UNIVERSITY OF THE WESTERN CAPE

Faculty of Community and Health Sciences

DETERMINANTS OF ADHERENCE TO TUBERCULOSIS THERAPY AMONG PATIENTS RECEIVING DIRECTLY OBSERVED TREATMENT FROM A DISTRICT HOSPITAL IN PRETORIA, SOUTH AFRICA

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A mini-thesis submitted in partial fulfillment of the requirement for the degree of masters in Public Health, the Faculty of Community and Health Sciences, School of Public Health, University of the Western Cape.

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KEY WORDS

DOTS

TB

TB patients

TB treatment

Treatment adherence

Adherence behavior

Poor adherence

Facilitating factors

Challenging factors

Pretoria West

ABSTRACT

Background: The incidence of tuberculosis in South Africa last measured at 834 in 2015 as reported by the World Bank. Out of these cases, only 54% cured and 13% of patients stop taking treatment. In Pretoria, Gauteng, comprehensive TB services are available in 87% of clinics and all these clinics offer the Directly Observed Treatment Short-course (DOTS) programme and help to diagnose TB and trace contacts. However, the average Pretoria district DOTS coverage has decreased from 88.8% to 84.7% in the last few years. The health district's cure rate as at 2012 is 61%, and its average rate of successful treatment of all new smear positive cases is 66% since 2005.

Certain factors that determine patients' adherence towards TB treatment have been identified to include demographic, psychosocial and health system related factors. However, the WHO identified factors responsible for or predisposing patients to discontinue the DOTS programme have not been investigated in the study setting.

Aim: The aim of this study was to assess the determinants of adherence to DOTS therapy amongst TB patients who commenced TB treatment at the TB clinic of a district hospital during April – June 2014.

Methodology: A quantitative study was conducted using a descriptive cross-sectional design. An inclusive sample was drawn from adults in the DOTS programme receiving first line treatment during the 6-month period prior to commencement of the research. The calculated sample size was 234 individuals. The data collection tools included a questionnaire, 2-day recall and 30-day recall instruments and pill counts. Data were analysed using EPI info version 7 which included descriptive statistics to measure level of adherence. Associations between identified factors and adherence to TB treatment were also determined.

Results: The final sample size was 80 participants of which 76% were male. The mean composite adherence rate was found to be 94% while the proportion of the patients who achieved adherence of 95% and above was 75%. Identified barriers to adherence include forgetfulness, lack of transport fare on clinic appointment days, patients not feeling well and so were not strong enough to attend clinic appointments. On the other hand, the role of treatment supporters and counseling were found to have a positive impact on adherence to DOT in this setting. The use of reminders such as cell phones and alarm-radios were also identified as facilitators to adherence. Patients' knowledge of consequences for not taking

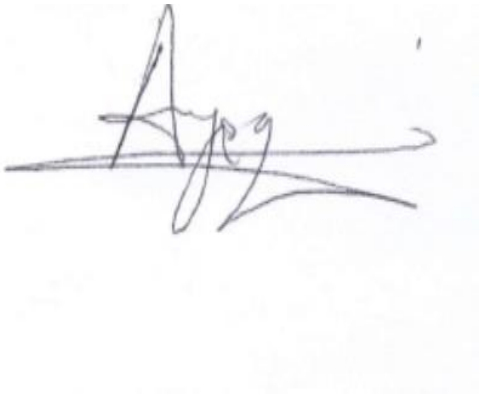
medications as prescribed, which is closely linked with counseling, was found to be significantly associated with adherence in this study.

Education status of participants was found to be significantly associated with adherence to DOTS ($p = 0.01$), when considering the pharmacy refill pill count as the adherence measure. Significant association was found between DOTS treatment regimens and 30-day recall adherence measures ($p = 0.002$). Significant association was also found for medication side effects and the adherence measures of 2-day recall, 30-day recall and pill count with $p = 0.04$; $p = 0.03$; $p = 0.05$ respectively There were significant associations between age and adherence with two of the adherence measures (30-day recall and pill count) at $p = 0.002$ and $p = 0.003$ level of significance respectively. Significant association was observed between duration of DOTS treatment when dichotomised using the mean treatment period (17 weeks) as the cut-off point and any of the adherence measures.

Conclusion: The factors identified in this study can be classified into patient related factors, economic factors, social factors and health care workers and health system related factors. Furthermore, the factors at these different levels impact on one another and their improvements need to be made at all these levels to address the challenges facing TB patients to achieve optimal treatment adherence. This study is the first study of its kind in the study location and the findings have provided useful baseline data on the adherence rates and some insights into the major factors that affect adherence among patients on DOTS at a Pretoria West District Hospital. However further qualitative and quantitative studies are required to explore the factors influencing adherence further.

DECLARATION

I, Olayinka Ayobami Aiyegoro, hereby declare that this study is a true reflection of my own research, and that this work, or part thereof has not been submitted for a degree or examination at any other institution of higher education.



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Unto the King Eternal, Immortal, Invisible, the only Wise one, be Glory and Honour forever, Amen.

DEDICATION:

This study is dedicated to:

God almighty (YAWEH);

My Wife- Adeola;

Moreover, to my Children- Precious, Bethel and Christina.

To God alone be all the Glory, Amen.

ABREVIATIONS

AFB	Acid-Fast Bacilli
CNR	Case notification rate
DOH	Department of Health
DOT	Direct Observed Therapy
DOTS	Direct Observed Therapy Short Course
MDR-TB	Multiple Drug Resistance Tuberculosis
PHC	Primary Health Care
PTB	Pulmonary Tuberculosis
SMS	Short Messaging Service
TB	Tuberculosis
UWC	University of the Western Cape.
WHO	World Health organization
XDR-TB	Extensively Drug Resistance Tuberculosis

DEFITIONS OF KEY TERMS

Non-Adherent

McLean (2003) describes a non-adherent patient as a patient who interrupts treatment for two consecutive months or more.

In this study, a non-adherent patient is a patient who misses two consecutive visits for medical appointment at the TB clinic and has not obtained any service from any other facility that offers TB services assuming that the patient does not take any TB medication during that period or later.

Notification rate

This is defined as the proportion of reported infectious cases such as TB

Treatment success rate

This is defined as is the proportion of TB patients who have been successfully cured and those who completed treatment.

Treatment outcomes

Treatment outcome is described by WHO (2007) as the end product of TB treatment. It includes the following: patients who are cured (smear positive patient converted to smear negative in the last month of treatment); completed treatment (a patient who has completed treatment but who does not meet the criteria to be classified as cured or failure); died (a patient who die for any reason during the course of treatment); failed treatment (a patient who is sputum smear positive at five months or later at the end of treatment); defaulter; transferred out (patient who is transferred to another facility and whose treatment outcome is unknown) and successfully treated (these are patients who have been cured and those who completed treatment).

Case notification

Beaglehole & Bonita (2004: 38), define case notification is as “the reporting system of infectious diseases that require prompt action for control.”

Treatment Supporter

A treatment supporter is a trained person, not necessarily a health worker who is chosen and trusted by the TB patient to make sure that the patient takes the treatment regularly until completion of the treatment duration (WHO, 2010). In this study, a DOT supporter is any person chosen by the health worker in consultation with the TB patient.

Infection rate

Infection rate is defined as "the proportion of the population from which a specific pathogen is isolated" (Vaughan & Morrow, 1998:40).

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CHAPTER ONE

INTRODUCTION

1.1. BACKGROUND TO THE STUDY

Mycobacterium tuberculosis is the causative agent of Tuberculosis (TB) an infectious disease. TB mycobacterium has predilection for the lungs, where it initiates pulmonary TB, although the mycobacterium can also infect other body parts and organs, where it may cause extra-pulmonary TB. TB disease is air-borne and the infection may spread faster when someone is in close proximity with a diseased individual especially in an overcrowded environment (Kumar et al, 2007).

According to the World Health Organisation (WHO) (2013), TB remains one of the world's deadliest communicable diseases even though it is avoidable and curable. TB mortality was reduced by 45% between 1990 and 2013 and the TB occurrence reduced by 41% during the same period (WHO, 2014). However, huge gaps exist in services to manage and treat the many TB patients, especially in developing countries, which is a major setback for the control of TB spread. In 2013, it was reported by WHO that an estimated 9.0 million people developed TB and 1.5 million died from the disease, 360 000 of whom were HIV-positive globally.

The five top ranking countries for TB prevalence are India, China, South Africa, Indonesia and Pakistan in the order of decreasing magnitude respectively (NDOH, 2013). Approximately 1% of the South African population develops TB disease every year (NDOH, 2011). The provinces affected the most are KwaZulu-Natal, the Western Cape, Eastern Cape and Gauteng, which combined have 80% of TB cases in South Africa. Of these, only 54% are cured and 13% of patients stop taking treatment (NDOH, 2011). TB is also the most common infection for the estimated 5.5 million South Africans living with HIV/AIDS (in a national population of approximately 48 million). In addition, the co-infection rate of HIV in South Africa is estimated at 73% of all TB cases, a rate the WHO classifies as a serious epidemic

(WHO, 2009). South Africa ranks the third highest in the world in terms of TB burden, with an incidence that has increased by 400% in the past 15 years (NDOH, 2011).

The first TB treatment medication developed in the 1940s and subsequently, the most effective first-line anti-TB drug, rifampicin, became available in the 1960s (WHO, 2014). Since then, the WHO has endorsed treatment for cases of drug-susceptible TB as a six-month program of four first-line drugs: isoniazid, rifampicin, ethambutol and pyrazinamide. The treatment for multidrug-resistant TB (MDR-TB) requires more expensive and more toxic drugs as a 20-month treatment regimen with a much lower success rate (WHO, 2014).

1.2. ANTITUBERCULOSIS THERAPY IN SOUTH AFRICA

The WHO guidelines for TB treatment recommend Directly Observed Treatment, Short-Course (DOTS) strategy to monitor patient medication adherence (WHO, 2012a; Frieden & Sbarbaro, 2007). This strategy includes treating TB using standardized rifampicin-based regimens of six-month duration for new TB cases and eight months for retreatment cases. The DOTS strategy focuses on five main points of action, these include; government commitment to control TB, diagnosis based on sputum-smear microscopy tests done on patients who actively report TB symptoms, direct observation short-course chemotherapy treatments, a definite supply of drugs, and standardized reporting and recording of cases and treatment outcomes. Treatment with properly implemented DOTS has a success rate exceeding 95% (WHO, 2012b).

After the end of apartheid rule in 1994, South Africa established the National Tuberculosis Programme (NTP). South Africa also developed an integrated National Strategic Plan (NSP) for HIV, STIs and TB (2012 - 2016) (NDOH, 2011). In South Africa, once diagnosed with TB, patients are provided with anti-TB medication and care free of charge under the DOTS programme, in line with the NSP HIV, STIs and TB control programme guidelines (NDOH, 2011). The targets set in the NSP for TB are to halve new TB cases and mortality by 2016 and to have no new TB infections, deaths or stigma by 2032. In order to respond to the dual epidemics of HIV and TB rationally, South Africa has become the world's largest provider of

preventative isoniazid TB therapy to HIV patients. An estimated 370,000 people living with HIV now receive the anti-TB drug to prevent the development of active TB (NDOH, 2011).

The central pillars of TB control in the NTP include diagnosing, treating and preventing TB in order to avoid TB deaths and reduce transmission. The South African NTP has substantially strengthened the TB control programme since inception in 1994, and the efforts of the NTP have contributed to a slow decline in TB case notification rates since 2009 (Churchyard et al, 2014). The NTP has developed an electronic recording and reporting system for drug-susceptible TB (ETR.net) and drug-resistant TB (EDR. net) (Mayosi et al, 2012). In addition, novel and sustainable solutions, such as the use of mobile phones and tablets to collect data in the field and in facilities, are used to strengthen the quality and use of data as well as patient management.

South Africa has made notable progress in improving access to TB control facilities, but the burden of TB remains enormous. The cure rates remain well below the 85% rate recommended by the WHO (WHO, 2012a). The NTP is faced with the challenge of integrating TB services into weak primary healthcare systems and the emergence of the HIV epidemic, which led to TB case rates multiplying between 1994 and 2012 (Abdool Karim et al, 2009).

The growing burden of MDR-TB and the emergence of extensively drug-resistant (XDR) TB in 2006 added a further burden to overstretched health services (Abdool Karim et al, 2009). However, this situation (i.e. the emergence of MDR-TB and extensively drug-resistant (XDR) TB can be reversed through ensuring high, sustained coverage of effective interventions for TB and HIV including in children and special populations (miners and prisoners). This will substantially reduce the burden of TB and result in the NSP targets being met (Abdool Karim et al, 2009). Finally, new anti-TB drugs, diagnostics and vaccines are required to accelerate progress towards TB elimination (WHO, 2012a).

1.3. ADHERENCE TO ANTITUBERCULOSIS THERAPY

Adherence to treatment is defined by WHO as: "the extent to which a person's behaviour-taking medication, following a diet, and or executing lifestyle changes, corresponds with agreed recommendations from a health care provider" (WHO, 2003:123). Non-adherence to medication described as the patient's refusal to adapt to administration of medications as prescribed (CDC, 2013a). Non-adherence to TB treatment medications, identified as the leading factor and barrier to TB eradication worldwide (Chaulk, et al, 1995; Daniel, 2006; Tumbo and Ogunbanjo, 2011; Ntshanga, Rustomjee and Mabaso, 2009; WHO, 2014; Munro et al, 2007). Non-adherence to TB treatment is a major challenge to global TB control because it poses a significant threat to both the individual patient and public health and is associated with higher transmission rates, morbidity, and costs of TB control programmes (Shargie & Lindtjorn, 2007). For the individual, drug resistance and emergence of resistant strains would result in an uncertain prognosis and the requirement of more toxic and complex drugs (Chesney, 2000). From a public health perspective, the emergence and transmission of drug resistant mycobacteria would not only impact negatively on the benefits intended by the DOTS programmes but would also result in increasingly more people requiring more expensive drugs, thus increasing the costs of the TB treatment programme (Chesney, 2000). This public health issue has been a major concern for the impact and feasibility of increasing accessibility of TB treatments to more patients in resource limited sub- Saharan Africa (Harries et al, 2001; Liechty & Bangsberg, 2003).

A variety of factors may impact on patient medication adherence, and thus efforts to improve medication adherence in general are more effective when they address multiple dimensions of adherence behaviours than single targeted interventions (Roter, et al., 1998; Charles, 2005). Adherence to treatment gives the opportunity to assess factors related to medication intake such as characteristics of the regimen, attitudes of the providers; socio-economic, cultural and environmental factors (WHO, 2003; Sagbakken, Frich & Bjune, 2008).

Although DOTS has been favoured to influence patient adherence to TB treatment and significantly enhance TB treatment outcomes (Daniel, 2006; Tumbo and Ogunbanjo, 2011; Ntshanga, Rustomjee, Mabaso, 2009), DOTS coverage and administration have been cited as challenges especially in developing nations as there are reports of insufficient or no TB

diagnostics to increase case detection, non-participation or non-inclusion of private practitioners in DOTS administration, the ever widening funding gap in DOTS-based programmes. Also, risk factors for continued TB transmission are not well addressed in most developing countries. For example, socio-economic health disparities are still very synonymous to health systems on Africa continent; this to a very large extent adds to the ease of TB transmission (Chaulk, et al, 1995; Daniel, 2006; Tumbo and Ogunbanjo, 2011; Ntshanga, Rustomjee and Mabaso, 2009).

Poor patient adherence to the treatment regimen is a major cause of treatment failure and of the emergence of drug-resistant TB. Previous research reported distance to treatment centres, gender, patient-caregiver relationship and communication, alcoholism and homelessness as the major determinants of adherence to anti-TB treatment (Tanguis et al, 2000; Naing et al, 2001; O'Boyle et al, 2002). Patient adherence to the standard anti-TB therapy in developing countries has been estimated to be as low as 40% (Al-Hajjaj & Al-Khatim, 2000). It is therefore important to find better ways to improving patient adherence to TB treatment. The present study was undertaken, to determine the extent of adherence and to evaluate the factors contributing to adherence in pulmonary TB patients receiving DOTS therapy at a Pretoria West hospital.

1.4. DESCRIPTION OF RESEARCH SETTING

The study location is the Tshwane Metropolitan District, Western Pretoria, Gauteng. The land mass area is approximately 6.17 km² with a population of 11535 (1869.99 per km²) and a total of 4084 (662.08 per km²) households (Statistics SA, 2011). This is a low socio-economic area and 10% of the total population of Pretoria live in this District (Pretoria West Palliative Care Forum, undated). The unemployment rate is currently estimated at 39.72%. Nine to twenty percent of the households have no income at all. There are 77 squatter camps in the district and poverty has increased by above 150% from 1994 to date (Pretoria West Palliative Care Forum, undated). Transport in the area is inadequate forcing patients to walk to health care facilities (Pretoria West Palliative Care Forum, undated). There are two district hospitals and one academic hospital in the district and, all three health facilities administer TB DOTS treatment.

This study was conducted among smear-positive TB patients diagnosed at the TB clinic of one of the district hospitals in Tshwane Metropolitan District. The hospital serves as a referral centre for the population of Pretoria West and adjacent informal settlements. The TB clinic registers and treats all diagnosed TB patients under the DOTS programme. The registers are compiled and reported monthly to the regional TB programme. The TB clinic has a record of about 1000 adult patients receiving DOT at the clinic, with an average monthly uptake of close to 100 patients. Approximately 98% of these DOT patients were on first line regimens. Patients on DOT receive treatment free of charge at the hospital. Patients for follow up appointments are seen at the clinic daily and the names of patients due for follow up on a particular day obtained from the computer at the clinic. The nurse checks the vital parameters like temperature, blood pressure and weight and then directs the patients to the doctor who prescribes the drugs and determines the next follow-up appointment date, which is usually after one month. Thereafter the patients go to the pharmacy where their remaining pills are counted and new ones dispensed. The total number of pills that the patient takes home is either recorded in the patients' health cards or on the pill container labels. Since the patients take their health cards home, the records at the hospital only reflect the number of pills that are dispensed to the patient and not the total number that the patient takes home.

The DOT provider (nurse) co-ordinates an agreed process of DOT with the patients in this clinic. Occasionally, the role of the DOT provider can be extended to include other healthcare professionals e.g. pharmacists. When the role of DOT provider is extended to non-healthcare professionals, training and information are provided to such individuals.

The clinic and its staff are committed to implementing and promoting measures to ensure the effective and safe management of patients referred for DOT. It is the policy of the clinic that healthcare professionals who have undertaken required education and training are facilitated to implement and promote the safe and effective management of persons referred for DOT in Primary Health Care.

In this clinic, all TB patients are the responsibility of the treating physician until their treatment has been successfully completed. The referring physician explains to the patient at the outset the rationale and the need for DOT in their specific case, confirms the patient's willingness to comply with DOT and requests DOT by completing the referral form including prescription(s). A copy of the DOT referral form is forwarded to the Tshwane District Health services support. The referring physician also advises when mask-wearing is necessary, inform the DOT provider when there is a change of medication, meet with patients who miss DOT doses to discuss problems with adherence, call and chair case-conferences as needed for non-compliant patients, facilitate hospital admission for patients who are unwilling to comply with DOT and for whom self-medication in the community is deemed inappropriate and also assist with the education and training of DOT providers.

In the clinic, there is a senior nurse who occupies the office of the Director of Public Health Nursing. She makes sure that appropriate personal protective equipment (PPE) is available as required by staff undertaking DOT, ensures robust governance structures in place to monitor and audit practice and to ensure patient safety, ensures systems are in place to facilitate education and training with regard to the management of DOT and use of PPE and also ensures that risk management policies and procedures are in place for reporting all adverse events, incidents, near misses and adverse drug events.

The staff supervising DOT administration is accountable for their practice; it is the responsibility of each DOT provider to be familiar with the main pharmacological actions, the usual dose, storage and stability of medication and frequency, route of administration and potential side effects and incompatibilities of the drugs in the management of clients referred for DOT. This includes appropriate observation of the patient i.e. observing them take their medications, report any difficulties/failures to the treating physician, ensure they take appropriate steps to develop and maintain competence with regard to the management of clients referred for DOT, adhere to all related policies, procedures, guidelines and protocols including risk management structures for DOT and to maintain appropriate documentation for DOT administration.

In the clinic, there is a referral pathway for patients; it involves that the prescribing clinician completes a referral form. The referral form is then forwarded with the prescription to the

relevant Director of Public Health Nursing (DPHN) and cc'd to the Director of Public Health and to the patient's next of kin. The DPHN forwards the referral form and prescription to the assistant DPHN who then contacts the Public Health Specialist. The assistant DPHN communicates the referral to the DOT provider. Any changes in medication is communicated in a timely manner by the prescribing clinician to the patient and to the DPHN.

The DOT provider (nurse or agreed person who is deemed responsible) co-ordinates an agreed process of DOT with the patient. This involves: ensuring that the medication has been obtained by the patient prior to the visit, confirming the identity of the patient at the time of the first visit, observing the client's condition and recording relevant information, verifying that the drugs to be taken are as prescribed. The DOT provider also observes the patient to ensure that the medication has been swallowed, document this in clients' records which include initialling the time and date that medications were taken, report any observed side effects of medications as soon as possible to the referring clinician, DPHN and line manager as appropriate. The DOT provider for each patient always applies the "five rights" of medication administration as follows: a) The right medication b) The right patient service c) The right dosage d) The right form e) The right time.

1.5. PROBLEM STATEMENT

In Pretoria West, comprehensive TB services are available in 87% of clinics offering the DOTS programme and helping to diagnose TB and trace contacts. According to the NDOH (2009), the average Pretoria West district DOTS coverage has decreased from 88.8% to 84.7% in the last few years. The average health district's cure rate is 61%, and its average rate of successful treatment of all new smear positive cases has been 66% since 2005. The negative trends in TB cure rate are attributable to patients' adherence responses to prescribed TB treatments (NDOH, 2009). WHO (2012a), reports have identified certain factors that determine patients' adherence towards TB prescribed treatments generally, which include: TB-related stigma and discrimination in the community, socio-economic status of patients, inadequate health system infrastructure, shortage of adequately trained health care workers, proximity of patients' residence to treatment sites, and many more unidentified factors (WHO 2012a). It is important to explore these factors in other environmental settings (i.e. Pretoria West in this case) and verify if the status quo is the same.

1.6. RATIONALE OF THE STUDY

The purpose of the study is to investigate local factors influencing the adherence of smear positive TB patients to the DOTS programme in order that recommendations could be offered to relevant health authorities in the district to improve adherence and hopefully increase the cure rate.

1.7. OUTLINE OF THE STUDY

CHAPTER 1

Chapter 1 provides a background to the study, a description of study setting and includes the formulation of the problem statement and rationale for the study.

CHAPTER 2

This chapter focuses on the review of the relevant literature. The literature review draws on issues on the global incidence of TB defaulting, strategies for management of TB, factors that contributes to treatment defaulting as well as theories that can be used to explain defaulting.

CHAPTER 3

This chapter explains the research methodology namely: the aims and objectives, the research design, the study population, sampling, data collection and analysis, rigor of the study, ethics considerations as well as limitations of the study.

CHAPTER 4

This chapter presents the study results.

CHAPTER 5

This chapter is a discussion of the results of the study in relation to other relevant literature.

CHAPTER 6

Conclusion and recommendations are made in this last chapter.

CHAPTER TWO

LITERATURE REVIEW

2. 1. INTRODUCTION

Although TB can affect anyone, the disease is believed to have poverty as its main risk factor. Those living in crowded, unhygienic habitats, those who suffer from malnutrition, or those who smoke tobacco; all are at very great risk of developing TB disease (WHO, 2002). In addition, those whose immune systems are compromised are at particular risk, which is why TB is the number one cause of death among people living with HIV (WHO, 2002).

In this chapter, the discussion of the literature focuses on TB management and control; factors promoting TB adherence; and finally, the barriers to adherence.

2.2. TUBERCULOSIS MANAGEMENT AND CONTROL

Since 1993, WHO has approved a holistic method of preventing the spread and initiation of new TB infections. This is a method that any government at all levels should adopt in meeting their responsibilities of managing tuberculosis epidemics within their population (Frieden & Sbarbaro, 2007). The method recommended by the WHO (2006a) to be the most effective TB intervention is DOTS for restraining the spread of TB in communities as alluded to earlier. WHO has reported that more than 30 million patients with TB have been treated with its five-element DOTS strategy, resulting in cure rates of more than 80% and default rates of 10% (WHO, 2006a).

The WHO's declarations on Global Plan to Stop TB emphasises:

• The need to expand DOTS by standardizing treatment regimen and appropriate TB case management

• Administration of TB treatment in a way that reduces the threat of acquiring TB drug resistance mycobacterium

• Giving all required support to patients in order to facilitate adherence to treatment and ultimately enhance the cure rate (Frieden and Sbarbaro, 2007).

The WHO launched the DOTS programme as the universally endorsed TB control approach in 1994 after recognizing TB as a leading world-wide public health epidemic (WHO, 2006b). Most National TB Control Programmes reported breakthroughs and made landslide progress in their TB management programmes when the DOTS strategy was employed. Subsequently, the strategy was expanded to form the Stop TB strategy, which is a build-up approach that seeks to climax the successes of the DOTS strategy (WHO 2006b).

2.2.1. Stop TB strategy

Most of the successes in TB control globally have been attributed to the DOTS strategy, especially in high TB burden countries (WHO 2006b). In order to address the remaining challenges, especially in regions where the TB epidemic has worsened (such as sub-Saharan Africa and Eastern Europe), a new strategy was developed, namely the Stop TB Strategy (WHO 2006b; Dye & Weil 2005). According to WHO (2006c), with DOTS as the central component, the Stop TB strategy set out steps which national TB control programmes, their partners and stakeholders needed to follow in order to improve their TB control programme. It elaborated the DOTS approach with six additional components, as follows: pursue rigorously DOTS expansion and delivery enhancement; address TB/HIV co-infection and MDR-TB challenges, health systems reinforcement; pro-active approach that include and engage all care providers; empower TB patients and enabling and encouraging TB related research. These components are expanded on next.

2.2.1.1. Rigorous Pursue of DOTS expansion and enhancement options

The Stop TB strategy requires all-inclusive and tenacious approaches that support other methods aimed at addressing social and environmental factors that contribute to the risk of individuals developing TB (WHO 2006b). Furthermore, DOTS strengthening is required in the following areas, namely: political commitment with increased and sustained financing; case detection through quality assured bacteriology; standardized treatment with supervision and support; effective drug supply and management systems; monitoring and evaluation systems; and impact assessment (WHO 2006b).

2.2.1.2. Address TB/HIV, MDR-TB and other challenges

The HIV epidemic has worsened the global burden of TB and increased the need to focus attention on strengthening the global TB and HIV programmes in order to tackle the two public health problems effectively (WHO 2004). TB has become the leading cause of death among people living with HIV, while infection with HIV is a large risk factor for latent TB infection to convert to active TB disease (WHO 2006c). The international standards for TB and HIV as set out by WHO are aimed firstly at decreasing the burden of TB among people living with HIV by strengthening intensive TB case finding, provision of Isoniazid preventive therapy for TB and HIV co-infected patients and TB infection control in healthcare and congregate settings. Secondly, the standards aim at decreasing the burden of HIV among TB patients through offering them HIV counselling and testing, HIV prevention and Cotrimoxazole prophylaxis, and HIV care and support, including provision of anti-retro virus therapy (ART) for eligible patients (WHO 2004). Therefore, collaborative activities between the TB and HIV programmes using the above strategies are being implemented as they help to control TB among HIV patients (Maher et al, 2002; WHO, 2006b).

The WHO describes multi drug resistance- tuberculosis (MDR-TB) as a threat to global TB control, worsened by: inadequate treatment for those suffering from it; increase in MDR-TB patients due to misuse of second line anti-TB medicines; and absence of new effective anti-TB medicines (WHO, 2006c). TB control programmes also need to pay attention to special population groups such as prisoners, refugees and other high-risk groups associated with high TB transmissions due to overcrowding and poverty (WHO 2006b).

2.2.1.3. Health systems strengthening

Improving access to quality healthcare services will benefit TB control and therefore TB control programmes should actively improve system-wide policy, human resources, financing, management, service delivery and information systems (WHO 2006b).

2.2.1.4. Engage all care providers (Public-Private Mix)

Many patients with early symptoms of TB consult private healthcare providers first and many such providers diagnose and treat TB (WHO 2006b). The diagnosis of TB needs to be made without delay and once diagnosed the correct treatment with adequate dosing needs to be instituted with proper follow up of such patients. Thus, engagement of all healthcare providers (both private and public) is of paramount importance. Evidence suggests that failure to engage all care providers used by those suspected of having TB and TB patients, hampers TB case detection, delays diagnosis, leads to incorrect diagnosis as well as inappropriate and incomplete treatment, increases drug resistance and places unnecessary financial burden on the patients and health systems (Uplekar, et al, 2001)

2.2.1.5. Empower people who have TB

To achieve greater commitment to fight TB, the Stop TB Strategy embraces the following methods: Advocacy, Communication and Social Mobilisation. Advocacy is encouraged to influence policy changes and ensure sustained financial and political commitment. Facilitation of communication between health care providers, TB patients and their communities is important in order to improve knowledge of TB and subsequently compliance to treatment. Social mobilization is encouraged to engage the communities, partners and stakeholders in the fight against TB (WHO 2006b).

2.2.1.6. Enable and promote TB research

Conducting locally relevant operational research can identify challenges and practical solutions that can be tested in the field before scaling up interventions (WHO 2006b). National Tuberculosis Control Programmes can thus develop new and effective strategies for TB control. The WHO (2006b) encourages TB programmes to facilitate and actively support research to develop new diagnostics, drugs, vaccines and treatments. Qualitative studies must be used to ascertain best intervention that would be practicable, maintainable, and that will be fully embraced by the patients and the health care services (Lienhardt and Rustomjee, 2006). This is believed to be the path toward making TB control more responsive and reflective of local health systems.

2.3. FACTORS PROMOTING ADHERENCE TO TB TREATMENT

Several strategies for promoting TB medication adherence have been investigated. These include:

(a) Interventions promoting better health care provider-patient communication about adherence. A number of studies have shown the importance of the relationship between healthcare workers and the patients as contributing to treatment compliance or non-compliance. Bam et al., (2005), in a study conducted in Nepal, found that the quality of the health care provider and patient interaction and relationship contributed to differences in treatment adherence. Similarly, a South African study (Peltzer, et al., 2002) established that the quality of health care provider and patient communication were associated with TB treatment compliance.

(b) Developing or improving existing adherence support services that are offered by a multidisciplinary team (nurse, physician, pharmacy, patient etc.). A multidisciplinary team of providers can provide adherence support that is both comprehensive and consistent in its message (Charles, 2005). A team may share office space and exchange information several times a day, or they may meet to exchange information once a month. A smooth, consistent communication between team members and patient is a facilitator to TB medication adherence (Charles, 2005).

(c) Directly observed therapy (which involves a health care worker, community care worker or family member directly monitoring patients swallowing their TB medication) (Volmink & Garner, 2007). DOT has been recommended as the standard of care for TB disease by the WHO as a keystone of its recommended strategy for global control of TB (WHO, 1999). It involves simply supervising the ingestion of every dose of treatment. DOT may be the most effective way to ensure completion of treatment for TB patients. However, Volmink & Garner (2007) conclude that there were not enough evidence to support DOT efficacy.

(d) Staff understanding of context. Staff members should be educated about relevant cultural beliefs and practices of the communities they serve, and should practice techniques for good communication with patients (Volmink & Garner, 2007). It is crucial to understand the patient population and identify and address socio-cultural differences, as misinterpretation of certain behaviours or intentions can adversely affect the patient-provider relationship. Patients who are uncomfortable or do not

understand providers or program staff may be less likely to initiate or complete treatment. (Volmink & Garner, 2007).

(e) Education and counselling: It was noted by Gebremariam et al, (2010); WHO (2003); Munro et al, (2007); that being knowledgeable about TB disease was also a facilitator of TB treatment adherence. Studies have shown that peer counselling was associated with higher self-esteem and sense of mastery, characteristics which in turn were associated with both the pulmonary (M'Imunya, Kredo & Volmink, 2012) and latent TB treatment completion (Morisky et al., 2001).

(f) Reminder systems and late patient tracers to help patients keep appointments: Reminder systems and late patient tracers are strategies to improve patients' adherence to tuberculosis screening, diagnosis, and treatment as used in some countries (Liu, et al., 2008). Liu and co-authors from this reviewed article affirmed that almost all the reminder trials, except one, show benefits of different types of reminders (visits made to patients, contacts by health workers, letters, telephone calls, e-mails and SMS text messages) compared to no reminder on adherence to tuberculosis clinic appointments, and the authors concluded that the trials show significantly better outcomes among those tuberculosis patients for which late patient tracers and reminders are used (Liu, et al., 2008).

(g) Incentives and enablers: The use of tangible incentives and enablers has been shown to increase treatment completion (White et al., 2002; Lutge et al., 2012). TB treatment programs regularly provide enablers, i.e. items or services that facilitate clinic attendance. Examples are food, food coupons, bus tokens, childcare facilities, pillboxes, pill splitters and crushers, utensils to administer liquid forms of medications, and calendars to mark off doses taken (Felton, 2004). Incentives are small rewards given to patients to encourage them to take their medications and/or keep their appointments. They may be offered at intervals during the course of treatment or reserved for treatment completion. Incentives can help motivate patients to complete a long treatment regimen, and can serve as rewards for good adherence.

(h) Social support to assist the patient in being adherent provided (Bosch-Capblanch, et al., 2007; Charles, 2005). The positive impact of social networks and social support on adherence has been demonstrated in studies of health issues including stress reduction, control of alcohol use, smoking cessation, weight loss, blood pressure monitoring, etc. Studies have specifically demonstrated the importance of social support for preventing the progression from latent to active TB disease, improving

adherence to TB treatment, and improving coping and quality of life (Chaisson, et al., 2001; El-Sadr, et al., 2001).

In addition, studies have shown that patients who received the support and care of their families and community were more likely to adhere to therapy and achieve cure (Macq et al., 2003; Nyirenda, et al., 2003; Adatu, et al. 2003; Kangangi, et al., 2003). In a study conducted in Ethiopia by Gebremariam et al, (2010), it was reported by the health professionals that patients who had family support and come to the clinics accompanied by either a family member or someone from within the community where they lived, are usually those who successfully complete their treatment. The same study also found that participation in TB clubs (small support groups of TB patients organised according to location of residence) was another facilitator. Observational studies performed in Kenya, Malawi, and Uganda showed that the choice of DOT supporter by the patient associated with the decentralization of treatment, improved treatment success rates (Nyirenda, et al., 2003; Adatu, et al. 2003; Kangangi, et al., 2003). Furthermore, studies in South Africa have reported improvements when lay health workers were involved in TB control (Kaplan, et al., 2016; Atkins, et al., 2010; Clarke, et al., 2005; Lewin, et al., 2005). A study in Nepal, demonstrated that both family and community DOT supporters can achieve good treatment outcomes; allowing a choice of treatment supporter provided the patients with the capacity to determine the mode of supervision that was the most appropriate for their daily life (Newell, et al., 2006). In addition, this community-based approach made it possible for community health workers to trace default patients and return them to treatment. Thiam et al. (2007), recommend that continuous monitoring of this kind of intervention by the district health team is critical for continuous positive outcomes. The authors also advise that the monitoring district health team should ensure regular supply and safe storage of medication in remote places, and regular updates of gathered patients' data.

TB containment is contingent to proactive treatment strategies to support the process of care for patients from detection of disease through the completion of treatment as prescribed (Lienhardt & Ogden, 2004). Reports from research studies have shown that interventions consisting of a holistic package of continuous efforts targeting all stakeholders in TB management and eradication, improved treatment outcomes (Lienhardt, et al., 2003; Lienhardt & Ogden, 2004). Well-coordinated public health interventions are mostly designed

to focus on several factors that in combination would best address the public health issues. This means that interventions developed to facilitate adherence to treatment will usually be complex with various resources coming into play in order to mitigate or combat the pressing public health menace (Lienhardt, et al., 2003). This will also be true for TB treatment as there can be several barriers to TB treatment adherence.

2.4. BARRIERS TO TB TREATMENT ADHERENCE

There are a number of challenges in fighting TB epidemics including the fact that diagnosis can be difficult, particularly in cases of multidrug-resistant forms of the disease (WHO, 2002). Also, TB treatment is difficult because, full blown TB involves six months of daily medication, hence, a major reason for non-compliance with TB treatment programme and a platform for the emergence of MDR-TB. MDR-TB requires up to two years of treatment at a cost up to 200 times more expensive than standard treatment (WHO, 2002).

Medication non-adherence is a major global major health issue, contributing to unfavourable treatment outcomes for a diseased individual (Christensen & Ehlers 2002; Kane et al, 2003). Patients may not be able to administer TB medication as prescribed because of many overarching circumstances and risk factors. However, these factors are not generic to all environments or individuals as they are largely contextual. These likely barriers to TB treatment adherence may be categorized as follows: patient-related factors, social factors, economic factors and health care and health system related factors (Govender & Mash, 2009).

2.4.1. Patient related factors:

Numerous factors have been cited and discussed to be patient related factors that act as barriers against DOTS TB treatments by several authors. These factors among many more include: Patient cultural beliefs about illness and treatment (Banerji, 1993; Sumartojo, 1993), ethnicity, gender and age, patient involvement in drug abuse and mental disorders such as depression or alcohol abuse (Hudelson, 1996). More often than not, when patients are diagnosed as having TB, communities immediately construct them as social and sexual

misfits in the society, which is often followed by exclusion from social interactions and relationships (Glynn et al., 2001). Where care is given in homes, a patient may experience feelings of intense loneliness and abandonment (Glynn et al., 2001).

A study by Date and Okita (2005) demonstrated that the educational levels of TB patients in Yemen were significant predictors of treatment compliance. Similarly, Belo, Luiz, Teixeira, Hanson and Trajman (2011) conducted a prospective study in Brazil and found that educational background is among the most important determinants of socio-economic status and that all deaths due to TB occurred in the group with a lower educational level. It can therefore be deduced based on these cited studies that educational level is a cogent factor in treatment adherence; that is, high education status is a facilitator to treatment adherence, while limited education status of the patients is a barrier to treatment adherence.

According to WHO (1999), some of the personal barriers postulated to be contributing to poor TB treatment compliance are: alcohol, substance abuse, depression and other psychiatric illnesses. Similarly, in a systematic review by Munro et al. (2007), depression, alcohol and substance abuse have been identified as factors that negatively influence compliance of patient on medications. The implications of patients taking alcohol while on treatment are twofold. Firstly, patients may forget to take their medicines when drunk, and secondly there may be more side effects to TB medicines, particularly when patients are taking other medicines, which may result in their being non-compliant (Munro et al., 2007). Smoking may also result in delayed healing from treatment, in turn giving the patients the false impression that the TB medicines are not working and cause them not to be compliant (Munro et al., 2007).

The personal beliefs of patients may constitute an important group of factors affecting adherence even in the presence of adequate access to treatment. In a qualitative review of literature from 1970 to 2005 comprising of more than 102 articles on factors affecting therapeutic compliance from the patients' perspective, the authors found that patients' misconceptions or erroneous beliefs contributed to non-adherence (Jin et al., 2008). The review showed that patients' fears about treatment, their belief that the disease could not be

controlled and their religious beliefs all contributed to the likelihood of non-adherence to therapy (Jin et al., 2008). Misconceptions can influence care-seeking behaviour, implying that if a TB patient misconceived the cause of the sickness, then care-seeking behaviour could also be faulty. The findings of a qualitative study conducted in Kenya on care seeking and attitude towards TB compliance, showed that some participants thought that environmental factors such as inhaling smoke and hot air from burning charcoal or sharing a house with domestic animals were the cause of their TB symptoms and therefore, if they can avoid these misconceived causes of their sickness, they will be healed and there will be no need for comprehensive TB treatments programme. Other patients thought that TB was contracted through alcohol consumption, water or sharing utensils (Ayisi et al., 2011). Similarly, in Ethiopia, some participants thought that 'evil spirits', sexual intercourse and 'the cold' were causes of TB (Gebremariam, Bjune and Frich, 2011). These misconceived causes of TB have contributed to TB patients' non-adherence to recommended TB treatments.

2.4.2. Social influences

Psychosocial issues like stigma and discrimination of TB patients have been cited as barriers in fighting TB epidemics; these psychosocial factors leave sick people too fearful to seek out treatment promptly. Several studies show that actual experiences and anticipations of stigma resulted in many patients hiding their diagnosis of TB or only disclosing it to selected people, mostly close families, which can impact negatively on adherence to TB treatment (Gebremariam, Bjune, & Frich; 2011, Courtwright &, Turner, 2010, Deribew et al, 2010). In a qualitative study to explore lay beliefs about TB and TB/HIV co-infection in Addis Ababa, Ethiopia, many TB patients believed that they were victims of stigma and discrimination because of their TB status (Gebremariam, Bjune, & Frich; 2011). Some believed that their stigma was mainly due to the fact that people associated TB with HIV. Many had seen other TB patients suffering from stigma and discrimination in their communities, and feared that the same might happen to them.

2.4.3. Economic factors:

Economic factors cover patients' employment status, socio-economic status, and cost of transport to clinic while undertaking TB treatment. Several studies on adherence to

medications especially DOTS have shown some associations between economic factors and adherence. According to Lamsal et al., (2009), poverty and TB are closely connected. They claim that the poor may have less flexibility regarding work and clinic attendance and less ability to pay for medications and transport. Nurses who took part in a phenomenological study by Sissolak, Marais & Mehtar (2011) conducted in Cape Town, South Africa, reported that their TB patients came from poor socio-economic conditions and lived far from the hospital. Some of them did not have decent housing because they lived in shacks, their nutritional status was poor and they were unemployed and had no money to travel to the hospital. The study found that all these factors contributed to low adherence level to TB treatment (Sissolak, Marais & Mehtar, 2011).

Studies in Nepal (Bam & Gunneberg 2006), Uzbekhistan (Hasker et al, 2008), Malaysia (O‟Boyle, et al, 2002), Swaziland (Pushpananthan, Walley & Wright 2000:), and Zambia (Needham & Godfrey Faussett 1998) indicated that cost of transport accounts for non-compliance to TB treatment. In the Malaysian study, cost and time of travelling to the treatment centre were major contributory factors associated with compliance to treatment, as non-compliant patients paid significantly more for transport than those compliant (O‟Boyle et al, 2002). A prospective cohort study in Southern Ethiopia to determine factors predicting treatment adherence among smear positive pulmonary tuberculosis patients found that among 404 TB patients on treatment, 20% defaulted treatment. Ninety-one percent of treatment interruptions occurred in the continuation phase, when they had higher cost of transport to a treatment facility (Shargie et al, 2007). One of the explanations for this finding might be that during this phase most of the symptoms disappear and patients may erroneously believe they are cured. This may encourage them to become reluctant to bear the extra burden of the cost of travel, time, and drug side effects (Shargie et al, 2007).

2.4.4. Health care and health system related factors

While the use of multidisciplinary services improves adherence, it has been recognized that a strengthened referral system, simple regimen (number of pills, and frequency of dosing) all improve adherence (Jin et al., (2008). One of the factors that may affect adherence has been found to be physician-patient relationship (Fochsen, et al., 2009; Munro et al., 2007; Jin et al., 2008). Prior research has suggested that collaborative communication between physician and

patient is associated with better adherence (Heisler et al, 2007; Naik et al, 2008; Schoenthaler et al, 2012). In a study conducted in northern California, USA, among 9,377 patients taking medications to lower their blood sugar, blood pressure or cholesterol, it was observed that 30% of participants were not necessarily taking their medications the way their doctors thought they were, due to lack of proper communications. On the other hand, in the same study, the rates for non-adherence were 4 - 6% lower for patients who felt their doctors listened to them, involved them in decisions and gained their trust (Ratanawongsa et al, 2013). The study suggests preparing doctors to be better communicators may help improve medication adherence and ultimately health outcomes (Ratanawongsa, et al 2013). In another study conducted in Auckland, New Zealand on physician-patient relationship and medication compliance by Kerse et al (2004), of almost 400 participants, it was concluded that a greater order of physician-patient concordance was associated with increased medication compliance. The authors suggested that "an emphasis on understanding and facilitating agreement between physician and patient may benefit outcomes in treatment/medication adherence" (Kerse et al, 2004:455).

Complex treatment has been cited as a factor that acts as a barrier to patients' compliance. Pill burden, pill fatigue, side effects and complexities and timing of dosing have all been cited as factors influencing adherence. For example, in a reviewed article of barriers and facilitators to anti-TB medication by Paliwal (2010), the study identified duration on medications and complexity of treatment as some of the factors that influenced adherence. It has been reported that adherence to TB treatment has direct association with the number of drugs prescribed in a treatment (Horne & Weinman 1999; Patal & Taylor 2002; Grant et al, 2003; Iihara et al, 2004), and correlated to the dosing times per day of all prescribed medications (Kass et al, 1986; Cockburn et al, 1987; Cramer et al, 1989; Eisen et al, 1990; Cramer 1998; Sung et al, 1998; Claxton et al, 2001; Iskedjian et al, 2002). It infers that the rate of compliance decreased as the number of daily doses increased; this is revealed in a compliance study that assessed pill counts and self-reports, where it was revealed that non-compliance increased as dosing times increased: 20% for once daily; 30% for twice daily; 60% for three times a day; and 70% for four times daily (Cramer et al, 1989). It has also been reported that, three times daily therapy was the frequent factor for poor adherence, and that the best improvement in adherence comes with the reduction of dosing frequency from three to two times a day (Jin et al, 2008). Similarly, a meta-analysis found that there was a

significant difference in compliance rate between patients taking antihypertensive medication once daily and twice daily (92.1% and 88.9%, respectively) (Iskedjian et al, 2002). Thus, simplifying the medication dosing frequency could improve compliance significantly.

DOTS Treatment observers are key to the success of tackling problems of acute non-adherence to treatment (Paliwal, 2010). According to Paliwal (2010), there are no universal criteria used in assigning treatment observer but in the choice of a treatment observer for a patient, the priority factor should be accountability of the observer to the health system. An observer could be members of the civil society, health care facility staff, social workers and members of non-governmental organizations, religious and ethnic leaders (Paliwal, 2010). In commenting on the importance of direct observation, Frieden & Sbarbaro (2007:409) concluded that "Perhaps what is most important is to ensure that the approach is patient-centered, with rigorous monitoring of and accountability for ensuring cure, and rapid intervention to increase cure rates if they are less than 85%".

A study evaluating DOT in South Africa demonstrated that the facilities with high DOT coverage had significantly better adherence rates than those with low DOT coverage ($p=0.045$) (Ntshanga, Rustomjee & Mabaso, 2009). In 2008–2009, the South African NTP implemented a national pilot project, the TB Tracer Project, to decrease default rates and improve patient outcomes, by constituting teams dedicated to following up TB patients (Podewils, et al, 2012). In an evaluation study based on data from routine national TB surveillance, it was revealed that sub-districts that participated in the TB Tracer Project had more patients who adhered to TB treatment and better treatment outcomes over the project period, in comparison to sub-districts that were not part of the tracer project (Podewils, et al, 2012; Bronner et al, 2012). Invariably, following up on patients with adequate traceability plans is a major player and inevitable facilitator to treatment adherence.

A Nigerian study reported that implementing DOTS in hospitals led to a significant increase in the number of patients completing treatment and a significant reduction in mortality among TB patients (Daniel, 2006), which meant that DOTS can help to ensure that patients adhere to and complete TB treatment regimens.

2.5. SUMMARY

Adherence has been identified as a key element in reducing the likelihood of the emergence of drug resistant TB mycobacteria. Hence, the global efforts towards increasing access to TB treatments through DOTS, especially in resource-limited settings, should match availability of TB medications with successful treatment outcomes to avoid the emergence of drug resistant strains. Though earlier apprehension of low levels of DOT adherence in resource-limited settings has been proven unfounded, adherence may still be a concern in such environments. Identifying contextual factors that affect adherence to DOTS is an important process in designing interventions aimed at sustaining optimal adherence levels.

Different context and people have their own peculiar characteristics; these factors are fundamental and germane to successful implementations of DOTS to TB patients in any environment or setting. Addressing psychosocial, demographic and health system factors that affect adherence are the hallmark of adherence enhancement (Laurenzi, Ginsberg & Spigelman, 2007). Improving adherence should be proactively done through identification of possible barriers during counselling and planning how to appropriately address them before the first drug prescription is made. Such strategies include those that encourage close patient-provider contact, social support and education and anticipating problems that may promote non-adherence.

The next chapter outlines the specific objectives of the present study and the methodology used in the study to achieve these objectives.

CHAPTER 3

METHODOLOGY

In this chapter the research methodology will be discussed in detail, covering aim of the study, study objectives, research design, population and sample, the research instrument, research assistants, data collection and analysis, ethics and reliability and validity.

3.1. AIM OF THE STUDY

The aim of this study was to assess the determinants of adherence to DOTS therapy amongst TB patients who commenced TB treatment at the TB clinic of a district hospital in Pretoria.

3.2. OBJECTIVES OF THE STUDY

The specific objectives of this study were:

I. To measure the level of adherence to DOTS in patients attending the TB Clinic in a Pretoria district Hospital.

II. To assess the associations of socio-demographic, cultural, religious and health systems factors with TB patients' level of adherence to DOTS at the TB Clinic.

3.3. STUDY DESIGN

A quantitative descriptive and analytical, cross-sectional study design was used for this study. According to Burns and Grove (2005), cross-sectional study designs examine participants simultaneously, irrespective of their stage of development but with an aim to describe differences in phenomena across stages. Data are collected at a point in time but with different study participants, as opposed to different points in time for the same participant (Brink 2007). Thus, the study is conducted in the present to determine what already exists; also, exposure and disease status are measured simultaneously (Joubert et al 2008). Cross sectional studies are relatively easy and not very expensive to conduct, since they involve data collection at one point in time only (Polit et al 2001). This study involved collection of

data over a 3-month period of time (April – June 2014) and was thus very economical. Also, a cross sectional study is useful for evaluating the relationship between exposures and outcomes (Gordis, 2004). In this study, associations were tested for various exposures, such as sex, educational level, distance from clinic, socio-economic status, alcohol use, DOT status and health system factors with the two outcomes (adherence and non-adherence).

A cross sectional study is an important step in first assessing the possibility of a relationship between an exposure and a disease before more complicated or expensive studies are undertaken, such as case-control and cohort studies (Gordis 2004; Stommel & Wills 2004). It is useful in identifying the factors associated with TB DOTS adherence or otherwise in a Pretoria West district clinic, which could pave the way for other studies that could identify the factors of treatment non-adherence more broadly.

However, the main disadvantage of cross-sectional studies is their failure to establish causation and the temporal relationship between exposure and disease or outcome as the two are measured simultaneously (Gordis 2004; Stommel & Wills 2004; Polit et al., 2001; Joubert et al., 2008). However, this was not a major limitation as this study aimed to identify associated factors and not necessarily the causes.

3.4. STUDY POPULATION

The study population constituted patients aged 18 years and above who registered for the DOTS programme at the TB clinic of a district hospital in Pretoria. Specific inclusion criteria were:

- Patients on first line regimens of DOTS for TB;
- Patients who had started on DOTS at the Hospital during the 6-month period prior (6 months before November 2014) to the commencement of the study.

The rationale for selecting the study population is that:

i. Adherence measures in patients under 18 years of age, may more likely have different factors to adherence in adults such as factors related to supervision of medication by caregivers' rather than particular choices made by the patients themselves.

ii. Patients visiting the hospital for a period of six months at least in order to gain the sample size required.

Only those patients who fitted the inclusion criteria and who were willing to participate were included in the study.

3.5. SAMPLE SIZE

The sample size was determined using EPI Info version 7 (CDC, 2013). The study population was estimated to be 1,000 (verbal communication with the TB clinic nurse) and the expected prevalence of patients achieving optimal adherence (taking > 95% of medication) was between 84% as the best acceptable rate and worst acceptable estimate was 80%. The estimates were based on two provider estimates using pill count records at the pharmacy (adherence pattern estimates from clinic pharmacy record for previous TB patients on DOTS). Using 95% confidence levels, the required sample size was determined to be 234.

An all-inclusive sampling method was applied in this study i.e. all the patients (215 individuals) on DOTS who fitted the inclusion criteria at the TB clinic for the sampling period (3 months) were approached for participation in the study. Their names were obtained from the TB clinic registers with the help of the nurses working in the clinic. Those who fitted the inclusion criteria but were not willing to participate in the study (135 individuals) were excluded, hence the small sample size of 80 individuals who consented to participate in the study.

3. 6. DATA COLLECTION TOOLS

In the current study, data was collected from the TB patients using a structured questionnaire at one point in time for each of the patients. While the data collection was at different times for the different patients, it was collected once for each of them. The data collection tool (see Appendix 1) was a structured questionnaire in English. The questionnaire was adapted from

those used in other adherence studies from developing countries (Kgatlwane et al., 2006; Irunde et al., 2005). The research assistants asked the questions verbally in Tshwana language and filled in the answers in English in the questionnaire. The research assistants were fluent in both English and the local language. The questionnaire was divided into three parts:

- ✓ The first part collected socio- demographic data;
- ✓ The second part collected data related to treatment, and;
- ✓ The third part collected data related to the adherence measurement tools.

Socio-demographic data

The socio-demographic variables included age, sex, marital status, level of education, place of residence and the nearest health facility.

Treatment data

Treatment data included duration on treatment, experience with side effects and knowledge of consequences of failing to take medication as prescribed. Data such as duration on treatment were collected as month while all the other questions were in a multiple-choice format. The question on treatment regimens were verified by comparing information from the patients' pill containers with the patients' health cards to ensure accuracy.

Adherence measurement tools

The third part of the questionnaire collected adherence data using three different measures: a 30-day self-report using a visual analogue scale, 2-day recall using a sun and moon chart and a pill count. The 30-day visual analogue scale required participants to pour beads from one container representing the pills they were supposed to have taken in a period of 30 days, into another container representing the pills actually taken in the same period. The pills left in the first container therefore represent the pills missed and adherence was measured using a line marked 1-10 on the first container. This was done for each drug in the regimen.

The visual analogue scales has been extensively used for assessment in a number of health domains and has therefore accumulated substantial support as a valid and efficient tool for use in assessment of medication adherence (Giordano et al., 2004; Amico et al., 2006; Bangsberg et al., 2000; Oyugi et al., 2004). Studies using pill count, visual analogue scales and questionnaires in monitoring adherence to treatment medications have reported good concurrence between pill count and visual analogue scales (Nackers et al., 2012; Amico et al., 2006; Bangsberg et al., 2000; Oyugi et al., 2004). Walsh, Mandalia and Gazzard (2002), also included visual analogue scales as an adherence assessment in the Medication Self-report Inventory, and when used to assess adherence to a single antiretroviral medication, visual analogue scales scores correlated significantly with Medication Events Monitoring data, pill counts, and viral load data. In this study, a 30-day self-report using a visual analogue scale was adopted to monitor adherence to TB medication based on the above cited published works.

The pill count was obtained by determining the number of pills returned, the number of pills dispensed in the previous refill and the number supposed to have been taken in a given period. This information was obtained from the pill containers and the patients' cards. Adherence was then calculated as the number of pills supposed to have been taken minus the number of pills missed in a given period as the numerator and the total number of pills supposed to have been taken in the same period as the denominator. This was calculated for each drug in the regimen and the average computed. Adherence rates that were over 100% using this adherence measure were recorded as 100%.

The two -day recall used a sun and moon chart that also indicated time in one-hour intervals. The participants were requested to state the time when the dose of each drug in the regimen was taken starting from the previous day to two days prior. Adherence was then calculated as a percentage of the interval between the doses in relation to the interval required.

3.7. DATA COLLECTION PROCEDURE

Two research assistants, (2 trainee nurses) conducted the interviews with patients on DOT at the hospital over a three-month period (April – June) from the time permission was granted

for the research. The two research assistants obtained the list of names drafted from the register on the days the participants had appointments at the clinic to identify the selected patients who were interviewed immediately after their appointments. The first assistant administered the first and second parts of the questionnaire and the second assistant the third part. The administration of the questionnaire done by the first research assistant was preceded by providing participants with an information sheet (see Appendix 3 and 4) and an informed consent form in their preferred language (see Appendix 2 and 5) accompanied by a verbal explanation of the purpose of the study and requesting their voluntary participation. Only after the participants had signed the consent form, did the interviews commence with questions being asked orally. The completed questionnaire was then coded using the patients' DOTS number before being passed on to the second research assistant.

The second assistant checked the questionnaire for completeness of information collected by the first assistant and then confirmed that the DOTS number on the questionnaire corresponds to the DOTS number on the patients' health card and that on the patient's pill containers. Next, the second assistant also completed details of the patient's treatment regimen on the questionnaire by confirming that the pills prescribed on the patients' file were the same as the pills or containers presented by the patient. This research assistant then proceeded with the 30 day and 2-day adherence self-report using the pill containers to ensure that adherence was reported for each drug in the regimen. This assistant also obtained pill count data from the patients' cards, pill containers and actual counting of the returned pills. The pill was counted on the patient's clinic appointment day for those pills taken/not taken between the last appointment day and the present day; which is approximately 30 days.

3.8. DATA MANAGEMENT AND ANALYSIS

All answers to questions requiring computing were entered on the questionnaire and double-checked by the researcher for completeness and accuracy at the end of each day. The researcher developed a written codebook detailing standard procedures and this was used to code the questionnaires, which were then double entered into Excel files by the two research assistants. The two files were then compared and anomalies or missing data between the two entries were checked using the questionnaires. The entered data were scrutinized for invalid

values and impermissible combinations and counterchecked with the questionnaires. These data were then exported into EPI Info version 7 (CDC, 2013).

Adherence was analysed both as a categorical variable which was expressed as high (> 95%), moderate (85% - 94%) and low adherence (< 85%) level; and as a dichotomous variable as optimal (> 95%) and sub optimal levels (95%). Bivariate analysis was done to test the significance of associations between outcome variables (2-day recall; 30-day recall; pill count; and composite measure) and predictor variables (age; sex; marital status; education level; disclosed status; regimens; medication knowledge; and reported side effects) separately. The p-value cut-off for significance was $P \leq 0.05$. The prevalence ratio and 95% confidence interval was used as the measure of effect of outcome and predictor variables on adherence.

3.9. GENERALIZABILITY

The small sample size of 80 participants in the study limits the generalizability of the results The results obtained have to be viewed with caution, as external validity might have been compromised by using such a small sample, rather than studying the entire population or a truly random sample.

3.10. VALIDITY AND RELIABILITY

Reliability and validity of a measuring instrument are very important (De Vos et al., 2007). To obtain valid and reliable data from the measuring instrument it is important to ensure that before administering the instrument it can be replicated and provide accurate information for the researcher to draw acceptable conclusions (Stommel & Wills 2004). Reliability arises from the stability and consistency of the measurement and provides an indication of the random error in the measurement (Burns & Grove 2005). In this study, measurement bias was reduced by the use of multiple adherence measures to ensure accuracy of adherence estimates, as strengths of one method compensate for the weaknesses of another. The measuring instruments in this study were not piloted due to lack of finance and time resources and most specifically because it was difficult to recruit willing participants.

However, the adherence measuring instruments in this study were adopted from other studies where they had been tested and proven as reported by Burns & Grove (2005) and De Vos et al., (2007). In order to ensure reliability of the measuring instrument, closed-ended questions were used in this study; this ensures that the participants give unbiased responses.

Validity is a measure of the truth or accuracy of a claim (Burns & Grove, 2005) and, according to Babbie (2004); it refers to how far a data collection instrument actually measures what it is supposed to measure. Validity has two aspects: firstly, that the instrument does in fact measure the concept it is intended to measure and secondly that it is measured accurately. Double-checking of recorded information and data in the questionnaire was carried out by the research assistants and confirmed by the chief researcher in order to ensure accuracy and completeness.

Social desirability is a perceptive bias in which participants answer to questioning in ways that make them seem more favourable or appealing to others. Participants can over-report their positive behaviours and under-report negative behaviours and qualities. Social desirability which is usually associated with self-reporting was minimized in this study by phrasing the adherence questions in a non-threatening manner and by the use of research assistants (who are clinic nurses and who are privy to the participants' attitudes to treatment and clinical history and therefore knew how to approach the participants and how to ask the questions) to administer the questionnaire to the participants, rather than the chief researcher.

The importance of truthful information in relation to the purpose of the study was explained to the participants, which hopefully reduced social desirability. Social desirability based on the use of clinic nurses were minimized by encouraging the participants to complete the questionnaires by themselves in the local language.

3.11. ETHICS

Verbal and written explanations about the study were given to the patients in their language of choice. They were also told that they could withdraw from the study at any time and that their withdrawal from the study would not compromise their treatment in any way. They

were also informed that their identities would be kept confidential. Verbal or written consent was obtained from the participants prior to participation. Approval for the study was obtained from the Senate Research Committee of the University of the Western Cape. Permission was also obtained from the District Health Manager and the facility manager of the research site. Permission to examine hospital records was secured from the District Hospital authorities. Careful measures were taken to treat the patients' medical records with confidentiality and this was conveyed to the participants. All identification data were stored in the computer database that was accessible only to the researcher and was password protected and was only shared with the supervisors.

CHAPTER 4

RESULTS

In this chapter, the research findings are presented and include socio-demographic information; clinical characteristics of participants; optimal adherence characteristics of participants; reasons for missing doses; facilitators for taking doses correctly; reasons for missing DOTS clinic appointments; and lastly factors affecting adherence to DOTS.

4.1. SAMPLE REALISATION

Sample size for this study calculated to be 234; however, patients who were willing to participate in the study during data collection were below the calculated sample size.

4.2. SOCIO-DEMOGRAPHIC CHARACTERISTICS OF PARTICIPANTS

A total of 80 DOT patients participated in the study. The majority of the participants were male (76.25 %, n=61), while 23.75% (19) were female; this is representative of the clinic clients (e.g. clinic data: male = 162; female = 54). Table 4.1 summarises the socio-demographic characteristics of the participants. The mean age of the participants was 36 years; 23 (28.75%) of the participants were in the 20-29-year age group; 22 (27.5%) of the participants were in the 30-39-year age group; 33 (41.25%) of the participants were in the 40-49 age group; 2 (2.5%) of the participants were in the 50-59 age group; and there were no representative participants from age group 60+ years in this study.

The marital status data of the participants revealed that 30 (37.5%) of the participants were married or cohabiting; 23 (28.8%) were divorced; 17 (21.3%) were single and 10 (12.5%) of the study participants were widowed. Slightly more than half of the participants (41[51.3%]) had attained primary education level status, while, 30 (37.5%) of the participants had secondary education level status. A total of 9 (11.3%) of the participants had no formal education, while none of the participants had achieved tertiary education status.

Table 4.1: Socio-demographic characteristics of TB Patients on DOTS (N=80)

Characteristics		**n (%)**
GENDER	Male	61 (76.25)
	Female	19 (23.75)
AGE (in years)	20-29	23 (28.75)
	30-39	22 (27.5)
	40-49	33 (41.25)
	50-59	2 (2.5)
	60+	0 (0)
MARITAL STATUS	Married /cohabiting	30 (37.5)
	Divorced	23 (28.8)
	Single	17 (21.3)
	Widowed	10 (12.5)
EDUCATION LEVEL	No Schooling	9 (11.3)
	Primary	41 (51.3)
	Secondary	30 (37.5)
	Tertiary	0 (0)
DISTANCE TRAVELLED	1 - 5 Kilometres	31 (39)
	6 - 10 Kilometres	16 (19)
	11 - 15 Kilometres	9 (11)
	16 - 20 Kilometres	10 (13)
	21 - 25 Kilometres	13 (16)
	>25 Kilometres	1 (2)

Table 4.1 also shows the distances travelled by the participants to the hospital. Thirty-nine percent of participants travelled up to five kilometres from their homes to the hospital; 43% and 16 % of the participants travelled between 6-20 kilometres and 21-25 kilometres respectively, to get to the hospital; while just 2% reported that they had to travel over 25 kilometres. The average distance travelled by all of the participants to arrive at the hospital was approximately 11 kilometres.

4.3. CLINICAL CHARACTERISTICS OF PARTICIPANTS

Most of the participants (88.8%, n=71) were on the first two-month intensive phase treatment combinations that contained Isoniazid + Rifampicin + Pyrazinamide + Ethambutol, while the remainder of the participants (11.2%: n=9) were on the continuation phase of the DOTS treatment.

Table 4.2 shows the length of time participants had been on DOTS programme. The mean duration those participants had been on DOTS treatment was approximately 17 weeks while the median duration on DOTS treatments was around 13 weeks. Approximately 43.8% (n=35) of the participants had been on DOTS for at least16 weeks.

Table 4.2: Clinical characteristics of participants (N=80).

DOTS REGIMEN	**Dosing Duration (Month)**	**No. (%)**
Isoniazid + Rifampicin + Pyrazinamide + Ethambutol	2	71 (88.8)
Rifampicin + Isoniazid	4	9 (11.2)
Duration on DOTS Treatment (Weeks)	**No. of DOTS Users (%)**	
≤ 12	10 (12.5)	
13 - 16	25 (31.25)	
17 - 20	31 (38.75)	
21- 24	12 (15)	
> 24	2 (2.5)	
Adherence Measure	**% Mean Adherence (SD)**	
30-day recall visual analogue	92.8 (5.73)	
2-day recall sun and moon chart	95.6 (3.10)	
Pharmacy refill record (pill count)	93.4 (5.16)	
Composite adherence of the 3 measures	94.0 (4.66)	

The mean adherence rates obtained using 30-day self-report (visual analogue), 2-day self-recall (sun and moon chart) and pill count were 92.8%, 95.6% and 93.4%, respectively. The mean composite adherence of the three measures gave an adherence rate of 94% (Table 4. 2).

Most (80%; n=64) of the participants reported having experienced some side effects with anti-TB medication, while all of the participants reported having disclosed their TB status to somebody else apart from the mandatory treatment supporter.

When asked about the consequences of failing to take anti-TB medication as prescribed, 80% (n = 64) of the participants answered that they understand that they would remain sick while 20% (n= 16) of the participants answered that the mycobacterium will develop resistance in their body and the drugs will not work later when they resume the treatment again. All of the participants answered that if they stopped taking their medication or stopped taking it correctly, their health will deteriorate and therefore become sicker. Any of the three answers was considered as DOTS knowledge.

4.4. OPTIMAL ADHERENCE CHARACTERISTICS OF PARTICIPANTS (N = 80)

The proportion of DOTS patients who achieved optimal adherence levels (95% and above) was 60%, 91% and 73% as measured by 30-day visual analogue, 2-day recall and pill count, respectively; the differences in optimal adherence values from the 3 methods used could mean effectiveness and sensitivities of one measurement technique over the other. Using the mean composite of the three adherence measures, it was found that 75% of the DOTS users had achieved optimal adherence levels (Table 4.3).

4.5. REASONS FOR MISSING DOSES

All of the participants reported that they had missed doses of their medications at one time or the other. Reasons given by the participants for missing doses varied from being away from pills (9%), reacted to medications (21%), forgetfulness (40%), alcohol use (10%) and lack of food (20%) (Table 4.4).

Table 4.3: Measure of adherence by Categories

ADHERENCE MEASURE	CATEGORY OF ADHERENCE		
	High (95-100)	**Medium (85-< 95)**	**Low (< 85)**
30 day visual analogue (N = 80)	48 (60%) (95% CI: 49.3-69.7%)	20 (25%) (95% CI: 15.5-33.5%)	12 (15%) (95% CI: 8.1-21.9%)
2 day sun & moon chart (N = 80)	72 (91%) (95% CI: 84.5-95.3%)	5 (6%) (95% CI: 2.5- 11.5%)	3 (3%) (95% CI: 1.4- 8.5%)
Pharmacy Pill count (N = 80)	58 (73%) 95% CI: 64.5-82.3 %)	13(14%) (95% CI: 9.5-20.9 %)	9(12%) (95%CI: 6.3-19.5%)
Composite adherence of the 3 measures (N = 80)	60 (75%) (95% CI: 63.5-78.4 %)	18 (22%) (95% CI: 18.9-32.2%)	2 (3%) (95% CI: 1.1-7.2%)

Table 4.4: Reasons for missing doses (N = 80)

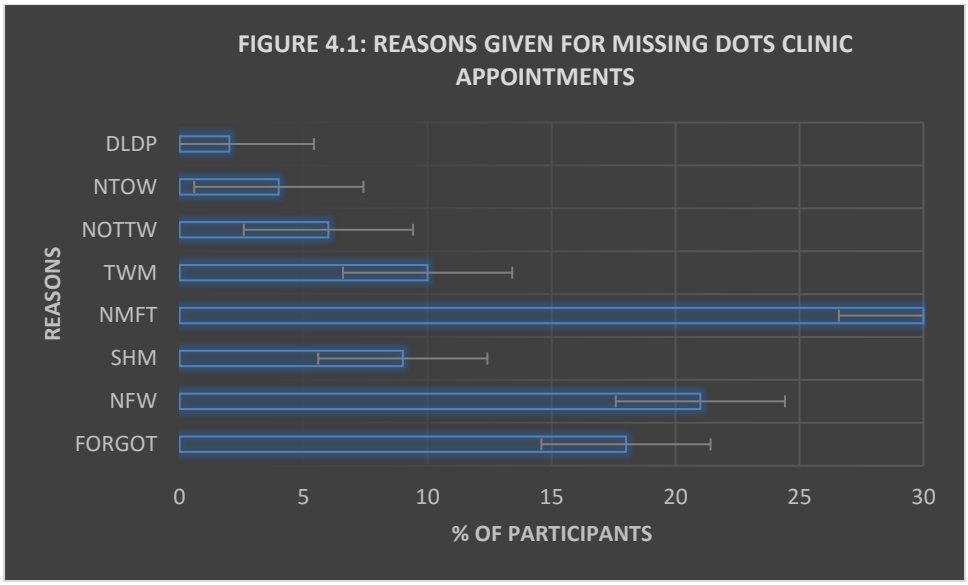
Cited Reasons	Number of participants (%)
Away from pills	7(9)
Reacted to medication	17 (21)
Forgot	32 (40)
Alcohol use	8 (10)
Lack of food	16 (20)

4.6. FACILITATORS FOR TAKING DOSES CORRECTLY

Seventy-two percent (n = 58) of the participants cited counselling and having treatment supporters as the main factors that facilitated in them taking their medicines correctly, while the remaining participants (28%, n = 22) mentioned using reminders like cell phones and radio as facilitators to remembering to take their medication on time.

4.7. REASONS GIVEN FOR MISSING DOTS CLINIC APPOINTMENTS

The main reason given by the participants (30%; n = 24) for missing their appointments was lack of transport money, while only 2% of the participants responded that not wanting to lose their day's pay was the main reason for missing medicine refill appointments.



LEGEND: FORGOT = Forgot; NFW = not feeling well; SHM = still have medicine; NMFT = no money for transport; TWM = tired with medicine; NOTTW = did not have anyone to travel with me; NTOW = could not have time off work; DLDP = did not want to lose a day's pay.

Figure 4.1: Reasons given for missing dots clinic appointments

4.8. FACTORS AFFECTING ADHERENCE TO DOTS TREATMENTS

Associations were tested between adherence and categorical variables. In the Chi square analysis, 2 × 2 tables were set up to test the associations between outcome variables (2-day recall; 30-day recall and pill count measures) and predictor variables (educational level; gender; DOTS regimens; medication side effects; distance to hospital; age and duration on DOTS treatment) separately. Association was tested using high and low adherence at 95% significance level ($p < 0.05$).

Table 4.5 illustrates the bivariate analysis using adherence in two categories. Education status of participants was found to be significantly associated with adherence to DOTS ($p = 0.01$), when considering the pharmacy refill pill count as the adherence measure. Gender was found to be significantly associated ($p = 0.03$; $p = 0.04$) with being adherent when using the 30-day visual analogue and the pharmacy refill count in the dichotomous categories. Significant association was also found between DOTS treatment regimens and 30-day recall adherence measures ($p = 0.002$). Another significant association was found among participants' reports

of medication side effects and the adherence measures of 2-day recall, 30-day recall and pill count with p = 0.04; p = 0.03; p = 0.05 respectively.

Table 4.5: Bivariate analysis of participants' variables using adherence in the two categories

	Optimal Adherence		
	2 day recall OR (95% CI) [p- Value]	**30 day recall OR (95% CI) [p- Value]**	**Pill Count OR (95% CI) [p- Value]**
Education status			
Primary school/no education vs Higher school education	0.14 (0.09-1.62) [0.14]	0.22 (0.13-3.77) [0.5]	0.32 (0.25- 3.77) [0.01]
Gender			
Female vs Male	0.29 (0.1-1.22) [0.28]	0.34 (0.09-1.66) [0.03]	0.28 (0.15-1.69) [0.04]
DOTS Regimen			
Isoniazid + Rifampicin + Pyrazinamide + Ethambutol vs Rifampicin + Isoniazid	0.04 (0.01-1.12) [1.54]	0.64 (0.22-3.16) [0.002]	0.28 (0.18-1.39) [0.99]
Medication Side Effect			
Yes vs No	0.16 (0.11-3.72) [0.04]	0.33 (0.14-1.32) [0.03]	0.24 (0.2-1.28) [0.05]
Distance travelled to clinic			
> 11 KM vs ≤ 11 KM	0.4 (0.84 -1.31) [0.15]	0.1 (0.78 – 1.38) [0.5]	0.5 (0.78 – 1.46) [1.15]
Age of Participants			
> 36 years vs ≤ 36 years	0.4 (0.94 -1.06) [0.2]	0.1 (0.71 – 1.32) [0.002]	0.38 (0.93 – 1.07) [0.003]
Duration on DOTS treatment			
> 17 weeks vs ≤ 17 weeks	0.4 (0.70 -1.43) [0.09]	0.1 (0.97 – 1.03) [1.75]	0.38 (0.77 – 1.29) [0.75]

Distance to the hospital was dichotomised using the mean distance of 11 km to the hospital as the cut-off point. Living within a distance of 11 km from the hospital was not significantly associated with being adherent to TB medication when using the 3 adherence outcome variables as the adherence measure. Age was dichotomised by using the mean age (36 years) as the cut-off point. There were significant associations between age and adherence with two of the adherence measures (30-day recall and pill count) at p = 0.002 and p = 0.003 level of significance respectively. Significant association was also observed between duration of DOTS treatment when dichotomised using the mean treatment period (17 weeks) as the cut-off point and any of the adherence measures.

4.9. SUMMARY

Eighty participants were included in this study, of which 76% were male. The mean composite adherence rate was found to be 94% while the proportion of the patients who achieved adherence of 95% and above was 75%. Identified barriers to adherence include lack of transport fare on clinic appointment days, patients not feeling well and so were not strong enough to attend clinic appointments and forgetfulness. The facilitators identified were having counselling, treatment supporters and the use of reminders such as cell phones and radios.

Education status of participants was found to be significantly associated with adherence to DOTS (p = 0.01), when considering the pharmacy refill pill count as the adherence measure. Significant association was found between DOTS treatment regimens and 30-day recall adherence measures; p-values of 0.002. Significant association was found among participants' reports of medication side effects and the adherence measures of 2-day recall, 30-day recall and pill count with p = 0.04; p = 0.03; p = 0.05 respectively There were significant associations between age and adherence with two of the adherence measures (30-day recall and pill count) at p = 0.002 and p = 0.003 level of significance respectively. Significant association was observed between duration of DOTS treatment when dichotomised using the mean treatment period (17 weeks) as the cut-off point and any of the adherence measures.

The next chapter will discuss the key findings within the context of the study setting.

CHAPTER 5

DISCUSSION

As far back as four decades ago, non-adherence to TB treatment has been recognised as the most challenging factor against global TB control (Addington, 1979); and, non-adherence to TB treatment is also recognised as the main barrier to the eradication of TB malady world-wide (Mason, 1986). Adherence to tuberculosis treatment can be particularly challenging as the findings of this study show.

The aim of this cross-sectional study was to provide baseline data on adherence levels and factors associated with adherence among patients receiving DOTS from the study TB clinic. This chapter discusses the main findings of the study and focuses on the areas of levels of adherence in study participants, gender disparity in notification rate and factors influencing DOTS adherence which are organised according to the following categories: patient related factors; medication related factors; socio-economic factors; health care worker and health system related factors.

5.1. LEVELS OF ADHERENCE IN STUDY PARTICIPANTS

The results found a mean composite adherence of 94% using the three adherence measures: 2-day self-report, 30-day self-report with visual analogue scale and Pharmacy pill counts. This means that 94% of all the pills that should have been taken by the patients were taken. However, this seemingly high mean adherence rate should not give rise to complacency, as the proportion of patients who achieved 94% and above adherence levels did not match it. Indeed, the proportion of patients achieving optimal adherence (> 95%) was only 75%. This finding highlights the disturbing fact that only three quarter of the patients on DOTS at the study TB clinic had sub optimal adherence rates and approximately 3% of these patients had adherence levels of less than 85%. The implications for this are that a large number of patients on DOTS may not be getting the full benefits of their treatment and might even be facing the risk of developing drug resistant forms of TB.

As very high levels of adherence are required in order for DOTS to achieve the intended treatment benefits, it is critical to have a clear understanding of the factors that influence the patient's ability to comply with the treatment requirements to address them and thus enhance adherence to DOTS (Chesney, 2000; Bangsberg et al., 2000).

5.2. GENDER DISPARITY IN NOTIFICATION RATE

Eighty patients on DOTS participated in the study with a male to female ratio of approximately 3:1. Research reports from other developing countries have testified to an increased notification rate of pulmonary TB in men (WHO, 2002). The male to female ratio found in this study setting is consistent with other studies where relatively high male to female ratio of patients on DOTS in comparison to the gender TB prevalence ratio have been observed (Khatri & Frieden 2000; Chakraborty 2004; Chan-Yeung et al., 2003). For example, the male to female ratio (3:1) of the 63 patients on DOTS at two district Hospitals in Indonesia (Widjanarko et al, 2009) was almost similar to the current study. From this present study, gender was found to be significantly associated ($p = 0.03$; $p = 0.04$) with being adherent when using the 30-day visual analogue and the pharmacy refill count in the dichotomous categories.

Differential access to the health care services among females due to socioeconomic and cultural factors, especially in the developing countries has long been considered important reasons for the difference in the TB notification rates between genders. Traditionally, women have poorer access to money, education, information, and health (Abdool-Karim et al., 2009). Furthermore, it has been found in a study from South Africa that the decision regarding a woman's treatment is made by the husband or senior members of the family. Women also have to depend on the men for their treatment-related expenses and mobility (Abdool-Karim et al., 2009). In a large house to house prevalence survey conducted in Bangladesh, a difference in the gender ratio (3:1) with an excess of cases in males was noted even after adjusting for confounding factors like income, awareness, and social stigma (Salim et al., 2003). On the other hand, a comparison between age and gender-specific prevalence and notification rates from 29 surveys in 14 countries suggested that the reasons for a low notification rate for TB in females was more due to biological factors than a differential access of the health care (Whitacre et al., 1995). Differences in the cellular immunity and

antibody response following immunization increased levels of CD4+ lymphocytes than men (Mair, et al., 2008) and influence of sex hormones (Whitacre et al., 1995) have all been implicated in the decreased incidence of TB in females. Although the gender disparity was not directly investigated in this study, evidence from the literature suggests that there are multiple factors biological and social that could explain the gender disparity found in this study.

5.3. FACTORS INFLUENCING DOTS ADHERENCE

Defaulting and poor treatment adherence threatens TB control, as partially treated patients are not cured and may develop multidrug-resistant TB. Several studies of factors associated to adherence have been conducted in many countries globally (Westaway and Wolmarans, 1994; Jin et al., 1993). A systematic review of qualitative research on patient adherence to TB treatment identified the facilitators to completing TB treatment as structural, social, health service-related and personal reasons (Munro, et al., 2007). Similarly, the factors associated with adherence can be grouped into those related to socioeconomic circumstances and conditions; those related to the patients; those related to the health workers and health system; and those related to the disease and its treatment (WHO, 2003).

5.3.1. PATIENT LEVEL FACTORS INFLUENCING ADHERENCE

The present study explored some factors that impeded or facilitated optimal adherence to DOTS among the patients at the study TB clinic. All of the participants reported that they had missed doses of their medications at one time or the other. At the patient level, reasons given by the participants for missing doses varied from being away from pills (9%), forgetfulness (40%) and alcohol use (10%).

Reasons for missing doses

Forgetfulness which was the main reason for missing doses may be related to being away from pills, which was another reason given for missing doses. Forgetfulness (i.e. forgot to take their medication with), which was cited by 40% of the participants, was associated with

the patients being away from home and thus finding themselves without their medication when the dose was due.

The results from this study is similar to a study among patients with TB in Northwest Ethiopia by Adane et al (2013) where about 6% of TB patients reported that they had a problem of forgetfulness. From that study it was concluded that those patients who had a problem of forgetfulness were seven times more likely to be non-adherent than their counterparts (AOR: 7.04, 95% CI 1.40– 35.13). From the present study underlying reasons for not taking medication with them may have been forgetting, some of these issues could be explored further and could be addressed by patient counselling.

Alcohol use as a barrier to DOTS adherence

About 10% of the participants reported that they had missed doses of their medications at one time or the due to alcohol use. According to a study in Tanzania by van den Boogaard et al, (2011), all of the study participants suggested that alcohol abuse was the most important barrier to TB treatment adherence, either because they knew that alcohol and TB treatment cannot be taken together or because alcohol abuse made them careless about their health. These could also be the reasons why the participants in the current study missed their doses. In another study by Naidoo et al (2013), it was emphasized that alcohol use or abuse is a significant predictors of non-adherence common to anti-TB therapy. The authors recommended that a comprehensive treatment programme addressing poverty, alcohol mis-use, tobacco use and psycho-social counselling is indicated for TB patients. The treatment care package needs to involve not only the health sector but other relevant government sectors, such as social development to address the social issues influencing treatment adherence.

Non-adherence to treatment believed at times to be a symptom of larger social and psychological problems in the patient (Naidoo et al., 2013). Few unconfirmed reports have suggested that those with the worst records of adherence are usually former prisoners and/or persons affected by alcohol and drug addiction. These patterns of addiction are, in turn, taken as indicators of unresolved psychological illness that makes successful treatment very

difficult to attain (Naidoo et al., 2013, van den Boogaard et al., 2011). However, the above mentioned psychological related factors (i.e. alcohol and drug addictions, being a prisoner) could not be confirmed as factors contributing to non-adherence in this study, but 10% of the participants affirmed to have missed their treatment due to alcohol uses.

Use of reminders as a facilitator to adherence

In the present study, about one quarter of the participants reported that using reminders like cell phones and radio have facilitated them remembering to taking their medication on time and correctly. Similarly, personal responsibility has been found to be an important aspect of adherence behaviour; patients who developed their own reminders adhered readily to TB medication regimen (Fong, 2004). In a study by van den Boogaard et al (2011), the participants perceived that amongst other factors such the presence of support from family members and friends, and the presence of helpful health care staff, the use of reminder cues was a facilitator for adherence. The participants in that study mentioned several reminder cues that helped them to remember to take their medication. Some participants used the alarm of a mobile phone to inform them when the time to take the medication had reached. Others placed their medication bottle somewhere where it was clearly visible, to remind themselves. In addition, most participants carefully selected an appropriate time for medication intake from that study (van den Boogaard et al., 2011). Therefore, it is clear that personal reminders are effective facilitators for TB adherence.

5.3.2. MEDICATION RELATED FACTORS

Adverse reaction to TB medication was cited by 20% of participants in the current study as a reason for non-adherence. Similarly, adverse reactions to TB treatment, including hepatic injury, were found to contribute to non-adherence elsewhere (Munro et al., 2007; Xia and Zhan 2007). In the present study patients also mentioned pill burden as being one of the major challenges of TB treatment as a high number of pills was perceived to be associated with potential damage to the body and a higher risk of not tolerating the drugs. Thus, active surveillance of patients' adverse reactions is suggested. To minimize the impact of adverse reactions, it is important that health staff provide concise pre-treatment counselling to patients and that they manage such side-effects with timely recommendations and services.

5.3.3. SOCIO – ECONOMIC FACTORS

According to Lamsal et al., (2009), poverty and TB are closely connected. They claim that the poor may have less flexibility regarding work and clinic attendance and less ability to pay for medications and transport. Nurses who took part in a phenomenological study by Sissolak, Marais & Mehtar (2011) conducted in Cape Town, South Africa, reported that their TB patients came from poor conditions and lived far from the hospital, the study found that these factors contributed to low adherence level to TB treatment (Sissolak, Marais & Mehtar, 2011).

Lack of food as a barrier to dots adherence

Lack of food was the second most common reason (33%) given by the participants for missing doses in the present study. This barrier may be due to an increased appetite as patients improve with DOTS use or to non-availability of food because the patient is too weak to work and therefore cannot afford to buy food - an issue that can be related to poverty.

Studies by Gebremariam et al., (2011); Maswanganyi et al., (2013); Munro et al., (2007), reported that the majority of patients believed that lack of food or intake of inadequate food was associated with more severe side effects and a difficulty to tolerate TB medications. The amount and quality of food needed and the degree of possible side effects were also believed by some patients from that study to be proportional to the medicine taken. The results of the present study indicate that, patients who had insufficient income mentioned the lack of food as a factor adversely affecting their treatment. Patients mentioned medication could be harmful on an empty stomach, and that it was better not to take medication if one had not eaten showing that they were aware of the implications of lack of food while on TB treatment.

DOTS and nutrition have been shown to be closely related (Gebremariam et al., 2011); results from this study have highlighted that provision of adequate nutrition is an issue that requires attention in patients attending the TB Clinic.

Lack of transportation and distance travel to hospital as barriers to dots adherence

Studies in Nepal (Bam & Gunneberg 2006), Uzbekhistan (Hasker et al, 2008), Malaysia (O‟Boyle, et al, 2002), Swaziland (Pushpananthan, Walley & Wright 2000:), and Zambia (Needham & Godfrey Faussett 1998) indicated that cost of transport accounts for non-compliance to TB treatment. In the Malaysian study, cost and time of travelling to the treatment centre were major contributory factors associated with compliance to treatment, as non-compliant patients paid significantly more for transport than those compliant (O'Boyle et al, 2002).

In the present study, the average distance travelled by the participants to arrive at the hospital was approximately 11 kilometres. Almost, 20% of the participants from this study travelled above 20 Kilometres to attend TB clinics; this could be a major contributory factor as to why optimal adherence could not be attained from this study's participants.

Our results suggest that addressing socio-economic factors such as providing early support in terms of food and financial assistance to at least cover transportation costs for patients with financial difficulties might facilitate adherence to DOTS treatment.

5.3.4. HEALTH CARE WORKER AND HEALTH SYSTEM RELATED FACTORS

A study in South Africa (Zwarenstein et al. 2000) found some benefit from DOT using lay health workers. A study in Swaziland (Wright et al. 2004) found no significant difference in cure rates between direct observation by community health workers (CHWs) and by family members. A Thai study (Kamolratanakul et al. 1999) found DOT to be effective, but they had adapted the original DOT model, including a choice of DOT (nearly all chose DOT by family members), supported by a once-weekly home visit from health workers.

A review of DOT and treatment adherence (Volmink et al. 2000) emphasized the importance of a wide array of interventions to promote adherence, such as reminder letters, financial incentives and increased supervision by staff. The study observed that factors such as the quality of interaction between patients and supervisors may be more relevant than the DOT

itself, and recommended that WHO make explicit both the mixture of inputs which are required to improve adherence and the additional resources which successful implementation of DOT usually requires.

Impact of treatment supporters

The value of treatment supporters as an adherence facilitator has been reported in some studies (Nwokike, 2005; Nachega, 2006). TB treatment guidelines require every patient on DOTS to have a mandatory treatment supporter to facilitate adherence, and clearly defined roles of the treatment supporter and the patient in adherence be known. In the present study, about 70% of the participants cited counselling and having treatment supporters as the main factors that encouraged them to take their medicines correctly. Similarly, in a study conducted in Ethiopia by Gebremariam et al, (2010), it was reported by the health professionals that patients who had family support and come to the clinics accompanied by either a family member or someone from within the community where they lived, are usually those who successfully complete their treatment.

Our findings suggest that adherence counselling by the treatment supporter might facilitate adherence. Therefore, treatment supporters should endeavour to provide patients with uniform and complete information on DOTS. Patients should be well informed about co-infection, side effects, pill burden and timing in the course of TB treatment. The treatment supporter should also discuss with the patient the importance of social support for adherence to treatment. Furthermore, according to the participants in this present study, apart from providing health education, health care staff could facilitate the patients' adherence to treatment by providing reminder cues and by ensuring supervision of medication intake. The role of the treatment supporter should therefore not be underestimated.

5.4. CONCLUSION

Adherence to anti-TB treatment is a major determinant of treatment outcome. In developing countries where inequities in access to health care are high and health resources are scarce the

magnitude and impact of poor adherence is assumed to be higher. The implication of this is that many patients experience difficulties in adhering to TB treatment.

The findings of this study identified barriers to adherence which include: lack of transport fare on clinic appointment days, patients not feeling well and so not strong enough to attend clinic appointments and most of the times forgetfulness. On the other hand, the facilitators of adherence identified from this study were counselling, treatment supporters and use of reminders such as cell phones and radios. Certainly the study assumes a position that there is an urgency to improve adherence among the patients on DOTS at the TB Clinic.

As this is the first study to attempt to measure adherence and identify factors that affect adherence among patients on DOTS at the TB Clinic, the findings of this study provide baseline data that could be useful in designing practical interventions to enhance adherence in the Hospital and other similar settings. The study also provides groundwork for qualitative and quantitative studies to explore and quantify these factors further and also serves as a template for further investigations on influence of adherence factors on DOTS, in order to address problems of non-adherence to TB treatment regimen.

5.5. STUDY LIMITATIONS

The study was restricted to the western district of Pretoria and the sample size of eighty participants is small. Accordingly, the findings cannot be generalized to other districts or to the whole country. The use of structured interviews prevented the interviewers from probing certain aspects of patients' behaviour and attitudes. The population for this study was generated from one TB clinic and therefore TB patients not registered at the participating TB clinic, but residing in the district, were not included in the study. Those TB patients who did not participate in this study might have had similar and/or different experiences affecting their adherence/non-adherence to TB treatment. In addition, qualitative studies would be beneficial to further explore the barriers and facilitators related to adherence and the ways that they interact to influence adherence. In addition, the clinic staff was used in administering questionnaires; this might have resulted in the participants being fearful and not willing to give accurate information, which could be a major limitation of the study.

Finally, it is likely that conducting the study in a hospital setting and using hospital staff might have inhibited some participants from expressing their personal views. To avoid this, the participants were reminded of the importance of truthful information in order to make recommendations for improvements to treatment adherence generally and that there would be no negative consequences to them.

CHAPTER 6

CONCLUSIONS AND RECOMMENDATIONS

6.1. CONCLUSIONS

Seeing that this study is the first study of its kind in Pretoria West, the findings have provided useful baseline data on the adherence rates and some insights into the major factors that affect adherence among patients on DOTS at one of the TB clinic in the region. Hence the findings may be useful in developing appropriate intervention strategies to improve and sustain optimal adherence in patients on DOTS in similar settings in South Africa. This is particularly important given the ongoing countrywide rollout of the DOTS programme in South Africa. However further qualitative and quantitative studies are required to further explore the factors influencing adherence in this or similar settings.

The study found that the mean adherence level among the sample of 80 patients on DOTS at the study clinic was 94%, while the proportion of patients who achieved adherence levels of 95% and above was 64%. Despite the reported high average adherence level, just less than two thirds of patients achieved optimum adherence levels; consequently, more than a third of the patients on DOTS at the study clinic run the risk of poor health outcomes and developing drug resistant forms of TB.

Thus, in view of the individual and public health implications of non-adherence, these findings indicate an urgent need to improve adherence levels among patients on DOTS at the study clinic. The higher adherence levels reported in similar clinical studies in other sub-Saharan African settings point to the feasibility of achieving greater adherence in this setting. In light of the scaling up of the DOTS program in South Africa, there is a need to not just monitor the levels of adherence, but also to identify and address factors that affect adherence so that an increasing number of patients on DOTS can achieve the full-intended benefits.

The main barriers to adherence identified in this study were forgetfulness at the patient level, lack of food and transport cost to attend clinic appointments at the socio-economic level. In addition, distance from home to the hospital was found to be significantly associated with adherence, with adherence decreasing with increasing distance. This barrier indicates that although DOTS is available at the study clinic free of charge, there are still issues of accessibility to many patients in terms of transport costs. Another cost related barrier to adherence among the patients on DOTS at the study clinic was the lack of food. Good nutrition is required for the restoration of the immune system, and so addressing a regular supply of food to patients on DOTS should be an important aspect of the DOTS Programme. It is therefore clear that socio-economic factors play a major role in TB treatment adherence.

Related to health system factors, the role of treatment supporters and counselling were found to have a positive impact on adherence to DOTS in this setting. Knowledge of consequences of not taking DOTS as prescribed, which is closely linked with counselling, was found to be significantly associated with adherence in this study, highlighting the influence of the treatment supporters on the individual patient's adherence behaviour. These facilitators to DOTS have been identified in other studies in Sub Saharan Africa and further developments in these services would add value to the DOTS Programme in the study clinic.

6.2. RECOMMENDATIONS

In accordance with the findings of this study, the following recommendations should be considered to assist in improving adherence among patients on DOTS at the study clinic.

• The community based DOTS programme should be better implemented so that the patients do not have to travel so far. Also, the feasibility of mobile clinics should be explored so that they could also be used to reach more TB patients.

• The on-going supportive role of the treatment supporter in adherence should be further encouraged and clearly defined to both the patients and the treatment supporters before commencement of DOTS, so as to facilitate adherence optimally.

It is also recommended that the TB program should ensure that treatment supporters receive the necessary incentives, recognition and psycho - social support to motivate them to give the required support to their patients.

• A counselling protocol should be improved at the hospital, so that all patients will have the same access to formal counselling as their individual cases may require.

• Alcohol abuse should be totally discouraged through adequate and timely counselling to patients. The complications that could arise as a result of using/abusing alcohol should be spelt out to the patients. They should also be referred for rehabilitation if necessary.

• Gender imbalances i.e. women's lack of independence in seeking health advice and treatment, reduced decision-making power and restricted mobility should be addressed by health and social development authorities as well as religious organisations in this location by having more awareness programs in the community. This will encourage more women to disclose their TB status and to adhere to DOTS treatment programmes.

The provision of food to patients on DOTS who require such assistance should be favourably considered and incorporated into the DOTS programme.

• Further studies involving both quantitative and qualitative methods, should be conducted to quantify and further explore the factors that influence adherence in this setting to gain a better understanding of these factors in order to improve the existing adherence levels.

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APPENDICES

APPENDIX 1: Questionnaire- Data Collection Tool.

Adherence Measurement for DOTS users' questionnaire

Date _____ Participant No._____ DOTS NO: ----------

1. Date of birth M_____Y_____

2. Sex

a). Male b). Female

3. Marital Status

a). Single b). Married /cohabiting c) Divorced d) Widowed

4. What is the highest standard that you have passed at school?

a) No schooling b). Grade 4 and below c). Grade 5 to 7 e). Grade 8 to 12 f) Tertiary

5. Where do you live? ----------

6. Nearest clinic/ health centre-------

7. When did you start DOTS? M_____ Y_____

8. Have you experienced any side effects with TB medication?

a). Yes b). No

8. What do you think would happen in your body if you skipped your anti-TB medicine? (Please tick one)

a). Remain sick b). Drugs won't work later on) c). Health deteriorates d) don't know e). Other (please specify)

9. Apart from your treatment supporter, have you disclosed your TB status to anybody else?

a). Yes b). No

10. If yes to Q9 who?

a). Brother/sister b). Parent c). Partner d) Child e). Other (please specify)

11. **Many people find it hard to take all their TB medicine exactly as prescribed. Which of the following reasons have caused you to skip your medicines or take them later than required? Please feel comfortable to answer this question truthfully (tick Max 3)**

a).Forgot b). No food c) Medicine exhausted d). Tired with the medicine e) did not have pills with you f). Reacted to the medicine g). Shared pills h).Feeling you had to hide medication from those around you i). Did not understand instructions j). Alcohol use k) Lack of care/support l). Others (specify please)

……

12. What is it that helps you to take your TB medicine regularly as prescribed? (Tick maximum 2)

a). Treatment supporter b).counseling c). Reminders (radio, cellphone, etc.) d). Other (please specify)

13. Many people find it difficult to collect their medicines or attend appointment on the date given by the doctor. Which of the following reasons have caused you to miss an appointment or not to collect your medicines? (Tick max 3)

a.). Forgot b). Ill/ not feeling well enough c). Still had medicines left d). no money for transport e). Tired with medicine f). did not have anyone to travel with me g). Could not have time off work h). Did not want to lose a day's pay i). Other (please specify)

14. Can I see your medicine please? ***Complete names of the medicines.*** a). Isoniazid (H) b). Rifampicin (R) c). Streptomycin (S) d) Ethambutol (E) e). Pyrazinamide (Z) f). Pyridoxine

15. 30 day recall using visual analogue.

Ask patient to pour out one lot of beads (representing ***all the pills they would take in any given month. Note: separately for each drug****). A glass full of beads is marked with a 0-10cm line. After pouring beads to an empty glass, estimate pills not taken by looking at the mark of beads remaining in the glass.*

Drug A_____cm Drug B_____cm Drug C_____cm Composite_____cm

16. 2-day recall using sun and moon chart

Mark "X" on each line the time when you took your Medicine **Yesterday?**	6 am  Morning	7 am	8 am	9 am	10 am	11 am	12  Mid-day	1 pm	2 pm	3 pm	4 pm	5 pm	6 pm  Evening	7 pm	8 pm	9 pm	10 pm	11 pm	12  Night
Drug A																			
Drug B																			
Drug C																			
Drug D																			

Mark "X" on each line the time when you took your Medicine the **Day before Yesterday?**	6 am  Morning	7 am	8 am	9 am	10 am	11 am	12  Mid-day	1 pm	2 pm	3 pm	4 pm	5 pm	6 pm  Evening	7 pm	8 pm	9 pm	10 pm	11 pm	12  Night
Drug A																			
Drug B																			
Drug C																			
Drug D																			

17. PHARMACY REFIL RECORD pill counts

Drug names (as in Q11)	**Example**	**Drug A**	**Drug B**	**Drug C**	**Drug D**
	D4t				
a). Previous date issued	2 AUG				
b). Quantity taken home (total)	66				
c). Quantity returned	11				
d). Date returned	1st Sept.				
e). Days since last issued	30				
f). Doses per day	2				
g). Total supposed to take	60				
h). Should have returned	b-g 66 - 60 = 6				
i). Pills missed	c-h 11- 6 = 5				
j). Percent adherence	g-i/g X 100 60-5/60X100				

……

APPENDIX 2: Consent form

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CONSENT FORM

Title of Research Project:

Determinants of Adherence to Tuberculosis therapy among patients receiving Directly Observed Treatment from a District Hospital in Pretoria, South Africa.

The study has been described to me in language that I understand and I freely and voluntarily agree to participate.

My questions about the study have been answered. I understand that my identity will not be disclosed and that I may withdraw from the study without giving a reason at any time and this will not negatively affect me in any way.

Participant's name……..

Participant's signature……..

Witness……..

Date……

APPENDIX 3: Information Sheet

APPENDIX 3

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INFORMATION SHEET

Project Title: Determinants of Adherence to Tuberculosis therapy among patients receiving Directly Observed Treatment from a District Hospital in Pretoria, South Africa.

What is this study about?

This is a research project being conducted by **Olayinka Ayobami Aiyegoro** at the University of the Western Cape. We are inviting you to participate in this research project because you will be able to help in giving relevant information that will make the research to be successful. Your answers will help the stakeholders in health industry to find solution to problems around patients' adherence to TB treatment. The purpose of this research project is is to investigate factors influencing the adherence of smear positive TB patients to the DOTS programme in order that recommendations for the improvement of the services rendered can be offered.

What will I be asked to do if I agree to participate?
You will be asked to complete a short questionnaire or be interviewed on your personal experience on TB treatment and DOT programme. The study location is in Western Pretoria in the Tshwane Metropolitan District. This study will be conducted among smear-positive TB patients diagnosed at the TB clinic of the hospital. All diagnosed TB patients above age eighteen under the DOTS programme at this facility during the study period are the study population.

Would my participation in this study be kept confidential?

We will do our best to keep your personal information confidential to help protect your confidentiality. Information obtained from you will be locked away in filing cabinets and storage areas, only the researcher will have access to this area. I will use identification codes only on data forms for identification and your name will never appear on any form and all

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information will be stored using password-protected computer files and information will be destroyed immediately after the study is completed.

If we write a report or article about this research project, your identity will be protected to the maximum extent possible.

What are the risks of this research?
There are no known risks associated with participating in this research project.

What are the benefits of this research?
This research is not designed to help you personally, but the results may help the investigator learn more about TB treatment adherence in this area. We hope that, in the future, other people might benefit from this study through improved understanding of the level of adherence and factors that influence adherence to DOTS therapy amongst TB patients who commenced TB treatment at the TB clinic of a district hospital in Pretoria.

Do I have to be in this research and may I stop participating at any time?
Your participation in this research is completely voluntary. You may choose not to take part at all. If you decide to participate in this research, you may stop participating at any time. If you decide not to participate in this study or if you stop participating at any time, you will not be penalized or lose any benefits to which you otherwise qualify. If there is anything that you are not comfortable to discuss, please say so.

What if I have questions?
This research is being conducted by **Olayinka Ayobami Aiyegoro; School of Public Health** at the University of the Western Cape. If you have any questions about the research study itself, please contact:

Olayinka Ayobami Aiyegoro

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Should you have any questions regarding this study and your rights as a research participant or if you wish to report any problems you have experienced related to the study, please contact:

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This research has been approved by the University of the Western Cape's Senate Research Committee and Ethics Committee.

APPENDIX 4: Tswana information sheet

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LEPHEPHA LA KITSA

Boikitsiso ba thumelo ya thuso e leng mo balwetseng ba TB baba bonag bophelo phepo e e tswang kwa dikantorong kgolo ya sepetlele sa Petoria kwa Afrika Borwa

Kokoanyo e e ka eng?

Se ke dipatlisiso tsa porojeke tsedi dirilweng ke Dikonketso Mofokeng kwa unibesiting ya kapa Bophirima (UWC)

Rego memela go tsaya karolo mo dipatlisisong tsa porojeke e, Ka gonne otla kgona lego thusa go fa kitso etla dirang legore dipatlisiso tse diatlege. Dikarabo tsa gago ditla thusa batshwara karolo mo lefapheng latsa pholo go bona tharabololo ya mathata a aparetseng balwetsi go oketsa go phekolwa ga TB.

Mosola wa dipatlisiso tse kego phuputsa mabaka a rotloetsang go tshwaetsana gogo maleba ga balwetsi ba TB, mo porogarameng ya DOTS gore re kgone re naganise ka bokgoni jwa tshebeletso e reka fanang ka yona.

Naa ke eng se nka se bolelelwang fa nka dumela go tsea karolo?

O tla kopiwa go araba dipotso di sekae/dile mmalwanyana kgotsa gore bolelela ka maitemogelo a gago mabapi le kalafo ya TB le porogarama ya DOTS. Lefelo la thuto lele ko Bophirima jwa Tshwane metropolitan district, thuto e etla tsamaisiwa mo balwetsing ba ba tshwaeditshweng Ka mogare wa TB ko bookelong kapa sepetlele. Balwetsi botlhe ba ba tshwaeditsweng ke mogare owa TB bale godimo ga dingwaga dile lesome leborobedi(18)kafatlase ga porogarama ya DOTS mo tsamaong ya thuto ya selekanyo sa batho.

A naa karolo ya me thutong e e tla tshireletswa sephiring?

retla dira kabo jotlhe jwa rona go boloka kitso ya bona mo sephiring. Kitso e etswang mogo wena etla lotlelelwa mo kabineteng ya difaele kgotsa ko karolong ya setoro, ke fela mmatlisisi yo otla fitlhelelang karolo eo. Ketla sebedisa kitsiso ya khouto fela mo foromong itshupo leina la gago gale kitla le bonala moforomong epe, dikitsiso tsotlhe ditla beiwa go sebedisiwe lefoko la sephiri kgotsa nomoro ya sephiri. Etlare morago ga

APPENDIX 4: Tswana information sheet

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thuto e efela re senye difaele tsotlhe mo computeng le kitso yotlhe kaga wena. Hare kwala repoto kgotsa buka ka dipatlisiso tsa porojeke e retla go sireletsa thata mogo kgonegang.

Naa dikotsi tse amanang le thuto e ke dife?

Ga gona dikotsi dipe tsedi amanang le go tsaya karolo modi patlisisong tse.

Naa ditshwanelo tsa thuto e ke dife?

dipatlisiso tse ga dia direlwa wena ka nosi. Ditlamorago dika thusa mmatlisisi go ithuta gole gontsi ka kalafo ya TB mo karolong e, re solofela gore mo isagong batho bangwe baka itseela sengwe gotswa mo thutong eo, ka tlhabololo ya seemo sa thotloetso ya DOTS go rotloetsa balwetsi gosimolola ka kalafi ya TB mo mafapheng a pholo le maokelo mo Tshwane.

A nna nka tsea karolo mo thutong ye le gone nkanne ka wa lesa go tsea karolo nako engwe le engwe?

Go tseyeng karolo mo dipatlisisong tseo kego ithaopa, o kanna wa itlhopela gosa tsee karolo mme haele gore o swetsa kago tsaa karolo mo dipatlisisong tse, o kanna wa emisa gotsaya karolo nako nngwe le nngwe. Haele gore o tlhopa gosa tsee karolo mo dithutong tse kgotsa hao emisa go tsaya karolo ka nako nngwe, gao kitla o fumana kotlhao kgotsa go latlhegelwa ke go itseela tse digo lebaneng.

Ha gonale sengwe seo sa batleng go bua ka sona,ka kopo bua jalo.

Fa kena a le dipotsiso?

Thuto ye e dirwa ke Olayinka Ayobami Aiyegoro: Lefapha la tsa Bophelo go tswa go Unibesithi ya Kapa Bophirima. Fa o kanna le dipotsiso dife ka thuto e o ka itshwaraganya le:

Olayinka Ayobami Aiyegoro
***Department of Public Health,* University of the Western Cape,**
Cell No: 0826227389
Work Telephone No: 0126729368
E-mail address: ayoyinkaaiyegoro@yahoo.com

APPENDIX 4: Tswana information sheet

FACULTY OF COMMUNITY AND HEALTH SCIENCES
School of Public Health

Private Bag X17, Bellville, 7535
South Africa
Tel: +27 (0) 21 959 2809/2166
Fax: +27 (0) 21 9592872
Email: soph-comm@uwc.ac.za
Website:
http://www.uwc.ac.za/faculties/chs/soph

Fa o k aba le dipotso mabupi le thuto ye le ditokelo tsa gago jalo ka motsua karolo kgots o na le bothala bo bo amangole thuto ye o ka tshwaraganga le:

Director:
Prof Helene Schneider
School of Public Health
University of the Western Cape
Private Bag X17
Bellville 7535
hschneider@uwc.ac.za

Dean of the Faculty of Community and Health Sciences:
Prof Jose Frantz
University of the Western Cape
Private Bag X17
Bellville 7535
jfrantz@uwc.ac.za

This research has been approved by the University of the Western Cape's Senate Research Committee and Ethics Committee.

A WHO Collaborating Centre for Research and Training in Human Resources for Health

UNIVERSITY of the WESTERN CAPE

A place of quality, a place to grow, from hope to action through knowledge

APPENDIX 5: Tswana consent form

FACULTY OF COMMUNITY AND HEALTH SCIENCES
School of Public Health

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Email: soph-comm@uwc.ac.za
Website:
http://www.uwc.ac.za/faculties/chs/soph

FOROMO YA DITETLELELO

Setlhakgolo sa porojeke: Boikitsiso ba thumelo ya thuso e leng mo balwetseng ba TB baba bonag bophelo phepo e e tswang kwa dikantorong kgolo ya sepetlele sa Petoria kwa Afrika Borwa

Thuto ye e tlhaloseditswe go nna ka leleme le ke le tlhaloganyang le gore kea ithaopa ebile kea dumela go tsea karolo.

Dipotsiso tsame ka thuto ye di arabilwe. Kea tlhaloganya gore boikitsiso ba me bo ka se bontshwe batho kantle le mmatlisisi gape le gore nka lesa go tsea karolo nako engwe le engwe kantle le go fa lebaka gape le gore se se ka se tshwenyane le nna leeseng.

Leina la Motsaakarolo.....

Lethswao kitsitso.....

Paki.....

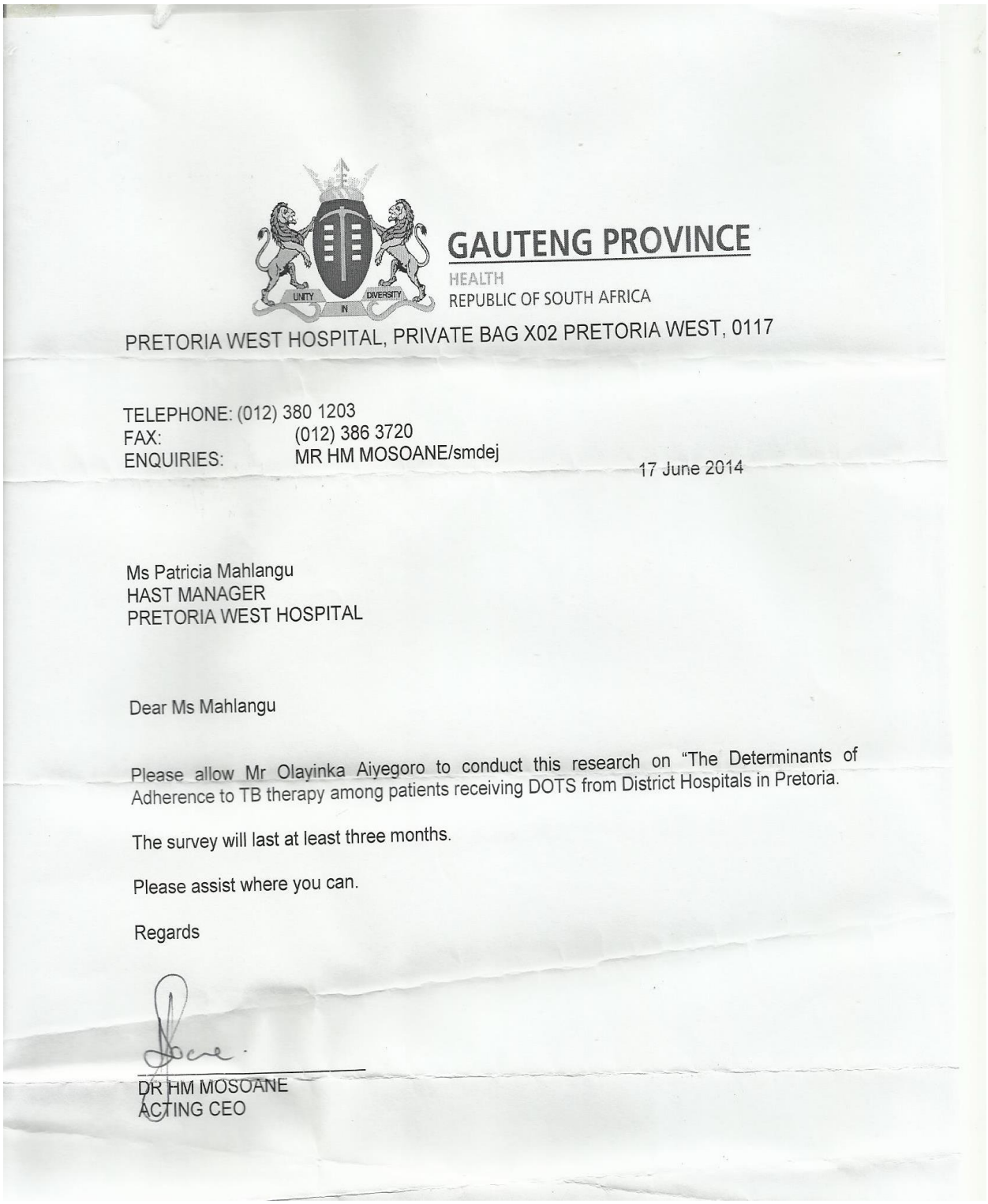
Letlha.....

APPENDIX 6: Participants Information Table

S/N	AGE (YRS)	SEX	MARITAL STATUS	EDUCATION	DISTANCE (KM)	DOTS DURATION (weeks)	SIDE EFFECT	DRUG SKIP EFFECT	TB DISCLOSURE	DRUG SKIP REASON	DRUG TAKING FACILITATOR	APPOINTMENT MISS	DRUG COMBINATION	30 DAY	2 DAY	PHARM REFILL
1	20	F	S	P	5	12	YES	YES	YES	FORGOT	REMIND	NFW	R+I	97	97	97
2	21	M	S	P	8	15	YES	YES	YES	NO FOOD	SUP&CO	SHM	I+R+P+E	96	96	96
3	22	M	S	S	14	15	YES	YES	YES	NO FOOD	SUP&CO	NMFT	I+R+P+E	99	99	99
4	23	M	S	P	16	14	YES	YES	YES	NO FOOD	SUP&CO	NMFT	I+R+P+E	98	98	98
5	24	M	S	S	5	15	NO	YES	YES	REACT	REMIND	NFW	I+R+P+E	95	95	95
6	24	M	S	P	7	18	YES	YES	YES	FORGOT	REMIND	TWM	R+I	98	98	98
7	21	M	S	P	14	16	YES	YES	YES	REACT	REMIND	FORGOT	I+R+P+E	92	96	92
8	23	F	S	S	18	20	YES	YES	YES	FORGOT	REMIND	NOTTW	I+R+P+E	89	89	89
9	22	M	S	P	19	13	YES	YES	YES	FORGOT	REMIND	NFW	I+R+P+E	95	95	95
10	24	M	S	S	5	19	YES	YES	YES	FORGOT	REMIND	NMFT	R+I	96	96	96
11	25	M	S	P	6	19	NO	YES	YES	FORGOT	REMIND	FORGOT	R+I	90	90	90
12	26	M	M	S	12	13	YES	YES	YES	FORGOT	SUP&CO	NFW	R+I	99	99	99
13	27	M	M	P	4	23	YES	YES	YES	FORGOT	SUP&CO	NMFT	R+I	95	95	95
14	28	F	M	S	18	12	YES	YES	YES	FORGOT	SUP&CO	FORGOT	I+R+P+E	98	98	98
15	29	M	M	P	30	24	NO	YES	YES	FORGOT	REMIND	TWM	I+R+P+E	94	95	94
16	29	M	S	S	3	17	YES	YES	YES	FORGOT	SUP&CO	NMFT	R+I	97	97	97
17	29	M	M	P	25	22	YES	YES	YES	FORGOT	SUP&CO	NOTTW	I+R+P+E	91	95	91
18	25	M	M	S	4	22	YES	YES	YES	FORGOT	REMIND	NFW	I+R+P+E	98	98	98
19	27	M	M	N	7	16	YES	YES	YES	REACT	SUP&CO	NMFT	R+I	92	95	92
20	26	M	S	P	2	18	YES	YES	YES	NO FOOD	SUP&CO	TWM	I+R+P+E	95	95	95
21	28	F	M	S	11	19	YES	YES	YES	REACT	REMIND	SHM	R+I	84	95	80
22	29	M	D	P	1	18	NO	YES	YES	REACT	SUP&CO	NTOW	I+R+P+E	95	95	95
23	26	M	S	S	21	17	YES	YES	YES	FORGOT	SUP&CO	NFW	I+R+P+E	80	95	84
24	30	F	M	P	5	12	YES	YES	YES	REACT	SUP&CO	NMFT	R+I	96	96	96
25	31	M	D	P	8	23	NO	YES	YES	REACT	SUP&CO	TWM	I+R+P+E	99	99	99
26	32	M	M	P	3	23	YES	YES	YES	NO PILLS	SUP&CO	NFW	R+I	80	84	80
27	33	M	S	P	24	16	YES	YES	YES	FORGOT	SUP&CO	NOTTW	I+R+P+E	96	96	96
28	34	M	D	P	2	21	NO	YES	YES	NO PILLS	SUP&CO	NFW	I+R+P+E	80	96	84
29	34	M	D	S	19	14	YES	YES	YES	NO PILLS	SUP&CO	FORGOT	R+I	95	95	95
30	33	M	S	P	9	20	YES	YES	YES	NO FOOD	SUP&CO	TWM	I+R+P+E	80	98	82
31	32	M	D	S	4	22	NO	YES	YES	NO PILLS	SUP&CO	NFW	I+R+P+E	98	98	98
32	31	M	S	S	5	15	YES	YES	YES	ALCOHL	REMIND	NMFT	R+I	98	98	98
33	33	M	D	P	24	19	YES	YES	YES	FORGOT	SUP&CO	NMFT	I+R+P+E	80	98	83
34	30	M	M	S	10	19	YES	YES	YES	FORGOT	SUP&CO	TWM	I+R+P+E	97	97	97
35	35	F	M	P	20	17	YES	YES	YES	FORGOT	SUP&CO	FORGOT	R+I	83	80	95
36	36	M	D	N	24	12	NO	YES	YES	FORGOT	REMIND	DLDP	I+R+P+E	99	99	99
37	37	M	M	S	24	21	YES	YES	YES	FORGOT	SUP&CO	NFW	I+R+P+E	80	99	84
38	38	M	M	S	2	20	YES	YES	YES	REACT	SUP&CO	NTOW	R+I	97	97	97
39	39	M	M	N	27	25	YES	YES	YES	NO FOOD	SUP&CO	NMFT	I+R+P+E	84	95	84
40	35	F	D	S	23	15	YES	YES	YES	REACT	SUP&CO	DLDP	I+R+P+E	95	95	95
41	36	M	M	P	15	18	YES	YES	YES	REACT	REMIND	NFW	R+I	83	95	99
42	37	M	M	S	21	18	YES	YES	YES	FORGOT	SUP&CO	NMFT	I+R+P+E	95	95	95
43	38	M	D	P	4	17	YES	YES	YES	FORGOT	SUP&CO	NOTTW	I+R+P+E	95	95	95
44	39	M	M	S	23	18	YES	YES	YES	FORGOT	SUP&CO	NFW	I+R+P+E	91	99	91
45	35	M	M	S	25	12	YES	YES	YES	FORGOT	SUP&CO	NMFT	R+I	90	94	90
46	40	F	D	P	14	18	YES	YES	YES	ALCOHL	SUP&CO	NTOW	I+R+P+E	96	96	96
47	41	M	W	S	5	17	NO	YES	YES	NO FOOD	REMIND	FORGOT	R+I	89	89	89
48	42	M	W	P	22	12	YES	YES	YES	ALCOHL	SUP&CO	NTOW	I+R+P+E	98	98	98
49	43	M	M	S	9	18	YES	YES	YES	FORGOT	SUP&CO	SHM	I+R+P+E	97	97	97
50	44	M	D	P	10	18	YES	YES	YES	ALCOHL	REMIND	NMFT	I+R+P+E	82	95	82
51	43	M	M	S	5	16	YES	YES	YES	NO FOOD	SUP&CO	NOTTW	I+R+P+E	96	96	96
52	42	M	M	S	9	19	YES	YES	YES	ALCOHL	SUP&CO	FORGOT	R+I	97	97	97
53	41	M	W	N	21	18	YES	YES	YES	FORGOT	REMIND	FORGOT	I+R+P+E	92	95	92
54	40	M	D	P	13	14	YES	YES	YES	REACT	SUP&CO	TWM	I+R+P+E	99	99	99
55	41	M	M	P	5	20	NO	YES	YES	NO FOOD	SUP&CO	NFW	I+R+P+E	94	95	94
56	42	M	M	P	19	17	YES	YES	YES	ALCOHL	SUP&CO	NMFT	R+I	96	96	96
57	43	M	W	S	8	13	YES	YES	YES	FORGOT	SUP&CO	NMFT	I+R+P+E	96	96	96
58	44	M	M	P	25	15	YES	YES	YES	REACT	REMIND	NFW	I+R+P+E	90	90	90
59	43	F	D	P	3	19	YES	YES	YES	ALCOHL	SUP&CO	NMFT	R+I	96	96	96
60	42	M	M	P	20	25	NO	YES	YES	FORGOT	SUP&CO	NMFT	I+R+P+E	98	98	98
61	41	M	D	S	18	14	YES	YES	YES	REACT	SUP&CO	TWM	R+I	95	95	95
62	40	F	M	N	4	23	YES	YES	YES	NO PILLS	REMIND	FORGOT	I+R+P+E	90	91	90
63	40	M	M	S	12	13	YES	YES	YES	NO FOOD	SUP&CO	NMFT	I+R+P+E	98	98	98
64	40	F	D	P	2	25	YES	YES	YES	ALCOHL	SUP&CO	NMFT	R+I	95	95	95
65	41	M	M	P	17	12	YES	YES	YES	NO FOOD	SUP&CO	NMFT	I+R+P+E	90	95	90
66	43	F	M	S	1	15	NO	YES	YES	REACT	SUP&CO	NFW	I+R+P+E	80	94	81
67	44	M	D	P	7	24	YES	YES	YES	FORGOT	REMIND	NMFT	I+R+P+E	90	94	90
68	44	F	W	P	3	18	NO	YES	YES	NO FOOD	SUP&CO	NMFT	R+I	97	97	97
69	49	F	W	S	4	24	YES	YES	YES	NO PILLS	SUP&CO	NMFT	I+R+P+E	89	99	89
70	46	M	D	P	10	12	YES	YES	YES	FORGOT	SUP&CO	NMFT	I+R+P+E	88	95	88
71	45	F	W	N	10	19	YES	YES	YES	REACT	SUP&CO	FORGOT	R+I	95	95	95
72	45	M	W	P	4	16	YES	YES	YES	NO PILLS	SUP&CO	FORGOT	I+R+P+E	87	95	87
73	48	M	D	P	2	20	YES	YES	YES	NO FOOD	SUP&CO	FORGOT	I+R+P+E	99	99	99
74	47	F	W	S	5	15	YES	YES	YES	REACT	SUP&CO	SHM	I+R+P+E	90	95	90
75	46	M	W	N	11	13	YES	YES	YES	FORGOT	REMIND	NFW	R+I	95	95	95

76	46	F	D	P	2	14	YES	YES	YES	NO FOOD	SUP&CO	SHM	R+I	92	95	92
77	48	M	D	P	6	12	YES	YES	YES	REACT	SUP&CO	FORGOT	I+R+P+E	97	97	97
78	49	F	D	N	5	14	YES	YES	YES	FORGOT	SUP&CO	NFW	R+I	98	98	98
79	54	F	D	N	2	12	YES	YES	YES	NO FOOD	REMIND	SHM	I+R+P+E	96	96	96
80	52	M	D	P	5	13	YES	YES	YES	NO FOOD	SUP&CO	FORGOT	R+I	95	95	95

APPENDIX 7: Permission to Conduct Research



GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

PRETORIA WEST HOSPITAL, PRIVATE BAG X02 PRETORIA WEST, 0117

TELEPHONE: (012) 380 1203
FAX: (012) 386 3720
ENQUIRIES: MR HM MOSOANE/smdej

17 June 2014

Ms Patricia Mahlangu
HAST MANAGER
PRETORIA WEST HOSPITAL

Dear Ms Mahlangu

Please allow Mr Olayinka Aiyegoro to conduct this research on "The Determinants of Adherence to TB therapy among patients receiving DOTS from District Hospitals in Pretoria.

The survey will last at least three months.

Please assist where you can.

Regards

DR HM MOSOANE
ACTING CEO

APPENDIX 8: Tshwane Research Committee Clearance Certificate

research

Dr Mulaine

110414

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

0826227389

Kuyasheshwa! Gauteng Working Better

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Enquiries: Dr. K. E. Letebele-Hartell.
e-mail: Manel.Letebele@gauteng.gov.za

TSHWANE RESEARCH COMMITTEE

CLEARANCE CERTIFICATE

Meeting: N/A

PROJECT NUMBER: 10/2014

Title: Determinants of Adherence to Tuberculosis therapy among patients receiving Directly treatment from a District Hospital in Pretoria, South Africa

Researcher: OlayinkaAyobamiAiyegoro

Supervisor:Ms. Suraya Mohamed

Department: Faculty of Community and Health Sciences

DECISION OF THE COMMITTEE

Approved

NB: THIS OFFICE REQUESTED A FULL REPORT ON THE OUTCOME OF THE RESEARCH DONE

Date: 18 March 2014

.....
Dr. K.E Letebele-Hartell
Chairperson Tshwane Research Committee
Tshwane District

.....
Mrs. M Morewane
Director: District Health Services Support
Tshwane District

NOTE: Resubmission of the protocol by researcher(s) is required if there is departure from the protocol procedures as approved by the committee.

17/6/14

Permission granted

Director ITR

APPENDIX 9: UWC research protocol approval letter to Conduct Research

UNIVERSITY of the WESTERN CAPE

OFFICE OF THE DEAN
DEPARTMENT OF RESEARCH DEVELOPMENT

9 December 2013

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:
Mr OA Aiyegoro (School of Public Health)

Research Project:	Determinants of adherence to tuberculosis therapy among patients receiving directly observed treatment from a district hospital in Pretoria, South Africa
Registration no:	13/10/42

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

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