.01) and type of area (OR=0.02 95% CI (1.00 – 1.13), p-value=0.05) were associated with compliance in the continuation phase. Overall, type of area (OR=0.03 95% CI (0.00 – 0.91), p-value=0.04) remains associated with treatment compliance. Treatment success is reported among 86.1% of patients. Poor treatment outcomes are associated with non-compliance in the initial phase (x^2 =49.98, p-value=<0.01), continuation phase (x^2 =98.81, p-value=<0.01) and overall (x^2 =110.02, p-value=<0.01).

Overall treatment compliance (89%) although higher than expected was lower than the WHO recommended 90% compliance. Very high compliance (97.2%) were reported in the initial

phase of treatment whilst compliance was also lower than desired (88.1%) in the continuation phase. Non-compliance recorded in the continuation phase is in agreement with the literature. Age and type of area are associated with compliance as reported in the continuation phase and overall in this study is new contribution of knowledge. The findings suggest that treatment compliance is associated with treatment success in both phases of treatment and overall. Low compliance especially in the continuation phase could lead to poor treatment outcomes such as prolonged infections, relapse, high TB mortality and drug resistance leading to increased programme costs. The study concludes that non-compliance results in poor treatment outcomes highlighting the need for interventions that address compliance in all phases but specifically within the continuation phase and amongst those at risk of having reduced compliance such as those in rural areas and young adult patients aged (15 – 34 years). Recommendations to the District Management Team and TB Programme Managers include: identification of measures that promote treatment compliance; support and monitoring of TB patients' compliance continuously; strengthening CB-DOT by increasing CB-DOT points and enhancing CB-DOT supporters' capacity as well as strengthening record keeping as a monitoring tool to increase compliance and improve treatment outcomes.

CHAPTER 1: INTRODUCTION

1.1 Overview of TB

Tuberculosis (TB) is a major health problem worldwide, with an estimated 9.0 million new cases reported in 2013 accounting for an estimated 1.5 million deaths in the same year. These reported cases and deaths are unacceptably high considering the fact that TB is preventable and curable (WHO, 2013). Of all the reported cases in 2013, 25% were in Africa and TB was reported to be the second leading cause of death in sub-Saharan Africa despite the availability of effective treatment (WHO, 2013; Stop TB Partnership, 2006). Africa is not on track for achieving the global TB mortality and prevalence targets and this may be attributed to resource constraints, conflicts and instability, as well as the widespread Human Immunodeficiency Virus (HIV) epidemic. The progress towards reaching the global targets is further affected by treatment defaulting and poor treatment compliance (Bam et al., 2005). About half of the patients diagnosed with TB globally do not complete their treatment and this has the potential for negative treatment outcomes such as prolonged infectiousness, treatment failure, drug resistance, relapse and death (Bam et al., 2005; Newell, 2006; WHO, 2003).

Namibia is one of the most affected countries in Africa, as shown by the very high case notification rate (CNR) of all forms of TB. About 11 145 cases were notified in 2012, equivalent to a CNR of 529 per 100,000 population. TB is widely dispersed in Namibia although its distribution varies by region. TB incidence in Namibia is increased through HIV as reflected by the HIV prevalence of 50% among TB patients as reported in the 2012-2013 annual TB report (MoHSS, 2013).

The country reported a TB treatment success rate of 83% in 2012, which is below the global target of 90% with a defaulter rate of 5%, treatment failure of 5% and mortality related to TB at 5%, while 2% of the patients were reported as transferred out (MoHSS, 2013). The 2012-2013 annual TB report (MoHSS, 2013) further reported an increase in the number of notified cases of drug-resistant TB (DR-TB) in the country from 2007- 2012.

TB treatment in Namibia is offered free of charge along with prevention, promotion and rehabilitation services and other services such as antenatal care, growth monitoring

promotion, immunization for children under 5 years as well as psychiatric treatment and anti-retroviral treatment (ART) (MoHSS, 2009).

Despite the continued efforts to control TB and eliminate it as a public health threat, Namibia continues to experience alarmingly high rates of TB. There are also reported cases of defaulters, treatment failure and TB related mortality. These challenges pose a problem to the effective implementation of the TB control programme (MoHSS, 2013).

1.2 World Health Organisation and TB control

In its efforts to control the burden of TB that prevails in many low and middle income countries and poses a major public health problem, the World Health Organisation (WHO) revived its global effort in 1991 through the development of the Directly Observed Treatment-Short course (DOTS) strategy (Raviglione and Pio, 2002; WHO, 2006). The DOTS strategy was developed by the WHO as a response to the inappropriate use of the basic medical technologies for proper diagnosis and treatment of TB in most parts of the world (Raviglione and Pio, 2002).

The WHO deemed the DOTS strategy appropriate for addressing the basic care elements needed for effective delivery of such technologies. One of the basic elements of the DOTS strategy is to ensure that there is standardised short-course chemotherapy in the management of all TB cases that should be administered under proper case management conditions that include Directly Observed Treatment (DOT) (MoHSS, 2010; Raviglione and Pio, 2002). This strategy was considered a reliable measure to ensure that patients are taking their TB medicines as prescribed in order to enhance patient adherence, reduce treatment interruption and improve treatment success (Raviglione & Pio, 2002). Therefore, DOTS treatment is administered to TB patients for the whole treatment duration in enhancing patients' adherence, reducing treatment interruption and improving treatment success (Raviglione & Pio, 2002; WHO, 2006). TB treatment is administered in two phases: the initial (intensive) phase, which is the first two months of treatment and the continuation phase that constitutes the last 4 months of treatment (WHO, 2006).

In the intensive phase patients are treated with four or more medicines Isoniazid, Rifampicin,

Pyrazinamide and Ethambutol (HRZE). These medicines are administered as a daily DOT for two months, to ensure that the majority of TB bacilli are killed and resistant bacilli have no chance of surviving. While in the continuation phase, patients are treated with fewer TB medicines Isoniazid, Rifampicin and Ethambutol (HRE) for 4 months because the population of live TB bacilli becomes smaller and the likelihood of containing resistant mutants is very small but these medicines are also provided as a DOT treatment. For all new TB patients, the DOT is recommended for the first two months of treatment and preferably for the full 6 months course (MoHSS, 2009; WHO, 2003). For patients on re-treatment the DOT is recommended for the full duration of treatment which is 6 - 9 months (Stop TB Partnerships, 2006; WHO, 2006).

Since DOTS is recommended for the entire treatment course, its implementation requires a patient-centred approach. Therefore TB treatment via the DOTS is organized in a way that it is accessible and affordable to all patients and their treatment supporters who are referred to as DOTS supporters. (MoHSS, 2009; WHO, 2006). The DOTS observations takes place at health facilities which is referred to as health facility-based DOT and at the community level which is known as community-based DOT (CB-DOT). Health facility-based DOT is provided at the health facility situated conveniently close to the patient's home or workplace. Patients are required to take their medications daily under the observation of the health care workers. Whereas CB-DOT has various options that include: workplace DOT, guardian-based DOT and community health worker-assisted DOT. Workplace DOT is either provided by the health worker at the workplace or by the lay person. While guardian-based DOT is provided by the lay person selected by the patient from his/her house or neighbourhood who is willing to take responsibility for the patient's TB treatment. Community health worker-assisted DOT is provided at the patient's house or at any agreed place by the community health worker in the neighbourhood of the patient, who takes responsibility for the patient's daily DOT (MoHSS, 2009; WHO, 2006).

After a decade of the DOTS implementation globally, another strategy which is an addition to DOTS strategy was launched in 2006. The Stop TB Strategy was launched with the aim of responding to or addressing the many challenges that could not be addressed by DOTS, particularly the challenges of drug-resistant TB, frail health systems, insufficient stakeholder (private provider and community) engagement as well as dependence on flawed medical technologies (Stop TB Partnerships, 2006; WHO, 2006). The Stop TB Strategy further aimed

at halving TB prevalence and TB related mortality reported in 1990 by 2015. This was to be done through the following components: pursuing high quality DOTS expansion and enhancement; addressing TB-HIV, MDR-TB and the needs of poor and vulnerable populations; health system strengthening; engaging all care providers; empowering TB patients and communities through partnerships and enabling and promoting research (Stop TB Partnerships, 2006; MoHSS, 2009; WHO, 2006). The Stop TB Strategy set the treatment success rate at 90% (WHO, 2006).

Enhanced TB treatment through the DOTS strategy and the Stop TB Strategy have saved many lives worldwide as their successful implementation has been associated with reduction in TB incidence and improved treatment outcomes in countries such as Peru, Cuba, and China, in some parts of India and in the USA (Lönnroth et al., 2009). However, studies have shown a worrisomely slow decline in TB burden and treatment success in sub-Saharan Africa and some parts of Europe. In Africa in the early 1980s and 1990s, the slow decline in TB burden has been attributed to the rapid increase of HIV (Lönnroth *et al*., 2009). According to the WHO (2013), there are still about 1000 or more cases per 100 000 people reported in South Africa and Swaziland in 2012 which is a strong indication of high TB burden in sub-Saharan Africa. Treatment success is reported by the WHO (2013) to be at its lowest in Europe with only 75% of all new cases successfully treated. However, Africa has also reported low treatment success rates in South Africa and Nigeria. . The low treatment success in Europe and Africa is mostly attributed to non-compliance with TB treatment (WHO, 2013).

1.3 TB control in Namibia

In Namibia, TB is managed through both the DOTS and the Stop TB Strategy as recommended by the WHO. DOTS has been adopted and implemented in Namibia from 1995 and was rolled out throughout the country by the end of 1996. DOTS is implemented at health facilities (health facility-based DOT) and at the community level (CB-DOT). Patients are observed swallowing the medicines by either the health care worker or any other person who has assumed co-responsibility for the patient's TB treatment for the entire treatment period, and these people that observe patients taking their treatment are referred to as DOT supporters (MoHSS, 2009). However, CB-DOT has not reached all the areas due to the

vastness of the districts and inadequate CB-DOT supporters both in terms of the number and expertise (MoHSS, 2009; MoHSS, 2010; MoHSS, 2013).

The Stop TB Strategy in Namibia was adopted and implemented in 2006 with the aim of complementing the DOTS effort. Through this new strategy, the TB prevalence and TB related mortality were expected to be lowered through: pursuing high quality DOTS expansion and enhancement; addressing TB-HIV, MDR-TB and the needs of poor and vulnerable populations; health system strengthening; engaging all care providers; empowering TB patients and communities through partnerships and enabling and promoting TB related research (MoHSS, 2009). The introduction of the Stop TB Strategy has seen a decline in TB prevalence and TB mortality in the country. In 2012, Namibia reported 11 145 cases equivalent to a CNR of 529 per 100 000 population. In 2007, 2008, 2009, 2010 and 2011, the country reported 15 244, 13 737, 13 332, 12 625 and 11 924 cases equivalent to CNR 722, 665, 634, 589 and 545 respectively. This represents a decline in TB prevalence, compared to the 11 145 cases reported in 2012, which translates to a CRN of 529 per 100 000 population. Maintaining the downward trend observed since 2007, TB related mortality declined from 8% reported in 2007 to 5% in 2012 (MoHSS, 2013). Though there is a downward decline in TB prevalence and mortality observed in the country, TB treatment success of 83% reported in 2012 remains lower than the WHO recommended TB treatment success of 90%.

TB services are offered by various categories of health care workers namely: doctors, nurses, field promoters and home-based care workers. The doctor's role is mainly limited to the diagnosis and management of TB complications. While nurses are the cornerstone of TB management and treatment as they are responsible for ensuring that the patients complete their treatment successfully. Field promoters are lay persons from the community who may be attached to the health facility or to other TB treatment points in the community and they have been trained on TB-DOT and TB case finding. Their roles are to provide support to the TB nurses regarding information, education and communication (IEC), observation of treatment, recording and tracing of patients who interrupt treatment. Community-based health care workers play the role of TB case-finding and CB-DOT as they are situated in the community and they act as DOT supporters for community health care worker-assisted DOT. Doctors and nurses are available at health facilities while field promoters and home-based care workers are only available at the clinics and in the community respectively (MoHSS,

2009).

Inadequate compliance with TB treatment has negative effects on TB control and has in most instances led to drug resistance and further spread of TB in the communities. This increases TB morbidity and mortality (Adane et al., 2013; Amuha et al., 2009; Naidoo et al., 2013). Therefore, increasing the effectiveness of the TB control strategies requires efforts that will optimize compliance with treatment and thus improve treatment success and ensure better treatment outcomes. That can be achieved if the compliance and the relationship between compliance and patient characteristics as well as treatment outcomes are known. This will enable the determination of the effects of treatment compliance on treatment outcomes. Acquiring such knowledge will enable targeted strategies to be devised.

1.4 Problem Statement

Despite significant efforts to control TB, and regardless of the availability of free and effective treatment, TB remains a major health problem and the second primary cause of death in Namibia (MoHSS, 2013). Windhoek District being ranked at number one on the disease burden in the country, reports the equivalent of 17% (1932 cases) of all reported TB cases in the country and a case notification rate of 567/100 000 population in 2012 (MoHSS, 2013). The district also recorded the highest mortality in the country, 4% of TB patients in the district. Though the DOTS strategy was implemented to enhance patient adherence, reduce treatment interruption and improve treatment success rates, there are still reported cases of default, treatment interruption and low rates of treatment success (MoHSS, 2009; MoHSS, 2013). Compliance with TB treatment in Namibia is not known as there is no information documented in the Namibian TB programme on how their patients comply with TB treatment. Thus the factors affecting TB treatment compliance as well as the effects of treatment compliance on treatment outcomes are not known in Windhoek District and Namibia at large because they were never explored. There are also very few studies that assessed compliance in Namibia that only explored the factors influencing compliance in general but not in the phases of treatment. Therefore this study attempts to investigate TB treatment compliance and measure the relationship between compliance and patient characteristics in different phases of treatment and overall as well as treatment outcomes in order to determine the effects of treatment compliance on treatment outcomes in the

Windhoek District.

1.5 Significance of the study

This study will provide insights into the overall TB treatment compliance and in the different phases of treatment, association of compliance across a range of patient characteristics as well as assess the relationship between treatment compliance and treatment outcomes. This is useful in determining the effect of treatment compliance on treatment outcome in Windhoek District. The information will contribute to the existing body of knowledge and provide new context specific information on TB management in the Windhoek District with possible lessons for other Namibian settings. The knowledge is crucial to TB programme management especially District Managers and service planners in developing targeted strategies to increase compliance and improve treatment outcomes. Moreover, those strategies are crucial to improving and increasing TB treatment success (cure and treatment completion) in the district through the promotion of compliance with TB treatment by TB patients in order to prevent TB defaulting, treatment failure, resistance and TB mortality.

1.6 Study outline

The report is presented in 6 Chapters.

Chapter 2 focuses on the review of the relevant literature pertaining to TB treatment compliance and its effects on treatment outcomes.

Chapter 3 describes the research methods used in the study with the specific focus on aims and objectives, type of research and design, study population, study setting, sampling procedure study variables, data collection methods, measures to prevent bias and ensure validity and reliability, statistical analysis and ethical considerations involved in the study.

In Chapter 4, the study findings will be presented. While Chapter 5 discusses the findings of the study.

The final Chapter addresses the conclusion and recommendations.

CHAPTER 2: LITERATURE REVIEW

Introduction

Tuberculosis is a major health problem worldwide, with more new cases reported yearly and an increase in TB mortality (WHO, 2013). According to Bam et al. (2006), non-compliance with TB treatment is one of the major barriers in achieving global TB control targets in most parts of the world regardless of strategies put in place globally to control TB. About half of the patients diagnosed with TB do not complete their treatment and this results in negative treatment outcomes such as prolonged infectiousness, drug resistance, relapse and death (Bam et al., 2006; Newell et al., 2006; WHO, 2011). This study is trying to determine the effects of treatment compliance on treatment outcomes for new PTB patients treated via DOTS in Windhoek District in Namibia.

This Chapter provides information on the purpose and scope of this review, a review of the literature pertaining to TB treatment compliance and its effects on treatment outcomes. It starts with the review on the importance of treatment compliance in TB management. Consequently, the review on compliance with DOTS TB treatment with a description of how TB treatment compliance is defined and measured elsewhere will also be presented. The review will also provide a summary of the existing evidence of treatment compliance among different treatment strategies as well as the associated TB treatment outcomes in such strategies. Factors influencing treatment compliance through the DOTS strategy will also be presented. The review will conclude by highlighting some of the gaps in knowledge regarding the effects treatment compliance has on different treatment outcomes.

2.1 Purpose of the literature review

The purpose of this literature review is to organise and systematically present what is known about TB treatment compliance by looking at what has already been studied and published in order to avoid unnecessary replication of information which wastes resources (Burns & Grove, 2005). Reviewing the relevant literature on TB treatment compliance and its effects

on treatment outcomes for PTB patients in various contexts is essential in validating and justifying the significance of this study.

2.2 Scope of literature review

In determining the effects of treatment compliance on treatment outcomes for PTB patients in Windhoek District in Namibia, the literature review has made use of the readings from different sources. Institutional reports, WHO materials, academic theses and articles from journals were reviewed. Information from African countries was relied on more as most African countries are similar to Namibia thus their information resonates with the Namibian context. Few studies from countries elsewhere were also included since TB treatment compliance is a worldwide concern. Since the terms compliance and adherence have been used "interchangeably in the past" (Farmer, 1999: 1074), both terms were considered in selecting and reviewing the relevant literature.

2.3 Literature reviewed

Numerous studies have been conducted worldwide to try and explore compliance with TB treatment via DOTS. Information on the importance of treatment compliance, compliance with DOTS treatment, treatment compliance among different treatment strategies, treatment compliance and associated treatment outcomes in different treatment strategies and factors influencing DOTS treatment compliance is presented below.

2.3.1 Importance of treatment compliance in TB management

Compliance with prescribed anti-TB treatment has many beneficial roles to play in TB control programmes especially programmes that fall under the DOTS strategy. In many TB programmes, treatment compliance has been associated with high TB cure rates and reduction in the emergence of drug resistance (Adane et al., 2013; Afns & Ji, 2010; Naidoo et al., 2013). Therefore correct and consistent compliance among TB patients receiving treatment through DOTS is required throughout the treatment period in order to achieve good treatment outcomes which is key to achieving high cure rates (Naidoo et al., 2013).

Compliance requires patients to take their TB treatment in a regular and consistent way in order to reduce the risk of treatment failure, relapse and development of drug resistant strains. According to Afns & Ji (2010), interruptions that occur especially in the early stages of treatment can cause an increase in the TB transmission rate. This is because the initial stage of treatment is regarded as the most infectious stage with many TB bacilli. This is also the stage where resistant bacilli survive if not properly treated, therefore it requires correct and consistent administration of medication in order to ensure that the majority of TB bacilli are killed and resistant bacilli have no chance of surviving. To prevent the increase in TB cases and the emergence of drug resistant TB, patients need to be encouraged to comply with their TB medication (Adane et al., 2013; Brust et al., 2010).

Non-compliance with TB treatment still poses a challenge in most TB control programmes (Adane et al., 2013; Amuha et al., 2009; Naidoo et al., 2013; Shargie & Lindtjørn, 2007). In Uganda and Ethiopia, like in other many countries in sub-Saharan Africa, poor compliance with TB treatment among patients with TB was reported to be a major problem (Adane et al., 2013; Amuha et al., 2009). In a cross-sectional study done in South Africa by Naidoo et al. (2013) on predictors of TB and ARV adherence, the authors argue that poor adherence with treatment was strongly associated with low cure rates of TB.

Studies further indicate that poor and inconsistent adherence like non-adherence have negative effects on TB control, and has in most instances led to drug resistance and further spread of TB in the community which increases morbidity and mortality (Adane et al., 2013; Amuha et al., 2009; Naidoo et al., 2013).

Many TB programmes have reported an increase in the health care costs related to the negative effects of non-compliance. Therefore, patients with TB are expected to have adherence of greater than 90% if they are to be cured (Adane et al., 2013; Amuha et al., 2009).

2.3.2 Compliance with DOTS TB treatment

Compliance with DOTS TB treatment is required if good treatment outcomes and treatment success that includes cure and treatment completion are to be achieved. According to

Awofeso (2008), TB treatment requires a treatment compliance of greater than 90% as recommended by the WHO in order to facilitate cure and to ensure treatment success. This was also indicated by Adane et al. (2013), Amuha et al. (2009) and Takarinda et al. (2012). Patients who took 95% of their prescribed medications were found to show high compliance while those who adhered for 40% and below demonstrated a low compliance in a study by Awofeso (2008).

Dye et al. (2005) indicated that treatment compliance has been commonly considered to be taking at least 80% of the prescribed treatment. This definition of compliance is consistent with the definition of non-compliance in a study conducted in Siberia that assessed barriers to successful TB treatment in Tomsk, where non-compliance was considered for all patients that missed 20% or more of the prescribed doses during the treatment period (Gelmanova et al., 2006).

In a study done in Uganda by Amuha et al. (2009) on non-adherence with anti-TB medications by TB/HIV co-infected patients, non-adherents were considered as patients that missed more than 10% (taken less than 90%) of the TB medication in five days preceding the survey. Adherence in this study was measured through a recall by the patients and it was calculated as the percentage of prescribed medications over five days that the patient has taken (Amuha et al., 2009). In a study by Bam et al. (2006) patients were deemed non-compliant if they missed more than 7 consecutive days of treatment in their entire treatment duration. Other studies that looked at compliance defined non-compliance as missing more than two consecutive months of treatment (Castelnuovo, 2010) and missing one dose in four days which is considered 25% of dose missed (Adane et al., 2013).

From the above discussion, it is clear that compliance has been defined and measured differently in different contexts, which poses a bit of a challenge to comparing compliance between different contexts. In a review conducted about compliance with anti-TB treatment in sub-Saharan Africa, the proportion of patients defaulting from treatment varied by phase of treatment from 11.3% in the initial phase to 29.6% in the continuation phase. Although the findings revealed a high rate of non-compliance, this non-compliance was limited to those patients that defaulted (missed two consecutive months of treatment), but did not assess other non-compliance. The author further acknowledged the heterogeneity in information and difference in the definition of compliance in the papers reviewed that prevented meta-analysis

to be performed. Thus the study could not confidently draw conclusions about the reasons for this high non-compliance, nor the effects of compliance on different treatment outcomes (Castelnuovo, 2010).

In the Ugandan study mentioned above, the prevalence of non-compliance with anti-TB treatment was 25% and non-compliance was more likely to be reported in the continuation phase than in the initial phase of treatment (Amuha et al., 2009). A cross-sectional study done in Gambia by Afns and Ji (2010) comparing health facility DOTS among TB patients before and after the introduction of daily DOTS also found that the majority of patients defaulted in the continuation phase of treatment because in that phase most of their main symptoms disappeared. These findings suggest that the continuation phase is the most problematic phase of treatment when it comes to compliance with TB treatment.

An institution-based cross-sectional survey conducted among TB patients in Ethiopia indicated non-compliance of 10% and 13.6% for patients assessed over a month and those assessed over four days respectively. The study further revealed that patients in their continuation phase of TB treatment were about seven times more likely to be non-adherent compared to the patients in the initial phase treated through DOTS (Adane et al., 2013). In a household survey conducted in Zambia by Kaona et al. (2004) non-compliance was recorded at 29.8%, and the study also indicated the continuation phase of treatment as the phase in which most treatment interruption occurs.

The findings of non-compliance being common in the continuation phase of treatment is consistent with Castelnuovo's (2010) findings; however this study only assessed one month compliance and did not look at the whole treatment duration which might have produced different findings. Compliance in this study was measured over the four days preceding the survey and all the patients that missed at least one dosage (25%) out of four doses were considered non-compliant (Adane et al., 2013) The study further acknowledged that DOTS with daily supervision for the whole treatment duration though yielding good results, could be a challenge for most patients, especially those co-infected with HIV that also require regular visits to ART clinics to collect their medications (Adane et al., 2013).

A cross-sectional study done in Tanzania by Mkopi et al. (2012) on adherence to TB therapy among patients receiving home-based DOT which is part of community-based DOT recorded

adherence of 75%. However adherence in this study was only measured at one point in time, thus the study recommends a cohort study to assess the rate of adherence throughout the full treatment course. This is deemed necessary in identifying the treatment phase that requires more support when it comes to treatment compliance (Mkopi et al., 2012).

This study has adopted the WHO recommended of compliance, whereby high compliance will be considered as patients that have taken 90% or more of their prescribed TB medications, while low compliance will be considered for all the patients who missed at least 40% of treatment. Those that have taken between 40% and 90% will be considered average compliance (Awofeso, 2008; Dye et al., 2005). Both average compliance and low compliance will be measured as non-compliance in this study. The study has taken this approach taking into consideration that it is the WHO recommendation, and there are a number of studies that have used the same approach that will enable comparisons to findings from different settings.

To summarise the above discussion, the WHO require a TB treatment compliance of greater than 90% in facilitating cure and achieving treatment success. Compliance has been defined and measured differently in different settings, but most of the studies have adopted the WHO recommendation. Compliance with TB treatment has been reported to be low in most studies, with the continuation phase of treatment identified as the most problematic phase when it comes to treatment compliance and one study recommending a cohort study to look into the rate of compliance. A WHO recommended compliance is adopted in this study to enable comparisons of the findings in different settings.

2.3.3 Treatment compliance across different treatment strategies

As mentioned in the introduction (Chapter 1), treatment via DOTS in Namibia is administered through different strategies namely: community-based DOT and health facility-based DOT. However, some TB programmes elsewhere are still offering TB treatment via self-administered treatment.

A cross-sectional study done in Gambia by Afns and Ji (2010), revealed compliance among patients treated via self-administered treatment and the patients treated with fixed-dose via DOTS. The findings indicate that those patients that received daily medication with fixed-

dose via DOTS were more likely to comply with their TB treatment because patients considered that option to be convenient for them. However, the study did not indicate the type of DOTS used in administering the fixed-dose, neither did it indicate how patients complied with their treatment in the initial and continuation phase of treatment (Afns & Ji, 2010).

A United States of America (USA) based retrospective study by Jasmer et al. (2004) compared treatment compliance among TB smear positive patients treated under DOTS and those treated through self-administered therapy. Similarly to the findings from the Gambian study, this study has also indicated that those patients treated through self-administered therapy had a high risk of non-compliance with the treatment regardless of the different methods used (Jasmer et al., 2004).

A review by Volmink & Garner (2007), compared treatment completion by TB patient treated through DOTS administered by health workers, family members, volunteers and those self-administering of treatment. The review did not find any statistical difference in treatment completion between the range of DOTS and self-administered treatment. However, the study did not indicate how patients complied with treatment on different types of DOT compared to self-administration. Thus, this review could not provide evidence for compliance on different types of DOTS and self-administration (Volmink & Garner, 2007).

A longitudinal study done in Tanzania by Van Den Boogaard et al. (2009) assessed adherence to community-based DOTS among the TB patients. The study findings indicate a high compliance of 96.3% among the patients treated under community-based DOT. Similarly, very high compliance (100%) were recorded in a study done in Iraq by Niazi and Al-Delaimi (2003) on the impact of community participation on treatment compliance and outcomes for TB patients treated via DOTS compared to health-facility based DOTS that recorded 14% compliance.

As revealed by the above discussion, most studies that compared TB treatment among different strategies did not indicate how patients complied with their treatment and some did not indicate the type of DOT used however few studies have indicated that compliance was higher among community-based DOT.

2.3.4 Treatment compliance and associated TB treatment outcomes in different treatment strategies

According to a study done in Tomsk, Russian Federation on the barriers to successful TB treatment by Gelmanova et al. (2006), non-compliance with TB treatment was identified to have significant adverse effects for the outcomes of TB treatment. The study classified treatment outcomes as good or poor. Good treatment outcomes were generally considered to be those patients who are cured and who completed their treatment, while poor treatment outcomes are considered those patients that defaulted, whose treatment failed and those that died while on TB treatment. About 66% of all poor outcomes experienced in this study occurred among those patients that did not comply with the therapy (Gelmanova et al., 2006). The high number of poor treatment outcomes among the patients that did not comply with the therapy in this study could be the important indication for the effects treatment compliance has on outcomes that needed further exploration in different contexts (Gelmanova et al., 2006). In addition, a study done in Iraq by Niazi and Al-Delaimi (2003) mentioned above also indicated the effects of treatment compliance on treatment outcomes. The study findings indicate that treatment compliance improved treatment cure rates.

The findings from the USA based study by Jasmer et al. (2004) also mentioned above, indicate a high cure rate for patients treated under DOTS compared to patients treated through self-administered therapy (97.8% versus 88.6%, $p < 0.002$). The study further reported a decrease in TB related mortality in patients treated under DOTS from the start of their treatment up to the end of the therapy (0% vs. 5.5%, $p = 0.002$). A review by Volmink and Garner (2007), also mentioned above did not find any statistical difference in treatment completion between the range of DOTS and self-administered treatment as indicated by the cure rate which was similar for both outcomes. However these studies did not indicate how the patients complied with their treatments.

Similarly, a Gambian study also mentioned above did not find statistical significant difference in treatment outcomes for patients treated through DOTS and those treated through self-administration. Cure rates, treatment completion rates, defaulter rate, treatment failures and death rates were closely related in these two treatment options (Afns & Ji, 2010).

A Namibian study by Zvavamwe and Ehlers (2009) assessed the efficacy of the community-

based DOTS programme compared to the standard hospital-based DOTS treatment in one of the Namibian regions. The findings indicate that those patients treated under community-based DOTS had better cure rates compared to those treated under health facility-based DOTS. Community-based DOTS was also associated with high cure rates in a study by Volmink and Garner (2007), Jasmer et al. (2004) and Newell et al. (2006). However, both the studies and the review could not confidently infer that community-based DOTS improved cure rates, because the TB patients who did not select the community-based treatment option might have been different from those that opted for community-based DOTS. This could have been established through further analysis (Volmink & Garner, 1997; Zvavamwe & Ehlers, 2009).

The above discussion indicates that non-compliance with TB treatment has adverse effects on treatment outcomes, while compliance improves cure rates. Higher cure rates were reported among patients treated under DOTS compared to self-administered treatment though some studies did not observe a significant difference between treatment outcomes.

2.3.5 Factors affecting DOTS TB treatment compliance

Several studies have been conducted to explore the factors affecting TB treatment compliance and identified the following factors as barriers and enhancers to TB treatment compliance: structural factors (financial burden, poverty and discrimination), patient factors (age, gender, motivation, knowledge, beliefs, attitudes, interpretations of illness, disease prognosis and medication side effects), social factors (community and family influence as well as social stigma), health care service factors (organization of treatment and care of TB patients) and other factors such as co-morbidities.

2.3.5.1 Structural factors

Many structural factors have been identified in previous research as factors influencing treatment compliance. An international systematic review by Munro et al. (2007) identified financial burdens as a structural factor mentioned in most of the reviewed studies influencing TB treatment compliance. In a study done in Gambia by Afns and Ji (2010), patients indicated that health facility-based daily medication increased their family expenditures

especially money spent on transport to and from the hospital. In other studies in sub-Saharan Africa and elsewhere, treatment interruption was associated with treatment costs either directly (paying for medications) or indirectly (hospital stays, transportation and change in a diet) (Barter et al., 2012; Greene, 2004; Lonnroth et al., 2009; Muture et al., 2011; Watkins & Plant, 2004). Studies have further highlighted that the difference between treatment options, work and indirect costs leads to expenses exceeding resources thus potentially pushing people into poverty (Greene, 2004; Munro et al., 2007). Studies further indicated that having TB had consequences for work and some patients hide their disease for fear of dismissal from their employment thus compromising their compliance with treatment (Barter et al., 2012; Edginton et al., 2002; Garner et al., 2007; Khan et al., 2000).

A study done in Burkina Faso on barriers faced by patients and community members in accessing and adhering to TB treatment has independently identified geography and poverty as some of the factors associated with treatment interruption. Geography and poverty influence attendance of the health centre initially for diagnosis and repeatedly for daily DOTS as their health centres are centralised and DOTS require daily direct observation (Sanou et al., 2004). These findings applies to most sub-Saharan countries, Namibia included because even if the services are decentralised, there are still some hard to reach areas that makes services inaccessible to the unemployed and other economically disadvantaged and thus impacting on their compliance with care.

Financial burden, work-related stigma, poverty and geography are some of the structural factors influencing TB treatment compliance identified in the above reviewed studies despite the difference in settings and difference in methodologies.

2.3.5.2 Patient/personal factors

There are a number of patient factors influencing TB treatment compliance. Treatment interruption was commonly attributed to lack of sufficient knowledge about TB, TB treatment, treatment duration and the consequences of non-compliance in most studies. In an international systematic review by Munro et al. (2007), non-compliance of TB treatment was attributed to insufficient knowledge about TB by TB patients. Findings from a Gambian study by Afns and Ji (2010) has also indicated that insufficient knowledge about TB among

TB patients contributed negatively to their treatment compliance. A descriptive cross-sectional study carried out in Nepal by Newell et al. (2006) revealed that 61% of the non-adherent patients indicated that they have stopped taking the treatment because they were feeling better and they attributed their treatment interruption to insufficient knowledge. These findings are consistent with the review by Munro et al. (2007) and with the study by Afns & Ji (2010). Newell et al. (2006) in a study conducted in Nepal further established that daily health education and knowledge of TB and its treatment were independently associated with adherence to treatment as confirmed by the multivariate analysis.

A retrospective study done in Morocco by Dooley et al. (2011) on the risk factors for TB treatment failure indicate that male gender was one of the risk factors associated with treatment failure. In their study, male TB patients were more than two times likely to default from their treatment compared to their female counterpart (Dooley et al., 2011). This is an indication that males were less compliant compared to the females. While a separate study done in Tanzania by Van Den Boogaard et al. (2009) found that women, children, rural areas' residents, newly diagnosed patients with smear-negative were most likely to be compliant with their TB treatment.

Personal behavioural factors such as substance abuse and alcohol consumption were also found to influence treatment compliance in a range of studies in sub-Saharan Africa and beyond (Dooley et al., 2011; Khan et al., 2005; Munro et al., 2007; Walley et al., 2001). Alcohol and other substances as well as mental illness are believed to alter individuals' behaviour, thus patients may forget to take their medications therefore leading to poor compliance.

Studies further indicate that beliefs about treatment efficacy, denial and difficulty in accepting the diagnosis as well as personal interpretation of illness, are some of the personal factors affecting treatment compliance (Awofeso, 2008; Gebremariam et al., 2010; Munro et al., 2007).

Some studies such as an international review by Munro et al. (2007) as well as the Gambian study by Afns and Ji (2010) highlighted the impacts of treatment requirements on patient's attitudes thus on adherence behaviour. Treatment requirements such as treatment duration that makes patients tired of taking the medications and fear of painful injections are some of

the factors that contribute to treatment interruption and non-compliance with the treatment (Afns & Ji, 2010; Awofeso, 2008; Munro et al., 2007).

A study done in Kyrgyzstan by Awofeso (2008) identified side-effects to medications as one of the factors influencing treatment compliance among TB patients. The study found that more serious side-effects such as hepatitis, dyspepsia, exanthema and arthralgia were attributable to the interruption and termination of treatment of up to 23% of patients (Awofeso, 2008).In most studies (Awofeso, 2008; Kaona et al., 2004), medication side-effects were mostly reported in the initial phase of treatment.

As discussed above, studies in sub-Saharan Africa and elsewhere identified insufficient knowledge, gender, substance abuse and alcohol consumption, patients' beliefs and attitudes and medication side effects as the patients' factors likely to have an influence on treatment compliance despite the difference in settings and methods used

2.3.5.3 Health service factors

There are health service factors believed to either promote or hinder patients' compliance with their TB treatment. A study done in Pakistan by Khan et al. (2005) indicated that for most patients, strategies used in administering treatment and care for TB patients through different types of DOTS plays a major role in treatment compliance. Patients feel that in most cases direct treatment observations are arranged to suit the treatment supporters schedule rather than that of the patients. This makes direct observation inconvenient and inflexible for patients thus potentially compromising compliance (Khan et al., 2005). In a Namibian study most of the participants (73%) preferred family members as their DOT supporter because they perceived them to be most convenient, acceptable and accessible (Zvavamwe & Ehlers, 2009).

Patient-centred approaches that allowed TB patients to choose the treatment option that was convenient and flexible to them was found to have improved the treatment outcomes for patients treated under both community and facility-based DOT. The approach further improved treatment success rates for patients who opted for community DOT rather than patients who chose facility-based DOT (Van Den Boogaard et al., 2009).

Studies identified the problems that are related to health-facility DOTS. Factors such as; availability and accessibility of health care facilities especially at the community level and availability of health workers were identified in some studies as factors influencing TB treatment compliance (Adane et al., 2013; Sanou et al., 2004). Other factors such as long waiting times, queues, poor TB medication availability lack of privacy and maltreatment by providers were identified in some qualitative studies both in sub-Saharan Africa and in other parts of the world as factors influencing health facility DOTS (Finlay et al., 2012; Greene, 2004; Harper et al., 2003; Khan et al., 2000; Watkins & Plant, 2004).

In some African studies and studies done elsewhere, health workers felt that daily DOTS increased their workload. Health workers attributed this workload to the treatment requirements where patients are seen and observed on a daily basis. For the proper implementation of the primary elements of DOTS, which is the monitoring of the progress of patients are also seen on regular basis for follow ups and sputum reviews (Afns & Ji, 2010; Podewils et al., 2013; Sanou et al., 2004; Van der Walt et al., 2007).

2.3.5.4 Social factors

Patients with TB do not only carry a burden of suffering from the disease, but their social life changes and are in most cases subjected to stigma and discrimination. In studies carried out in Kenya (Ayisi et al., 2011), Nigeria (Odusanya & Babafemi, 2004) and South Africa (Pronyk et al., 2001), discrimination against TB patient by family members, friends, co-workers and employers was strongly associated with treatment non-adherence and delay in seeking treatment. In a Gambian study, stigma was more prominent among females compared to their male counterpart (Afns & Ji, 2010). Stigma and discrimination does not only affect compliance and cause a delay in seeking treatment but further impact on TB control and it is more prevalent mostly in developing countries (Abioye et al., 2011; Cramm et al., 2010; Cramm et al., 2010; Kipp et al., 2011).

In a cross-sectional study conducted in Nigeria, TB patients reported that stigma was common, forcing patients to hide their sickness, thus affecting their adherence to treatment (Abioye et al., 2011). Munro et al. (2007) in their systematic review identified peer influence,

lack of family and spouse support as some of the social factors that were strongly associated with non-compliance because of their strong influence on treatment taking behaviour. In a Gambian study by Afns and Ji (2010), full compliance with TB medication was described as a very challenging activity that requires patients to sacrifice important family responsibilities. A study done in South Africa by Cramm et al. (2010) on TB treatment initiation and adherence indicated that younger patients received more support from their family and friends compared to older TB patients and it helped them to comply more with their treatment. In a separate study by Govender (2009) on reasons why TB patients are not adhering to their treatment in South Africa, findings indicated that social support received from family and partners were significantly associated with adherence, while social support from friends was not associated with treatment adherence.

Social factors influencing TB treatment compliance identified in this review were: stigma and discrimination as well as lack of social support despite the difference in study settings and study methods.

2.3.5.5 Other factors

The other factors associated with either compliance or non-compliance were co-morbid conditions such as cardiovascular diseases, diabetes and HIV. These conditions require patients to take additional medications in addition to TB treatment. Studies from sub-Saharan Africa and elsewhere indicated that patients may either comply because they want to get better, or they may decide not to comply because they feel worthless or they may become tired of taking a lot of medications (Bagchi et al., 2010; Bam et al., 2006; Brust et al., 2012; Daftary, 2012; Faurholt-Jepsen et al., 2012; Kaona et al., 2004; Munro et al., 2007). Non-compliance with anti-TB treatment was considered high in the Ethiopian institutional cross-sectional study by Adane et al. (2013) and being HIV positive was significantly associated with non-compliance. The authors attributed non-adherence to TB among HIV positive patients to the number of pills that TB/HIV co-infected patients have to take and the adverse effects of anti-TB medication that are more common in HIV infected patients. They further indicated that HIV/AIDS co-infected patients may be less motivated to take their medication. In a South African study, non-compliance with TB treatment among TB patient co-infected with HIV was attributed to poor integration between HIV and TB programmes (Atkins et al, 2011). TB/HIV co-morbid was also strongly associated with non-compliance in a Ugandan

study by Amuha et al. (2009).

This review identified co-morbidities such as cardiovascular diseases, diabetes and HIV as other factors influencing treatment compliance among TB patients.

2.4 Gaps in knowledge

Though the literature has provided a great amount of information on TB treatment compliance, most studies were either surveys or reviews and they could not indicate how compliance has been in all the phases of treatment and throughout the treatment duration. The studies have also not provided information on how compliance is distributed across a range of patients' characteristics in different phases of treatment. Very few studies provided information on how compliance influences the treatment outcomes and the information was insufficient to draw conclusions on about the impacts of compliance on treatment outcomes. There are also very few studies that assessed compliance in Namibia. These gaps make this study imperative in providing new insights about TB treatment compliance and contribute to the available data in order to enable targeted interventions to be devised.

Summary

This literature review aimed at presenting the information available about TB treatment compliance in order to validate and justify the significance of the study. This was done through reviewing of the relevant literature on both compliance and adherence from reports and journals. The review mainly focused on the importance of treatment compliance, compliance with DOTS treatment, treatment compliance among different treatment strategies, treatment compliance and associated treatment outcomes in different treatment strategies and factors influencing DOTS treatment compliance. Correct and consistent compliance with prescribed TB treatment has been associated better treatment outcomes while non-compliance with TB treatment has been identified as a problem in many TB programmes and it is associated with increase in TB morbidity, poor treatment outcomes and an increase in health care costs. The WHO requires a TB treatment compliance of greater than 90% in facilitating cure and achieving treatment success. Compliance has been defined and measured differently in different settings, but most of the studies have adopted the WHO recommendation. Compliance with TB treatment has been reported to be low in most studies,

with the continuation phase of treatment identified as the most problematic phase when it comes to treatment compliance and one study recommending a cohort study to look into the rate of compliance. A WHO recommended compliance is adopted in this study to enable comparisons of the findings in different settings. Most studies that compared TB treatment among different strategies did not indicate how patients complied with their treatment and some did not indicate the type of DOT used, studies that did however have indicated that compliance was higher among community-based DOT. Non-compliance with TB treatment has adverse effects on treatment outcomes, while compliance improves cure rates. Higher cure rates were reported among patients treated under DOTS compared to self-administered treatment though some studies did not observe a significant difference between treatment outcomes. Financial burden, work-related stigma, poverty and geography are some of the structural factors influencing TB treatment compliance identified in the reviewed studies. Studies identified insufficient knowledge, gender, substance abuse and alcohol consumption, patients' beliefs and attitudes and medication side effects as the patients' factors influencing treatment compliance. Treatment strategies as well as availability and accessibility of health care services were identified by many studies as the health service factors influencing TB treatment compliance. Social factors influencing TB treatment compliance identified in this review were: stigma and discrimination as well as lack of social support. Co-morbidities were identified as other factors influencing treatment compliance among TB patients. In the efforts to fill the gaps identified in the literature, this study is trying to provide new insights about TB treatment compliance and contribute to the available data in order to enable targeted interventions to be devised.

CHAPTER 3: METHODS

Introduction

This Chapter focuses on the aims and objectives of the study, as well as the type of research and design used in this study. The study population, study setting, sampling procedure and the criteria used in the selection of the study participants will also be discussed. The Chapter will also describe the variables studied, methods used for extracting the data as well as the strategies used in the study to prevent bias and to ensure validity and reliability. Finally, the Chapter will discuss the statistical analyses conducted and the ethical considerations involved in the study.

3.1 Aims and objectives

3.1.1 Aim

The aim of the study was to investigate TB treatment compliance and measure the relationship between patient characteristics as well as treatment outcomes and compliance among adult patients (age 15 and above) with PTB treated in Windhoek District during 1st January 2013 and 31st December 2013, in order to determine the effects of treatment compliance on treatment outcomes.

3.1.2 Objectives

The study objectives were:

- To determine TB treatment compliance in these patients;
- To compare compliance between initial and continuation phase of treatment;
- To measure the association between patient characteristics and compliance;
- To determine the prevalence of different treatment outcomes among these patients and
- To measure the association between TB treatment compliance and treatment outcomes.

3.2 Study setting

The study was conducted in Windhoek District, the largest district in Namibia and the only District in the Khomas region (one of the 13 regions in Namibia) where the capital city of Namibia is situated. Windhoek District is divided into Windhoek urban and rural of which the urban is the larger part of the District, while Windhoek rural is the portion of the district that consists of the farms at the outskirts of the city (NSA, 2011).

According to the Namibian Statistics Agency (NSA) Namibia's 2011 population and housing census (2014), Windhoek District has the total population of 342 141, of which almost equal numbers are women and men, with an annual growth rate of 3.1% in 2011. Ninety five percent of the population is living in urban areas. There are 89 438 households, with an average size of just under 4 persons per household. The age composition of the population suggests that those 15-59 years make up 69% of the total district's population.

The proportion of the people who are literate in Windhoek District is reported at 97%. About 39% of the district's population has completed primary education and 31% has completed secondary education. Seventy four percent of the population aged 15 years and above are economically active while 30% of the eligible population is unemployed (NSA, 2014). About 56% of the district population lives below the poverty line and there is also high inequality as indicated by a Gini-coefficient of 0.5 (NSA, 2014).

There are 12 government health facilities (seven Primary Health Care clinics, two Primary Health Care Centres, and two big hospitals of which one is an intermediate hospital and another a national referral hospital for specialized care). The District TB Unit is hosted in the intermediate hospital and it serves as a referral hospital for 3 other regions surrounding Khomas region in which Windhoek is based. All the clinics and health centres in the district offer basic health care services of which TB treatment is one, and it is offered free of charge, not only in Windhoek District but in the whole country. Daily, weekly, bi-weekly and monthly DOT is offered at 12 DOT points in the whole district which includes 9 health facilities and 3 community DOTS centres. There are also 6 private hospitals and several private consulting rooms that also offer TB treatment for fees and mostly cater for the middle and high income groups of the society (MoHSS, 2012).

3.3 Study type and design

This was an observational analytic study, using a quantitative approach. A retrospective cohort design was used in this study in order to determine TB treatment compliance, factors influencing compliance and the effects compliance have on different treatment outcomes within this cohort. The study design is useful in examining the 'possible relationship between exposures and outcomes" (Joubert & Ehrlich, 2012:79), the effect compliance has on treatment outcomes can also be determined. The cohort in this study was Pulmonary TB (PTB) patients started on TB treatment for the first time during the period of 1st January 2013 to 31st December 2013.

3.4 Population and sampling

The targeted population were treatment cards of all adult PTB patients (15 years and above) treated on DOT in Windhoek District. While the study population comprised treatment cards of all new cases of adult PTB both sexes who were treated on DOT in Windhoek District during the study period. This study population was chosen so that by the time the study commenced patients would have completed 6 months of treatment and have available outcome measures. The study population size was 766 cases.

Inclusion criteria

- Treatment cards of all new adults PTB patients who received their TB treatment in the public health services via DOT in Windhoek District regardless of their HIV status were included in the study.
- Treatment cards of all new adults PTB (PTB) patients started on TB treatment for the first time during the period of 1st January 2013 to 31st December 2013.
- Treatment cards with some missing information were included in the study but were excluded from some analysis.

Exclusion criteria

- Treatment cards of patients with multi-drug resistance TB (MDR-TB), extensively drug-resistant TB (XDR-TB) or other forms of TB, complications such as TB meningitis, patients on alternative TB drugs that require different treatment durations

were excluded from the study because they require extended or varying duration of treatment.

- Patients whose TB treatment cards were missing were excluded from the study.

Using the District TB register, all patients that met the inclusion criteria were selected to be part of the study population. In this study, the study population and study sample are the same as there was no sampling done. In total 352 (46%) patients met the inclusion criteria and their treatment cards were all included in the study. The table below illustrates how the final cohort was selected to be part of the study and eventually analysed.

Table 1: New PTB patients treated in Windhoek District between 1st January 2013 and 31st December 2013. n=766

Category of patients	Number (N)	Percentage (%)
Other forms of TB such as Pleural Effusion	78	10
TB complications such as TB meningitis	13	2
Patients with Drug resistance TB	7	1
Children under the age of 14 years with only PTB	207	27
Missing TB treatment cards	109	14
Patients that met the inclusion criteria	352	46
Target population	**766**	**100**

After operationalization of the inclusion and exclusion criteria as indicated above, 352 patients' treatment cards were included in the study.

3.5 Data collection method

Data collection method presents how the data was collected and the measures that were performed.

3.5.1 Data collection

Data was extracted by the researcher from the TB treatment cards using a data extraction tool **(Appendix A)**. The data extraction tool was developed based on the data available on the standard Namibian TB treatment cards used for all TB patients on DOT in accordance with WHO standards. All patients that have met the inclusion criteria were selected from the TB register and their TB treatment cards were extracted for data collection.

Treatment cards of these patients were reviewed at the end of their TB treatment, to assess their compliance, socio-demographic and clinical factors affecting compliance, as well as their treatment outcome thus enabling the evaluation of the effects their compliance had on their treatment outcomes. Data collected from the treatment cards included: socio-demographic data and clinical data that included the diagnostic classification, type of DOT and HIV status. Data on TB therapy and other medication the patient has taken as collected by the staff at the beginning of the treatment were also extracted. Compliance was measured in all phases of treatment by collecting data on daily doses taken/missed in the initial phase and in the continuation phase as well as the overall doses taken/missed. Overall compliance was calculated by adding compliance in the initial phase to the compliance in the continuation phase. Data on co-morbidities and side effects as well as patient education verification (at the beginning of the treatment, and the end of the initial phase and at 5 to 6 months of treatment) and treatment outcome were also collected. Compliance was determined through the calculation of the total number of doses taken in comparison with the number of doses supposed to be taken.

Retrospective data collection took place at the District TB unit's outpatient department. At the beginning of the treatment and during other events occurring during the treatment such as co-morbidities, side-effects data was collected and recorded by doctors and nurses. While data on daily doses and patients' knowledge through education verification at the end of each treatment phase is collected and recorded by nurses for those treated under health facility-based DOT and by DOTS supporters for those treated under community-based DOT. TB treatment cards of all TB patients that were treated at different DOTS centres in the District are kept at the District TB unit. The researcher made use of a separate form for data collection (data extraction tool) for each patient's treatment card and ensured that all patients' treatment cards were kept safe at all times while in her possession.

3.5.2 Measures

The dependent variables were: treatment compliance (by looking at compliance in the initial phase, continuation phase and overall) and treatment outcomes (cured, treatment completed, defaulted and died). While the independent variables that were collected included socio-demographic variables (age, gender, employment status and type of area) and clinical

variables (diagnostic classifications, type of DOT, HIV status, TB therapy doses taken (initial phase, continuation phase and overall); TB therapy doses missed (initial phase, continuation phase and overall), co-morbidities, other medications taken, alcohol consumption, medication side-effects and knowledge of TB through patient education verification).

In determining the proportion of the doses taken out of the total doses the patient was supposed to take in 6 months; patient's treatment cards were reviewed to count the actual number of doses taken as recorded in the treatment cards. In the initial phase of treatment 62 doses were supposed to be taken while in the continuation phase 119 doses were supposed to be taken. A total of 181 doses were supposed to be taken by all patients fully treated over the 6 months treatment period.

Compliance was measured in the two phases and for overall compliance. Patients who took 90% of the prescribed treatment per treatment phase were considered to have good compliance. Those patients that had taken between 40% and 90% of the prescribed doses were considered to have moderate compliance, while patients that have taken less than 40% of their treatment were considered to have poor compliance. Patients with good compliance were considered compliant while those with moderate and poor compliance were considered non-compliant. Overall compliance was calculated by adding compliance in the initial phase to the compliance in the continuation phase. This measurement could however not be performed for patients who died, defaulted and transferred out in the initial phase of treatment.

Different treatment outcomes were obtained from the treatment cards as recorded at the end of 6 months of treatment or at the time treatment was ended.

3.6 Data analysis

Data collected was entered and analysed using Epi Info 7. Before data analysis, the data was cleaned and coded. Data cleaning and coding ran concurrently with data collection. The data extraction tools were checked for completeness and consistency before being entered into Epi Info. Raw data was coded into numerical and categorical variables to enable data analysis. Records in Epi Info were also checked and double checked for correctness and completeness against the data extraction tools.

Descriptive statistical analyses were used to summarize the data, measure central tendency and dispersion. Frequencies and proportions were used to summarize univariate categorical data. While for numerical data, means and standard deviations were used.

Analytical statistics were used in bivariate analysis using chi-squared p-value (x^2) to test for association between patients' characteristics and compliance in different phases of treatment. These analyses were limited to those demographic and clinical variables that did not have a lot of missing data, to avoid the influence of missing data on the findings. Association was also tested between compliance in the various stages of treatment and treatment outcomes to determine the effects of compliance on treatment outcomes. In this analysis, age groups were collapsed into two groups namely; young adults were considered as patients aged 15 – 34 years while older adults were considered as patients aged 35+ years. HIV status in this analysis was only done for those with known HIV status (positive and negative). Treatment outcomes were also collapsed into two categories, namely; treatment success (good treatment outcomes) were considered for those patients that are cured and those who completed their treatment, while poor treatment outcomes were considered for patients that defaulted, died, transfer out and those whose treatment failed before and after 5 months of treatment.

A 5% confidence limits and 95% confidence interval was used in determining the significance level of the findings. To control variables for other associations, a multivariate regression using a logistic regression model was performed on variables that showed a statistically significant association in a bivariate analysis with a chi-squared p-value <0.05.

3.7 Validity and reliability

To ensure internal validity, selection bias was reduced by the use of inclusion and exclusion criteria. All the records from the study population that met the inclusion criteria were included in the study. Information bias was reduced through standardization of the data abstraction tool and ensuring that the information flow in the data extraction tool is the same as the information in the patients' treatment cards. The data extraction tool was pre-tested on 10 randomly selected records. This was done to ensure that the tool measures what it is intended to measure (Bonita et al., 2006). The tool was adjusted accordingly based on the results of the pre-test and the adjusted tool was used for data collection. Initially, the tool was

not made to capture missing data for most of the variables, but after the pre-test, the researcher had to adjust the tool for it to be able to capture the missing information which was notable in most of the records. A repeated measure on at least 5% of the data abstraction forms against the patients' records was also done to ensure consistency and reliability of measurements (Bonita et al, 2006). External validity was ensured by having clear inclusion and exclusion criteria.

3.8 Generalisability

The results from this study will be generalized to all new adult PTB patients with no drug resistant strains and no other forms of TB on DOTS in Windhoek District and to new adult PTB patients with no drug resistant strains and no other forms of TB in similar settings in Namibia. This is because of similarities of the population and the likelihood of similar compliance and similar effects on treatment outcome.

3.9 Ethical considerations

Ethics permission was granted by University of the Western Cape Senate Research Committee **(Appendix B)**. There were no individual consents for participants because there were no participants but rather reviewing of patients' treatment cards. Written permission to conduct the study was sought from the Permanent Secretary **(Appendix C)**, while permission to access patient's records was sought from the Khomas Health Regional Director **(Appendix D)** and the Intermediate Hospital Katutura's Medical Superintendent **(Appendix E)** respectively.

Permission to conduct the research was obtained from the Ministry of Health and Social Services' Permanent Secretary through the Ministry's Research Unit **(Appendix E)**, as well as from the Medical Superintendent of the Intermediate Hospital Katutura who is in charge of the District's TB Unit **(Appendix F)**.

Anonymised data was extracted from the patients' records by the researcher. Extraction was done at the TB outpatient department. Patients' records are confidential documents that were safeguarded as required by the health ethics; therefore information obtained was kept fully confidential with no person other than the researcher allowed any access to the information.

Since this was a record review using existing data, there was no anticipated emotional harm involved in the study. The study findings will benefit the TB programme in devising targeted actions based on the study findings. The study findings will be presented to the District Management Team as well as to the District TB programme coordinators. The Ministry's Research Unit and the District will be provided with the copy of results that will be kept for future reference.

Summary

The study aimed at investigating TB treatment compliance and its association on patient characteristics as well as treatment outcomes in order to determine the effects of compliance on treatment outcomes in Windhoek District. A quantitative observational analytic study using a retrospective cohort design was adopted. Treatment cards of new adult PTB patients treated under DOTS in the District during a specified period that met the inclusion criteria (352) were included in the study and there was no sampling done. Data was collected using data extraction tool in extracting the data from the patients TB treatment cards. Selection and information bias was eliminated by using clearly defined inclusion and exclusion criteria using a pre-tested standardized tool. Statistical analysis using descriptive and analytic statistics was done using Epi Info 7 to determine the prevalence of compliance, treatment outcomes and to measure the associations. Institutional Review Board approval and gate-keeper approval was granted by relevant institutions. The next Chapter (Chapter four) will present the study findings.

CHAPTER 4: RESULTS

Introduction

This Chapter presents the findings of the study, starting with the description of the socio-demographic and clinical characteristics of the study sample and findings about compliance in both phases of treatment and overall as well as treatment outcomes. The Chapter will further show the analysis of the variables associated with compliance, by looking at the chi-squared p-values and multivariate logistic regression odds ratios (OR) to determine the associations. Finally, findings about the association between compliance and treatment outcomes will be presented in order to determine the effects of compliance on treatment outcomes.

4.1 Characteristics of the study population

4.1.1 Socio-demographic characteristics

Table 2: Socio-demographic characteristics of new adult PTB patients treated in Windhoek District between 1st January and 31st December 2013 stratified by sex at baseline. n=352

Socio-demographic characteristics	**Sex**		**Total N (%)**
	Female n (%)	Male n (%)	
Age groups			
15 – 24	27 (20.5)	32 (14.6)	59 (16.8)
25 – 34	49 (37.0)	70 (31.8)	119 (33.8)
35 – 44	28 (21.2)	66 (30.0)	94 (26.7)
45 – 54	19 (14.4)	37 (16.8)	56 (15.9)
55 +	9 (6.9)	15 (6.8)	24 (6.8)
	132 (100)	**220 (100)**	**352 (100)**
Age range (years)	15 - 85	15 - 85	***15 - 85***
Mean age (years), SD	35.1 ± 12.6	36.9 ± 11.3	***36.2 ± 11.8***
Employment status			
Employed	4 (3.0)	10 (4.6)	14 (4.0)
Unemployed	16 (12.1)	15 (6.8)	31 (8.8)
Not recorded	112 (84.9)	195 (88.6)	307 (87.2)
	132 (100)	**220 (100)**	**352 (100)**
Type of area			
Rural	12 (9.1)	12 (5.5)	24 (6.8)
Urban	120 (90.9)	208 (94.5)	328 (93.2)
	132 (100)	**220 (100)**	**352 (100)**

The largest proportion of the study cohort were adults aged 25 to 34 years 119 (38.8%) that comprised more females 49 (37%) than males 70 (31.8%).While the smaller portion of this population 24 (6.8%) came from older adults aged 55 years and above. The majority of the records 307 (87%) did not indicate the employment status of the patients and more males 195 (88.6%) did not have their employment status recorded. Employment could therefore not be included in further analysis due to the missing data. Ninety-three percent (328) of the patients came from urban areas, with a larger proportion of males 208 (94.5%) living in urban areas.

4.1.2 Clinical characteristics

Clinical information about the study population is presented in two tables. Table 3 presents the clinical information that was collected at the beginning of the treatment, referred to as the baseline, while Table 4 presents the clinical information specifically co-morbidities that was collected throughout the treatment duration (pre-treatment, at the end of the initial phase and at the end of the continuation phase).

Table 3: Clinical characteristics of new adult PTB patients treated in Windhoek District between 1st January 2013 and 31st December 2013 stratified by sex at the baseline. n=352

Patients' clinical information	**Sex**		**Total n (%)**
	Female n (%)	Male n (%)	
Diagnostic classification			
Pulmonary TB smear positive	105 (79.5)	163 (74.1)	268 (76.1)
Pulmonary TB smear negative	20 (15.2)	38 (17.3)	58 (16.5)
Pulmonary TB no smear	7 (5.3)	19 (8.6)	26 (7.4)
	132 (100)	**220 (100)**	**352 (100)**
Type of DOT			
Close relative	6 (4.5)	2 (0.9)	8 (2.3)
Guardian-relative, neighbour	3 (2.3)	1 (0.5)	4 (1.1)
Community Health Worker	5 (3.8)	12 (5.5)	17 (4.8)
Community-based DOT	*14(10.6)*	*15 (6.9)*	*29 (8.2)*
Health Facility-based DOT	*118 (89.4)*	*205 (93.1)*	*323 (91.8)*
	132 (100)	**220 (100)**	**352 (100)**
HIV status			
Negative	68 (51.5)	100 (45.4)	168 (47.7)
Positive	60 (45.5)	104 (47.3)	164 (46.6)
Unknown	4 (3.0)	16 (7.3)	20 (5.7)
	132 (100)	**220 (100)**	**352 (100)**

The majority of the patients 268 (76.1%) were treated for Pulmonary TB smear positive,

which was reported more among females 105 (79.5%) (Table 3). Ninety two percent (323) of the patients were treated under health facility-based DOT and the majority of males.

According to the records, 168 (48%) of the patients were HIV negative, while 164 (46.6%) were HIV positive. The prevalence of HIV among new adult patients treated in Windhoek District between 1st January 2013 and 31st December 2013 was 46.6%.

Table 4 presents how co-morbidities were distributed across the phases of treatment stratified by sex. There was no much difference in co-morbidities recorded at the commencement of TB treatment 148 (42.1%) and co-morbidities recorded at the end of each phase of treatment, with 143 (45.6%) and 132 (45%) at the end of the initial and continuation phase of treatment respectively. HIV was the most frequently recorded co-morbidity in all phases of treatment with 142 (96%) at the beginning of the treatment and 126 (96.9%) at the end of the continuation phase of treatment.

Table 4: Clinical information on co-morbidities of the 352 new adult PTB patients treated in Windhoek District between 1st January 2013 and 31st December 2013 in the phases of treatment stratified by sex. n=352

Patients' clinical information	**Sex**						**Total N (%)**		
	Female n (%)			Male n (%)					
	Pre-treatment	**Initial phase**	**Continuation phase**	**Pre-treatment**	**Initial phase**	**Continuation phase**	**Pre-treatment**	**Initial phase**	**Continuation phase**
Co-morbidities recorded									
Yes	54 (40.9)	49 (42.6)	44 (41.5)	94 (42.7)	94 (47.2)	86 (46.2)	148 (42.0)	143 (45.5)	130 (44.5)
No	78 (59.1)	66 (57.4)	62 (58.5)	126 (57.3)	105 (52.8)	100 (58.8)	204 (58.00)	171 (54.5)	162 (55.4)
	132 (100)	**115 (100)**	**106 (100)**	**220 (100)**	**199 (100)**	**186 (100)**	**352 (100)**	**314 (100)**	**292 (100)**
Co-morbidities conditions									
HIV	50 (92.6)	48 (98.0)	44 (100)	93 (98.9)	93 (98.9)	82 (95.4)	143 (96.6)	141 (98.6)	126 (96.9)
Others	4 (6.4)	1 (2.0)	-	1 (1.1)	1 (1.1)	4 (4.6)	2 (3.4)	2 (1.4)	4 (3.1)
	54 (100)	**49 (100)**	**44 (100)**	**94 (100)**	**94 (98.9)**	**86 (100)**	**148 (100)**	**143 (100)**	**130 (100)**

4.2 Treatment compliance and treatment outcomes

Table 5: Treatment compliance and treatment outcomes of new adult PTB patients treated in Windhoek District between 1st January 2013 and 31st December 2013 by sex. n=352

Compliance and Treatment outcomes	**Sex**		**Total**
Compliance	Female	Male	
Mean Anti- TB dosages taken, SD	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*
Initial phase	61.7 ± 14.6	63.2 ± 15.0	**62.6 ± 14.8**
Continuation phase	111.3 ± 27.6	109.9 ± 31.1	***110.5 ± 29.9***
Overall	173 ± 42.2	173.1 ± 46.1	***173.1 ± 44.7***
Compliance	n (%)	n (%)	N (%)
Initial phase			
Good compliance	128(97.0)	214(97.2)	342 (97.2)
Compliant	*128(97.0)*	*214(97.2)*	*342 (97.2)*
Moderate compliance	3(2.2)	4 (1.9)	7 (2.0)
Poor compliance	1(0.8)	2 (0.9)	3 (0.8)
Non-compliant	*4 (3.0)*	*6 (2.8)*	*10 (2.8)*
	132(100)	**220 (100)**	**352 (100)**
Continuation phase*			
Good compliance	101 (87.8)	179 (88.2)	280 (88.0)
Compliant	*101 (87.8)*	*179 (88.2)*	*280 (88.0)*
Moderate compliance	11(9.6)	13 (6.4)	24 (7.6)
Poor compliance	3(2.6)	11 (5.4)	14 (4.4)
Non-compliant	*14 (12.2)*	*24 (11.8)*	*38 (12.00)*
	115 (100)	**203 (100)**	**318 (100)**
Overall*			
Good compliance	102 (88.7)	181 (89.2)	283 (89.0)
Compliant	*102 (88.7)*	*181 (89.2)*	*283 (89.0)*
Moderate compliance	10 (8.7)	13 (6.4)	23 (7.2)
Poor compliance	3 (2.6)	9 (4.4)	12 (3.8)
Non-compliant	*13 (11.3)*	*22 (10.8)*	*35 (11.0)*
	115 (100)	**203 (100)**	**318 (100)**
Treatment outcomes			
Cured	73 (63.5)	118 (56.5)	191 (58.9)
Treatment completed	29 (25.2)	59 (28.2)	88 (27.2)
Treatment success	*102 (88.7)*	*177 (84.7)*	*279 (86.1)*
Defaulted	4 (3.5)	14 (6.7)	18 (5.6)
Died	8 (7.0)	13 (6.2)	21 (6.5)
Treatment failure	1 (0.8)	5 (2.4)	6 (1.8)
Poor treatment outcomes	*13 (11.3)*	*32 (15.3)*	*45 (13.9)*
	115(100)	**209 (100)**	**324 (100)**

*Compliance in the continuation phase and overall compliance was not measured for the 34 patient that either died, defaulted or those that were transferred out in the initial phase of treatment, therefore it was only measured in 318 records.

Table 5 presents information on compliance and treatment outcomes of adult PTB patients treated via DOTS in Windhoek District stratified by sex.

Compliance in the initial phase of treatment was measured in all 352 patients' records. While in the continuation phase and overall, compliance was only measured in 318 records excluding the records of patients that either died, defaulted or those that were transferred out in the initial phase of treatment.

In the initial phase, 342 (97.2%) patients were compliant almost equally distributed between males 214 (97.2%) and females 128 (97%). In the continuation phase, 280 (88%) patients were compliant, with compliance recorded slightly more in males 179 (88.2%) than females 101 (87.8%). Whereas for overall compliance, 283 (89%) patients were compliant with males 181 (89.2%) showing slightly better compliance than females 102 (88.7%).

The initial phase displayed high compliance while compliance in the continuation phase was similar to overall compliance (88.7%).

As indicated in Table 5, treatment outcomes were measured only in 324 patients, excluding those patients who are transferred out. This gives the prevalence of different treatment outcomes among adult PTB patients treated via DOTS in Windhoek District over a specified period. . Treatment success in all 324 patients was 86.1% over six months as indicated by 191 (58.9%) cure and 88 (27.2%) treatment completed. There was no significant difference in treatment success between males and females.

Moreover, 18 patients (5.6%) defaulted to give a defaulter rate of 51 per 1000 TB cases per 6 months. Males 14 (6.7%) defaulted more compared to 4 (3.5%) females. Six and half percent (21) of the patients died, this outcome was observed more among females 8 (7%). Treatment failure occurred in about two percent (6) of the patients and it was recorded more among males 5 (2.4%) than among females with less than one percent. Poor treatment outcomes as represented by those patients that defaulted 18 (5.6%), died 21 (6.5%) and whose treatment failed 6 (1.8%) was reported at 45 (13.9%).

4.3 Association between a range of patients' characteristics and compliance in the initial, continuation phase and overall treatment compliance

Association between socio-demographic and clinical characteristics and compliance of the 352 new adult PTB patients was based on the observed percentages and the chi-squared (x^2) p-values. Those variables that showed an association of p-value=0.05 and below were analysed further using a multivariate regression to control for other associations.

4.3.1 Association between patients' characteristics and compliance in the initial phase of treatment

Table 6: Association between patients' characteristics and compliance of new adult PTB patients treated in Windhoek District between 1st January 2013 and 31st December 2013 in the initial phase of treatment. n=352

Patients' characteristics	Compliant n (%)	Non-compliant n (%)	x^2	P-value
Socio-demographic information				
Age category				
Young adults (15 – 34)	172 (96.6)	6 (3.4)	0.37	0.54
Older adults (35+)	170 (97.7)	4 (2.3)		
Sex				
Male	214 (97.3)	6 (2.7)	0.03	0.86
Female	128 (97.0)	4 (3.0)		
Type of area				
Rural	22 (91.7)	2 (8.3)	2.81	0.09
Urban	320 (97.6)	8 (2.4)		
Clinical information				
Diagnostic classification				
Pulmonary TB smear positive	261 (97.4)	7 (2.6)	0.21	0.64
Other PTB (smear negative and no smear)	81 (96.4)	3 (3.6)		
Type of DOT				
Community-based DOT	28 (96.6)	1 (3.4)	0.04	0.83
Health Facility-based DOT	314 (97.2)	9 (2.8)		
HIV status				
Negative	164 (97.6)	4 (2.4)	0.14	0.70
Positive	159 (97.0)	5 (3.0)		

*statistically significant association

There were no statistically significant associations observed between patients' socio-demographic and clinical characteristics and compliance in the initial phase of treatment. However, it is should be noted that the results of type of area (x^2=2.81, P value=0.09) were

approaching the significance level in this phase with majority of patients from urban areas complying with 97.6% compared with those from rural areas 91.7%.

4.3.2 Association between patients' characteristics and compliance in the continuation phase of treatment

Table 7 presents association between patients' socio-demographic and clinical characteristics and compliance of the 318 new adult PTB patients.

Table 7: Association between patients' characteristics and compliance of new adult PTB patients treated in Windhoek District between 1st January 2013 and 31st December 2013 in the continuation phase of treatment. n=318

Patients' characteristics	Compliant n (%)	Non-compliant n (%)	x^2	P-value	Multivariate logistic regression	
Socio-demographic information					Odds ratio (95% CI)	P-value
Age category						
Young adults (15 – 44)	136 (84.5)	25 (15.5)	3.97	0.05*	4.13 (1.72 – 9.90)	<0.01*
Older adults (35+)	144 (91.7)	13 (8.3)				
Sex						
Male	179 (88.2)	24 (11.8)	0.01	0.92		
Female	101 (86.8)	14 (12.2)				
Type of area						
Rural	15 (62.5)	9 (37.5)	16.11	<0.01*	0.02 (0.00 - 0.13)	0.05*
Urban	265 (90.1)	29 (9.9)				
Clinical information						
Diagnostic classification						
Pulmonary TB smear positive	214 (88.4)	28 (11.6)	0.14	0.70		
Other PTB (smear negative and no smear)	66 (86.8)	10 (13.2)				
Type of DOT						
Community-based DOT	22 (81.5)	5 (18.5)	1.21	0.27		
Health Facility-based DOT	258 (88.7)	33 (11.3)				
HIV status						
Negative	137 (87.8)	19 (12.2)	0.01	0.92		
Positive	127 (88.2)	17 (11.8)				

*statistically significant association

In the continuation phase of treatment and among age categories, very high compliance was observed among older adults (patients aged 45+years) with 91.7%. These results (x^2=3.97, P value=0.05) indicate a marginal statistically significant association.

As in the initial phase of treatment, the majority of patients from urban areas complied (90.1%), whereas patients from rural areas compliance were lower with 62.5%. The results (x^2=16.11, p-value=<0.01) indicate a statistically significant association.

In the multivariate regression using a logistic regression model, the only variables that showed a significant association in this phase were age (OR=4.3 95% CI (1.72 – 9.90), p-value=<0.01) and type of area (OR=0.02 95% CI (0.00 – 0.13), p-value=0.05). The odds of compliance are 4.13 among older adults (patients aged 45+years) in comparison with young adults (patients aged 15 – 34 years). While the odds of compliance is 0.02 for patients from rural areas compared to patients from urban areas.

In the continuation phase of treatment, age and type of area were associated with compliance with older adults (patients aged 35+years) more likely to comply than young adults (patients aged 15 – 34 years) and patients from rural areas less likely to comply with their treatment than those from other communities.

4.3.3 Association between patients' characteristics and overall compliance

Table 8 presents association between the socio-demographic and clinical characteristics of the 318 new adult PTB patients and overall compliance based on the observed percentages and chi-squared p-values and multivariate logistic regression odds ratio and p-values.

Among age categories, overall compliance was similar to the initial and different to that in the continuation phase of treatment. High overall compliance 92.4% were observed in older adults (patients aged 45+ years). The results (x^2=3.58, P value=0.04) show a statistically significant association between age and overall treatment compliance as in the continuation phase of treatment, with older adult patients more likely to comply with their treatments than young adults.

As in the initial and continuation phase of treatment, a large number of patients from urban

areas complied (91.2%), whereas patients from rural areas' compliance was relatively low with 62.5%, like in the continuation phase. The results (x^2=18.60, P value=<0.01) indicate a statistically significant association between type of area and overall treatment compliance.

Table 8: Association between patients' characteristics and overall compliance of new adult PTB patients treated in Windhoek District between 1st January 2013 and 31st December 2013. n=318

Patients' characteristics	Compliant n (%)	Non-compliant n (%)	x^2	P-value	Multivariate Logistic regression	
Socio-demographic information					Odds ratio (95% CI)	P-value
Age category						
Young adults (15 – 34)	138 (85.7)	23 (14.3)	3.58	0.04*	1.03 (0.18 – 7.83)	0.08
Older adults (35+)	145 (92.4)	12 (7.6)				
Sex						
Male	181 (89.2)	22 (10.8)	0.02	0.89		
Female	102 (88.7)	13 (11.3)				
Type of area						
Rural	15 (62.5)	6 (37.5)	18.60	<0.01*	0.03 (0.00 – 0.91)	0.04*
Urban	268 (91.2)	26 (8.8)				
Clinical information						
Diagnostic classification						
Pulmonary TB smear positive	217 (89.7)	25 (10.3)	0.47	0.49		
Other PTB (smear negative and no smear)	66 (86.8)	10 (13.2)				
Type of DOT						
Community-based DOT	22 (81.5)	5 (18.5)	1.70	0.19		
Health Facility-based DOT	261 (89.7)	30 (10.3)				
HIV status						
Negative	139 (89.1)	17 (10.9)	0.00	0.95		
Positive	128 (88.9)	16 (11.1)				

*statistically significant association

As in the continuation phase of treatment, those variables that showed a statistically significant association including age and the type of area were analysed further in a multivariate regression using a logistic regression model to control for other factors. The results show that in the model age is not associated with overall compliance (OR=1.03 95% CI (0.18 – 7.83), p-value=0.08) although the results were approaching significance indicating that older adult patients have higher compliance than young adult patients. The type of area

(OR=0.03 95% CI (0.00 – 0.91), p-value=0.04) remains statistically significant, with the odds of compliance 0.03 for patients from rural areas compared to patients from urban areas.

4.4 Association between compliance and treatment outcomes

Table 9 presents the association between compliance in each phase of treatment, as well as on overall compliance, and treatment outcomes to assess the relationship between treatment compliance and treatment outcomes. These associations are based on the observed percentages, bivariate chi-squared p-values.

Table 9: Association between compliance in all phases of treatment and treatment outcomes of new adult PTB patients treated in Windhoek District between 1st January 2013 and 31st December 2013. n=352

Treatment compliance	**Treatment success**	**Poor treatment outcomes**	x^2	**P-value**
Initial phase n=324				
Compliant	278 (88.5)	36 (11.5)	49.98	<0.01*
Non-compliant	1 (10.0)	9 (90.0)		
Continuation phase n=313				
Compliant	263 (95.6)	12 (4.4)	98.81	<0.01*
Non-compliant	16 (42.1)	22 (57.9)		
Overall compliance n=313				
Compliant	266 (95.7)	12 (4.3)	110.02	<0.01*
Non-compliant	13 (37.1)	22 (62.9)		

*statistically significant association

In the initial phase poor treatment outcomes appeared higher among those patients who did not comply with their treatment 9 (90%) compared to only 36 (11.50%) poor outcomes observed among those patients who were compliant with their treatments. Treatment success was 278 (88.50%) among patients that complied with their treatment and much lower 1 (10%) among those patients that did not comply with their treatment. The results (x^2 =49.98, P value=<0.01) show a statistically significant association between treatment compliance in

the initial phase of treatment and treatment outcomes. This clearly indicates that those patients who are non-compliant in this phase of treatment have poorer treatment outcomes while those with good compliance have good treatment success.

In the continuation phase, treatment success amongst compliant patients seems to increase (95.6%) as does treatment success amongst those non-compliant 16 (42.1%). The results (x^2 =98.81, P value=<0.01) still show a statistically significant association between treatment compliance in the continuation phase of treatment and treatment outcomes. The chi-squared test result further indicates a strong association between treatment compliance in the continuation phase and treatment outcomes.

Overall, treatment success appeared higher among those patients that complied with their treatment 266 (95.7%) compared to those patients who were less compliant with their treatment 13 (37.1%). Poor treatment outcomes seemed higher among the patients that complied less with their treatment 22 (62.9%). The results (x^2 =110.02, P value=<0.01) show a statistically significant association between overall treatment compliance and treatment outcomes. The chi-squared test result further indicates strong association between treatment compliance throughout the initial and continuation phase of treatment and treatment outcomes.

Summary

The study findings are based on the records of 352 new adult PTB patients treatment via DOTS in Windhoek District over a specified period. The analyses comprised 63% males and 37% females aged 15 to 82 years with a mean age of 36.2 years and a standard deviation of 11.8 years. The largest proportion of the study population were adults age 25 – 34 years; from urban areas; on health facility-based DOT; with PTB smear positive and HIV negative patients. HIV prevalence is recorded at 46.6%. Treatment success among the cohort was 86.1%. In the initial phase of treatment there were no factors that appeared to be associated with compliance. In the continuation phase of treatment age and type of area are associated with compliance with older adult patients aged 45+ years more likely to comply and patients from rural areas less likely to comply with their treatment. Overall, type of area is associated with treatment compliance while the relationship with age is no longer observed in the regression model. The results further indicate that poor treatment outcomes are associated

with non-compliance while treatment success is associated with compliance.

CHAPTER 5: DISCUSSION

Introduction

This Chapter discusses the findings of the study in line with the study objectives and in relation to the literature. Compliance with TB treatment remains important to the success of TB control programmes (Adane et al., 2013; Afns & Ji, 2010; Naidoo et al., 2013). This study contributes to the knowledge of TB treatment compliance, by revealing some important information on compliance, factors affecting compliance and the effects of TB treatment compliance on treatment outcomes in new adult PTB patients treated on DOTS in Windhoek District in Namibia. In keeping with the study objectives, the discussion will look at overall compliance as well as compliance in the two key phases of treatment. The discussion will further look at the factors associated with compliance as well as the association between treatment compliance and treatment outcomes in order to determine the effects of treatment compliance on treatment outcomes as well as the limitations of the study.

The key findings of the study show that overall treatment compliance was 89% with initial phase and continuation phase, 97.2% and 88% respectively. Treatment success among the cohort was 86.1%.

There were no factors associated with compliance in the initial phase of treatment, while in the continuation phase of treatment age and type of area were statistically significantly associated with compliance. Older adult patients aged 45+ years were more likely to comply with their treatment than young adult patients aged 15 – 34 years, while patients from rural areas were less likely to comply with their treatment compared to patients from urban areas. Overall, type of area is statistically significantly associated with treatment compliance, with patients from rural areas less likely to comply with their treatment compared to patients from rural areas. The results further suggest that treatment compliance seems to have an effect on treatment outcomes. Compliance is statistically significantly associated with treatment success.

5.1 Treatment compliance

The study shows overall compliance as well as compliance in the initial and continuation phase of treatment in Windhoek District among adult PTB patients treated under DOTS. The study indicated high compliance in the initial phase of treatment (97.2%). Compliance is higher than the WHO recommended 90% compliance as indicated by the literature (Adane et al., 2013; Awofeso, 2008; Takarinda et al., 2012). The continuation phase and overall compliance were higher than expected, 88.1% and 89% respectively but below the WHO's 90% recommended compliance as indicated by the literature (Adane et al., 2013; Awofeso, 2008; Takarinda et al., 2012). This indicates that patients were more compliant with their treatments in the initial phase of treatment and became less compliant/ non-compliant in the continuation phase of treatment, which has affected their overall compliance. High compliance in the initial phase of treatment which is above the WHO recommended compliance is a good indication for TB treatment compliance in Windhoek District. It indicates that patients in Windhoek District are capable of complying with their treatment throughout their treatment duration if support is given to both the patients and the treatment supporters. This will enable the District to achieve and surpass the WHO recommended treatment success.

In this study non-compliance varies by the phase of treatment from about 12% in the continuation phase to less than 3% in the initial phase. A review by Castelnuovo (2010) on compliance with anti-TB treatment in sub-Saharan Africa non-compliance from ranged from 11.3% to 29.6%. Another study done in Uganda reported the prevalence of non-compliance with TB at 25% and a study from Ethiopia found non-compliance of 10% to 13.6% (Adane et al., 2013; Amuha et al., 2009). However, it should be noted that in Castelnuovo's (2010) review compliance in the studies was determined through defaulters, while this study assessed compliance based on WHO's recommended 90% use of prescribed medication. The Ethiopian and Ugandan studies assessed compliance over four days and five days preceding their surveys respectively, which is also different from the way compliance was measured in this study.

Looking at non-compliance identified in this study that varies from 2.8% to 11.9% in comparison to non-compliance findings from other studies, non-compliance in this study is relatively lower. This could be due to the different measures used in other studies. Unlike

other studies previously conducted, this study assessed overall compliance over the whole treatment duration which is 6 months and compliance was also assessed in both phases of treatment separately. The method used in this study to measure compliance was useful in determining how non-compliance was occurring throughout the treatment duration and should enable recommendations for targeted interventions to be devised.

In many TB programmes, treatment compliance has been associated with high TB cure rates and reduction in the emergence of drug resistance (Adane et al., 2013; Afns & Ji, 2010; Naidoo et al., 2013). Therefore, consistent compliance in TB patients receiving treatment through DOTS is required throughout the treatment period for the achievement of good treatment outcomes which is key to achieving high cure rates (Naidoo et al., 2013). This study found that compliance has not been consistent throughout the treatment duration and the continuation phase of treatment was found to be the most problematic phase when it comes to treatment compliance. The highest non-compliance reported in this study of about 12% was reported in the continuation phase of treatment. These findings concur with the literature from sub-Saharan Africa that found the continuation phase to be the most problematic phase when it comes to compliance with TB treatment (Afns & Ji, 2010; Amuha et al., 2009; Castelnuovo, 2010).

Non-compliance with TB treatment in the continuation phase of treatment could be due to a number of factors. Studies attributed treatment interruption mostly to lack of sufficient knowledge about TB, TB treatment, treatment duration and the consequences of non-compliance (Munro et al., 2007; Afns & Ji, 2010). Studies further attribute treatment interruptions to the disappearance of symptoms that occurs mostly in the continuation phase of treatment (Munro et al., 2007; Newell et al., 2006). Since most patients in this study were treated under health facility based DOT, non-compliance in the continuation phase could also be due to financial burdens as Munro et al. (2007) and Afns and Ji (2010) have indicated that health facility-based daily medication have the potential of increasing family expenditures especially money spent on transport to and from the hospital. However, this study could not provide conclusive evidence on the factors contributing to non-compliance with TB treatment in the continuation phase of treatment but rather recommends that future studies explore this.

5.2 Factors influencing TB treatment compliance

Compliance with TB treatment remains beneficial in TB control programmes especially programmes that fall under the DOTS strategy. In many TB programmes, treatment compliance has been associated with high TB cure rates and reduction in the emergence of drug resistance (Adane et al., 2013; Afns & Ji, 2010; Naidoo et al., 2013). Treatment compliance can only be achieved if factors influencing compliance are known. Some of the most cited factors affecting TB treatment compliance in sub-Saharan Africa and beyond include financial burdens (Munro et al. 2007), treatment costs (Barter et al., 2012; Greene, 2004; Lonnroth et al., 2009; Muture et al., 2011; Watkins & Plant, 2004), geographic area (Sanou et al., 2004), insufficient knowledge about TB among TB patients (Munro et al., 2007; Newell et al., 2006), gender (Dooley et al., 2011; Van Den Boorgard et al., 2009).

Other factors such as personal behaviours including substance abuse and alcohol consumption (Dooley et al., 2011; Khan et al., 2005; Munro et al., 2007; Walley et al., 2001), personal interpretation of illness and cure (Awofeso, 2008; Gebremariam et al., 2010; Munro et al., 2007), medication side-effects (Awofeso, 2008; Kaona et al., 2004) were also cited. Social factors, health service factors and other factors such as co-morbidities were also identified as factors influencing TB treatment compliance (Barter et al., 2012; Greene, 2004; Lonnroth et al., 2009; Munro et al., 2007; Muture et al., 2011; Watkins & Plant, 2004). This study assessed some of these factors in the initial phase and continuation phase of treatment as well as overall. This was to assess how these factors were occurring in the treatment duration and to see if there was an association with compliance.

In this study, the findings indicate that there were no factors associated with compliance in the initial phase of treatment. While in the continuation phase age and type of area were statistically associated with compliance, with patients older adult patients aged 45+ years more likely to comply with their treatment compared to patients from other ages. In the continuation phase older adult patients aged 45+ years' compliance could be due to a number of factors. This age category represents older people, whose level of responsibility might be higher compared to that of younger adults. Most of these adults are at the helm of their employment, therefore they are likely to take all the responsibilities; those related to their employment and those related to their health. Being employed also means that their accessibility to care is better than that of the younger adults. In the absence of the literature

confirming that the above mentioned reasons are the actual reasons why the older adult patients are complying, this study is not providing conclusions on why that age category is more likely to be compliant than all the younger adults. But rather identifying the gaps that need to be filled by future research.

The findings about the type of area being associated with compliance are similar to the findings of a study done in Burkina Faso (Sanou et al., 2004), who indicated that geography has got an influence on health centre attendance for daily DOTS. However, in Sanou et al.'s (2004) study, patients from rural areas were more compliant with their treatment compared to patients from urban areas. This was because most patients in their study were treated via CB DOTS because it was more accessible to them. In this study, many patients were treated through health facility-based DOT, because there were more health facility-based DOT in the district than CB DOT (MoHSS, 2013).

5.3 Treatment outcomes

There was not much difference in treatment outcomes reported in this study and the national treatment outcomes reported by the MoHSS (2013).This study has reported a cure and treatment completed of 58.9% and 27.2% respectively. This translates into treatment success of 86.1% over six months, which is higher than expected because it is slightly higher than the national treatment success of 83% and the treatment success of 85% reported in a study done in Nepal (MoHSS, 2013; Newell et al., 2006). This study's treatment success is however still lower than the WHO target of 90% (Stop TB Partnerships, 2006; WHO, 2006).

The cure reported in this study appeared lower in comparison to the study by Jasmer et al. (2004) that indicated a very high cure of 98% among TB patients treated under DOTS in the USA. The study further reported a defaulter of 5.6% which is slightly higher than the national defaulter that was reported at 4% (MoHSS, 2013). The defaulter was however low compared to Castelnuovo's (2010) findings of 11.3% to 29.6% as the defaulter in a number of sub-Saharan African studies. Moreover, the TB mortality of 6.5% reported in this study appeared slightly higher than the reported national and district TB mortality (MoHSS, 2013). The treatment failure of 1.8% as reported in this study is slightly below the national TB treatment failure that was reported at 5% (MoHSS, 2013). The findings about treatment outcomes from this study are helpful in providing context specific information as well as for comparing these

treatment outcomes with the WHO recommendations and findings on treatment outcomes from elsewhere.

5.4 Effects of treatment compliance on treatment outcomes

The findings from this study suggest that treatment compliance seems to have an effect on treatment outcomes with compliance associated with treatment success. This was indicated in both phases of treatment and overall. In the initial phase of treatment, compliance was associated with treatment success as in the continuation phase and overall. Looking at the chi-squared test results (Table 9) that indicated a strong association, it is clear that those patients that complied with their treatment had higher treatment success than those that were non-compliant. These findings are in agreement with Gelmanova et al. (2006) who found that non-compliance with TB treatment has significant adverse effects for TB treatment outcomes. The findings also confirm that compliance with TB treatment is important to the success of TB control programmes because it promotes higher treatment success (Adane et al., 2013; Afns & Ji, 2010; Naidoo et al., 2013).

5.5 Limitations

Since the study has made use of secondary data, the findings are limited to the information that was available in the patients' treatment cards. The factors affecting compliance were also limited to those documented in the patients' treatment cards. However, the study findings are still useful in providing information about compliance and its distribution among demographic and clinical variables as well as its effects on treatment outcomes. Some data were also incomplete in some patients' treatment cards particularly data on co-morbidities, side-effects, alcohol consumption and knowledge of TB through patient education verification. Though records with some missing data were included in the descriptive analysis, they were excluded from further analysis in order to prevent their effects on the study findings. Acknowledging these limitations allows for proper interpretation of the findings and avoidance of assumptions.

Summary

Overall compliance and treatment success among adult PTB patients treated via DOTS in Windhoek District between 1st January 2013 and 31st December 2013 were higher than expected but slightly lower compared to the WHO recommended treatment compliance and success. Initial phase of treatment recorded higher treatment compliance, while compliance was slightly low in the continuation phase of treatment. Non-compliance recorded in this study was much lower than all the other studies. Continuation phase was identified to be the most problematic phase when it comes to compliance and these findings are in agreement with the literature. Age and type of area are associated with compliance and in the continuation phase of treatment while type of area is associated with overall compliance and this is also new contribution of knowledge. The findings from this study suggest that treatment compliance seems to have an effect on treatment outcomes. Treatment compliance is associated with treatment success in both phases of treatment and overall. The next Chapter (Chapter six) presents conclusions on the study and recommendations for practice and further research based on the study findings.

CHAPTER 6: CONCLUSIONS AND RECOMMENDATIONS

Introduction

This Chapter provides the conclusions from the study and recommendations for practice and further research about the effects of treatment compliance on treatment outcomes in Windhoek District.

6.1 Conclusions

The study conclusions are based on the study's key findings and discussions. In determining the effects of treatment compliance on treatment outcomes for adult PTB patients treated via DOTS in Windhoek District in Namibia between the 1st January 2013 and 31st December 2013, the study investigated TB treatment compliance and measured the relationships between treatment compliance and patients' characteristics. It also assessed the relationship between compliance and treatment outcomes. The study revealed some interesting findings about TB treatment compliance in Windhoek District. Overall treatment compliance of 89% for new PTB patients treated via DOTS in Windhoek District was reported in this study. This compliance was higher than expected but slightly lower than the WHO recommended 90% compliance. Compliance was also lower than desired at 88.1% in the continuation phase of treatment. However as supported by the literature, very high compliance (97.2%) was reported in the initial phase of treatment (Adane et al., 2013; Awofeso, 2008; Takarinda et al., 2012) It can be concluded that slightly lower than desired overall compliance in Windhoek District is likely due to the reduced compliance in the continuation phase of treatment. The continuation phase of treatment continues to appear to be a relatively problematic phase when it comes to TB treatment compliance; although relative to other contexts compliance is still good. Factors related to the increase in compliance in the initial phase of treatment and the reduced compliance in the continuation phase were not explored in this study. If not addressed the reduced compliance during continuation could lead to poor treatment outcomes such as prolonged infections, relapse, high TB mortality and drug resistant TB. These adverse outcomes may further increase the TB programme's costs.

Treatment success (86.1%) among adult PTB patients treated via DOTS in Windhoek District was also higher than expected but slightly lower compared to the literature and WHO treatment success (90%). It can be concluded that Windhoek District is still below the WHO treatment success target.

Type of area showed an overall significant association with compliance, as well as in the continuation phase of treatment while age showed a significant association with compliance in the continuation phase of treatment. Patients from rural areas were less likely to comply with their treatments compared to patients from other areas, while older adult patients aged 45+ years were more likely to comply with their TB treatment compared to young adults aged 15 – 34 years. It can be concluded that older age 45+ years increase the chances of TB treatment compliance in the continuation phase of treatment while rural areas reduce the chance of TB treatment compliance in the overall and in the continuation phase of treatment.

Non-compliance is associated with poor treatment outcomes while compliance is associated with treatment success. The study concludes that the effect of treatment compliance on treatment outcomes is that non-compliance causes poor treatment outcomes while compliance leads to better treatment outcomes.

6.2 Recommendations

The following recommendations emanate from the study's conclusions. The recommendations should be used to improve compliance and its effects on treatment outcomes in the District and for further research.

6.2.1 Recommendations to improve compliance in Windhoek District

In order to increase compliance, decrease non-compliance and improve treatment outcomes in Windhoek District, the following recommendations are made for the consideration of the District Management Team and Programme Managers.

- Create awareness about the importance of TB treatment compliance at the community level and during all phases of treatment to enhance treatment compliance and improve treatment success.
- District Management Team and the District TB Co-ordinators to consider additional or different mechanisms to support rural patients, young adults and all the patients in the continuation phase of treatment to increase their treatment compliance.
- Create awareness about treatment compliance among TB patients and treatment supporters at the beginning of the treatment and in particular at the end of the initial phase and during the continuation phase to address reduced compliance during this phase.
- Continuous support and monitoring and to patients in the continuation phase of treatment from relatives, CB-DOT supporters, health facility-based treatment supporters and the District Management Team should be enforced to ensure compliance in this phase.
- Continuous support and monitoring of younger adults (15 – 34 years) in the continuation phase of treatment from relatives, DOTS supporters and the District Management Team should be enforced to ensure compliance among these age category in the continuation phase.
- Strengthen the district's CB-DOT by increasing CB-DOTS points and enhancing CB-DOTS supporters' capacity in terms of the number and skills. This is to ensure that patients from rural areas who might be challenged in accessing health care facilities treated under are well monitored and encouraged to comply with their treatment through CB-DOT.
- Strengthen record keeping and ensure that all the important information about the patients are recorded completely and accurately in order to ensure proper monitoring of the patients and to ensure availability of data for future research.

6.2.2 Recommendations for further research

- Since this research was unable to provide a good measure about the factors influencing compliance, a prospective study involving interviewing TB patients as they start their TB treatment and following them up to the end of their treatment is required to ensure that all the factors influencing compliance are explored.

- Further studies should consider exploring the impacts of socio-economic factors on treatment compliance.
- Study exploring kinds of psycho-social and logistic support that patients might find helpful from the health services when entering the continuation phase to ensure compliance is recommended.
- Effects of demographic, socio-economic and clinical factors on treatment outcomes also need to be explored.
- Reasons why older adults are more compliant and younger adults are less compliant with TB treatment in the continuation phase need further exploration.
- Reasons why patients from rural areas are less compliant with their TB treatment also need to be investigated further.

Summary

Overall treatment compliance (89%) for new PTB patients treated via DOTS in Windhoek District were reported in this study. This compliance was higher than expected but slightly lower than the WHO recommended 90% compliance. Very high compliance (97.2%) were reported in the initial phase of treatment. Compliance was also lower than desired 88.1% in the continuation phase of treatment. It can be concluded that slightly lower than desired overall compliance in Windhoek District is likely due to the reduced compliance in the continuation phase of treatment. The continuation phase of treatment continues to appear to be a relatively problematic phase when it comes to TB treatment compliance; although relative to other contexts compliance is still good though it falls below the recommended compliance. If not addressed the reduced compliance during continuation could lead to poor treatment outcomes such as prolonged infections, relapse, high TB mortality and drug resistant TB. These adverse outcomes may further increase the TB programme's costs. Windhoek District's treatment success is below the WHO's treatment success targets. Being an older adult, male, from urban areas, diagnosed with PTB smear positive, treated under health facility-based DOT increases the chances of compliance. While being older adults aged 45 – 54 years and patients from urban areas are more likely to comply with their treatment due to a number of factors. Non-compliant patients are more likely to have poor treatment outcomes than compliant patients while compliant patients

are more likely to have a treatment success than non-compliant patients. The District Management Team and TB Programme Managers are encouraged to use this study's findings and recommendations in devising strategies required in increasing compliance, decreasing non-compliance and improving treatment success.

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APPENDICES

Appendix A: Data Extraction Tool

UNIVERSITY OF THE WESTERN CAPE
School of Public Health

Private Bag X17 ● **BELLVILLE** ● 7535 ● South Africa
Tel: 021- 959 2809, Fax: 021- 959 2872

A. DEMOGRAPHIC INFORMATION

1. Code number ☐
2. Age in years ☐
3. Sex
   - 3.1 Male ☐
   - 3.2 Female ☐
4. Employment status
   - 4.1 Employed ☐
   - 4.2 Unemployed ☐
   - 4.3 Not recorded ☐
5. Residence: _____
6. Type of area:
   - 6.1 Urban ☐
   - 6.2 Rural ☐

B. CLINICAL INFORMATION

7. Diagnostic Classification
   - 7.1 Pulmonary TB smear positive ☐
   - 7.2 Pulmonary TB smear negative ☐
   - 7.3 Pulmonary TB no smear ☐
8. Type of DOTS (Enter code)

8.1 Health Facility DOTS: ☐

8.2 Community Based DOTS: ☐

8.3 Other: Specify ☐ _____

DOTS codes: close relative (1); Guardian-relative, neighbor (2); Workplace (3); Health Facility (4); Community Health Worker (5); Other (6) specify

9. HIV Status

9.1 Positive ☐

9.2 Negative ☐

9.3 Unknown ☐

10. Anti-Tuberculosis Therapy

10.1 Date Started ☐

10.2 Date ended ☐

10.3 Initial Phase: Dosages Taken ☐ Dosages Missed ☐

10.4 Continuation Phase: Dosages Taken ☐ Dosages Missed ☐

11. Compliance in Percentages (%) Compliance (Enter compliance code)

11.1 Initial Phase ☐ ☐

11.2 Continuation Phase ☐ ☐

11.3 Overall compliance ☐ ☐

Compliance classifications: good compliance 80% and above (1); moderate compliance 40% - 79% (2); poor compliance 39% and below (3).

C. CO-MOBIDITIES AND SIDE-EFFECTS

12. Any documented co-morbidity? If yes, specify.

12.1 Pre-treatment: Yes ☐ No ☐ _____

12.2 2 months of treatment: Yes ☐ No ☐ _____

12.3 5 – 6 months of treatment: Yes ☐ No ☐ _____

13. Other Medicines taken? If yes, specify:

13.1 Pre-treatment: Yes ☐ No ☐ _____

13.2 2 months of treatment: Yes ☐ No ☐ _____

13.3 5 – 6 months of treatment: Yes ☐ No ☐ _____

14. Any documented alcohol consumption?

14.1 Pre-treatment: Yes ☐ No ☐

14.2 2 months of treatment: Yes ☐ No ☐

14.3 5 – 6 months of treatment: Yes ☐ No ☐

15. Any documented side effects? If yes, enter code and for other enter code and specify.

15.1 Pre-treatment: Yes ☐ No ☐ _____

15.2 2 months of treatment: Yes ☐ No ☐ _____

15.3 5 – 6 months of treatment: Yes ☐ No ☐ _____

Side effects codes: skin rash (1); Jaundice (2); Confusion (3); Visual impairment (4); Shock (5); Renal failure (6); Poor appetite (7); Nausea/Vomiting (8); Abdominal pain (9); Joints pain (10); Burning/numbness or tingling sensation in the hands or feet (11); Drowsiness (12); Other (13) specify.

D. KNOWLEDGE ON TB

16. Patient Education Verification

	Pre-treatment			**At 2 months of treatment**			**At 5-6 months of treatment**		
	Yes	No	Not recorded	Yes	No	Not recorded	Yes	No	Not recorded
16.1 Knowledge of what TB is?									
16.2 Knowledge on how TB is spread?									
16.3 Knowledge on how to avoid infecting others?									
16.4 Knowledge on how TB is treated?									
16.5 Knowledge of whether TB can be cured?									
16.6 Knowledge on TB treatment and treatment duration?									
16.7 Knowledge on the importance of taking									

TB medications every day?									
16.8 Knowledge on the difference between TB and HIV/AIDS?									
16.9 Knowledge on the importance of knowing one's HIV status if infected with TB?									
16.10 Knowledge on the importance of having a DOTS supporter?									
16.11 Knowledge of the common side-effects and how they are handled?									
16.12 Knowledge of the serious side-effects that should be reported to the hospital immediately?									
16.13 Knowledge on whether TB can relapse?									

E. TREATMENT OUTCOME

17. Treatment Outcome after 6 months of treatment

17.1 Cured ☐

17.2 Treatment Completed ☐

17.3 Treatment failure before 5 months of treatment ☐

17.4 Treatment failure after 5 months of treatment ☐

17.5 Defaulted ☐

17.6 Transfer out ☐

17.7 Died ☐

Appendix B: Permission from University of the Western Cape Senate Research Committee

UNIVERSITY of the
WESTERN CAPE

OFFICE OF THE DEAN
DEPARTMENT OF RESEARCH DEVELOPMENT

18 December 2014

To Whom It May Concern

I hereby certify that the Senate Research Committee of the University of the Western Cape approved the methodology and ethics of the following research project by:
Ms EN Nepolo (School of Public Health)

Research Project:	Effects of treatment compliance on treatment outcomes for Pulmonary Tuberculosis patients on directly observed treatment-short course in Windhoek District, Namibia.
Registration no:	14/10/37

Any amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.

The Committee must be informed of any serious adverse event and/or termination of the study.

Ms Patricia Josias
Research Ethics Committee Officer
University of the Western Cape

Private Bag X17, Bellville 7535, South Africa
T: +27 21 959 2988/2948 . F: +27 21 959 3170
E: pjosias@uwc.ac.za
www.uwc.ac.za

Appendix C: Permission request letter for the Permanent Secretary

UNIVERSITY OF THE WESTERN CAPE
School of Public Health

Private Bag X17 ● **BELLVILLE** ● 7535 ● South Africa
Tel: 021- 959 2809, Fax: 021- 959 2872

24 October 2014

The Permanent Secretary

Ministry of Health and Social Services

Private Bag 13198

Windhoek

Namibia

Dear Sir

Re: Request for permission to conduct a study on the "Effects of treatment compliance on treatment outcomes for Pulmonary Tuberculosis patients on Directly Observed Treatment-Short course in Windhoek District in Namibia".

I am Ester Ndahekelekwa Nepolo**,** a Masters of Public Health Student at the University of the Western Cape. I am asking for your permission to access patients' information in conducting the above mentioned study because you are the person in charge of the Ministry of Health in which the study will be conducted. The study will be undertaken as a partial fulfilment for the completion of the Masters of Public Health Degree.

The purpose of this study is to determine whether patients' compliance with TB treatment through DOTS has got an effect on TB treatment outcomes. The study will look at the overall treatment compliance and to assess factors influencing compliance as well as relationship between compliance and different treatment outcomes for PTB patients on DOTS in Windhoek District. The results of this study could be used to contribute to the existing body of knowledge and provide context specific information on TB management in the District, which is crucial for

TB management and development of targeted strategies in promoting TB treatment compliance through DOTS in order to improve treatment success, prevent default, treatment failure and TB mortality.

A quantitative retrospective study will be used in this study, making use of all patients' records (patient treatment cards) of all new adult PTB cases of both sexes who were treated on DOTS in Windhoek District from 01 January 2013 to 31 December 2013. I will use the permission to access the District TB register where I will look at the eligible patients' records for inclusion in the study. All eligible records will be included in the study.

The TB treatment cards from the eligible files will then be collected for data collection using the data extraction tool that will require the following information: demographic information, clinical information such as type of DOT received and diagnostic classification, co-morbidities and side effects, patient education verification as well as and treatment outcome. The data collected will be analysed using Epi info 7 for data entry and analysis; to determine compliance with TB treatment, frequencies and proportions of risk factors as well as prevalence of different treatment outcomes.

The data collection will take place at the District TB outpatient, where all the District records are kept. The data collection will take 3 – 4 weeks. Therefore I also request your permission to use the TB outpatient department space during data collection. Using the TB outpatient space will enable me to maintain the confidentiality of the information contained in the records and also to safe keep the records. To help protect patient's confidentiality, the collected information will be kept at the safer place (locked cabinet), and the data will finally be stored in a password protected computer files. To maintain anonymity, no names will be included on the data abstraction tools, codes will be used instead and only the researcher will know those codes and no one else can link the information on the coded forms to any patient's information. If we write a report or article about this research project, the identity of the patients will not be revealed.

Since there will not be any direct interaction between the researcher and the patients' whose files will be reviewed in the study, there are no known risks associated with this research project. The study findings will benefit the TB programme in devising targeted actions based on the study

findings. The study findings will be presented to the District Management Team as well as to the District TB programme coordinators. The Research Unit of the Ministry and the District will be provided with the copy of results that will be kept for future references. This research has been approved by the University of the Western Cape's Senate Research Committee and Ethics Committee.

If you have any questions about the research study itself, please contact me ***Ester Ndahekelekwa Nepolo*** at: P.O. Box 7647, Katutura, Namibia; Cell phone number +264 811244083, email address: eshaama80@gmail.com or my Supervisor: Dr. Lucia Knight, University of the Western Cape, Private Bag X17, Bellville 7535, Telephone: +27 21 959 2243, Email address: lnight@uwc.ac.za

Thank you for considering my request. I have attached my research proposal and the data abstraction tool as well as the Ethical Clearance from University of the Western Cape's Senate Research Committee and Ethics Committee.

Kind regards,

Ester Ndahekelekwa Nepolo

Appendix D: Permission request letter for the Khomas Health Regional Director

UNIVERSITY OF THE WESTERN CAPE
School of Public Health

Private Bag X17 ● **BELLVILLE** ● 7535 ● South Africa
Tel: 021- 959 2809, Fax: 021- 959 2872

24 October 2014

The Regional Director

Khomas Regional Health Directorate

Ministry of Health and Social Services

Private Bag 13198

Windhoek

Namibia

Dear Madam

Re: Request for permission to access patients' information in conducting the study on "Effects of treatment compliance on treatment outcomes for Pulmonary Tuberculosis patients on Directly Observed Treatment-Short course in Windhoek District in Namibia".

I am Ester Ndahekelekwa Nepolo**,** a Masters of Public Health Student at the University of the Western Cape. I am asking for your permission to access patients' information in conducting the above mentioned study because you are the person in charge of Khomas Health Regional Directorate in which the study will be conducted. The study will be undertaken as a partial fulfilment for the completion of the Masters of Public Health Degree.

The purpose of this study is to determine whether patients' compliance with TB treatment through DOTS has got an effect on TB treatment outcomes. The study will look at the overall treatment compliance and to assess factors influencing compliance as well as relationship between compliance and different treatment outcomes for PTB patients on DOTS in Windhoek

District. The results of this study could be used to contribute to the existing body of knowledge and provide context specific information on TB management in the District, which is crucial for TB management and development of targeted strategies in promoting TB treatment compliance through DOTS in order to improve treatment success, prevent default, treatment failure and TB mortality.

A quantitative retrospective study will be used in this study, making use of all patients' records (patient treatment cards) of all new adult PTB cases of both sexes who were treated on DOTS in Windhoek District from 01 January 2013 to 31 December 2013. I will use the permission to access the District TB register where I will look at the eligible patients' records for inclusion in the study. All eligible records will be included in the study.

The TB treatment cards from the eligible files will then be collected for data collection using the data extraction tool that will require the following information: demographic information, baseline information such as type of DOT received and diagnostic classification co-morbidities and side effects, patient education verification as well as and treatment outcome. The data collected will be analysed using Epi info 7 for data entry and analysis; to determine compliance with TB treatment, frequencies and proportions of risk factors as well as the prevalence of different treatment outcomes.

The data collection will take place at the District TB outpatient, where all the District records are kept. The data collection will take 3 – 4 weeks. Therefore I also request your permission to use the TB outpatient department space during data collection. Using the TB outpatient space will enable me to maintain the confidentiality of the information contained in the records and also to safe keep the records. To help protect patient's confidentiality, the collected information will be kept at the safer place (locked cabinet), and the data will finally be stored in a password protected computer files. To maintain anonymity, no names will be included on the data abstraction tools, codes will be used instead and only the researcher will know those codes and no one else can link the information on the coded forms to any patient's information. If we write a report or article about this research project, the identity of the patients will not be revealed.

Since there will not be any direct interaction between the researcher and the patients' whose files will be reviewed in the study, there are no known risks associated with this research project. The study findings will benefit the TB programme in devising targeted actions based on the study findings. The study findings will be presented to the District Management Team as well as to the District TB programme coordinators. The District will further be provided with the copy of results that will be kept for future references. The study has been approved by both the University of Western Cape Ethics committees and the Ministry of Health and Social Services Research Management Committee.

If you have any questions about the research study itself, please contact me ***Ester Ndahekelekwa Nepolo*** at: P.O. Box 7647, Katutura, Namibia; Cell phone number +264 811244083, email address: eshaama80@gmail.com or my Supervisor: Dr. Lucia Knight, University of the Western Cape, Private Bag X17, Bellville 7535, Telephone: +27 21 959 2243, Email address: lnight@uwc.ac.za

Thank you for considering my request. I have attached the approval letter from the Ministry of Health and Social Services through the Permanent Secretary's office and the data abstraction tool.

Kind regards,

Ester Ndahekelekwa Nepolo

Appendix E: Permission request letter for the Intermediate Hospital Katutura's Medical Superintendent

UNIVERSITY OF THE WESTERN CAPE
School of Public Health

Private Bag X17 ● **BELLVILLE** ● 7535 ● South Africa
Tel: 021- 959 2809, Fax: 021- 959 2872

24 October 2014

The Medical Superintendent

Intermediate Hospital Katutura

Ministry of Health and Social Services

Private Bag 13198

Windhoek

Namibia

Dear Sir/Madam

Re: Request for permission to access patients' information in conducting the study on "Effects of treatment compliance on treatment outcomes for Pulmonary Tuberculosis patients on Directly Observed Treatment-Short course in Windhoek District in Namibia".

I am Ester Ndahekelekwa Nepolo**,** a Masters of Public Health Student at the University of the Western Cape. I am asking for your permission to access patients' information in conducting the above mentioned study because you are the person in charge of Windhoek Health District in which the study will be conducted. The study will be undertaken as a partial fulfilment for the completion of the Masters of Public Health Degree.

The purpose of this study is to determine whether patients' compliance with TB treatment through DOTS has got an effect on TB treatment outcomes. The study will look at the overall treatment compliance and to assess factors influencing compliance as well as relationship

between compliance and different treatment outcomes for PTB patients on DOTS in Windhoek District. The results of this study could be used to contribute to the existing body of knowledge and provide context specific information on TB management in the District, which is crucial for TB management and development of targeted strategies in promoting TB treatment compliance through DOTS in order to improve treatment success, prevent default, treatment failure and TB mortality.

A quantitative retrospective study will be used in this study, making use of all patients' records (patient treatment cards) of all new adult PTB cases of both sexes who were treated on DOTS in Windhoek District from 01 January 2013 to 31 December 2013. I will use the permission to access the District TB register where I will look at the eligible patients' records for inclusion in the study. All eligible records will be included in the study.

The TB treatment cards from the eligible files will then be collected for data collection using the data extraction tool that will require the following information: demographic information, baseline information such as type of DOT received and diagnostic classification, diagnostic evaluation and monitoring of progress, co-morbidities and side effects, patient education verification as well as and treatment outcome. The data collected will be analysed using Epi info 7 for data entry and analysis; to determine compliance with TB treatment, frequencies and proportions of risk factors as well as prevalence of different treatment outcomes.

The data collection will take place at the District TB outpatient, where all the District records are kept. The data collection will take 3 – 4 weeks. Therefore I also request your permission to use the TB outpatient department space during data collection. Using the TB outpatient space will enable me to maintain the confidentiality of the information contained in the records and also to safe keep the records. To help protect patient's confidentiality, the collected information will be kept at the safer place (locked cabinet), and the data will finally be stored in a password protected computer files. To maintain anonymity, no names will be included on the data abstraction tools, codes will be used instead and only the researcher will know those codes and no one else can link the information on the coded forms to any patient's information. If we write a report or article about this research project, the identity of the patients will not be revealed.

Since there will not be any direct interaction between the researcher and the patients' whose files will be reviewed in the study, there are no known risks associated with this research project. The study findings will benefit the TB programme in devising targeted actions based on the study findings. The study findings will be presented to the District Management Team as well as to the District TB programme coordinators. The District will further be provided with the copy of results that will be kept for future references. The study has been approved by the University of Western Cape Ethics committees, Ministry of Health and Social Services Research Management Committee through the Permanent Secretary's office and by the Khomas Regional Health Director.

If you have any questions about the research study itself, please contact me ***Ester Ndahekelekwa Nepolo*** at: P.O. Box 7647, Katutura, Namibia; Cell phone number +264 811244083, email address: eshaama80@gmail.com or my Supervisor: Dr. Lucia Knight, University of the Western Cape, Private Bag X17, Bellville 7535, Telephone: +27 21 959 2243, Email address: lnight@uwc.ac.za

Thank you for considering my request. I have attached the approval letter from the Khomas Regional Health Director and the data abstraction tool.

Kind regards,

Ester Ndahekelekwa Nepolo

Appendix F: Permission from the Permanent Secretary

9 – 0/0001

REPUBLIC OF NAMIBIA

Ministry of Health and Social Services

Private Bag 13198
Windhoek
Namibia

Ministerial Building
Harvey Street
Windhoek

Tel: 061 – 203 2562
Fax: 061 – 222558
E-mail: hnangombe@gmail.com

OFFICE OF THE PERMANENT SECRETARY

Ref: 17/3/3
Enquiries: Ms. H. Nangombe

Date: 18 November 2014

Ms. Ester Ndahekelekwa Nepolo
P.O. Box 7647
Katutura
Windhoek
Namibia

Dear Ms. Nepolo

Re: Effects of treatment compliance on treatment outcomes for Pulmonary Tuberculosis patients on Directly Observed Treatment-Short course in Windhoek District, Namibia.

1. Reference is made to your application to conduct the above-mentioned study.

2. The proposal has been evaluated and found to have merit.

3. **Kindly be informed that permission to conduct the study has been granted under the following conditions:**

3.1 The data to be collected must only be used for completion of Masters of Public Health Degree;
3.2 No other data should be collected other than the data stated in the proposal;
3.3 A quarterly report to be submitted to the Ministry's Research Unit;
3.4 Preliminary findings to be submitted upon completion of the study;
3.5 Final report to be submitted upon completion of the study;
3.6 Separate permission should be sought from the Ministry for the publication of the findings.

Yours sincerely,

Andrew Ndishishi (Mr)
Permanent Secretary

PERMANENT SECRETARY 19 NOV 2014 Republic of Namibia MINISTRY OF HEALTH AND SOCIAL SERVICES

"Health for All"

Appendix G: Permission from the Medical Superintended of Intermediate Hospital Katutura

Republic of Namibia

Ministry of Health and Social Services

Private Bag 13215 **WINDHOEK** Namibia	Intermediate Hospital Katutura Independence Avenue **WINDHOEK**	Telephone (061) 203 4004 Telefax (061) 222706

Enquiries: Dr. N. T. Amagulu — Date: 02 December 2014

THE OFFICE OF THE MEDICAL SUPERINTENDENT

Ms. Ester Ndahekelekwa Nepolo
P. O. Box 7647
Katutura
Windhoek
Namibia

RE: **PERMISSION FOR RESEARCH ON EFFECTS OF TREATMENT COMPLIANCE ON TREATMENT OUTCOME FOR PULMONARY TUBERCULOSIS PATIENTS ON DIRECTLY OBSERVED TREATMENT-SHORT COURSE IN WINDHOEK DISTRICT AT KATUTURA INERMIDIATE HOSPITAL, TB UNIT**

This office hereby grants you permission to do research on effects treatment and outcomes for Pulmonary Tuberculosis patients at Intermediate Hospital Katutura.

Thank you.

Yours in Health,

DR. N. T. AMAGULU
MEDICAL SUPERINTENDENT

MINISTRY OF HEALTH
AND SOCIAL SERVICES
P/BAG 13215
WINDHOEK NAMIBIA
02 -12- 2014
INTERMEDIATE HOSPITAL KATUTURA