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Factors associated with extreme nonadherence to tb treatment among adult defaulters attending Gqeberha clinic between 2018 and 2019

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UNIVERSITY OF THE WITWATERSRAND



FACULTY OF HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH

FACTORS ASSOCIATED WITH EXTREME NONADHERENCE TO TB TREATMENT AMONG ADULT DEFAULTERS ATTENDING GQEBERHA CLINIC BETWEEN 2018 AND 2019.

By

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Research report submitted for the degree of MSc in Epidemiology, Field of Implementation Sciences.

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20 February 2024

DECLARATION

I, Elisha Chipise make the declaration that this research report is my own original work. It is being submitted in partial fulfillment of the requirements for the Degree of Master of Science in Epidemiology (Field of Implementation Science) at the University of the Witwatersrand, Johannesburg. It has not been submitted either in part or full for any degree or examination at this or any other University.

Signature,



Chipise Elisha

DEDICATION

I dedicate this research report to my loving wife and family for their unwavering support and encouragement throughout this journey and to God the Almighty for granting me sufficient grace, strength, and wisdom to successfully complete this task.

ABSTRACT

Background

Tuberculosis remains a significant public health problem in sub-Saharan Africa leading to high morbidity, mortality, social and economic implications. Tuberculosis is a curable condition that can be eliminated. However, global efforts towards ending TB are under threat from patients' nonadherence to effective TB treatment. This study aimed to determine the prevalence and factors associated with extreme nonadherence to TB treatment among adult defaulters attending Gqeberha clinic in South Africa.

Methods

The study is a secondary data analysis of a cross sectional study on TB defaulters attending Gqeberha clinic. The analysis included 144 participants with minimum age of 18 years who had defaulted treatment between April 2018 and September 2019. TB nonadherence and study characteristics were described using frequencies and percentages. Extreme nonadherence was defined by an aggregate score of at least 4 based on the Morisky Medication Adherence 8-item scale (MMA8). The prevalence of extreme nonadherence was estimated using percentage frequencies while univariable and multivariable logistic regression modelling were performed to identify the factors associated with extreme nonadherence.

Results

There were 18(12.9%) TB defaulters who had extreme nonadherence. The majority of TB defaulters 65.2% (n=90) were men. All participants involved had a minimum age of 18 years. 73.4% (n =102) of the study participants stayed in formal dwellings, 79.1% (n =110) were unemployed, 68.8% (n =95) had not attained matric level qualification and 78.4% (n =109) were either single, divorced or separated. A larger proportion of participants, 79.9% (n =111) stayed within 5km radius of Gqeberha clinic, 65.5% (n =91) experienced shorter waiting times and 84.2% (n =117) acknowledged constant availability of medicines at the health facility. However, 69.1% (n =96) did not have a family member who encouraged them to attend clinic visits, 64% (n =89) lacked adequate food whilst taking medication, and 80.6% (n=112) had inadequate income to cover their basic needs whilst on treatment. After adjusting for covariates, those who took other medication besides TB treatment had 0.33 times odds (95% CI: 0.11-0.97) of extreme

nonadherence compared to their contrasting peers. All the other factors were not significant in the adjusted model.

Conclusion

The prevalence of extreme nonadherence to TB treatment among adult defaulters was low. The participants involved in the study were from low-income families with the majority being unemployed, having low educational attainment and lacking adequate food during treatment course. The use of multiple drugs was significantly associated with lower odds of extreme nonadherence. There is need to intensify programs aimed at improving adherence to treatment if the end TB by 2035 goal is to be realized.

Keywords

Tuberculosis (TB), extreme nonadherence, defaulter,

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DEFINITION OF TERMS

Tuberculosis - an infectious disease caused by a bacteria called mycobacterium tuberculosis.

Adherence - the correct and consistent use of treatments as prescribed by the healthcare provider.

Treatment default- interruption of treatment for at least two consecutive months

Cure rate – percentage of people who successfully complete treatment course.

Default rate- percentage of people who interrupt treatment for at least two consecutive months.

Multidrug resistant TB(MDRTB)- tuberculosis resistant to either rifampicin or isoniazid

Extensively drug resistant TB(XDRTB)- a form of MDRTB which includes resistance to any fluoroquinolone plus at least one second line injectable.

Extreme nonadherence- situation where patients have a higher probability of defaulting treatment owing to the existence of critical factors. In this study it is defined by a total score of at least 4 after aggregation of scores based on the Morisky Medication Adherence tool (MM8).

Recurrent TB- development of new TB infection in a patient who previously successfully completed TB treatment course.

ABBREVIATIONS AND ACRONYMS

AIDS	AQUIRED IMMUNE DEFICIENCY SYNDROME
HIV	HUMAN IMMUNODEFFICIENCY VIRUS
TB	TUBERCULOSIS
WHO	WORLD HEALTH ORGANISATION
SSA	SUBSAHARAN AFRICA
MDRTB	MULTIDRUG RESISTANT TUBERCULOSIS
XDRTB	EXTENSIVELY DRUG RESISTANT TUBERCULOSIS
STI	SEXUALLY TRANSMITTED INFECTION
MTSF	MEDIUM TERM STRATEGIC FRAMEWORK
NSP	NATIONAL STRATEGIC PLAN
NDP	NATIONAL DEVELOPMENT PLAN
SANAC	SOUTH AFRICAN NATIONAL AIDS COUNCIL
PIP	PROVINCIAL IMPLEMENTATION PLANS
NDOH	NATIONAL DEPARTMENT OF HEALTH
MMA8	MORISKY MEDICATION ADHERENCE 8-ITEM SCALE
HREC	HUMAN RESEARCH ETHICS COMMITTEE
VIF	VARIANCE INFLATION FACTORS

CHAPTER 1: INTRODUCTION

1.1 Background

The global pandemic tuberculosis (TB), caused by inhalation of mycobacterium tuberculosis, is preventable and can be cured with highly effective and affordable regiments(1). Despite this, approximately 1.5 million lives have been lost worldwide in 2020 according to the World Health Organization (WHO) Global TB report of 2021(1). Without intervention, 50-65% of TB cases will succumb to TB within 5 years(2).In 1993, TB was declared a public health emergency by WHO(3). Ever since, the pandemic has caused social and economic distress of catastrophic proportions. WHO estimates that 13 billion United States dollars is required annually to cover the costs of TB prevention, diagnosis, and treatment to meet the End TB by 2035 goal(1). The projected global TB incidence for the year 2023 is 9.9 million.

Tuberculosis (TB) remains a serious public health concern in sub-Saharan Africa. According to WHO, in 2020 there were an estimated 1.8 million cases of TB in the region, which accounted for around a quarter of the global burden of TB(1). TB is a major public health problem in SSA, where the burden of the disease is high. In 2019, the incidence of TB in SSA was 225 cases per 100,000 people, compared to a global incidence of 130 cases per 100,000 people(4) . The high TB burden in SSA is attributed to factors such as poverty, malnutrition, overcrowding, and HIV co-infection (5,6). HIV is a major risk factor for TB in SSA, as it weakens the immune system and increases the risk of developing active TB disease(7). In 2019, 57% of people with TB in SSA were also living with HIV(4).

One of the major challenges in TB control in SSA is the high rate of treatment default. Treatment default occurs when patients stop taking their medication before completing the full course. This can happen for various reasons, such as adverse effects of the medication, lack of education about the importance of completing the full course, and stigma associated with the disease (8). The World Health Organization (WHO) defines treatment default as a patient who interrupts treatment for two or more consecutive months (1). In 2019, the treatment success rate for TB in SSA was 83%, with the subsequent 17% either succumbing to the disease or failing to complete their treatment course(4). The treatment success rate varies by country, with some countries in SSA having default rates as high as 30% (9).

South Africa, a country located in Sub-Saharan Africa, is among the 30 high-burden TB countries which contribute 87% of global TB incident cases(1,5). The national TB prevalence study conducted in 2018 revealed that the bacteriologically confirmed TB prevalence rate was 737 cases per 100 000 people(10). About 360 000 new cases were identified in 2019 and 58 000 patients succumbed to the disease. The shocking statistics confirm the status of TB being the principal cause of mortality in South Africa(11). The cure rate of TB treatment is defined as the proportion of TB patients who have been cured of the disease after completing their treatment course. In South Africa, the TB cure rate has improved over the years, but it is still below the global target of 85%. According to the WHO Global TB Report of 2020, the TB cure rate in South Africa was 81% in 2019(4). The low cure rate is due to several factors, including poor patient adherence, drug-resistant TB, and inadequate healthcare infrastructure.

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Treatment nonadherence in the context of TB refers to the failure of a patient to complete their full course of TB treatment as prescribed by their healthcare provider. Nonadherence can take different

forms such as missing doses, interrupting treatment, or stopping treatment prematurely(9). Non-adherence does not only harm the individual but also puts the public's health at risk because it could prolong the illness and raise the danger of sustained community spread. Also, the proper therapy for resistant TB strains demands the use of prolonged, specialized treatment regimens with additional antibiotics, raising the cost and decreasing the likelihood of cure (12). Systematic evaluation of TB treatment should be promoted since it aids in identifying the major obstacles to effective treatment and supports the surveillance of populations at risk like TB defaulters attending Gqeberha clinic.

1.2 Literature review

1.2.1 Tuberculosis situation in South Africa

South Africa is working towards the global goal of ending TB by 2035(13,14). According to the World Health Organization, the estimated number of incident TB cases in South Africa was 454,000 in 2010, and it decreased to 301,000 in 2020. The estimated number of patients successfully treated for TB increased from 259,000 in 2010 to 297,000 in 2020. The estimated number of patients on treatment for TB increased from 329,000 in 2010 to 379,000 in 2020(1). These numbers indicate some progress in TB control in South Africa, but more efforts are needed to achieve the global targets for TB control. It is important to note that these numbers are estimates and may not reflect the actual number of TB cases and treatment outcomes in South Africa.

Additionally, South Africa has a huge burden of Multidrug resistant TB which has been increasing steadily over the past decade. From 2010 to 2020, there were a total of 127,514 cases of MDR-TB in South Africa. The number of cases increased from 11,022 in 2010 to 14,547 in 2020(5,9,15). However, the percentage of MDR-TB cases among all TB cases has remained relatively stable at around 2-3%. The treatment success rate for MDR-TB in South Africa has also improved over the years. In 2010, the treatment success rate was 53%. By 2020, it had increased to 73%(16,17).

However, the treatment success rate for extensively drug-resistant TB (XDR-TB) remains low at around 40%.

COVID-19 pandemic has had a huge impact on TB services in South Africa, with disruptions to TB diagnosis and treatment. This has likely contributed to a decrease in the number of TB cases reported in 2019 compared to previous years(18).

Overall, while there have been increases in the number of MDR-TB cases in South Africa over the past decade, there have also been improvements in treatment outcomes. However, there is still a long way to go in the fight against TB, particularly in the context of the COVID-19 pandemic.

1.2.2 The National Strategic Plan for TB in South Africa

The National Strategic Plan(NSP) of 2017-2022 was established to address challenges in the management and scale up of quality HIV, TB and STIs services in South Africa(19).It provides a strategic framework for multi-sectoral partnership with the aim of reducing burden of HIV, TB and STIs in South Africa. Provinces are tasked to develop tailor made Provincial Implement Plans (PIP) which are aligned to the broader strategic objectives. This strategy enables the development and implementation of healthcare services that are aligned with the specific needs of communities(20). The NSP is in line with the Medium Term Strategic Framework (MTSF) and is part of National Development Plan (NDP)(21). The NSP was developed through multiple stakeholder consultations and is based on current evidence. It was approved by the South African National AIDS Council (SANAC) and national cabinet.

1.2.3 TB treatment in South Africa

The South African National Department for Health (NDOH) provides TB treatment free of charge (8). Treatment is rolled out in two phases namely the intensive phase and the continuation phase. During the intensive phase, patients are given rifampicin, isoniazid, ethambutol and pyrazinamide

as fixed dose combinations with weight adjustment for a period of 2 months. According to a study by Chirwa and colleagues, the critical period to achieve sterility is the intensive phase (9) hence advocacy for optimal adherence must be maximized. The direct observation treatment (DOT) strategy is often optimized during the intensive phase with patients reporting to their nearest healthcare facility to take their daily treatment doses. The continuation phase is characterized by a reduced pill burden from the usual 3 or 4 tablets to 2 tablets per day and a more relaxed DOT where treatment support is transferred to family and caregivers. During this phase patients are provided with rifampicin and isoniazid for 4 months. To achieve cure, patients must take at least 90% of their prescribed regimen (10).

1.2.4 Adherence to TB medication

Adherence to TB medication is a major predictor of the treatment outcome (11). The effectiveness of TB treatment depends on the timely provision of the correct regimen and strict compliance to treatment for the prescribed duration(22).Treatment interruption results in a myriad of complications affecting individuals, families, communities and nations at large(9,23). Despite the importance of strict adherence to treatment, the default rate in South Africa is still high. A study conducted in Free State province in South Africa by Kigozi and colleagues revealed that the default rate was 7,2% (12). Several pieces of literature have shown that nonadherence levels differ by geographical location, study population and duration involved in calculating nonadherence(6,24–26). Nonadherence is therefore complex, dynamic and multifactorial.

1.2.5 Extreme Nonadherence to TB medication and related factors

1.2.5.1 ***Intolerable side effects***

Extreme or high-level nonadherence refers to a situation where patients have a higher probability of defaulting treatment owing to the existence of critical factors. A single critical factor may lead to default or may combine with other factors leading to default as shown in Fig 1. One such factor is the presence of intolerable side effects. In a study conducted by Schaberg, 23% of participants defaulted TB treatment in the intensive phase owing to the side effect profile of pyrazinamide, isoniazid and rifampicin. The most intolerable side effects were arthralgia (joint pain), hepatotoxicity (liver damage) and exanthema (widespread rash) (14).

1.2.5.2 ***Lack of food and poverty***

Lack of food is a well-known critical factor for default in families in the lower wealth quantiles. Qualitative studies have revealed that patients in the intensive phase of treatment often complain about hunger and the need to take the pills on a full stomach. When food is not available, patients may resort to skipping doses resulting in suboptimal adherence (15). Poverty is a chief driver of the TB pandemic as it often dictates the housing type, access to quality health services, and availability of food. In a review of incentives for TB treatment, Lutge and colleagues discovered that provision of US$15 vouchers to patients on treatment improved treatment completion by 28% compared to the control group (16). This suggests that poverty eradication efforts can help in lowering default rates.

1.2.5.3 ***Family support***

Family support is an important factor in TB treatment adherence, as patients may face various challenges in adhering to their treatment regimen, such as medication side effects, financial constraints, or difficulty attending appointments(27,28). Family members can provide practical assistance and emotional support to help patients overcome these challenges and stay on track with their treatment. Additionally, family members can ensure that patients take their medication

through daily reminders. Family members who participate in TB clubs can gain a better understanding of the challenges faced by patients with TB and provide support and encouragement to help them adhere to their treatment(29).

Several studies have demonstrated the effectiveness of family support and clubs in improving treatment adherence and outcomes in TB patients. For example, a study by Cherkaoui and colleagues found that patients who had family support were significantly more likely to complete their TB treatment than those who did not have family support(30). Weiand and colleagues found that patients who participated in a TB club with their family members had higher rates of treatment success and were more likely to complete their treatment than those who did not participate in a club(31).

1.2.5.4 Lack of Knowledge

Lack of knowledge about tuberculosis (TB) and its treatment is a significant barrier to adherence. Patients who are not adequately informed about TB may not understand the importance of completing their full course of treatment, may not know how to properly take their medications, and may not be aware of the potential risks and benefits of TB treatment(32). Several studies have identified that patients who did not understand the importance of completing their full course of TB treatment were more likely to experience treatment failure or relapse(9,33,34).

1.2.5.5 Health care system and provider factors

One important factor is the quality of care provided by healthcare facilities. Patients who perceive the quality of care to be poor may be less likely to adhere to their treatment regimen. Mesfin and colleagues found that patients who reported dissatisfaction with the quality of care provided by their healthcare facility were more likely to have poor treatment adherence(35). Poor quality

services could be influenced by lack of adequate training of healthcare workers. Quality services must be patient centred, safe, effective, timely, efficient and equitable(36).

Another important factor is the availability of diagnostic and treatment services. Patients who have difficulty accessing these services may be less likely to adhere to their treatment regimen(37). When patient fail to access their treatments, they inevitably default leading to extreme nonadherence. Several studies have indicated that patients who had to travel long distances to access TB diagnostic and treatment services were more likely to have poor treatment adherence(33,38).

In addition, the attitudes and behaviour of healthcare providers can also affect treatment adherence. Patients who feel stigmatized or discriminated against by healthcare providers may be less likely to adhere to their treatment regimen. A study by Adane and colleagues revealed that patients who perceived stigma from healthcare providers were more likely to have poor treatment adherence(39).

1.2.5.6 ***Substance misuse***

Substance misuse, including alcohol, smoking and illicit drug abuse, can significantly affect nonadherence to tuberculosis (TB) treatment. Substance misuse is associated with a range of social, economic, and health problems, which can make it difficult for individuals to adhere to their TB treatment regimen. Several studies have shown that substance misuse is associated with poor adherence to TB treatment resulting in higher rates of treatment interruption and treatment failure among patients with TB(17,31,39). Substance misuse can also impact the effectiveness of TB treatment by interfering with drug metabolism and reducing drug absorption, which can lead to treatment failure and drug-resistant TB. Additionally, substance misuse can increase the risk of adverse drug reactions and drug interactions(9,40).

1.2.5.7 ***Pill burden, Comorbidities and Herbal medicine use***

Pill burden, which refers to the number of pills or medication doses that a patient must take each day, can be a significant barrier to adherence. Patients with high pill burdens may find it difficult to remember to take all of their medications at the correct times or may experience unpleasant side effects that make them hesitant to take their medication. Separate studies conducted by Schaberg and Jim indicated that high pill burden was a significant predictor of poor adherence to TB treatment(41,42).

Comorbidities, or the presence of other health conditions in addition to TB, can also impact adherence to TB treatment. Patients with comorbidities may be less likely to adhere to their TB treatment regimen if they are also managing other health conditions or experiencing side effects from other medications. Of note Pablos and Quaschning separately revealed that patients with comorbidities such as HIV and diabetes were more likely to experience treatment failure or relapse than patients without comorbidities(43,44).

Herbal medicine use may affect nonadherence to tuberculosis (TB) treatment by interfering with the absorption and metabolism of TB drugs resulting in reduced effectiveness of TB medications. Additionally, the use of herbal remedies may delay the diagnosis and treatment of TB, leading to more severe disease and poorer treatment outcomes(45).

1.2.5.8 ***Forgetfulness***

Forgetfulness was independently associated with defaulting treatment in most of the studies (11,17,18). The effect could be augmented by the low level of education, lack of caregivers and

reminders (10,19). Furthermore, the migratory pattern of patients particularly those with informal vocations may also result in default as they may forget to carry their pills along.

1.2.5.9 ***Symptomatic disease***

Researchers have had conflicting findings on the role of symptomatic disease in enhancing nonadherence. Akilew and colleagues argue that when patients remain symptomatic despite strictly abiding by treatment they may feel discouraged because of the lack of improvement in the clinical condition. This subsequently leads to treatment default (11). The resolution of symptoms was also associated with defaulting treatment as patients felt better and thought completing the regimen was no longer necessary (10,20).

1.2.5.10 ***Phase of treatment***

The phase and duration of treatment have been reported as determinants of non-adherence. TB treatment is offered for at least 6 months and can even be prolonged to as long as 24 months in the event of highly resistant TB strains. This chronicity of treatment may be discouraging to some patients who may subsequently default. Most studies have shown that default normally occurs in the continuation phase (15). This is partly explained by the transfer of treatment supervision to community and family members who may have competing interests. However, some researchers have identified the intensive phase as the most defaulted period (5,21).

1.2.5.11 ***Vicarious experience***

Vicarious experience, which refers to a patient's observation of other individuals' experiences with tuberculosis (TB) treatment, can play a role in nonadherence to TB treatment. Patients who observe negative experiences, such as adverse side effects or lack of improvement in symptoms, in others may become discouraged or fearful and may be more likely to discontinue their own

treatment(46,47). On the other hand, positive vicarious experiences, such as observing successful treatment outcomes in others, may motivate patients to adhere to their treatment regimen(47).

1.2.6 Conceptual Framework

Fig 1 shows a conceptual model which illustrates the various factors identified in the literature as important determinants of non-adherence. The model was adapted from Reda (22) who categorized determinants of adherence to treatment as medication; healthcare system; healthcare provider; patient; sociocultural and disease-related factors. There is an interdependence between critical factors leading ultimately to extreme non-adherence. Extreme nonadherence impacts the patient outcomes resulting in death (23), TB relapse (24,25), resistant TB strains (20,26,27), extrapulmonary complications of TB and sustained community transmission (9).

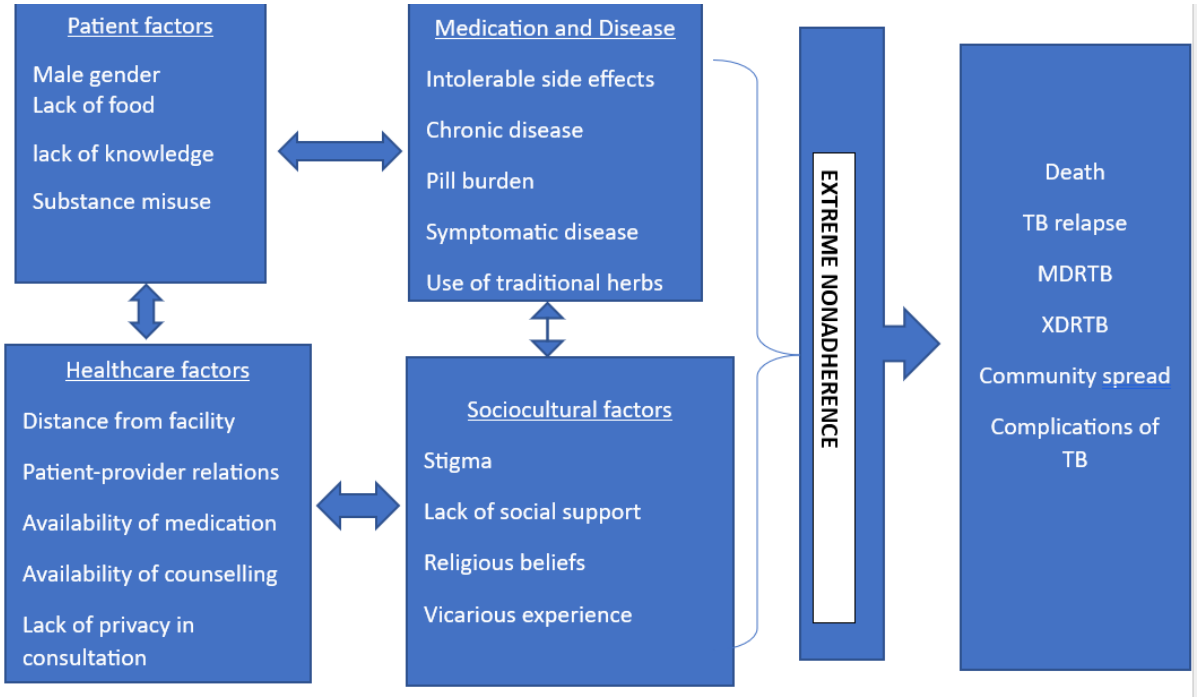


Figure 1: Factors influencing nonadherence to TB treatment: adapted from Reda (22)

1.3 Problem statement

South Africa established a national TB cure rate target of 85%, however, a number of provinces have fallen short of this landmark with some recording cure rates as low as 41% (48). Despite the epidemiological information provided, not many studies on the subject have been carried out in the Nelson Mandela district.. There is a gap in particular in the knowledge of the prevalence of extreme nonadherence to TB treatment and factors associated with it in the area

1.4 Justification

TB is a curable disease. The correct and consistent use of efficacious combination therapy as prescribed will cut the chain of transmission (22). The study will show the factors that lead to extreme nonadherence in one of the high TB burden districts in South Africa. The knowledge of extreme nonadherence factors will enable the formulation and implementation of sustainable tailor-made interventions rather than ad hoc generalizations. The study will also enable the formulation of algorithms for the identification of patients at high risk of default and address their needs with the aim of retaining them to care.

1.5 Research Question

What are the factors associated with extreme nonadherence among adult defaulters attending the Gqeberha clinic in Nelson Mandela District, South Africa between April 2018 and September 2019?

1.6 Aim

To estimate the prevalence of extreme nonadherence to TB treatment and determine the factors associated with extreme nonadherence to TB treatment among adult defaulters attending Gqeberha clinic in Nelson Mandela District, South Africa between April 2018 and September 2019.

1.7 *Objectives*

1. To describe the characteristics of adult defaulters attending Gqeberha clinic in Nelson Mandela District, South Africa between April 2018 and September 2019.
2. To determine the prevalence of extreme nonadherence to TB treatment among adult defaulters attending Gqeberha clinic between April 2018 and September 2019.
3. To establish the factors associated with extreme nonadherence to TB treatment among adult defaulters attending Gqeberha clinic between April 2018 and September 2019

2 METHODOLOGY

2.1 Description of Primary study

The primary study was conducted in Nelson Mandela district by Best Health Solutions with the aim of identifying reasons for default among clients attending Gqeberha clinic. 144 participants were identified from an electronic TB register of adults receiving TB services between April 2018 and September 2019 at Gqeberha clinic. All patients who were willing to be interviewed and consented were interviewed in their homes using a structured questionnaire. The study employed a mixed method approach.

2.2 Study design.

Secondary data from a cross sectional study was used to determine the factors associated with extreme nonadherence to TB medication among adult defaulters attending Gqeberha clinic in Nelson Mandela district.

2.3 Study site

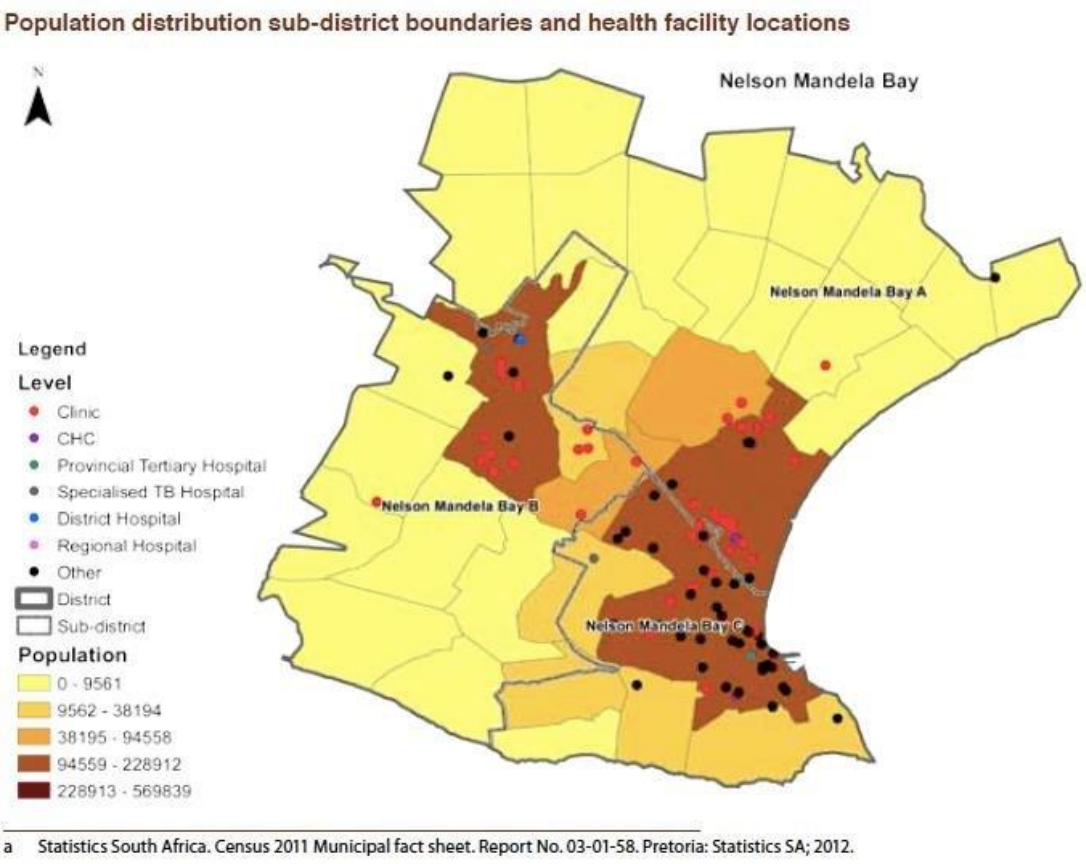


Figure 2: Map of Nelson Mandela District(49)

The study was done in Nelson Mandela district which is situated on the Southern coast of South Africa, in the Eastern Cape province. Gqeberha clinic is found in Walmer township and has a population of 1 334 883 people according to the Community Survey of 2016(50). The economy of Nelson Mandela is driven chiefly by manufacturing, finance and community service. However, the unemployment rate is high and was estimated to be about 37% according to the Census of 2011. About 38.7% of the population was found to be living below the poverty datum line from

the Census of 2011. Over the period between 2008 and 2018, the population growth rate of Nelson Mandela district stood at 1.47% which is almost double that of the Eastern Cape province which is 0.94%. Lastly, about 6.9% of the population live in informal dwellings which are often referred to as shacks(50). Poor socioeconomic status, overcrowding and poor housing type have been documented in literature as risk factors for contracting TB.

2.4 Study population.

The study population comprised adults who defaulted TB treatment at Gqeberha clinic in Nelson Mandela between April 2018 and September 2019. This clinic was chosen because it has historically reported high numbers of TB defaulters in Nelson Mandela district. Adults in the study were defined as people with at least 18 years of age.

2.5 Sampling

The study utilized all participants from the primary study who consented, therefore the sample size was 144. The power of the study was estimated to be 95.0 using Stata Version 17. The calculations and assumptions for power calculation are shown in appendix 8.

2.5.1 Inclusion criteria

- Defaulters identified from the TB register at Gqeberha clinic between April 2018 and September 2019
- On anti-tuberculosis drugs for at least 3 months,
- At least 18 years of age
- completed informed consent.

2.5.2 Exclusion criteria

- Incomplete records on treatment adherence responses shown in section 3.5 of the questionnaire in appendix 6.

2.6 Data collection

Data was sought from the Gqeberha clinic gatekeeper by registering online on the Best Health Solutions website and applying for permission to use the dataset. A structured validated questionnaire was utilized in the primary study which focused on factors relating to healthcare system, medicines, socio-economic variables and demography of patients attending Gqeberha clinic. The research tool had 25 questions highlighting the determinants of non-adherence and is attached in appendix 6.

2.7 Data management and analysis

2.7.1 Data cleaning

Deidentified data from the primary study was used. A search for missing data, out-of-range data, duplicates and wrong formats was carried out. Data inconsistencies were checked and corrected with the subsequent recording of changes made to the database.

2.7.2 Data backup

The 3-2-1 rule was be employed in a backup of data. Three forms of backup were used namely a flash disk, external hard drive and online backup. The data was encrypted, and password protected in all forms of backup. Google Drive was utilized as the online storage method whereas the flash disk was stored at a remote site from the researcher.

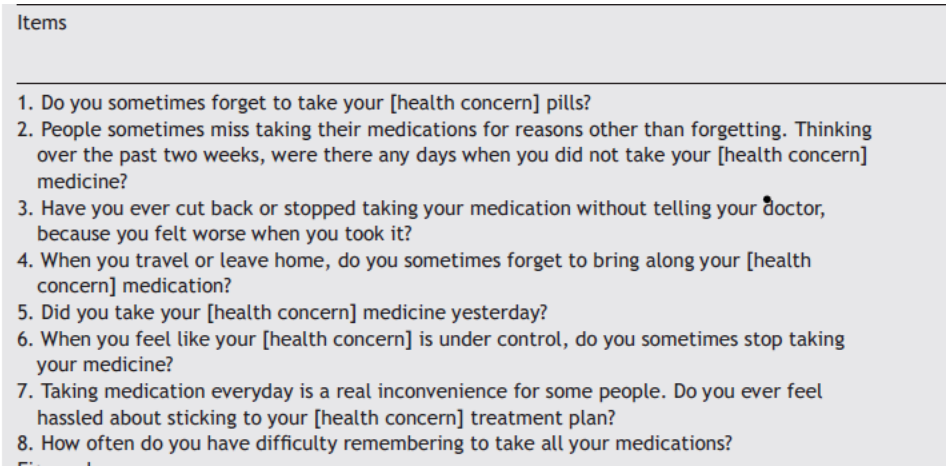
2.7.3 Data archiving

Data was archived in compliance with the regulations of the University of Witwatersrand. The data dictionary, codebook and complete documentation of variables was provided.

2.8 Outcome variable

The primary outcome was extreme nonadherence which was coded 1. This was measured using the Morisky Medication Adherence 8-item scale (MMAS-8)(51).The MMAS-8 scale was chosen because of its extensive use in literature in studies where adherence was self-reported(51–54). Additionally, it helps to assess the impact of behaviour on adherence patterns(51). Moreover, the research instrument used in the primary study assessed adherence using questions on the MMAS-8 scale. The outcome was derived from scores generated from section 3.5 of the adherence questionnaire in the appendix 6. Only 7 questions were available (excluding question: Did you take your medication yesterday?). A “yes” response was assigned a score of 1 and a “no” was equated to a score of 0. The last question which has ordinal responses was recoded so that the “never” and “Once in while” responses were treated as a “no” whilst the remaining responses were

treated as “yes”. The total score range was 1-7. Extreme nonadherence was defined by a score of at least 4 whilst nonextreme nonadherence was be represented by a score below 4(55).



Items
1. Do you sometimes forget to take your [health concern] pills?
2. People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your [health concern] medicine?
3. Have you ever cut back or stopped taking your medication without telling your doctor, because you felt worse when you took it?
4. When you travel or leave home, do you sometimes forget to bring along your [health concern] medication?
5. Did you take your [health concern] medicine yesterday?
6. When you feel like your [health concern] is under control, do you sometimes stop taking your medicine?
7. Taking medication everyday is a real inconvenience for some people. Do you ever feel hassled about sticking to your [health concern] treatment plan?
8. How often do you have difficulty remembering to take all your medications?

Figure 3: Morisky Medication Adherence 8 item scale(54)

2.9 Exposure variables

The exposure variables were classified as patient factors, sociodemographic factors, health system factors and disease and medicine-related factors as shown in Table 1 below.

Table 1: List of variables extracted.

1.0	DEMOGRAPHIC INFORMATION	
1.1	**Ethnicity**	
1.2	**Gender**	

1.3	**Type of dwelling**	
1.4	**Employment status**	
1.5	**Income**	
1.6	**Age**	
1.7	**Marital status**	
1.8	**Highest Education status**	
2.0	PATIENT SATISFACTION	
2.1	**Healthcare workers treat me with respect and dignity**	
2.2	**Healthcare workers provide all information**	
2.3	**Medication pickup is done in clean areas**	
2.4	**Medication pickup is done in safe areas**	
2.5	**Medication is always available**	
3.0	HEALTHCARE SYSTEM FACTORS	
3.1	**I would prefer to pickup my medication outside clinic hours (8am-5pm)**	
3.2	**The waiting time to pickup medication is always less than 2 hours**	
3.3	**I stay less than 10km from this clinic**	
4.0	SOCIOECONOMIC FACTORS	
4.1	**I am always having adequate food while taking my medication**	
4.2	**My income can cover my basic needs**	
4.3	**It costs me less than R50 to pickup my medication**	
5.0	DISEASE AND MEDICINE RELATED FACTORS	
5.1	**Did you experience any medication side effects whilst taking TB treatment?**	
5.2	**Did side effects make you stop taking treatment?**	
5.3	**Where you taking any other medications beside TB treatment?**	

5.4	**Did this treatment have any effect on you taking TB treatment?**	
6.0	FAMILY SUPPORT	
6.1	**I live with my family**	
6.2	**Did you tell your family that you have TB?**	
6.3	**My family ensures that I take my medication**	
7.0	TREATMENT ADHERENCE (OUTCOME VARIABLE)	
7.1	**Do you sometimes forget to take your pills?**	
7.2	**Thinking over the past two weeks, were there any days when you did not take your medicine?**	
7.3	**Did you cut back or stopped taking your medication without telling your doctor/ nurse, because you felt worse when you took it?**	
7.4	**When you travel or leave home, do you sometimes forget to bring along your medication?**	
7.5	**When you feel like your health is under control, do you stop taking medication?**	
7.6	**Taking medication every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?**	
7.7	**How often do you have difficulties remembering to take your medications?**	

2.10 Data Analysis

Data from the primary study was imported into Stata version 17. All data management was done in Stata. The descriptive statistics was performed in Stata version 17.

Analysis of Objective 1: ***To describe the characteristics of adult defaulters attending Gqeberha clinic in Nelson Mandela District, South Africa between April 2018 and September 2019.***

Categorical variables such as educational level, ethnicity and nationality were presented in table 2 using frequencies and percentages. The continuous variables: age, income and household size were summarised by mean, standard deviation, median and interquartile range.

Analysis of Objective 2: ***To determine the prevalence of extreme nonadherence to TB treatment among adult defaulters attending Gqeberha clinic between April 2018 and September 2019***

Pearson's Chi-square and Fishers exact were utilized to generate cell frequencies used to estimate the overall prevalence of extreme nonadherence against the explanatory variables as appropriate.

Analysis of Objective 3***: To establish the factors associated with extreme nonadherence to TB treatment among adult defaulters attending Gqeberha clinic between April 2018 and September 2019***

Univariate binary logistic regression was performed between the outcome and each explanatory variable to assess association. This was reported by odds ratios (OR), 95% confidence intervals and p- values. The level of significance was set at 0.05. The data is presented in Table 3. Multivariable logistic regression analysis was conducted on all explanatory variables. Model building was done using the stepwise forward variable selection with a cut off set at 0.2. The results are displayed in table 4 and indicate adjusted Odds ratios (aOR) and corresponding 95% confidence intervals and p-values. Variance Inflation factors (VIF) were checked to detect multicollinearity in model building.

2.11 Ethical Considerations

Ethical clearance was applied from the Medical Human Research Ethics Committee (HREC) of the University of the Witwatersrand. This is shown in appendix 3. In addition, authorization to use the dataset was sought from the gatekeeper as shown in Appendix 4. The dataset was used strictly for academic purposes only.

3 CHAPTER THREE: RESULTS

This section presents the results of the study in response to the study objectives. Tables were utilized to display study findings. Descriptive statistics were presented using percentages, proportions and frequencies. Univariate and multiple logistic regression results were reported using odds ratios (OR), adjusted odds ratio (AOR), and their corresponding 95% confidence intervals (CI) and p- values as appropriate.

3.1 Description of study participants

A total of 144 participants were enrolled in the primary study. However, only 139 (96.5%) managed to complete records on the treatment adherence questionnaire section. Table 2 below summarises the study characteristics. The overall number of TB defaulters who had extreme nonadherence was 18 (12.9%). Most TB defaulters 65.2% (n=90) were men. The median age of participants with extreme nonadherence was 35.5(IQR: 29;41) whilst those with nonextreme nonadherence had a median age of 32(IQR: 24;41). 73.4% (n =102) of the study participants stayed in formal dwellings, 79.1% (n =110) were unemployed, 68.8% (n =95) had not attained matric level qualification and 78.4% (n =109) were either single, divorced or separated. A larger proportion of participants, 79.9% (n =111) stayed within 5km radius of Gqeberha clinic, 65.5% (n =91) experienced waiting times of less than 2hours at the health facility and 84.2% (n =117) acknowledged constant availability of medicines at the health facility. However, 69.1% (n =96) did not have a family member who encouraged them to attend clinic visits, 64% (n =89) lacked adequate food whilst taking medication, and 80.6% (n=112) had inadequate income to cover their basic needs whilst on treatment.

Table 2: Description of study characteristics of adult defaulters attending Gqeberha clinic

Characteristics	Overall n (%)	Nonadherence to TB treatment	
		Nonextreme nonadherence N= 121(87.1%)	Extreme Nonadherence N=18(12.9%)
Gender			
Female	48(34.8)	43 (35.8%)	5(27.8%)
Male	90(65.2)	77(64.2%)	13(72.2%)
Type of Dwelling			
Formal	102(73.4)	90(88.2%)	12(11.8%)
Informal	37(26.6)	31(25.6%)	6(33.3%)
Employment Status			
Employed	29(20.9)	26(21.5%)	3(16.7%)
Unemployed	110(79.1)	95(78.5%)	15(83.3%)
Marital status			
Married	30(21.6)	26(21.5%)	4(22.2%)
Not married	109(78.4)	95(78.5%)	14(77.8%)
Highest education level			
Matric level and above	43(31.2)	40(33.3%)	3(16.7%)
Below Matric	95(68.8)	80(66.7%)	15(83.3%)
Waiting time to pick up medication is always less than 2hours			
Yes	91(65.5)	80(66.1%)	11(61.1%)
No	48(34.5)	41(33.9%)	7(38.9%)
I stay less than 5km from this clinic			
Yes	111(79.9)	97(80.2%)	14(77.8%)
No	28(20.1)	24(19.8%)	4(22.2%)
It cost me less than R50 to pick up my medication per visit			
Yes	134(96.4)	116(95.9%)	18(100%)
No	5(3.60)	5(4.1%)	0(0%)
Health workers treat me with respect and dignity			
Yes	63(45.3)	53(43.8%)	10(55.6%)
No	76(54,7)	68(56.2%)	8(44.4%)
Health workers provide all the information about my medication			
Yes	62(44.6)	56(46.3%)	6(33.3%)
No	77(55.4)	65(53.7%)	12(66.7%)
Medication pickups are done in safe areas			
Yes	119(85.6)	102(84.3%)	17(94.4%)
No	20(14.4)	19(15.7%)	1(5.6%)
Medication pickups are accessible to the disabled			
Yes	117(84.2)	101(83.5%)	16(88.9%)
No	22(15.8)	20(16.5%)	2(11.1%)

My medication is always available			
Yes	130(93.5)	113(93.4%)	17(94.4%)
No	9(6.5)	8(6.6%)	1(5.6%)
My family encourages me to attend clinic visit			
Yes	43(30.9)	39(32.2%)	4(22.2%)
No	96(69.1)	82(67.8%)	14(77.8%)
My family encourages me to adhere to medication			
Yes	62(44.6)	54(44.6%)	8(44.4%)
No	77(55.4)	67(55.4%)	10(55.6%)
My family ensures that I have taken my medication			
Yes	35(25.2)	32(26.4%)	3(16.7%)
No	104(74.8)	89(73.6%)	15(83.3%)
My family accompanies me to clinic visits			
Yes	6(4.3)	6(5.0%)	0(0%)
No	133(95.7)	115(95.0%)	18(100%)
Clubs encourage couple counselling and testing			
Yes	84(60.4)	73(60.3%)	11(61.1%)
No	55(39.6)	48(39.7%)	7(38.9%)
I always have adequate food whilst taking medication			
Yes	50(36.0)	43(35.5%)	7(38.9%)
No	89(64.0)	78(64.5%)	11(61.1%)
My income can cover my basic needs			
Yes	27(19.4)	22(18.2%)	5(27.8%)
No	112(80.6)	99(81.8%)	13(72.2%)
Where you taking other medication whilst on TB medication?			
Yes	83(59.7)	75(62.0%)	8(44.4%)
No	56(40.3)	46(38.0%)	10(55.6%)
Age in years			
Mean (sd)		34(11,7)	35.3(10.3)
Median (IQR)		32(24;41)	35.5(29;41)
Number of people per household			
Mean (sd)		4.2(1.6)	4.4(1.5)
Median (IQR)		4(3;5)	4(3;6)
Average monthly income			
Mean (sd)		R947(1788)	R894(1874)
Range (minimum-maximum)		(R0;R5200)	(R0;R6500)

Table3 :Distribution of responses of participants with extreme nonadherence to TB treatment

Morisky Medication Scale instrument	N=18	
	Yes [n(%)]	**No [n(%)]**
Do you sometimes forget to take your pills?	17(94.4)	1(5.6)
People sometimes miss taking their medication for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your medicine?	18(100.0)	0(0.0)
Did you cut back or stopped taking your medication without telling your doctor/ nurse, because you felt worse when you took it?	2(11.1)	16(88.9)
When you travel or leave home, do you sometimes forget to bring along your medication?	8(44.4)	10(55.6)
When you feel like your health is under control, do you stop taking medication?	13(72.2)	5(27.8)
Taking medication everyday is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?	13(72.2)	5(27.8)
How often do you have difficulties to remember to take your medications?	**More than once [n(%)]**	**Once or never[n(%)]**
	13(72.2)	5(27.8)

Table 3 shows the distribution of responses by participants who had extreme nonadherence. All participants reported failure to take medication for some days in the past two weeks whilst 94.4%(n=17) reported forgetfulness as reason for nonadherence to treatment. The majority of participants with extreme nonadherence divulged improvement in health status as a reason for nonadherence. 72.4% (n=13) disclosed that taking medication daily was a real inconvenience.

3.2 Factors associated with extreme nonadherence to TB treatment.

3.2.1 Univariate analysis

Factors associated with extreme nonadherence to TB treatment were assessed using logistic regression model shown in table 4. At univariate level, none of the explanatory variables showed a statistically significant relationship with the outcome variable.

Table 4: Univariate analysis of factors associated with extreme nonadherence to TB treatment.

Characteristics	**Univariate Model**	
	OR (95% CI)	P-Value
Age	1.01 (0.97-1.05)	0.646
Number of people per household	1.12 (0.82-1.54)	0.461
Average monthly income	1.00 (0.99-1.00)	0.907
Gender		
Female	Ref	
Male	1.45 (0.48-4.35)	0.505
Type of Dwelling		
Formal	Ref	
Informal	1.45 (0.50-4.20)	0.491
Employment status		
Employed	Ref	
Unemployed	1.37 (0.37-5.09)	0.640
Highest Education level		
Below Matric	Ref	
Matric level and above	0.40 (0.11-1.46)	0.166
Marital Status		
Not married	Ref	
Married	1.04 (0.32-3.44)	0.944
Waiting time to pick up medication is always less than 2hours		
Yes	Ref	
No	1.24 (0.45-3.44)	0.677
I stay less than 5km from this clinic		
Yes	Ref	
No	1.15 (0.35-3.83)	0.814
Health workers treat me with respect and dignity		
Yes	Ref	
No	0.62 (0.23-1.69)	0.353
Health workers provide all the information about my medication		
Yes	Ref	
No	1.72 (0.61-4.89)	0.307
Medication pickups are done in safe areas		

Yes	Ref	
No	0.32 (0.04-2.52)	0.276
Medication pickups are accessible to the disabled		
Yes	Ref	
No	0.63 (0.13-2.96)	0.560
My medication is always available		
Yes	Ref	
No	0.83 (0.10-7.06)	0.865
My family encourages me to attend clinic visit		
Yes	Ref	
No	1.66 (0.51-5.39)	0.395
My family encourages me to adhere to medication		
Yes	Ref	
No	1.01(0.37-2.73)	0.988
My family ensures that I have taken my medication		
Yes	Ref	
No	1.80 (0.49-6.62)	0.378
Clubs encourage couple counselling and testing		
Yes	Ref	
No	0.97 (0.35-2.67)	0.950
I always have adequate food whilst taking medication		
Yes	Ref	
No	0.87 (0.31-2.40)	0.782
My income can cover my basic needs		
Yes	Ref	
No	0.58 (0.19-1.79)	0.341
Where you taking other medication whilst on TB medication?		
No	Ref	
Yes	0.49 (0.18-1.33)	0.163

3.2.2 Multiple logistic regression

Table 5 shows the factors associated with extreme nonadherence to TB treatment among adult defaulters after adjusting for all covariates. Those who took other medication besides TB treatment had 0.33 times odds (95% CI: 0.11-0.97) of extreme nonadherence compared to their contrasting peers. This was the only statistically significant finding with p-value of 0.044.

Table 5:Final adjusted model of factors associated with extreme nonadherence to TB treatment.

Characteristics	Univariate Model		Adjusted Model	
	OR (95% CI)	P-Value	OR (95% CI)	P-value
My income can cover my basic needs				
Yes	Ref		Ref	
No	0.58 (0.19-1.79)	0.341	0.43 (0.12-1.47)	0.177
Health workers treat me with respect and dignity				
Yes	Ref		Ref	
No	0.62 (0.23-1.69)	0.353	0.42 (0.14-1.26)	0.123
Were you taking other medication whilst on TB medication?				
No	Ref		Ref	
Yes	0.49 (0.18-1.33)	0.163	0.33 (0.11-0.97)	0.044*
Health workers provide all the information about my medication				
Yes	Ref		Ref	
No	1.72 (0.61-4.89)	0.307	2.27 (0.74-6.97)	0.152
My family encourages me to attend clinic visit				
Yes	Ref		Ref	
No	1.66 (0.51-5.39)	0.395	2.26 (0.66-7.74)	0.194
Highest Education level				
Below Matric	Ref		Ref	
Matric level and above	0.40 (0.11-1.46)	0.166	0.31 (0.08-1.25)	0.100

3.2.3 Model diagnostics

Post estimation tests indicated that the fitted adjusted model was a good fit (p-value =0.376) and had an area under curve of 71,2% which is high. The post-regression multicollinearity analysis of the final logistic regression model showed a VIF score of 1.84 indicating no significant multicollinearity between the covariates.

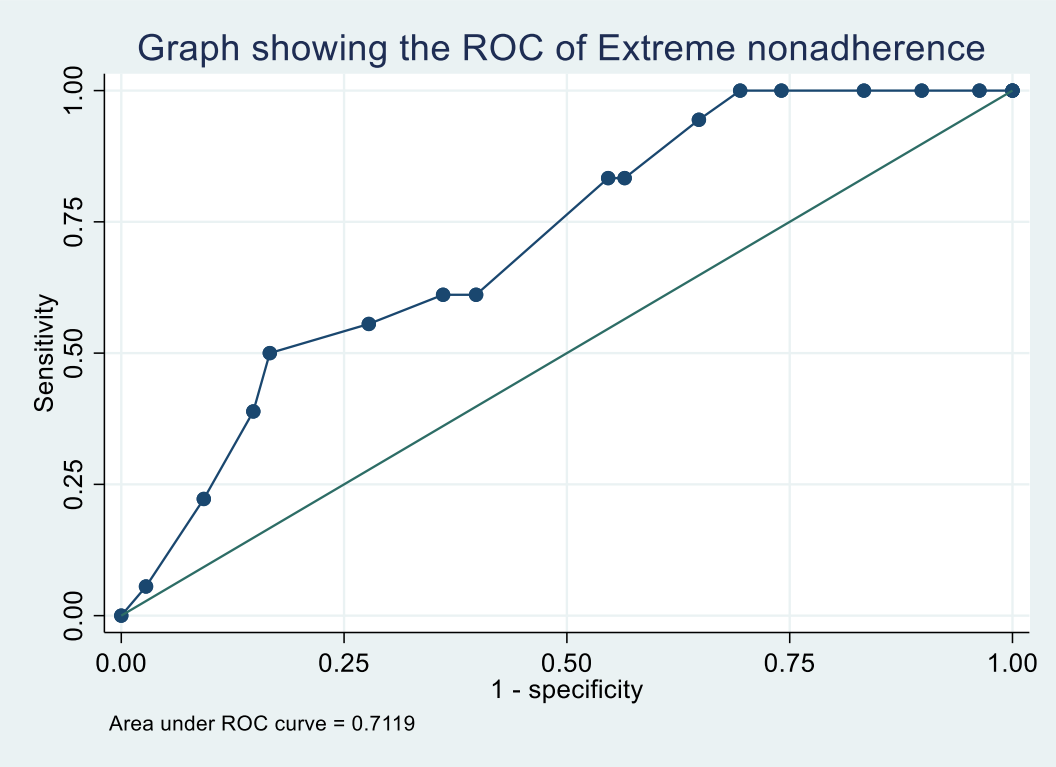


Figure 4: ROC Analysis of Extreme nonadherence to TB treatment among adult defaulters

4 Chapter 4: Discussion

This section presents the discussion of the results of the study in relation to similar studies. The aim of the study was to determine the factors associated with extreme nonadherence to TB treatment among adult defaulters attending the Gqeberha clinic in Nelson Mandela District, South Africa between April 2018 and September 2019. The participants involved in the study were of the lower wealth quantile. The prevalence of extreme nonadherence to TB treatment was 12.9% and multiple drug use was the only statistically significant factor associated with extreme nonadherence.

4.1 Prevalence of Extreme nonadherence and sociodemographic profile

The study revealed that the prevalence of extreme nonadherence to TB treatment among adult defaulters attending Gqeberha clinic was 12.9%. This is a novel finding. A Malawian study by Chirwa and colleagues revealed that the levels of nonadherence to treatment ranged from 1.3% to 22.9% depending on the phase of treatment and the number of treatment days missed(22). Ajema and colleagues discovered that in Southern Ethiopia the levels of nonadherence to TB treatment ranged between 10% and 16.5% basing on treatment days missed(9).The findings were similar to my study although different methods were used in calculating levels of nonadherence. The participants in the study were from low-income families with the majority being unemployed, having low educational attainment, not currently married and having inadequate food. Additionally, the majority of the defaulters were men. These findings support the evidence that TB is disease of poverty whose risk factors include unemployment, male sex and low educational attainment(1,27,39)

4.2 Factors associated with extreme nonadherence.

4.2.1 Use of multiple drugs

The study revealed that multiple drug use was protective against extreme nonadherence (aOR = 0.33, 95% CI: 0.11-0.97). Richard Grant and colleagues had a similar finding which they identified high medication adherence rates among patients on multiple drugs(56). Similarly, a Brazilian study by Rodriguez showed a high adherence rate to multiple drugs of 86.5%(57). This finding might be explained by the fact patients who have several long-term illnesses (multimorbidity) may have adjusted to taking treatments routinely. Furthermore, they are more informed on consequences of nonadherence owing to interacting with healthcare professionals on multiple occasions. On the contrary, most studies have identified the use of multiple drugs as a barrier to adherence to treatment(53,58–60).Mekonnen and Azagew's study in Ethopia showed a 6 times odds of nonadherence to TB treatment in patients with comorbidities(58).Patients

without comorbidities were also noted to have better quality of life in a study by Yadav and colleagues(53). Multiple reasons have been gathered which include pill burden, adverse drug reactions and drug to drug interactions. Additionally, the economic impact of multiple drugs is often heavy on low- and middle-income families where a financial constraint may be felt leading to treatment default(61).

4.2.2 Provision of health information

The study revealed that 66.7% (12/18) of the extreme non adherers had not received health education at the facility. The study showed no association between provision of health education and extreme nonadherence to TB treatment (aOR=2.27, 95% CI: 0.74-6.97). This is contrary to most studies which have revealed that patients who are cognizant of the side effect profile of their prescribed medication are more likely to adhere to treatment(27,54,62,63). The provision of information on Tuberculosis empowers communities on its etiology, mechanism of spread and prevention methods. Additionally, patients are equipped with knowledge on the correct dose, frequency and duration of treatment, drug interactions, and raises the awareness on potential side effects(20,27).

4.2.3 Educational level

68.8% of the participants had not attained matric level. Interestingly, the majority of the extreme non adherers (83.3%) had an educational attainment below matric level. Attainment of higher levels of education is often associated with better comprehension of instructions on treatment regimens and ultimately leads to improved adherence(64,65). Contrary to findings in reviewed literature, the study showed no association between educational attainment and extreme nonadherence (aOR = 0.31, 95% CI: 0.08-1.25).

4.2.4 Family support

Family support was assessed in this study by variables which identified participants who had a family member encouraging them to attend clinic visits, accompaniment to clinic appointments and encouragement on treatment adherence at home. The study revealed that 69.1% (96/138) of the participants had no one to encourage them to attend clinic visits. Similarly, the majority of extreme non adherers (14/18) attested to lack of encouragement to attend clinic appointments. Of note, all extreme no adherers had no one to accompany them to attend clinic visits. 55.4% of the defaulters had no one to encourage them on treatment adherence at home. A similar trend was

observed among the extreme non adherers where 55.6% (10/18) lacked family encouragement to adhere to treatment at home. There was no association between family encouragement and extreme nonadherence (aOR=2.26, 95% CI : 0.66-7.74). This finding is contrary to most studies which have identified the importance of family support in improving treatment adherence(2,20,37,66). An appraisal of compliance to TB in India by Motappa and colleagues revealed that nonadherence to TB treatment was 9.22 times higher in participants who lacked family support(28).

4.3 Strengths of the study

The study was conducted in one of districts with the highest TB burden in South Africa hence it provides an insight on the common challenges experienced by the population. The study therefore serves as a steppingstone where hypotheses can be generated for future studies.

4.4 Influence of limitations on study results

The dataset used was designed to solely meet the purposes of the primary study. As a result, some important variables in the conceptual framework were absent such as HIV status, substance use, presence of comorbidities and presence of adverse side effects. The study relied on self-reporting of adherence which may have introduced social desirability and recall bias. This could have overestimated the measure of association. The study findings are not generalizable since the study was conducted in one clinic. The small sample size might have affected the significance of multiple factors hence the need for larger studies.

4.5 Conclusion

The prevalence of extreme nonadherence to TB treatment among adult defaulters was low. The participants involved in the study were from low-income families with the majority being unemployed, having low educational attainment and lacking adequate food during treatment course. The use of multiple drugs was significantly associated with lower odds of extreme nonadherence. There is need to intensify programs aimed at improving adherence to treatment if the end TB by 2035 goal is to be realized.

4.6 Recommendations

Tuberculosis is a disease of poverty hence eradication of poverty is crucial. The government of South Africa should come up with strategies aimed at empowering the marginalized societies and improving employment rates among disadvantaged populations. The department of health (DOH) should intensify information, education and communication (IEC) programs to improve the awareness of Tuberculosis and emphasize treatment adherence. Community driven interventions (CDIs) can be utilized in the distribution of TB treatment particularly in the continuation phase. This will help to retain patients particularly males who have a poor health seeking behaviour. The concept of treatment clubs can also be utilized during the continuation phase. In this method, patients who are being treated for TB are gathered in groups based on proximity of their respective households. A club representative will be tasked to distribute treatment to his peers. Treatment clubs can also help patients to share their experiences on the treatment journey and hence gain emotional support along the way. Family support is a crucial aspect in ensuring adherence to treatment for patients on long-term regimens. Therefore, it is important for healthcare professionals to encourage patients to attend clinic visits with relatives or guardians.

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5 APPENDIX

5.1 Appendix 1: Plagiarism declaration

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I ELISHA CHIPISE (Student number: 2604549) am a student registered for the degree of MASTERS EPIDEMIOLOGY IMPLEMENTATION SCIENCE in the academic year 2024.

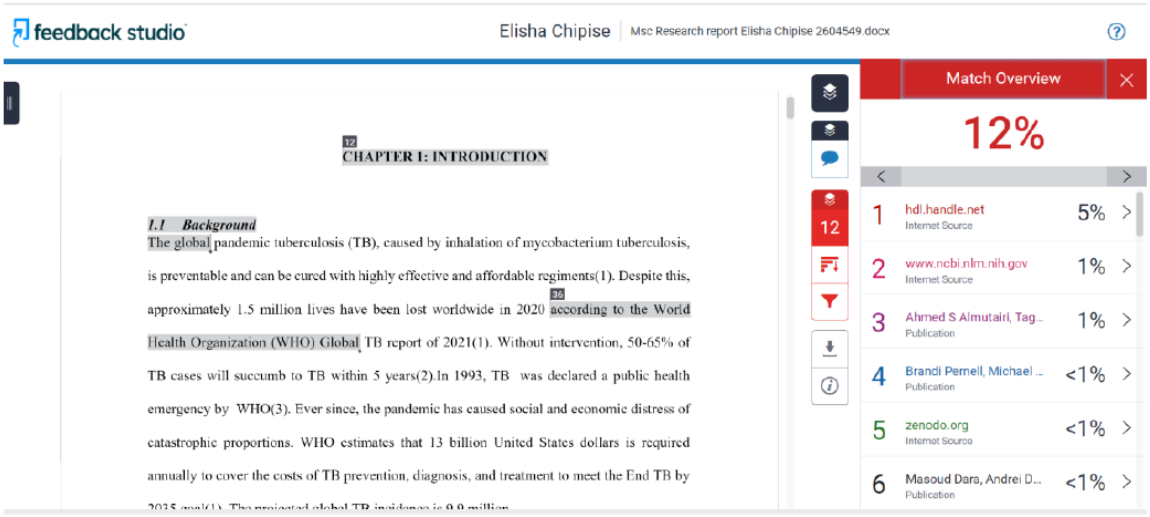
I hereby declare the following:

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

Signature:  Date: 20/02/2024

1

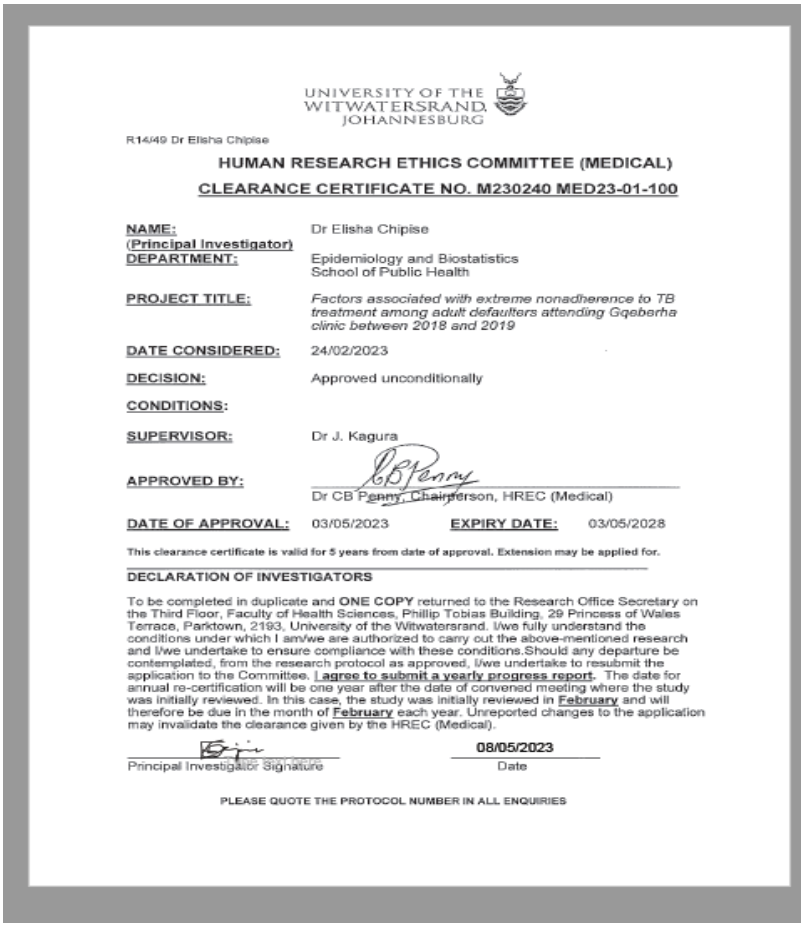
5.2 Appendix 2:Turnit in Report



Name of Supervisor: Dr Juliana Kagura

Signature : 

5.3 Appendix 3:Human Ethics Certificate



UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R14/49 Dr Elisha Chipise

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M230240 MED23-01-100

NAME: (Principal Investigator)	Dr Elisha Chipise
DEPARTMENT:	Epidemiology and Biostatistics School of Public Health
PROJECT TITLE:	*Factors associated with extreme nonadherence to TB treatment among adult defaulters attending Gqeberha clinic between 2018 and 2019*
DATE CONSIDERED:	24/02/2023
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr J. Kagura
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	03/05/2023 **EXPIRY DATE:** 03/05/2028

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

DECLARATION OF INVESTIGATORS

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

Principal Investigator Signature — **08/05/2023** Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

5.4 Appendix 4:Permission letter from Gatekeeper

The Best Health Solutions
6 2nd Street, Orange Grove, Johannesburg, South Africa Phone: +27 (0)11 057 6661 Fax: +27 (0) 86 598 5221
E-Mail: info@besthealthsolutions.co.za Web: www.besthealthsolutions.co.za

07 February 2023

To whom it may concern

Re: Consent to use data

I hereby give permission to Elisha Chipise, a Masters in Epidemiology in Implementation Science student at the University of Witwatersrand to access and use data on TB defaulters from Gqeberha clinic owned by Best Health Solutions. The data will be used for verification, cleaning, analysis, reporting and publishing.

The data will only be used to fulfill the requirements of the Masters in Epidemiology in Implementation Science at the University of Witwatersrand. The data may not be reproduced in any form without the permission of Best Health Solutions. Use of the data for other purposes will not be permitted.

Your assistance will be greatly appreciated

Dr. Ndumiso Tshuma
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5.5 *Appendix 6:Adherence questionnaire*

	Section 1: Demographic Measures											
1	Ethnicity	Black 1	White 2	Asian 3	Coloured 4	2	Gender	Male 0	Female 1			
3	Type of dweling	Formal 1	Informal 2		4	Employment status		Unemployed 1	Employed 2			
5	Nationality	South African 1	Non South African 2		6	Average monthly income			7	Age		
8	Marital Status	Single 1	Married 2	Divorced 3	Cohabitating 4	Widowed 5						
9	Highest Education	below matric 1	Matric 2	Certificate 3	Diploma 4	Degree 5	10	Number of people in household				
	Section 2: Health status											
11	Date tested TB positiv	month/ year	12	Date started TB Treatme	month/ year	13	umber of tablets currently taken daily			2	3	4
	Section 3: Measurement of immediate outcome											
	Indicate the extent to which you agree or disagree to the following statements where											
	1= Strongly Disagree, 2= Disagree, 3= Neutral/ Don't know, 4= Agree, 5= Strongly Agree											
	Section 2. Service Delivery Factors							1	2	3	4	5
	3. Healthcare system related							1	2	3	4	5
14	I would prefer picking my TB medication outside clinic hours (8am -5pm)							1	2	3	4	5
15	The waiting time to pick up medication is always less than 2 hours							1	2	3	4	5
16	I stay less than 10 km from this clinic							1	2	3	4	5
	3.4 Patient satisfaction											
18	Healthcare workers treat me with respect and dignity							1	2	3	4	5
19	Healthcare workers provide all the health information							1	2	3	4	5
20	Medication pick ups are done in clean areas							1	2	3	4	5
21	Medication pick ups are done in a safe area							1	2	3	4	5
22	My medication is always available							1	2	3	4	5
	Section 3. socio-economic factors											
	Socioeconomic variables											
23	I am always having adequate food to eat while taking medication							1	2	3	4	5
24	My income can cover my basic needs							1	2	3	4	5
25	It cost me less that R50 to pick up my medication per visit							1	2	3	4	5
	3**.3 Family support**											
26	I leave with my family											
27	Did you tell your family that you have TB											
28	My family ensures that I have taken my medication											
	Disease and medicine related											
29	Did you experience any side effects when you were taking TB treatment?							Yes		No		
30	Did side effects made you to stop taking taking treatment?							Yes		No		
31	Were you were taking any other medicines besides TB treatment?							Yes		No		
32	Did this treatment also have effect in you taking TB treatment?							Yes		No		
	3.5 Treatment adherence											
33	Do you some times forget to take your pills?							YES		No		
34	People sometimes miss taking their medication for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your medicine? If Yes how many ?							Yes		No		
35	Did you cut back or stopped taking your medication without telling your doctor/ nurse, because you felt worse when you took it?							Yes		No		
36	When you travel or leave home, do you some times forget to bring along your medication?							Yes		No		
35	When you feel like your health is under control, do you stop taking medication?							Yes		No		
36	Taking medication everyday is a real inconvinience for some people. Do you ever feel hassled about sticking to your treatment plan?							Yes		No		
37	How often do you have difficulties to remember to take your medications?							Once a while	Sometimes	Usually	All the times	Never

5.6 Appendix 7:Codebook

	Definition	Primary Data set	Secondary Data set	
Gender	Male or Female	Female 1 Male 2	Female 0 Male 1	
Type of dwelling	Type of housing structure where one resides	Formal 1 Informal 2	Formal 0 Informal 1	
Employment status	Whether one is employed or unemployed	Employed 1 Unemployed 2	Employed 0 Unemployed 1	
Monthly income		Continuous variable	Continuous variable	
Age	Age in years	Continuous variable	Continuous variable	
Marital status	The condition of currently living with a spouse or not.	Divorced 1 Married 2 Single 3 Widowed 4	Not married 1	Divorced/ Single/Widowed
			Married 0	Married
Education level		Certificate 1 Diploma 2 Matric 3 Below matric 4	Below matric 0	Below matric
			Above Matric 1	Certificate/Diploma/ Matric
Household size	Number of people living in each household	Continuous variable	Continuous variable	
Pill burden	Number of pills taken by patient daily	Continuous variable	Continuous variable	
Picking hour preference	Whether patients prefer to collect medication outside working hours (8am – 5pm)	Strongly disagree 1 Disagree 2 Neutral 3 Agree 4 Strongly agree 5	Prefer clinic hours 0	strongly disagree/disagree/neutral
			Prefer outside clinic hours 1	strongly agree/agree
Waiting time to medication pickup****	Whether the waiting time for picking up	Strongly disagree 1 Disagree 2 Neutral 3	Wait time <2 hours 0	Agree/Strongly agree

	medication is less than 2 hours	Agree 4 Strongly agree 5	Wait time > 2hours 1	strongly disagree/disagree/neutral
Variable	Definition	Primary Data set	Secondary Data set	
Distance from facility	I stay less than 5km from this clinic	Strongly disagree 1 Disagree 2 Neutral 3 Agree 4 Strongly agree 5	Facility distance <5km 0	Agree/Strongly agree
			Facility distance >5km 1	strongly disagree/disagree/neutral
Cost of medication pick up	It costs me less than R50 to pickup my medication	Strongly disagree 1 Disagree 2 Neutral 3 Agree 4 Strongly agree 5	pick up cost <R50 0	Agree/Strongly agree
			pick up cost >R50 1	Strongly disagree/Disagree/Neutral
Respectful treatment	Healthcare workers treat me with respect and dignity	Strongly disagree 1 Disagree 2 Neutral 3 Agree 4 Strongly agree 5	Respectful treatment 0	Agree/Strongly agree
			Unrespectful treatment 1	Strongly disagree/Disagree/Neutral
Health information provision	Healthcare workers provide all information	Disagree 1 Neutral 2 Agree 3	health education provided 0	Agree
			no health education provision 1	Neutral/Disagree
Medication pickup in safe areas	Medication pickup is done in safe areas	Neutral 1 Agree 2 Strongly agree 3	Meds picked in safe area 0	Agree/Strongly agree
			Meds picked in unsafe area 1	Neutral
Accessibility of medication access points	Medication pickup area is accessible to disabled patients	Strongly disagree 1 Disagree 2 Neutral 3 Agree 4 Strongly agree 5	Meds picked in accessible area 0	Agree/Strongly agree
			Meds picked in inaccessible area 1	Strongly disagree/Disagree/Neutral
Medication availability at facility	Medication is always available at health facility	Disagree 1 Neutral 2 Agree 3 Strongly agree 4	Meds always available 0	Agree/strongly agree
			Meds not always available 1	Disagree/neutral
Family encouragement on clinic visits	My family encourages me to attend clinic visits	Disagree 1 Neutral 2 Agree 3 Strongly agree 4	Family encourages clinic visits 0	Agree/strongly agree
			No family encouragement 1	Disagree/neutral
	My family encourages me	Strongly disagree 1 Disagree 2	Family encourages adherence 0	Agree

Family encouragement on adherence	to adhere to treatment	Neutral 3 Agree 4	Family doesn't encourage adherence 1	Disagree/ Neutral / Strongly disagree
Monitoring of adherence by family	My family ensures that I have taken medication	Strongly disagree 1 Disagree 2 Neutral 3 Agree 4 Strongly agree 5	Family monitors adherence 0	Strongly agree/Agree
			Family doesnt monitor adherence 1	Strongly disagree/Disagree/Neutral
Variable	Definition	Primary Data set	Secondary Data set	
Family accompanies patient to treatment	My family accompanies me to clinic visits	Strongly disagree 1 Disagree 2 Neutral 3 Agree 4 Strongly agree 5	Family accompanies to clinic 0	Strongly agree/Agree
			Family doesnt accompany to clinic 1	Strongly disagree/Disagree/Neutral
Club couple counselling and testing	Clubs encourage couple counselling and testing	Strongly disagree 1 Disagree 2 Neutral 3 Agree 4 Strongly agree 5	Club encourages couples 0	Strongly agree/Agree
			Club doesnt encourage couples 1	Strongly disagree/Disagree/Neutral
Availability of food	I always have adequate food while taking my medication	Strongly disagree 1 Disagree 2 Neutral 3 Agree 4 Strongly agree 5	Always have food 0	Strongly agree/Agree
			Don't always have food 1	Strongly disagree/Disagree/Neutral
Adequate income	My income can cover basic needs	Strongly disagree 1 Disagree 2 Neutral 3 Agree 4 Strongly agree 5	Adequate income 0	Strongly agree/Agree
			Inadequate income 1	Strongly disagree/Disagree/Neutral
Polypharmacy	Where you taking any other medication besides TB ?	No 1 Yes 2 yes 3	No 0 Yes 1	
Forgetting Medication	Do you some times forget to take your pills?	No 1 Yes 2	No 0 Yes 1	
Missed doses	Thinking over the past two weeks, were there any days	No 1 Yes 2	No 0 Yes 1	

	when you did not take your medicine?			
Cutback on medication	Did you cut back or stopped taking your medication without telling your doctor/ nurse, because you felt worse when you took it?	No 1 Yes 2	No 0 Yes 1	
Forgetting medication during travel	When you travel or leave home, do you sometimes forget to bring along your medication?	No 1 Yes 2	No 0 Yes 1	
Asymptomatic defaulters	When you feel like your health is under control, do you stop taking medication?	NO 1 No 2 Yes 3	No 0	NO , No
			Yes 1	Yes
Daily dosing is inconvenient	Taking medication everyday is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?	No 1 Yes 2	No 0 Yes 1	
Frequency of forgetting medication	How often do you have difficulties to remember to take your medications?	All the time 1 Once a while 2 Sometimes 3 Usually 4	Once or never 0	Once a while
			More than once 1	All the time, Sometimes, Usually
Nonadherence		Sum of scores (Forgetting Medication+ Missed doses + Cutback on medication+ Forgetting medication during travel + Asymptomatic	Continuous variable	

		defaulters + Daily dosing is inconvenient+ Frequency of forgetting medication)		
Nonadherence categories(binary outcome)			Extreme Nonadherence	Sum score >= 4
			Non extreme nonadherence	Sum score <4

5.7 Appendix 8: Power calculation

Outcome variable: Extreme nonadherence

Independent variable used for power calculation availability of food during treatment.

Significance level: 0.05

To estimate the power of the study, a significant critical factor for extreme nonadherence: lack of food, was be used. The proportion of extreme nonadherence in the group without food was assumed to be 0.6 whereas the proportion of extreme nonadherence in the group with food was estimated to be 0.3. Assuming an equal number of people in the group that has access to food and the one without food. This gave a power of 95.90% using Stata version 17 for computations.

```
. power twoproportions 0.6 0.3,n(144)

Estimated power for a two-sample proportions test
Pearson's chi-squared test
H0: p2 = p1  versus  Ha: p2 != p1

Study parameters:

        alpha =    0.0500
            N =       144
  N per group =        72
        delta =   -0.3000  (difference)
           p1 =    0.6000
           p2 =    0.3000

Estimated power:

        power =    0.9590
```