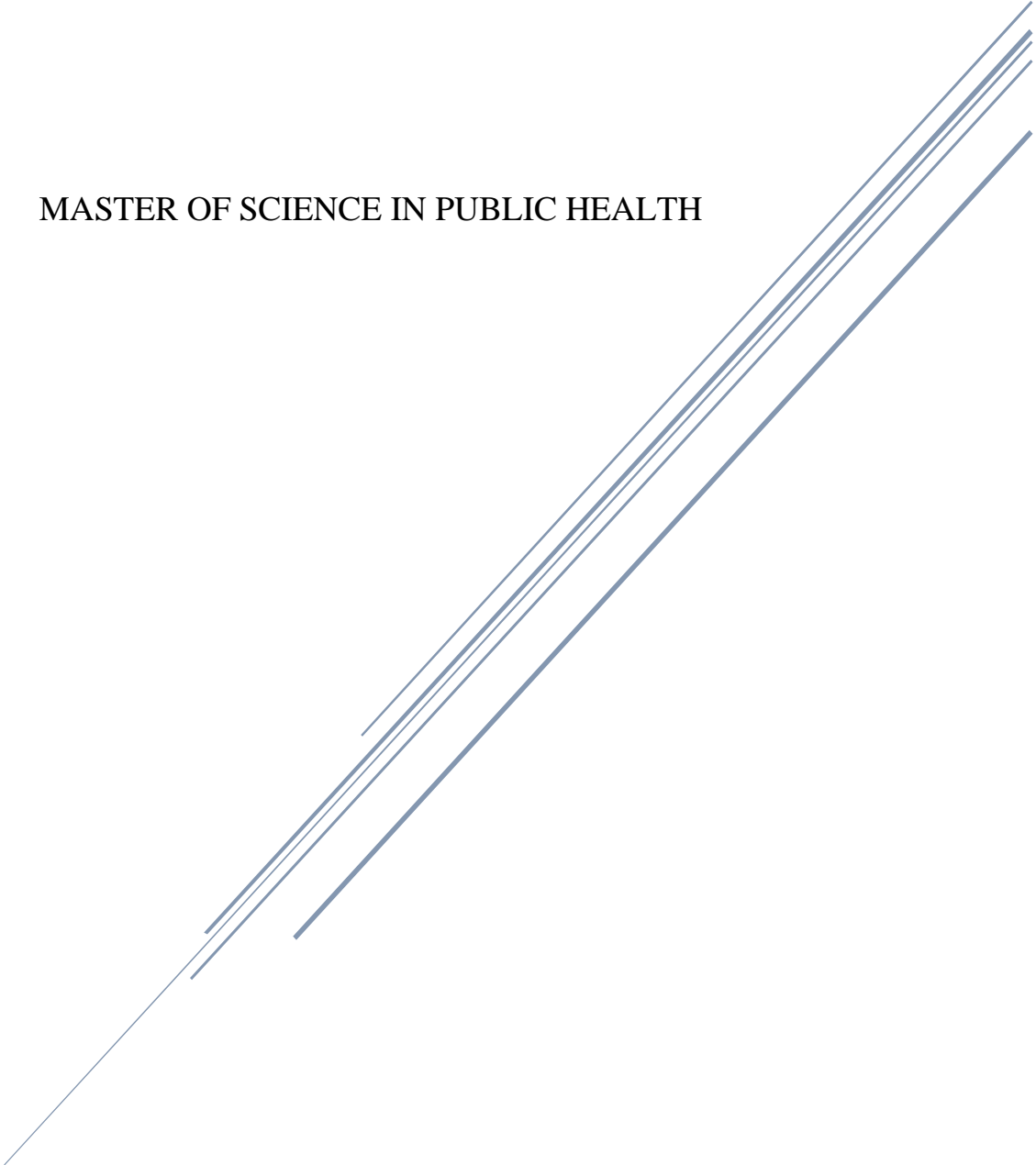# EXPLORING FACTORS INFLUENCING TREATMENT ADHERENCE AMONG TB PATIENTS IN NIGERIA

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MASTER OF SCIENCE IN PUBLIC HEALTH

KIT (Royal Tropical Institute) Vrije University Amsterdam

Exploring factors influencing treatment adherence among TB patients in Nigeria

A thesis submitted in partial fulfilment of the requirement for the degree of Master of Science in Public Health

By

ALHAJI KONNEH

SIERRA LEONE

Declaration:

Where other people's work has been used (from either a printed or virtual source, or any other source), this has been carefully acknowledged and referenced in accordance with academic requirements.

The thesis **Exploring factors influencing treatment adherence among TB patients in Nigeria** is my own work.

Signature

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Dedication

This work is dedicated to the memory of the brave people who lost their lives to tuberculosis while looking for care and comfort. Your strength and determination are still inspiring as we fight against the relentless disease.

Lists of Abbreviations

TB	Tuberculosis
CBDOT	Community-Based Direct Observe Therapy
DAT	Digital Adherence Technologies
DOT	Direct Observe Therapy
FMoH	Federal Ministry of Health
HCW	Health Care Worker
HIV	Human Immunodeficiency Virus
LGA	Local Government Area
LMIC	Low and Middle-Income Country
MDR-TB	Multi-Drug Resistant Tuberculosis
NTBLCP	National Tuberculosis Leprosy Control Program
SMS	Short Message Services
SSA	Sub-Saharan African
VDOT	Video Direct Observe Therapy
WHO	World Health Organisation

Definition of terms

Adherence to TB medication: Adherence is the degree to which a patient's actual drug-taking behaviour matches the treatment plan. A measuring of how well patients follow medication schedule (1).

Tuberculosis (TB): TB is an infection that is spread by germs called Mycobacterium tuberculosis. It mostly affects the lungs. People with pulmonary tuberculosis pass on the infection through the air when they cough, sneeze, or spit, putting germs into the air. (2).

Direct Observe Therapy (DOT): A process in which TB drugs are given by a trained health professional or a designated person who is not a family member, and the patient is closely watched as they swallow each dose (3).

Digital Adherence Technology (DAT): These are tools specifically created to assist individuals with tuberculosis in adhering to their medication regimen (4).

Lost to follow-up (LTFU): LTFU is when a patient has begun their treatment but stopped taking medications for an extended period before returning for further treatment (5).

Treatment completed: A TB patient with a positive smear test who finished treatment but no smear examination results were available at the end. It covers smear-negative and extra-pulmonary cases (5).

Cure: This means that a person with TB who was smear-positive at the start of treatment and ended up being smear-negative by the seventh month (5).

Abstract

Background: Tuberculosis is a contagious illness that leads to high death rates in Nigeria. Even though free treatment is available for infected patients and the disease is treatable, the disease remains challenging due to patients not following the treatment plan.

Objective: This study aims to investigate the factors that affect adherence to TB treatment among patients in Nigeria. The purpose is to provide the Federal Ministry of Health with evidence-based interventions to address the problem effectively.

Method: The method involved conducting a literature search on Google Scholar, PubMed, ScienceDirect, and VU Library to find published articles, including quantitative and qualitative studies and grey literature. The findings were presented using the Donut framework.

Result: Based on findings, factors that appear to influence treatment adherence include; patient-related lack of knowledge of the causes of TB and treatment duration, perceived well-being, and level of education of the patients. Socioeconomic were community stigmatisation and discrimination, lack of social support, alternative medication and poverty. Health system factors were negative attitudes of healthcare workers (HCWs) and distance to a health facility, while medication and condition factors were medication side effects, and comorbidity, respectively.

Conclusion: In Nigeria, adherence to TB treatment remains challenging due to the interplay of factors, including knowledge gap, stigmatisation, poverty, lack of social support and attitude of service providers. Interventions such as effective patient education and counselling, training of (HCWs), and inventive packages can help the Federal Ministry of Health to control tuberculosis.

Keywords: Factors, Tuberculosis, Medication adherence, Nigeria,

Word count: 12,093

Introduction:

As a public health officer, my passion and commitment lie in working with communities and striving to improve the lives of others. Five years ago, I embarked on a health promotion job to increase community awareness about the importance of early and appropriate health-seeking practices. During this time, I had the opportunity to interact with TB patients, particularly those who had defaulted on their treatment, gaining valuable insights into their challenges and reasons for not seeking timely care. It became evident that many issues influencing their health-seeking behaviour were beyond their control.

Furthermore, I dream of becoming an infectious diseases public health specialist in the near future, aiming to hold a significant position. This aspiration has fuelled my interest in conducting an extensive literature review to explore the factors hindering TB patients' medication process and identify sustainable evidence-based interventions that can improve poor medication adherence among patients.

This thesis is organised into five chapters, each serving a distinct purpose. The first chapter provides an in-depth explanation of the country's background, socioeconomic and sociocultural aspects, an overview of Tuberculosis and the structure of service delivery within the health system. In the second chapter, I highlight the burden of TB and justify the need for conducting this study. I also outline the specific objective to be achieved through the literature review and describe the methodology employed. The third chapter presented the findings from the extensive literature review of bother the factors influencing TB patients' medication adherence and the evidence-based interventions that have shown promise to improve adherence rates. Lastly, the fourth chapter discusses the key findings, draws meaningful conclusions, and proposes recommendations based on the identified evidence-based interventions. By doing so, I hope to improve TB patients' adherence to their medication regimen and ultimately make strides in combatting infectious diseases effectively.

Chapter One

1.0 Background

1.1 Geographical and Demographic Information:

Nigeria is one of the Sub-Saharan Africa (SSA) countries in the western part of Africa. It shares a boundary with neighbouring countries Niger and Chard in the north and northeastern part, respectively, Cameroon in the east, Benin in the west and surrounded by the Atlantic Ocean to the south. Nigeria Occupies an area of 923,768 square kilometres (6).

Nigeria has a remarkable topography, characterised by plains and plateaus located in the north and southern parts of the country and savannah grassland across the country, with the majority in the centre of the country (6). Nigeria is further grouped into six geographic and political regions, subsequently separated into 32 states, each further divided into Local Government Areas (LGAs). In total, there are 774 LGAs in Nigeria see—figure 1 (7).

Nigeria is one of Africa's most densely occupied nations and 7th most populated globally. According to the United Nations Population Fund (UNFP), Nigeria has over 200 million, with 43% and 54% of the country's population below the age of 15 and between the ages of 15 and 64, respectively (8).

The country has a vast cultural and ethnic diversity, and there are over 250 ethnic groups, with the majority being Hausa, Yoruba, and Igbo (9). The country's official language is English, but over 500 other local languages are spoken, with the majority of the population in the northern part of the country being Muslim (50%), followed by Christian (48.1%). Less than 2% practise other religions in Nigeria's centre and southern part (10).
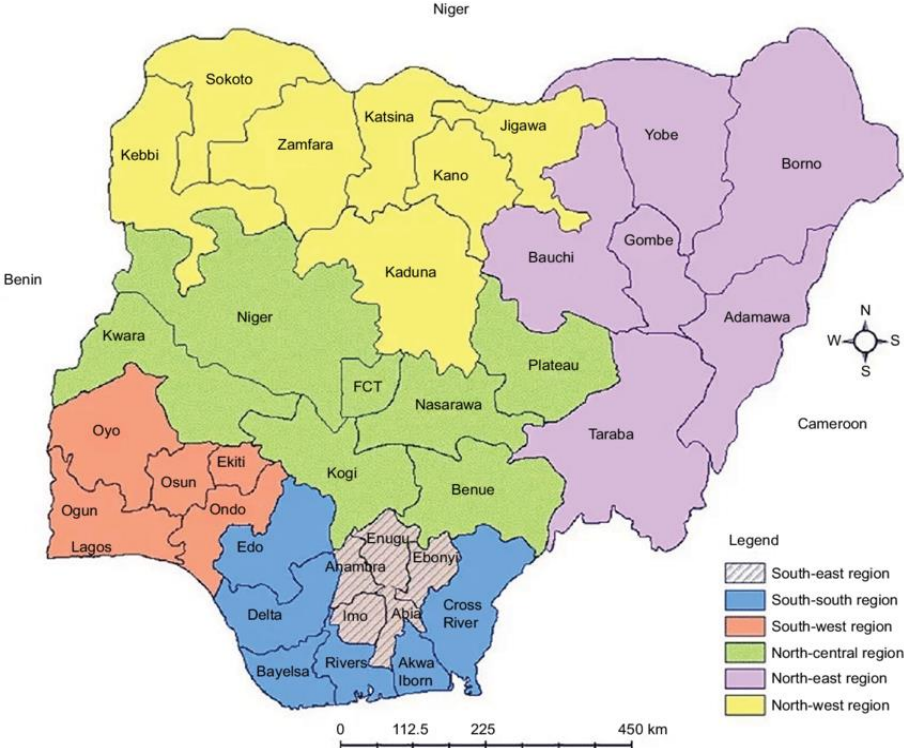
Figure 1**: Map of Nigeria showing the geographical and political division** (11)

1.2 Socio-Economic situation:

According to the world bank, Nigeria is one of the leading oil producers globally, and its oil production contributes significantly, about 2/3, to the country's state revenues. However, this is not reflected in most of the population, with 4 out of every 10 Nigerians living below the poverty line (12). For example, a National Bureau of Statistics multidimensional poverty survey reported that 63% of Nigerians are poor, meaning they can't afford essential health and social needs (13).

1.3 Nigeria Health system structure:

Nigeria operates a diverse healthcare system, with its population receiving health services from public and private healthcare providers with a mixture of modern and traditional healthcare systems. The healthcare system is divided into three levels, primary healthcare, Secondary healthcare, and tertiary healthcare system, with services provided by Local Government Areas, State Government, and Federal Government, respectively (14–16). See Figure 2. The Federal Ministry of Health administratively monitors Nigeria's health system.

Primary health is located at the community level, mainly as the gateway to the secondary healthcare level. At the primary level, community health workers and nurses provide services such as health promotions and prevention, diagnosis and treatment of common and minor illnesses and injuries at this level.

Medical doctors provide services such as managing and treating complex illnesses and injuries at the secondary healthcare level. In contrast, the tertiary healthcare level, located at the federal level, provides highly complicated medical services for patients either referred from the secondary healthcare level or admitted (16).

However, with all these structures and levels of healthcare services, only 43% of the Nigerian population has access to healthcare services. Leaving 57% with no healthcare services (17).
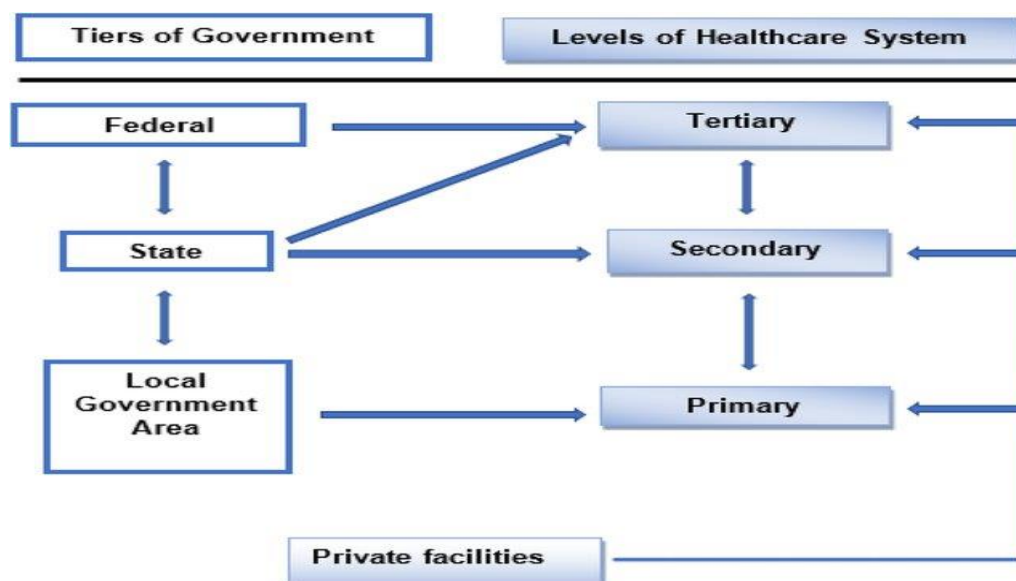
Figure 2: Nigeria's healthcare service level (15)**.**

1.4 Health expenditure

According to the WHO, the current health expenditure is 3.03% of the Gross Domestic Product (GDP). In comparison, the total health budget as a percentage of the total national budget is 5.9% in 2022. This is lower than the 15% recommended during the Abuja declaration (18). This has resulted in the general population being burdened with high out-of-pocket (OOP) expenses. According to the WHO global health expenditure 2020 data, 74.7% of healthcare financing is from OOP expenses (19).

1.5 Overview of Tuberculosis Burden in Nigeria

Although Nigeria is experiencing epidemiological transmission with an increase in the incidence of non-communicable diseases, it is essential to note that communicable diseases still account for most of the sickness and death in the country (20). They account for about 72% of death.

Among these infectious diseases, tuberculosis, in particular, remains the primary cause of mortality from a single infection agent. Nigeria witnesses over 240,000 deaths each year and nearly 600,000 new cases of this preventable and curable disease (21).

Various contributing factors drive the increasing burden of TB in Nigeria. Data from the WHO 2019 Global TB Reports shows that Malnutrition, HIV infection, diabetes, and alcohol use disorder are linked to 20%, 12%, 3%, and 1% of tuberculosis cases in Nigeria, respectively (22).

Furthermore, the prevalence of HIV among TB patients varies across the six zones in Nigeria. The northwest zone reports a 4% rate; the northeast reports 8%; the southwest reports 9%; the southeast reports 16%; the north centre reports 19%; and south-south reports 21%. (23).

1.6 Tuberculosis Services in Nigeria

Since the World Health Organisation (WHO) declared TB a public health threat, strategies have been formulated to control and prevent the disease. One of the strategies was implementing directly observed therapy (DOT) to accomplish a 50% and 75% decrease in TB prevalence and death rates, respectively, by 2025 (24).

These implementations were initiated by the authority in charge of TB services in Nigeria, the National TB and Leprosy Control Program (NTBLCP), through health facilities. The services involve testing suspected TB patients and providing direct observation medications to patients for 6 or 9 months, depending on the level of infection (25).

With support from international and local partners in 2019, 12,606 public and private health facilities were equipped to provide direct observation therapy (DOT) services. Meanwhile, 28 hospitals are trained to offer services to drug-resistant TB cases. These services have been decentralised to the community level to increase coverage. However, only 31% of the 40562 health facilities in Nigeria are equipped to offer TB services. (23,24)

With the increase in TB-HIV coinfection, there is an active collaboration between the NTBLCP and healthcare workers. Their efforts have mainly focused on capacity building in managing TB cases, MDR-TB cases, and TB-HIV coinfections. This effort has increased the notification of TB cases from 31,164 in 2002 to 120,266 in 2019 (24).

1.7 National Tuberculosis Control Programm Organogram

The NTBLCP runs the tuberculosis program and is a unit in the Department of public health with the Federal Ministry of Health. The NTBLCP activities are aligned along the country's three governance levels: federal, state and LGAs, as presented in Figure 3 (24,26).

At the federal level, the primary duty of the NTBLCP is to engage in policy development aimed at controlling TB, allocating resources, providing career development, monitoring and evaluating activities and rendering technical guidance to state programmes (24,26).

At the state level, the NTBLCP is responsible for providing logistical support to the state and LGAs and monitoring and evaluation activities within both levels. Besides coordinating and monitoring activities, the NTBLCP offers technical support to stakeholders and staff at the state and LGA levels (24,26).

The LGA level is called the implementation level, where TB cases are detected and treated with support from the Local Government TB supervisor through the collaboration of local partners and community-based organisations. Most of the activities at this level include providing support to the state programme by conducting training and support in detecting non-compliant TB patients. Supervise healthcare workers to ensure that treatment guidelines are adhered to and that patient information is captured, analysed and presented quarterly at the LGA level to inform decision-making (24,26).
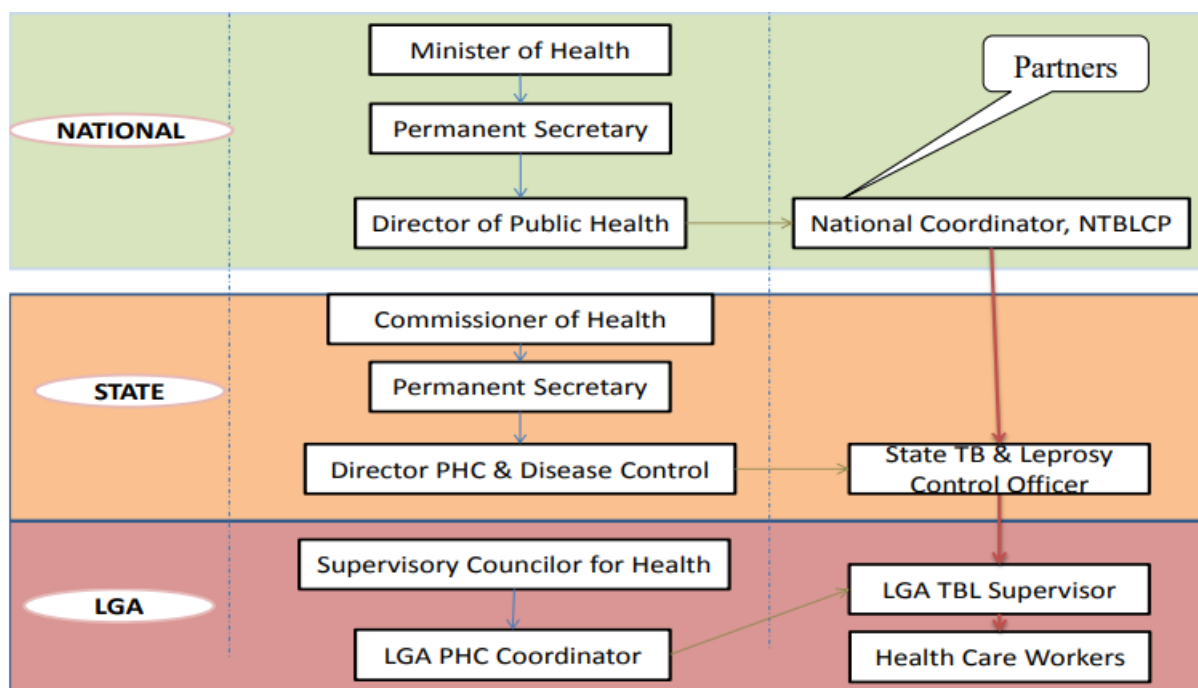
Figure 3: Organisational chart showing the relationship of the operational levels of the NTBLCP (26)**.**

Chapter Two

2.0 Problem statement, and Justification and Objectives

2.1 Problem statement

As per the WHO report, TB continues to be among the ten leading causes of global death and stands as the primary contributor to deaths caused by a solitary infectious agent ranking above HIV/AIDS. In 2021, an estimated 10.6 million people were infected with TB, and 1.5 million TB deaths globally; sadly, of all the 10.6 million TB cases, only 6.4 million TB cases have been detected, diagnosed and treated by TB programs worldwide (27). Among those infected, men account for 56.7%, with a global treatment success rate of 86% below the WHO 95% treatment success rate target, which has led to a continual increase in Multi-Drug Resistant TB (MDR-TB) (27). Among the countries that contribute to the high burden of TB, the WHO Africa Region contributed to 23% of all the new TB infections making Africa one of the contributors to the high TB burden (28).

Tuberculosis remains a significant public health issue in Nigeria; according to the WHO's 2022 report, Nigeria currently occupies the second position in Africa and 7th position globally among countries that significantly contributes to the high TB burden, with the country recording over 540,000 cases every year (22)(29). In 2021, a total of 467,000 TB cases were recorded, translating to an incidence of 219 TB cases per 100,000 population. Males are more likely than females to contract tuberculosis. Specifically, men and women aged 15 years and above accounted for 56% and 37% of TB infections, respectively, while children below 15 years accounted for 7% (27). (see Figure 3)

TB accounted for more than 10% of the total death in Nigeria in 2022 (30). The mortality rate is also high among young adults; for instance, the Institute for Health Metrics and Evaluation 2019 data revealed that adults between the ages of 15 and 49 accounted for 5.14% of the total death among this age group (31).

Like many other African nations, Nigeria relies primarily on the directly observed therapy (DOT) short-course strategy for managing tuberculosis (32). To achieve the goal of ending TB by 2025 set forth by WHO, Nigeria implemented the Stop TB plan in 2015, intending to achieve a 90% detection and treatment rate (33).

However, non-adherence to TB medication remains the key challenge in controlling Tuberculosis in Nigeria (34). For example, a study by Ofoegbu observed an adherence rate among HIV-negative and HIV-positive TB patients to be 78.5% and 48.8%, respectively, below the WHO target (5).

Non-adherence to TB medication poses a significant threat to the patients, community, family and the nation. Such non-adherence reduces the chance of returning to work and increases catastrophic health expenditure, negatively affecting the patient's family and the poor economic viability of the affected workforce. (35). According to the WHO 2022 report, 71% of individuals with TB experience catastrophic health costs while seeking care (27).

Medication adherence has been extensively investigated, and some of these factors that influence patients' adherence to medication as prescribed have been grouped into five categories, patient-related factors, diseases/condition-related factors, medication-related factors, socio-economic and socio-cultural factors and healthcare system-related factors (1).

However, some factors can be intentional, such as deciding not to take medication, while others may be non-intentional, such as forgetting to take medicine (36).

TB case notifications, 2021

Total new and relapse	204 725
- % tested with rapid diagnostics at time of diagnosis	63%
- % with known HIV status	97%
- % pulmonary	98%
- % bacteriologically confirmed ^	79%
- % children aged 0-14 years	7%
- % women (aged ≥15 years)	37%
- % men (aged ≥15 years)	56%
Total cases notified	207 785

Figure 3: TB notification rate (27)

2.2 Justification

To reduce Nigeria's high tuberculosis burden and meet the Sustainable Development Goal 2030 target, the NTBLCP relies heavily on TB patients adhering to their prescribed treatments. Treatment for tuberculosis involves taking multiple medications daily for several months to years, and failing to complete the recommended course of treatment can have adverse consequences. Such negative effects include an increased chance of treatment failure, community transmission of TB, and even death (37).

Although the NTBLCP has implemented interventions to mitigate the tuberculosis burden in Nigeria by ensuring access to quality care, treatment outcomes are still not optimal (33). In 2019, the proportion of patients with all forms of TB and TB-HIV who completed treatment was only 87% and 76%, respectively, which falls short of the global target rate of 95%. While lost to follow-up and death rates in both patients were 6% and 8%, and 5% and 13, respectively (23). (See Figure 4)

Furthermore, there is an increasing rate of drug-resistant TB. Based on the findings of the first national DR-TB survey in 2010 (38) and a systematic review of MDR-TB studies conducted in 2021 (39), it is evident that the proportion of DR-TB cases has been on the rise over time. The data shows that the percentage of DR-TB cases in new TB patients increased from 2.9% in 2010 to 6% in 2021, while in previously treated cases, it escalated from 14.3% in 2010 to 32% in 2021 (38,39). Drug-resistant TB is more dangerous since it has limited treatment options, is more expensive, has significant side effects and is mostly less effective.

Therefore, exploring the factors most likely to influence adherence to medication and treatment outcomes, especially in settings with limited resources, is essential given the considerable costs that poor treatment outcomes have on patients and the health system (37).

Hence, it is important to review the existing body of studies on the factors affecting treatment adherence and offer recommendations that might assist FMoH, NTBLCP, and other nations in

a similar situation in designing and implementing adherence strategies based on recognised situational factors.
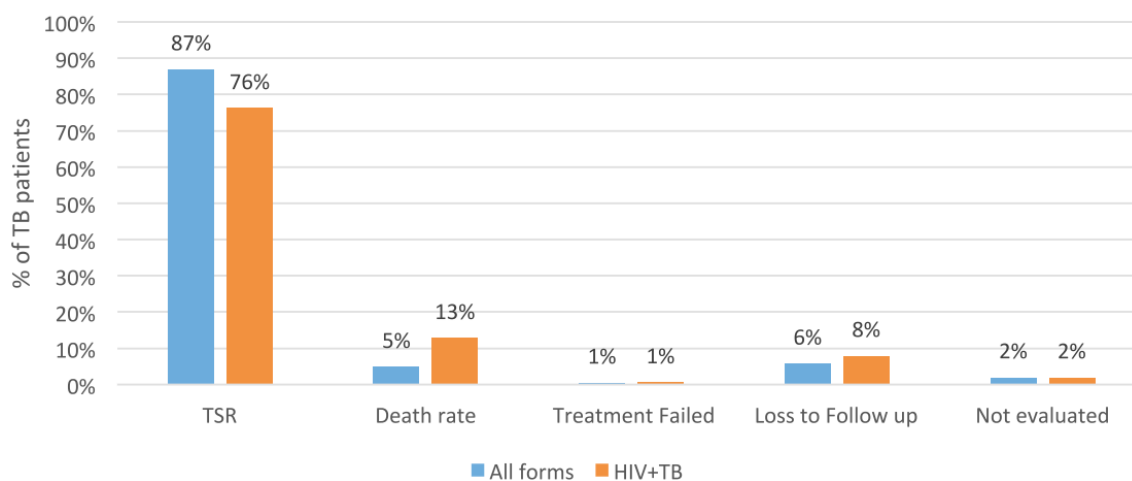
Figure 4: Treatment outcome of all forms of TB and TB-HIV patients in 2019 (23)**.**

2.3 Objectives

The study aims to explore the factors influencing treatment adherence among tuberculosis patients and provides recommendations to the Federal Ministry of Health for effective interventions.

2.3.1 Specifics Objectives

1. Explores the individual factors influencing treatment adherence among tuberculosis patients.
2. Identify the socio-economic and socio-cultural factors influencing treatment adherence among tuberculosis patients.
3. Identify the medical and condition/disease-related factors influencing treatment adherence among tuberculosis patients.
4. Explore the healthcare system-related factors influencing treatment adherence among tuberculosis patients.
5. Identified best practices or interventions to enhance TB treatment in Nigeria and provide recommendations to the Federal Ministry of Health.

Chapter Three

3.1 Methodology: A literature review.

Database: The study primarily involved an extensive literature review, which included searching and retrieving published articles across various databases, including Google Scholar, PubMed, Scopus, ScienceDirect, and the VU library.

Secondly, search engines, including Google and Google Scholar, were used to conduct a preliminary search and retrieve published articles, including quantitative, qualitative and mixed studies and grey literature. Additionally, Reference chaining (snowballing) was done on most published articles exploring factors influencing medication adherence among TB patients to find additional information.

Furthermore, reports from Nigeria's Federal Ministry of Health and valuable information from local and international organisations which provided enough relevant to the development of the thesis were incorporated. The retrieved articles were summarised into a table and grouped under common categories such as title, author, factors/determinations, findings and interventions.

Search Strategy factors:

In the first step of the process, a single keyword was used to do an initial search, followed by a combination of these keywords using the "AND" and "OR" Boolean operators to narrow the search results. Keywords including "Factors" AND "Tuberculosis", AND "Medication Adherence", AND "Nigeria were used. The word "Nigeria" was not used as a search term for studies outside Nigeria, as indicated in Table 1. Selection criteria were used to get more relevant articles, including selecting important articles by reading the abstract, glancing, and skimming.

Search string for evidence-based Interventions:

In other to provide practical and evidence-based recommendations to address the issue of poor medication adherence among TB patients in Nigeria. A different search string with the combination of keywords, as indicated in Table 2, was conducted to identify published articles and grey literature on evidence-based interventions to improve medication adherence among TB patients.

Table 1**: Search table showing the combination of keywords, MESH terms and Boolean operator.**

	Factors		Condition		Issues		Location
Patient-related	Age **OR** "Marital Status" **OR** "Education Status" **OR** Lifestyle **OR** Belief **OR** Attitude and beliefs about TB **OR** Perceived well-being **OR** knowledge/Health literacy	**AND**	"Tuberculosis" OR Mycobacteria Tuberculosis OR TB	**AND**	"Medication Adherence" OR "Medication Compliance" OR Adherence OR 'Drug Adherence" OR "Drug Compliance" OR "Medication Nonadherence" OR Loss-to-follow-up OR Default	**AND**	Nigeria OR Sub-Saharan Africa OR Africa OR LMICs
Socioeconomic	Gender **OR** Stigma and discrimination **OR** **Alternative medication OR** poverty **OR** Family/friend support **OR** Occupations						
Health system	Distance to TB services **OR** Drug availability **OR** Attitude of service providers **OR** Waiting time **OR** Financial constraints **OR** Health Policies						
Medical related	Actual or perceived side effects **OR** Complex regimens **OR** Duration of treatment						
Condition related	Co-morbidity **OR** TB-HIV						

Table 2:Search table for the combination of keywords for evidence-based intervention.

Objective	Intervention		Keywords		Locations
Evidence-based interventions or best practices to improve medication adherence	Community-based Direct Observe Therapy OR Cognitive and Behaviour Intervention OR Education OR Treatment Supporter OR Social Support OR Incentive package OR mHealth intervention	AND	"Enable factors" OR "Best practices" OR "Reminder" OR "Education"	AND	Nigeria OR West Africa OR Sub-Saharan Africa OR LMIC

3.2 Inclusion criteria

During the literature search, articles that were used for this thesis include:

- Articles that aimed to explore at least one factor (including patient factors, socio-economic and cultural factors, health system-related factors, medical-related factors, and diseases/conditions factors) influencing medication adherence or compliance among TB patients in Nigeria.
- Articles exploring factors influencing medication adherence among TB patients are published in English, and those studies were conducted either in Nigeria, Sub-Saharan Africa or in other low and middle-income countries from 2000 to 2023.

The articles on factors influencing adherence to TB treatment among TB patients were selected from 2000–2023 to gain insight into factors influencing adherence to TB treatment over the past two decades. The year 2000 was chosen because that was when TB started getting global attention and at the same time when DOT services in Nigeria reached 100% geographical coverage. And including papers from Sub-Saharan Africa LIMC because TB is a global problem, and knowing what is happening in other places will help us figure out why most TB patients have trouble sticking to their treatment.

3.3 Exclusion criteria

Articles that were not used for this thesis include:

- Articles that did not mention or assess at least one of the factors associated with TB treatment adherence or TB medication adherence.
- Articles published before 2000, not published in English, and those not conducted in Nigeria, Sub-Saharan Africa or any low and middle-income countries.
- Adherence studies containing children, pregnant women, and those conducted in prisons.

3.4 Study Limitation:

The study has certain limitations, primarily due to its nature as a literature review. This is because the investigation is built on gathered ideas from published articles and grey literature, such as reports and theses. Additionally, the study is restricted to only articles published in English and therefore did not use information from articles published in other languages, even when they were conducted within the geographical scope of this thesis.

3.5 Conceptual Framework

To effectively and efficiently carried out a literature review and guide the development of my thesis, a series of searches was conducted for a conceptual framework. During the investigation, several frameworks were identified to establish factors influencing adherence to medication or providing recommendations for improving medication adherence.

One of the frameworks was the socio-ecological model mentioned most of the determinants of adherence. However, the author did not include the psychological factor of it (40). Another framework was the planned behaviour model; here, the author focuses more on the behaviour factors leaving out the structural component of medication adherence (41). The third framework

was Wekesa's conceptual framework; here, the author included the various adherence factors such as individual, medical, community-related and structural factors but also failed to include demographic characteristics and condition-related factors (42). Therefore, using any of the above-listed frameworks to fully understand the factors influencing treatment adherence and also to address the objectives of the study fully will be difficult.

Another framework identified during the search was the WHO medication adherence framework called the "Donut Framework", developed from a synthesis of 120 frameworks that identify adherence gaps and provide recommendations for improving medication adherence (43). The framework offers a comprehensive approach to identifying factors/determinants that influence treatment adherence. The framework includes patient-related, socioeconomic, healthcare system, medical, and condition-related factors, as indicated in Figure 4 (43).

Conceptual Model for Factors Contributing to Medication Adherence

Condition-related factors (n=55)
- Disease control (i.e., symptoms, complications, severity, acute events/ deterioration, impact on lifestyle)
- Disease characteristics (i.e., cognitive deficit, symptom bother, consequence)
- Patient specific (i.e., co-morbidities, time since diagnosis, declining health)

Medication-related factors (n=65)
- Medication regimen (i.e., complexity, dosage, type, pill burden, interference in routine, clarity of instructions on label, regimen familiarity)
- Medication effects (i.e., side effects, safety, efficacy, benefits, patient experience)
- Medication properties (i.e., cost, physical properties, formulation)

Healthcare system/HCP-related factors (n=69)
- HCP characteristics (i.e., relationship, communication, trust in provider, clinical care, ability to relate, provision of training/ follow-up, prescription practice, patient education)
- Healthcare system-related factors (i.e., access, provider continuity, cost, drug supply, regulation processes, quality of health services, information support, insurance coverage)

Patient-related factors (n=102)
- Cognitive and psychological factors (i.e., perceptions, beliefs, concerns, knowledge/ health literacy, emotions, motivation/goals)
- Behavioral factors (i.e., organization, planning, lifestyle)
- Priorities (i.e., quality of life, other competitive needs)
- Non-modifiable characteristics (i.e., demographics, experience, type of user, physical factors)
- Family/ caregiver characteristics (i.e., hesitancy, support, relationship)

Socioeconomic factors (n=78)
- Social/ environmental factors (i.e., social context, interaction, support, culture, language, stigma, norms, external influences, sociodemographic, promotional prompts, environment)
- Lifestyle factors (i.e., alcohol, drug use)
- Economic factors (i.e., income, education, occupation, living condition, insurance)

Figure 5: Conceptual model for factors contributing to medication adherence (43).

Patient-related factor

Within the patient-related factor, various aspects play a role in influencing medication adherence. This encompasses cognitive and psychological factors like perception, beliefs, and education. Additionally, behavioural elements such as lifestyle choices and planning impact adherence. Priorities, which involve considerations like quality of life and competing needs, also contribute. Furthermore, non-modifiable characteristics, including demographic traits and family and caregiver features like hesitancy, support, and relationship dynamics, are all considered significant influences on medication adherence.

Socioeconomic factor

Within the Socioeconomic realm, a range of factors come into play that influence medication adherence. These encompass socio/environmental factors, such as social context, support systems, stigma, societal norms, and sociodemographic considerations. Lifestyle elements, including alcohol and drug use, also have an impact. Economic factors like income, education,

occupation, living conditions, insurance-related factors including gender, and socioeconomic influences on medication adherence.

Healthcare system-related factor

Several factors have been identified as influencing adherence to TB medications within the health system-related domain. These include aspects of healthcare practices like the quality of relationships, communication, trust in healthcare providers, and the availability of training and patient education. Additionally, health system-related factors play a role, such as access to care, continuity of healthcare providers, the cost of treatment, drug availability, drug supply, regulation process, quality of health services, information support, and insurance coverage.

Medical-related factor

Within the framework, the medical-related factor examines various issues influencing TB patients' medication adherence. These encompass aspects like the medication regimen, including complexity, dosage, and pill burden. Additionally, medication effects, such as side effects, safety, efficacy, and perceived benefits. Moreover, medication properties like cost and formulation also shape medication adherence among TB patients.

Condition-related factor

Within the framework, the condition-related factor delves into several issues that impact patient medication adherence. These encompass aspects like disease control, which considers symptoms, complications, severity, and the overall impact on lifestyle. Additionally, disease characteristics, including cognitive deficits, were taken into account. Patients-specific factors, such as co-morbidities and the time since diagnosis, are also recognized as challenges influencing medication adherence among patients.

Chapter Four

4.0 Introduction of the Results section

The results presented in this chapter are drawn from twenty-nine included articles published in Nigeria and over 34 articles from other parts of Sub-Saharan Africa. Most (>70%) of the articles were cross-section studies, with few retrospective cohort and experimental study designs. Most of the study participants were drug-sensitive TB patients, with few studies on patients with drug-resistant TB. Most of the included articles use the five domains of medication adherence to determine the influencing factors of medication among TB patients. These domains include patient-related factors, socioeconomic-related factors, health system-related factors, medication-related factors and condition-related factors. The modified framework shown in figure 6 was used to present the results based on the findings from the reviewed articles.
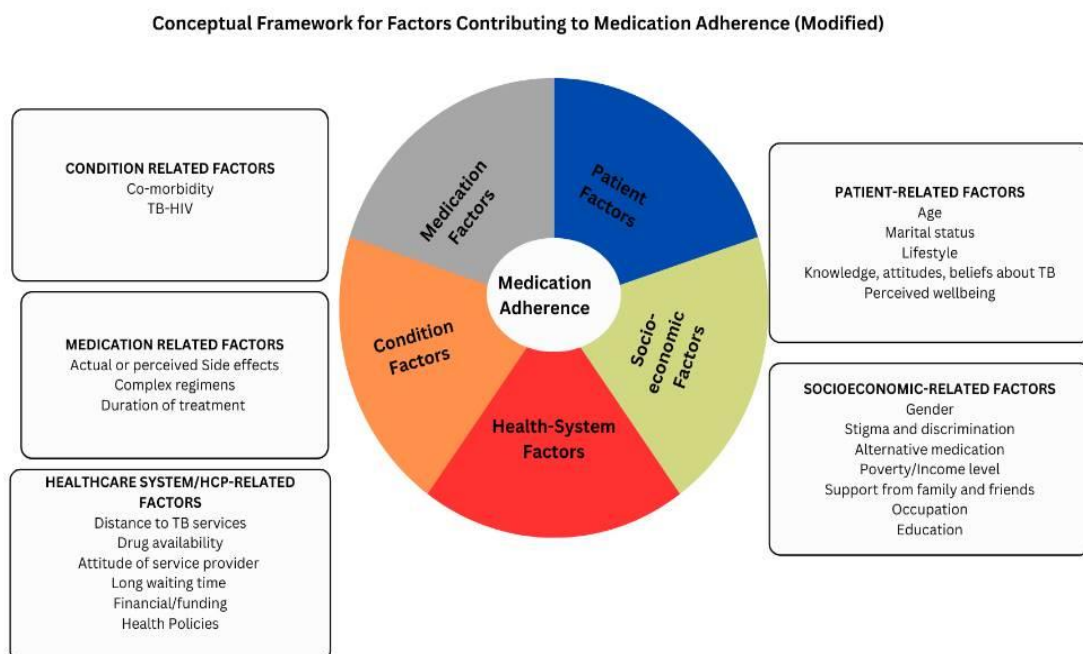

Figure 6: Adapted conceptual framework for factors contributing to medication adherence[1].

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[1] Source: Adapted from Peh et al 2021 by author

4.1 Patients related factors

4.1.1 Age of the Patients

Demographic factors, such as age, have long been investigated as one of the elements influencing medication adherence. Several articles mentioned the connection between age and medication adherence (44–48). Almost half of the studies that accessed age as a factor reported that older adults were more likely to interrupt their treatments (45,48–50); for instance, a cross-sectional study carried out in the plateau state by Alobu et al. (2014) reported that older adults age 30 years and above were more likely to default treatment than the younger adults due to the presence of dementia among older adults (45). It is suggested that older patients who experience comorbidity, social isolation and inability to access care easily make it challenging to adhere (45). In another cross-sectional study, adults aged 30 years and above were two times more likely to interrupt their treatment (AOR 1.5, 95% CI 1.2 – 2.1) (51). These conclusions were supported by studies conducted in Ethiopia and South Africa (47,52).

Only one study that was conducted in the northern part of Nigeria reported contradicting findings; they found that younger adults below the age of 25 years were more likely to miss their treatment than older adults above 65 years due to peer influence and low level of experience of TB medication as compared to more experienced adults (44).

However, two studies found no association between the patient's age and medication adherence (53,54). The study did not provide further justification for the findings.

4.1.2 Marital Status

The effect of marital status as a factor on medication adherence was documented by most included articles. Most studies concluded that married TB patients were more likely to interrupt treatment than TB patients who were single or widows/widowers (34,55,56).

In one of the cross-sectional studies by Iweama et al. (2021), they found that married couples were at high risk of not adhering to their TB treatment (AOR 120.49, 95% CI 5.38 – 271.1) than those that were single; it is believed that married patient particularly women, may miss their medication due to the responsibilities of caring for a family member. (34). Another study conducted in a teaching hospital in Nigeria reported a similar finding that adherence level was lower among married patients than among single patients (58.5%) (55).

Only one cross-sectional study, which was conducted in the northern part of Nigeria, documented that non-adherence to anti-TB medication was higher among those that were either single (20%) than those that were married (7.5%); it is believed that single patient lacks the needed social support thus in the process of providing for themselves may miss taking their routine medication. (44).

However, one study conducted in a tertiary hospital in central Nigeria found no association between marital status and adherence to TB medication (57). Moreover, the sample size was relatively small, thus affecting the statistical power of the analysis.

4.1.3 Lifestyle of Patients

All the included articles concluded that lifestyle, such as alcohol consumption, negatively affects medication adherence (48,58–60). Ajao et al. (2014), in their cross-sectional study, mentioned that most of the TB patients that were involved in drinking alcohol interrupted their anti-TB

medication than others who did not take alcohol, as alcohol influences the thinking ability of the patients, which makes them forget leading to treatment interruptions (38.3%) [p<0.001] (58). A study conducted in Lagos by Adejumo et al. (2016) also found that treatment interruption was higher among smokers (58.3%) than TB patients who did not smoke. Since smoking reduces, the effectiveness of the medication and patients may interpret that the drugs are not effective, thus leading to treatment interruptions (59).

These findings agreed with those reported in studies in Kenya, Ethiopia and East Africa (61–63). The Ethiopian study found that TB patients who consume alcohol were three times more likely to interrupt their treatment than patients who do not drink alcohol [AOR, 2.99; 95% CI 1.41 – 6.36] due to judgement impairment which affects patient's ability to remember taking their drug or follow-up visit leading to treatment interruptions (63). Also, young adults, due to peer influence, tend to ignore health advice given to them by health workers, thereby continue consuming alcohol which in turn leads to treatment interruptions (64).

4.1.4 Knowledge attitude and belief about TB and Medication adherence

Several studies have documented the influence of knowledge, attitude and belief in the existence of the diseases and the efficacy of drugs on treatment adherence among TB patients in Nigeria (56,60,65–67). For instance, Akhimien et al. (2014) found that TB patients who lacked prior knowledge of treatment durations were six times more likely to interrupt treatment [AOR: 6.1; CI 95%: 2.8-13.2] (48). Similarly, a study conducted in a Nigerian tertiary institution revealed that individuals with limited knowledge about the causes of TB, side effect and medication duration were seven times at risk of defaulting treatment than individuals with adequate knowledge [AOR, 6.7; 95% CI 1.79 25.5; P = 0.005] (57). Similar findings were also documented In Ethiopia, where inadequate knowledge about the disease was a cause of treatment interruption among TB patients (68).

Forgetting anti-TB drugs has also been identified as a common reason for treatment interruptions (65,69). Additionally, in rural Lagos, some individuals believe that TB is caused by evil spirits or witchcraft and cannot be cured by anti-TB drugs, leading to non-compliance with treatment (70). Believing that TB is caused by witchcraft was also reported by studies in other sub-Saharan African countries to be associated with treatment interruption (61,64,71–76).

It is believed that patients with inadequate knowledge of treatment duration after the intensive phase of treatment may perceive disappearing symptoms as a cure, while those believing witchcraft to be the cause of TB may seek spiritual or traditional help, thus leading to treatment interruptions (68,70).

4.1.5 Educational status

Educational status is crucial in providing job opportunities and equipping individuals with the necessary knowledge and skills to manage their health and illnesses. Most included studies underscore the importance of education in medication adherence (49,55,58,65). Thomas et al. (2018) and Ajao et al. (2014) concluded that TB patients with higher educational status were more likely to take their drug as prescribed than TB patients with lower or no formal education (49,58). Similarly, studies conducted in Southeastern Nigeria concluded that individuals with higher education were more likely to exhibit higher medication compliance rates than those with lower education levels (55,65). Patients with higher education understand the importance of medication and have good job opportunities than uneducated patients, which enables them

to finance associated TB treatment costs like food and transportation, which will encourage them to adhere to their treatment (55,65)

Contradicting findings documented that TB patients with no formal education (19.4%) had a higher compliance rate than educated TB patients (4.3%), likely because educated patients are caught up with work and cannot keep up with their treatment appointments, thus leading to treatment interruption(44). It is suggested that uneducated patients mostly have treatment supporters, which enable them to adhere to treatment (46). One study found no association between educational status and medication adherence (77).

4.1.6 Perceived well being

All the included studies conducted in Nigeria that investigated the link between perception and medication adherence concluded that most patients perceived the disappearance of signs and symptoms as a cure (44,56,58,60). Studies conducted in Osun State and northern Nigeria have documented the influence of perceived well-being on the continuity of anti-TB medication (44,58). These studies found that over 40% of participants were less motivated to continue treatment after completing the intensive phase, as they believed they were cured due to the disappearance of signs and symptoms. Similarly, Kaona et al. (2004) reported that 38.6% of TB patients interrupted their treatment because they felt much better and saw no reason to continue medication, which was attributed to poor counselling and lack of knowledge about treatment duration (76). This highlights the importance of effective counselling before and during treatment.

Contradictory findings were reported in a South African study, where TB patients were demotivated to continue treatment due to the presence of symptoms while on medication resulting in treatment interruptions (78). However, feeling well was also a motivational factor for some TB patients. In a qualitative study, *a TB patient expressed* (79).

> *"Since I know the duration of my treatment, whenever I see changes and feelings of wellness, It motivates me to complete using my drugs as I am assured of being cured"* (77).

4.2 Sociocultural and Socioeconomic

4.2.1 Gender

Gender influences treatment adherence among TB patients significantly; however, most studies found no association between gender and treatment adherence (48,49,54,65,80).

While only two studies (44,56) found an association between gender and medication adherence, in one of the case-control studies, it was documented that males were three times more likely to default treatment than women [OR 3.05; 95% CI 1.60-5.80] (56). Anyaike (2013) also observed that among patients that interrupted treatment, 95% of them were male (44). Similar findings of male defaulting treatment were also reported in Ghana, Ethiopia and Tanzania (80–82). It is believed that males are considered the head of the family and, in the process of providing for the family, may likely miss treatment appointments, thus leading to treatment interruption (44,56).

However, contradictory findings were reported in another Ghanaian study, where males exhibited a three-fold increase in adherence rate compared to females. [OR = 2:978, 95%CI = 1:173-7:561; p = 0:022] (83), **although the research team provided no reasons for such findings**.

4.2.2 Stigma and Discrimination

TB is highly associated with poverty and disproportionately affects marginalised and rural populations, exposing them to stigma and discrimination. Most of the studies conducted in rural and urban Nigeria reported an association between stigma and discrimination and medication adherence (57,60,70,84). Stigma and discrimination against TB patients discourage them from continuing treatment or seeking help, resulting in treatment interruptions (70).

In a cross-sectional study by Sariem et al. (2013), it was reported that among TB patients that interrupted treatment (14.3%), 66% of them were abandoned by community and family members due to their TB status (57). A qualitative study also documented Stigmatisation against TB patients, as one community member expressed (70).

> *"I cannot eat with a person who has this kind of disease, and if there is anything we need to do together, I will avoid the person"* (63).

Consequently, patients refrain from disclosing their status to friends and family and fear visiting publicly known DOT sites due to fear of stigma and discrimination (85). At the same time, some TB patients and their treatment supporters were restricted from sharing public places like public toilets and bathrooms (64).

4.2.3 Alternative medication

Several studies across Nigeria have reported using alternative medication among TB patients, especially when both formal and informal medical practices are done side-by-side. This encourages patients to seek care from informal sectors due to easy access and affordability (86–88).

A cross-sectional study conducted in Benin City, Nigeria, documented that individuals who used alternative medication were two times more likely to interrupt treatment than patients who never used alternative medicine [OR 1.95; 95%CI 1.02 -3.73] (56). The use of herbal medication was also reported in a study conducted in Lagos. However, the percentage of herbal medicines used was not mentioned due to the qualitative nature of the study (70). Similarly, a cross-sectional study conducted in rural Nigeria reported that of the 450 study participants, 85% of them use alternative medication (50). These findings align with studies conducted in Ethiopia and Kenya (61,63,68,75).

It is suggested that easy access and affordability of such alternative medications, fear of side effects, stigma, and discrimination were the most cited reason for interrupting treatment (56,68,86).

4.2.4 Family and Friend Support

Aside from providing medication support to patients, the impact of treatment supporters from friends and family on TB patients' adherence has been well-documented (44,59,80,89).

More than half of the review articles concluded that patients who were given social support by either family, friends or community members were more likely to adhere to their medication (44,60,84,89–91). A cross-sectional study conducted by Anyaike et al. (2013) documented that individuals who received support from friends and family members had a higher adherence rate (20%) compared to those without support (9.8%) (44). Similarly, treatment interruption was also reported by Madukaji et al. (2021), where among the 96 TB patients that defaulted treatment, 86.5% had no treatment supporters (60).

Several reasons for adherence were also documented, including receiving monetary help from family members (89,92), assistance with collecting medication on behalf of elderly patients (71), monitoring of the medication process and reminders of clinic visits by supporters (93).

However, despite the importance attached to support given by friends and family members to improve adherence as documented in several studies (60,79,85,94), one contradicting finding was reported by Adejumo et al., where default rate was higher in patients with treatment supporters (44.4%) compared to those without treatment supporters (34.7%) Likely because treatment supporters were not living together with the patients, and treatment supporters are chosen by HCWs without due consideration of the NTBLCP guidelines. (59).

4.2.5 Poverty/Level of Income

Tuberculosis is highly prevalent among low-income earners and marginalised individuals, which significantly impacts treatment adherence (95). Poverty appears to be a factor affecting compliance with treatment in all the identified studies in Nigeria (34,50,56,60,89). A cross-sectional study conducted in Northern Nigeria concluded that TB patients in the low-income group were at a high risk of treatment interruption due to a lack of money to provide food and transportation (60). Similarly, in Northwestern Nigeria, patients with monthly earnings between ₦100,000 (USD 133.16) and ₦199,00[2] (USD 264,99) were prone to non-adherence (34).

Similar findings were reported in southern Ethiopia, where TB clients with low income were forced to interrupt treatment due to financial constraints in paying for transportation, accommodation and food, especially when the medication needed to be taken on an empty stomach (85,96).

Inability to afford associated costs, such as paying for food and transportation (61,79,97) and accommodation[3] (75,98,99), were among the most frequently cited reasons for treatment interruption among TB clients in Ethiopia, Kenya, and South Africa.

4.2.6 Occupational Status

The occupational status of TB patients significantly influences their adherence to anti-TB medication. Employed patients have a greater advantage in funding the associated costs of TB treatment, while unemployed patients face limitations in financing such expenses, which can impact treatment adherence (61,100).

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[2] "₦" is the currency symbol for the Nigeria currency called Naira.
[3] Accommodation because they need to travel to another town for treatment

Most of the included articles did not explore the effect of occupational status on medication adherence; among the few articles that explored, two of them reported that TB patients who are employed were more likely to interrupt treatment than unemployed (55,89)

In a retrospective cohort study conducted in the Southeastern part of Nigeria, it was documented that the compliance rate among employed patients was higher (33.3%) compared to unemployed patients (17.1%) (55). The above findings align with studies conducted in other Sub-Saharan African countries (61,100).

Contrary to the above findings, a cross-sectional study conducted in Ghana found that adherence rates were higher in unemployed patients (83%) compared to daily farm workers (61%); it is believed that many of the farm workers prioritise their job over clinic appointments, thus leading to treatment interruptions (46).

Despite the known influence of occupational status on medication adherence, one study conducted in Southeastern Nigeria reported no differences between employed and unemployed patients regarding treatment adherence (65).

4.3.0 Healthcare System Factor

4.3.1 Attitude of Healthcare Workers (HCWs)

The relationship and attitude of HCWs towards their patients significantly influence treatment adherence among TB patients (70). More than half of the published articles in Nigeria concluded that the negative attitude of HCWs contributes to patients interrupting their treatment (48,57,60,70,91,101). For instance, one of the cross-sectional studies conducted in Plateau state, Nigeria, by Ibrahim et al. (2014) documented that among the 76 participants, 73.4% interrupted treatment because of the negative attitude of HCWs (91). Similar findings were established in the Southwestern part of Nigeria, where it was reported that 83.3% of the 33 patients interrupted their medication because of the ill-treatment of HCWs.

Negative HCW attitudes were identified as reasons for treatment interruptions, including scolding patients for not following treatment instructions (64), providing incorrect treatment guidance, and failing to obtain patient consent (59).

Only one qualitative study documented a positive attitude of HCWs towards their patient which motivated the patient to continue their medication. A patient explains how the HCW's behaviour inspired him to comply with his treatment (90).

> *" I feel motivated to use my drugs when the health workers shows care and support and responds to my questions promptly" (27-year-old Male Self-employed, FGD)* (90).

Attitudes such as providing a listening ear to patients, conducting follow-up visits (75), and offering encouragement and motivation to continue treatment (85,102) were identified as positive HCWs' attitudes that motivate patients to adhere to their treatment.

4.3.2 Distance to Health Facility / DOT Site

The accessibility of healthcare facilities from the homes of TB patients is crucial for adherence and completion of treatment. Most studies reported that patients staying far from the DOT site

were more likely to interrupt treatment (48,56,58,60,77,89–91). For example, a cross-sectional study that was conducted in Plateau state, Nigeria, found that patients residing 5 kilometres away from the DOT site were more likely to miss their clinic appointments [AOR, 11.3; CI 95% 5.7, 22.2] (48). However, data on distance were self-reported, which may not be entirely accurate. Similarly, it was reported that patients who could not handle the associated fees of daily clinic attendance due to long distances were forced to interrupt their medication (60).

Factors include longer distances to the DOT site (46,56) and increased travel time to reach the DOT site (60). And inaccessibility of the DOT site due to geographical barriers like mountains and hills (103), coupled with the inability of patients to afford transportation costs due to poverty, make it difficult to reach the DOT site, were most of the reported reasons why patient interrupted their medications. This issue is particularly prevalent in Nigeria, where DOT services are unevenly distributed (25).

These findings align with studies conducted in Kenya and Ethiopia (57,79), where it was also reported that patients living far from the DOT site were more likely to interrupt treatment than those living close (81).

However, few studies from other parts of Ethiopia found no association between the distance of the DOT site and patients' adherence (52,104). This could be attributed to the study location and the fact that the participants recruited stayed very close to the DOT sites.

4.3.3 Availability of Drug

The availability of drugs at the DOT site during patient visits has a significant influence on treatment adherence. A cross-sectional study conducted in the plateau state by Ibrahim et al. (2014) concluded that among the 71 participants, 71% of the patients interrupted their treatment because the anti-TB drugs were unavailable at the DOT site during their visits (91). Though TB drugs are free, disruption of the supply chain system in Nigeria causes a stockout of drugs at DOT sites (105).

It is believed that patients will perceive the unavailability of drugs at the DOT site during the visit to be time and resources wasted, especially for patients staying far away from the DOT site, creating inconveniences and lack of trust in the health system, thus leading to treatment interruption (106).

However, these findings are not supported by a study conducted in Rivers State, Nigeria, where Tobin-West et al. (2016) found no association between drug availability at the DOT site and treatment adherence; this was because patients received their complete medication package at the time of admission (107).

4.3.4 Waiting Time

It is important to note that many studies in Nigeria have not explored the relationship between waiting time and treatment adherence. However, studies in Sub-Saharan Africa have shown that the duration patients take in a health facility for them to be treated has a greater link to their treatment compliance (61,68,104). A correlation was found between waiting time and treatment compliance in a study conducted in Osun State, Nigeria. Patients waiting for one or more hours before receiving attention were likelier to default on their treatment [p<0.001]. This is particularly for daily wage earners who may experience income loss while away from their jobs, leading to treatment interruptions (58). Similar findings were also documented in an Ethiopian

study, where patients who experienced longer waiting times than expected were at high risk of defaulting treatment [AOR = 14.260; 95% CI: 2.135–95.241] (81).

Moreover, prompt attention from HCWs, and also giving patients the opportunity to select a suitable time for their clinic appointments have been associated with better compliance with TB medication (64)

4.3.5 Financial Constraints

It is worth knowing that only a few studies have investigated the impact of funding on medication adherence among TB patients. However, few of the identified studies documented a funding gap in the NTBLCP which influences the implementation of the activities, subsequently leading to treatment interruption among TB patients (25,105,108).

The successful implementation and coordination of the NTBLCP heavily relies on its financial pillar. However, the effective coordination between the levels of structure to achieve the program's strategic objectives is hindered by inadequate and or delayed disbursement of funds by the government (26)

The lack of financial accountability and responsibility at the LGAs levels has also undermined the fight against TB, disrupting the daily operation of DOT services (26). This funding gap has led to inefficiencies in DOT sites and service providers, particularly in tracking lost-to-follow-up patients and monitoring other TB activities (25).

During a qualitative study, a health worker expressed frustration over the lack of funds to support their work (108).

> . *"....we don't get money for making calls, we are not even reimbursed when we use our money, today, I still called a patient with my phone. Nobody is paying for the calls ..."* (103)

Similar findings were reported in studies conducted in Ghana and Uganda that unsustainable funding of TB activities contributes to unsustainable outreach activities and monitoring of activities, which subsequently contributes to non-compliance among TB patients (64,108–110).

4.3.6 Health Policies

It is important to note that there is still limited evidence exploring the effect of health policy on medication adherence among TB patients (25). Ensuring the protection of the rights and welfare of patients, especially those affected by tuberculosis, is crucial for effective disease control (111). While there are existing policy frameworks for the prevention, testing, and care of TB patients on a free basis, there are some weaknesses, such as the lack of specific TB legislation and well-defined regulations on confining TB patients (25). The weakness of these legislations contributes to stigma and discrimination faced by TB patients in their workplaces, homes and communities, resulting in treatment interruptions (112). A study on the governance of TB concluded that weak legal protection, such as unclear policies on mandatory conferment of TB patients, exposes them to stigma and discrimination, which mostly leads to disclosure of status, thus leading to treatment interruption (25).

Furthermore, the exclusion of TB diseases from the National Health Insurance Scheme creates financial burdens and inequitable access to health services, especially for poor TB patients. This

further increases treatment interruption among TB patients due to the resulting catastrophic expenditure (50).

4..4.0 Medication-Related Factors

Actual or perceived side effects, treatment durations, the number of pills, and the complexity of the drug regimens all influence treatment adherence among TB patients. From the reviewed literature, side effects (53,58,91,94,103,106,113), complex regimens (89,102,103,114), and treatment durations (44,45,79,114,115) were cited as factors affecting treatment adherence among TB patients.

In Osun state, extra-pulmonary TB patients who experienced side effects were less likely to adhere to treatment (58). Similarly, a study in Plateau state found that among the 76 participants, 80% of them did not comply with treatment due to fear of medication side effects (91). Skin irritation, specifically rash, was cited as a common reason for treatment interruption (64). Similar findings were reported in the southeastern part of Nigeria and other Sub-Saharan African countries (94,103,106,113). In Ebonyi state, Nigeria, a retrospective cohort study found that TB Patients on longer treatment drugs were more likely to interrupt their medication than those on shorter treatment duration [AOR 1.6; 95% CI 1.1 - 2.2] (45). Moreover, the intake of multiple pills was also a contributing factor to treatment interruptions (65).

It is suggested that patients experiencing side effects may perceive the drugs as causing more harm than good and may decide to stop the medication, while those on longer treatment durations may question the effectiveness of the anti-TB drugs; such perception leads to treatment interruption (108,114,115).

4.5.0 Comorbidity

Studies done within hospitals and in surrounding communities in Nigeria have documented that Individuals with TB who have HIV are more likely to have their treatment stopped. (51,58,59,65). Adejumo et al. found that TB-HIV coinfected patients were less likely to comply with their treatment than TB patients without HIV (59). According to research in southeastern Nigeria, 61% of 59 TB patients undergoing HIV medication had halted their TB treatment. (65). Treatment interruptions among TB-HIV patients have also been documented in other Sub-Saharan African countries (61,63,78,80,113).

It is believed that fear of stigma and discrimination, difficulties in managing the burden of TB and HIV medication, denial of HIV status among newly diagnosed TB patients, side effects, and inadequate counselling by health workers have been cited as reasons for treatment interruptions (47,59,75,78).

However, Alobu et al. found no association between TB-HIV coinfected patients and treatment adherence (45). This finding may be attributed to the retrospective study design used by the research team, and at the same time, the data used were routine health information; therefore, it cannot be generalised.

Table 3: Summary of factors and evidence-based interventions

Factors	Findings influencing medication adherence	Evidence-Based Interventions
Patient-related factor	• Lack of knowledge of causes of TB and treatment duration. • Forgetting to take the drug. • Harmful lifestyle (smoking and alcoholism) • Perceived well-being • Belief in the cause and cure of diseases.	• Cognitive and behavioural intervention: Educating the patients about the cause of the disease's treatment options and counselling. Thus addressing the lack of knowledge and harmful lifestyle. • SMS Reminder: Send a message to patients to alert them on medication intake and clinic appointments, thus addressing forgetfulness.
Socioeconomic/sociocultural	• Poverty • Stigma and discrimination • Use of alternative medication • Lack of social support • Being employed	• Social support: providing emotional and financial support to patients, thus addressing stigma and discrimination and improving community acceptance. • Incentive/economic package: supporting less privileged patients with food and financial support to enable them to afford transportation costs for treatment and address nutritional challenges.
Health system factor	• Negative of healthcare workers • Accessibility of DOT sites and long waiting time • Inadequate funding	• Incentive/economic package: To motivate HCWs, especially those not on salary. • CBDOT: Decentralising DOT services at the community level, especially in remote areas, thus addressing the issue of inaccessibility. •
Medical-related factors	• Adverse side effects and too many pills.	• Enhance health education: Educate patients on potential medication side effects to address negative perceptions.
Comorbidity	• TB-HIV coinfection	• CBDOT: Decentralising DOT services at the community level, especially in remote areas, thus addressing the issue of inaccessibility. • Enhance health education: Educate patients on potential medication side effects to address negative perceptions.

4.6 Interventions to improve medication adherence

To improve medication adherence among TB patients in Nigeria, It is vital to consider context-appropriate and data-driven interventions to enhance medication adherence. The challenges of non-adherence have been tackled through several intervention strategies, including short message services (SMS), video direct observation therapy (VDOT), Real-time medication monitoring pillbox, 99DOTs, offering digital adherence technologies (DAT), incentives, education, treatment supporters targeting patient, community member, friends and family member, and implementing CBDOT.

4.6.1 Short Message Services (SMS)

Several studies have investigated the impact of SMS reminders on medication adherence (116–118). This involves sending motivational messages to patients daily to ensure they do not forget to take their medication (118). SMS reduces patients' inconveniences in getting to DOT sites (115) and encourages clinic attendance, especially for subsequent appointments (119).

Using SMS as a way to improve medication adherence depends on the situation. Some studies show promising results, while others show mixed or neutral results. More study needs to be done with larger sample sizes and more rigorous methods for conclusive results.

In a randomised control trial, Gashu et al. found that SMS significantly improved medication adherence, with an adherence rate of 79% in the intervention group compared to 66.4% in the control group. However, their study only focused on patients with phones, limiting its generalizability to the entire TB population (120). Similarly, an intervention study in Mozambique reported that 97% of the 76 participants in the intervention group claimed to have never missed a clinic appointment due to an SMS reminder (121).

On the other hand, a study in Cameroon found no difference in treatment success between the intervention and control group, possibly due to a high dropout rate among patients and weak application of the SMS intervention (117). Similar findings were reported in Uganda, although the intervention was well-received and accepted by patients and HCWs (122).

4.6.2 Video Direct Observation Therapy (VDOT)

VDOT is a medication adherence intervention that involves recording a video of the patient while they take their medication. This is either done by the patient or their treatment supporter. The video is then securely stored and sent to a database for evaluation by the HCW (123) (figure 5). The patient also receives instructions from HCWs through this method, increasing patients' autonomy and reducing in-person clinic visits (124,125).

VDOT is good for improving medication adherence. However, before recommending such an intervention to improve medication adherence, careful thought must be taken considering the mixed evidence and implementation challenges.

A cohort study conducted in Uganda found that the VDOT intervention improved adherence; among the 50 participants, 85% adhered to their medication, and 92% expressed satisfaction with VDOT. (126). Similar results were documented in Vietnam, where patients expressed a high willingness to use VDOT (127).

Although VDOT is known to maintain privacy and improve adherence by involving direct HCW supervision, there are concerns about patients falsifying video recordings to indicate

medication adherence when they have not actually taken their medication. Additionally, worries about the confidentiality and security of videos, internet connectivity issues, and unstable electricity supply in rural areas and among low-income earners may make implementation challenging (126).
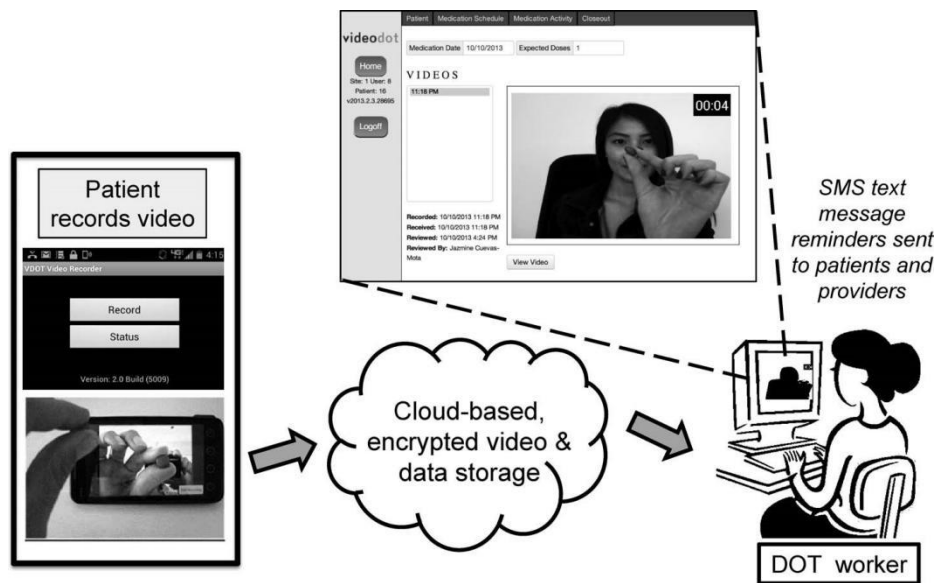

Figure 6**: Video direct observe therapy; a schematic diagram** (123)

4.6.3 Real-Time Medication Monitoring Pillbox

The medication pillbox (see Figure 6) is a device that has been utilised to enhance medication adherence, particularly in cases where patients may forget to take their medication. Whenever the patient takes a drug from the pillbox, a signal is sent to the server indicating that the patient has taken their medication. If the patient fails to open the pillbox, the server promptly sends an SMS notification to the patient's phone, informing them of their oversight (see Figure 7) (128).

The real-time drug device shows promise in improving poor medication adherence. However, more research is needed for conclusive evidence. And implementation challenges with the internet, electricity, and socioeconomic issues must be addressed, as presented in the findings below.

In a pilot study conducted in Tanzania, the real-time medication device improved adherence significantly. Among the five TB patients included in the study, the median adherence rate was 99% (IQR 97 – 99%). However, there was no comparison group to indicate that the intervention led to the outcome. Additionally, the smaller sample size used in this study limits its generalizability to the entire TB population (128). In another study by Liu et al. (2015), the device reduced non-medication compliance by 40% to 50% (129).

The pillbox device accurately detects non-adherence events and is highly accepted by patients and HCWs (130). It has also been shown to reduce catastrophic costs for patients as compared to routine DOT interventions (131).

However, implementing this intervention requires highly educated patients and those from high-income groups. It also requires stable internet and electricity supply, which may make it challenging to implement in rural areas and among patients with lower socioeconomic status (132).

Figure 7: The pillbox container used for medication intake (128).
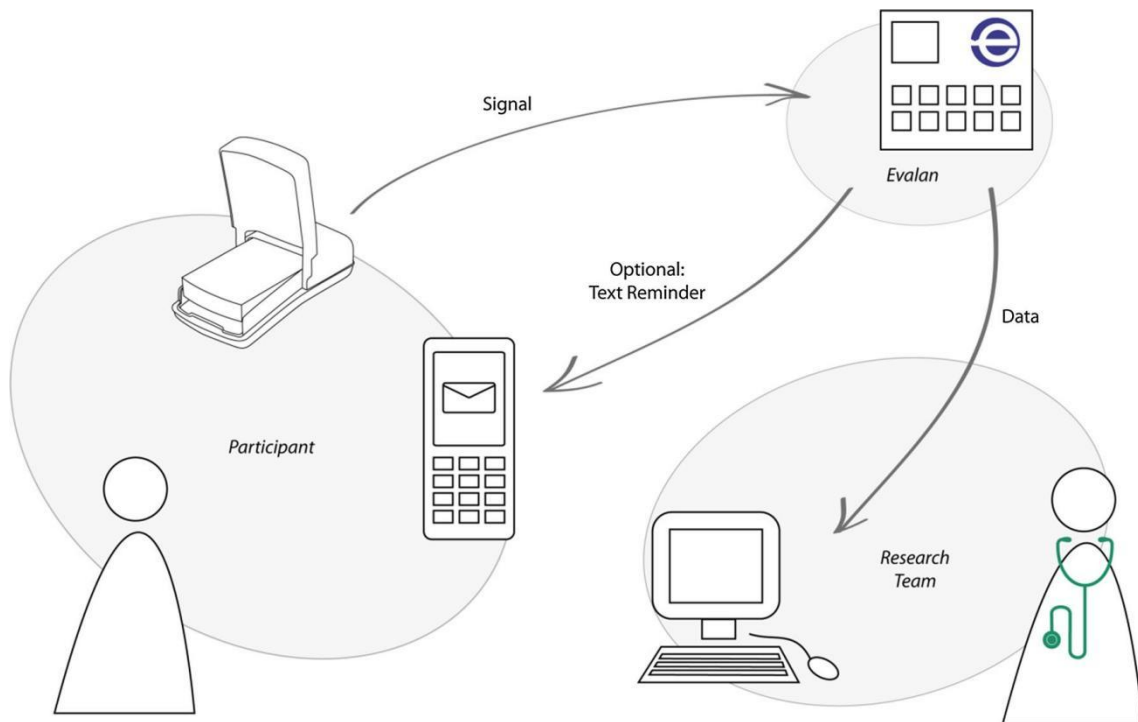
Figure 8: A schematic diagram of real-time medication monitoring (128).

4.6.4 99DOTS

99DOT is a novel Digital Adherence Technology (DAT) tool that utilises a combination of packaging and basic phone to track patient medication intake. As depicted in Figure 8, the medication blister is enclosed within customised paper envelopes sealed by the HCW. Patients reveal a hidden phone number by tearing perforated flaps on the envelope and proceed to make a too-free call using their personal or family member's phone. The call is recorded as an adherence event and later evaluated by the HCWs (133).

Different studies have come to a different conclusion about how well the 99DOTs system improve medication adherence. More study is needed for a definitive conclusion and problems with implementation need to be solved.

For instance, the 99DOTs system was implemented in Uganda, where patients and HCWs found the intervention very easy to use, leading to an increased adherence rate of 96.4% among the observed patient. However, the intervention had no comparison group to validate if the intervention directly resulted in a high adherence outcome (134). Similarly, an Indian study documented an adherence rate of 96% among the 150 patients that were included in the 99DOTS implementation (135).

However, studies conducted in Uganda (136) and India (137) found no association between the intervention and treatment success rate. This lack of association was attributed to poor implementation and interaction of HCWs, inadequate monitoring, and patients' inability to use the system effectively, leading to underestimating the intervention's effectiveness.

Despite the high acceptability of the intervention, challenges such as poor network coverage, inadequate social support, unstable electricity supply, and the unavailability of the phone, especially among less privileged populations, affect its effective implementation (138)

Figure 9**: 99DOTS Demonstrations** (133)

4.6.5 Cognitive and Behaviour Interventions

Several studies have documented the impact of patients' knowledge of the diseases and counselling to promote behavioural changes (48,55,65). Cognitive intervention empowers patients to make informed decisions and actively manage their health condition (139). It also helps reduce stigma and discrimination while fostering acceptance among both patient's family and community members (140).

Cognitive interventions like educating and counselling patients have been shown to help patients take their medication as prescribed. This leads to better treatment outcomes and lowers the rate of non-adherence.

For example, in a quasi-experimental study by Sariem et al., patients who received knowledge and counselling were four times more likely to have a successful treatment outcome than those in the control group (p<0.01; CI=1.5-8.4). (139). Similarly, in Ethiopia, counselling and educating the patients on the importance of medication adherence also helped reduce non-adherence from 19.4% at baseline to 9.5% at the endpoint in the intervention group. In comparison, non-adherence increased from 19.4% to 25.4% in the control group. However, the involvement of HCWs to collected information from patients may influence the responses of the patient leading to bias or overestimation (141).

Having low or no knowledge of the cause of diseases has been documented to influence poor adherence and increase loss to follow-up (142). At the same time, effective and continuous counselling improves medication adherence, especially for long-term treatment (53,98,143).

4.6.6 Community-Based Direct Observe Therapy (CBDOT)

CBDOT is an approach aimed at improving medication adherence, particularly for patients staying in communities with limited or no access to DOT sites (144). It helps reduce inconveniences such as covering longer distances, facing longer waiting hours in DOT sites, and dealing with stigma and discrimination when visiting DOT sites for medication (48,81). At the same time, it relieves pressure on the limited available resources in health facilities.

CBDOT shows promise in helping patients adhere to their medication because of its high case-holding rates and treatment success. For instance, a retrospective study on CBDOT intervention in Benun state, Nigeria, documented that the approach recorded a 95% case holding with only a 5% loss to follow-up, underscoring the importance of CBDOT in improving medication adherence (145). In Ethiopia, the extension of DOT services in rural areas and care provided by close community members resulted in an increased treatment success rate of 75% among the 178 patients who completed the treatment (146). While it was also noted in a randomised control trial that CBDOT is more cost-effective than the hospital-based DOT system, with less loss to follow-up patients, 3% (2/27) in the CBDOT compared to the 20% (15/27) loss to follow-up patients in the hospital-based DOT (147).

Several studies have documented the high acceptability of CBDOT by patients, especially older patients and women, due to its convenience in terms of accessibility and affordability (57,148,149).

4.6.7 Treatment Supporters

Assistance provided by friends, family members, and community members has been documented to improve medication adherence significantly. This support can take various forms, including financial aid and emotional or psychosocial support. Such help fosters effective communication and ensures drugs are taken on time (92).

Based on the findings, it is conclusive that supportive interventions, including financial aid, provision of food, and encouragement from family members, improve medication adherence, for instance.

A study conducted in Ethiopia found that support in the form of financial aid and the provision of food improved medication adherence among patients (102). Similarly, another Ethiopian

study reported similar findings, indicating that support is crucial in enhancing medication adherence (79).

In a qualitative study in Nigeria, a female participant expressed how instrumental her family members were in ensuring she completed her treatment, as described in her own words (92).

> *"For me, it was very traumatic to start taking drugs I have not been used to… but I got so many encouragements, people around me… And probably to be frank, if not for their encouragement and everything, I would have stopped; because this is my last month, I wouldn't have taken it this far, I would have stopped, but they encouraged me that I had to complete the period of medication." Female TB patient (92).*

The positive influence of treatment supporters is further evident in a study conducted in Zimbabwe, where patients who received social support from family members had better health-related quality of life than those who did not receive such support (150).

4.6.8 Incentive support to improve medication adherence

Tuberculosis, like many other chronic diseases, requires a more extended treatment duration, consequently affecting the affected person's economic productivity (151). Providing a financial package to support additional associated costs (transport, food and accommodation costs) carried by the patient has significantly improved medication adherence (152).

Among the three studies exploring the impact of incentive support on medication adherence, all reported that incentive packages improve medication adherence, for example. An economic intervention package implemented in Ebonyi state documented a reduction of catastrophic expenditure from 59.5% to 10.7% in the intervention group and an increased treatment success rate from 71.1% to 86% due to decreased loss to follow-up cases (152). However, due to an uncontrolled quasi-experimental design, the findings may be prone to bias and confounding, and the smaller sample size limits the generalizability of the results.

Another qualitative study conducted in Ebonyi state also documented the positive impact of incentive packages on medication adherence. It highlighted how such interventions resulted in high acceptability and increased clinic attendance among TB patients, especially those less privileged (89), *as expressed by a 46-year-old patient*.

> *'I thank you for providing us this money…most times when I want to come to the hospital I borrow money for transportation then when I collect the money I will go and pay back' (IDI, 45-year-old female (74).*

A randomised control trial in South Africa found that those who received economic support had a higher adherence rate, 10% higher than those in the control group. However, the interventions and control groups had no significant difference in treatment success. This might be attributed to the inefficient implementation of the intervention (153).

Chapter Five

5.0 Discussions

Chapter five of this thesis will include discussions of findings, conclusions and recommendations to the government and NTBLCP.

Adherence to TB medication among TB patients in Nigeria is vital to improving treatment outcomes and the overall goal of the NTBLCP to control TB within the general population.

The main objective of this study was to investigate the factors influencing medication adherence among TB patients in Nigeria and provide recommendations to government stakeholders, partners, and the Ministry of Health through NTBLCP.

According to the articles reviewed, the following were identified as the most reported factors influencing TB treatment adherence within and outside Nigeria, within the patient-related domain, including poor knowledge of TB, cultural beliefs, harmful lifestyle choices, and perceived well-being.

Poor knowledge was often interconnected with other factors, including the absence of counselling by healthcare workers or the influence of cultural beliefs. Patients not educated or counselled may think the disappearance of symptoms as a cure or side effect of the drug as a medication reaction; thus, they stop taking the medication. While people with deep cultural beliefs were also found to lack knowledge of TB causes and treatment, influencing their adherence to TB medication. Poor adherence to TB medication due to a lack of knowledge, and cultural beliefs, was also documented in Ethiopia (154). Similarly, harmful lifestyle practices, including alcohol consumption and smoking, negatively influences treatment adherence. Patients who consume alcohol mostly forget to take their TB treatment due to intoxications, thus leading to non-adherence. Harmful lifestyle practices were also documented in a systematic review conducted in LMICs to influence medication adherence among TB patients (155). Moreover, perceived well-being was also mentioned in most of the studies to influence medication adherence. Patients not educated on the importance of treatment and treatment completion were often reported to stop their medication halfway during treatment, either due to disappearing symptoms or the presence of signs and symptoms during the treatment.

To address these challenges that influence TB treatment adherence under the patient-related domain, interventions including effective patient education and counselling have been introduced, where patients are educated on the importance of treatment completion and counselled on the effect of harmful lifestyle choices. In Nigeria and Ethiopia, effective education and counselling of patients before and during treatment show promising outcomes by reducing non-adherence and improving treatment outcomes.

This review also documented that stigma, discrimination, alternative medication, poverty, lack of treatment support, and unemployment were the most commonly cited socioeconomic factors associated with poor TB treatment adherence.

Stigma and discrimination were associated with poor TB treatment adherence, which was prevalent in TB-HIV coinfected patients, uneducated patients, and those living in rural areas. Due to the belief that TB is caused by witchcraft and evil spells, community or family members

segregate themselves from the patient; this act discourages patients from disclosing their status or asking for help, thus leading to treatment interruption.

Effective interventions, including the involvement of friends and family members to provide social support for patients, have been identified to counteract stigmatisation and discrimination. Social support has demonstrated promising outcomes by promoting greater acceptance within the community. Whereby patients receive emotional, physical, and financial aid, thus motivating them to continue treatment. Research conducted in Zimbabwe and Nigeria has underscored the positive impact of support from friends and family, fosters community acceptance and improves medication adherence.

Moreover, traditional remedies were also found to influence medication adherence negatively. The issue of traditional or alternative medicines was more prevalent in patients with cultural beliefs in the cause of TB and individuals lacing awareness about the underlying causes of the disease and available treatment choices. The practice of resorting to traditional remedies has been observed in other contexts to impact treatment adherence negatively (154).

To counteract these challenges, interventions focused on adequately educating patients and community members about the correct approach to TB treatment have proven effective in enhancing TB treatment by raising awareness and disseminating accurate information. Studies conducted in a similar context show that patients receiving educational intervention were less likely to use traditional remedies.

This review also identified certain groups at a higher risk of treatment interruptions; workers, married couples, and older patients. Among these, married women tended to forget their treatment due to the demands of domestic work, while older patients faced difficulties remembering because of cognitive impairments. Employed patients were also prone to medication forgetfulness due to their busy schedules, ultimately contributing to treatment interruptions.

Interventions like sending daily SMS reminders to patients have proven effective in addressing the issue of forgetfulness. These reminders not only provide information about health and motivation but also help patients remember to take their medication consistently, which in turn improves their adherence to TB medication. This intervention has demonstrated positive outcomes, such as increased clinic attendance and improved adherence rates among patients who received SMS reminders in Mozambique. The use of SMS reminders in Nigeria to improve TB medication will be viable, considering the extensive mobile usage among the general population.

Additionally, this review identified Poverty as a significant factor influencing treatment adherence. Poverty was high among unemployed patients and mostly those living in rural areas and deprived communities; it was observed that poor or low-income patients could not pay for transportation and provide food during treatment, making it difficult to access care and adhere to treatment. Patients lacking a reliable social support system also confronted similar difficulties, thus leading to non-adherence. The correlation between impoverished conditions and inadequate adherence to TB treatment is supported by existing literature (156).

Addressing this issue, Evidence suggests that incentive-based interventions, including financial support to economically disadvantaged patients, can improve treatment adherence. Offering assistance in the form of food and transportation to those in need enables them to overcome the

financial barriers that hinder their ability to remain consistent with treatment. Evidence from Nigeria shows that TB patients given incentive support were more likely to continue treatment and have good treatment outcomes.

Findings from this review document that negative attitudes toward patients, long waiting times, uneven distribution of DOT sites and the delayed disbursement of funds to DOTs sites are the most common health system-related factors associated with poor TB treatment. There is a scarcity of adequately trained staff to manage TB cases, causing an overwhelming workload for the limited staff. Most HCWs are volunteers and lack the knowledge and skills to educate and counsel patients effectively. In some instances, patients are being scolded by HCWs for not adhering to treatment instructions. Additionally, some patients may spend up to an hour or more before receiving treatment due to the high workload. This unfriendly attitude of HCWs and long waiting times demotivate patients from continuing treatment. The unfriendly attitude of HCWs was also documented in other reviews to influence medication adherence (154,157). Training and posting a designated TB staff, motivation, and monitoring HCWs are some interventions to improve medication adherence.

Moreover, inaccessibility to DOT sites, either due to distance or geographical barriers, was documented in this review to negatively influenced medication adherence. DOT sites are unevenly distributed across Nigeria, with the majority concentrated in urban areas, making it difficult for patients in remote rural areas to access these services. This comes with additional costs that some patients, especially those staying in hard-to-reach areas, struggle to afford, thus resulting in discontinuation of treatment. However, interventions, including decentralising DOT services through CBDOT, mobile clinics and outreach services, can reduce the gap of inaccessibility and improve medication adherence. The decentralisation of DOT services in rural areas through the CBDOT will be more feasible by using the community volunteer structures established by the NTBLCP.

Furthermore, this review also found that financial constraints affect medication adherence. The limited and delayed disbursement of funds from the federal and local governments affects the implementation of DOT services. This affects the performance of the DOT services and hinders the proactiveness of the staff, resulting in challenges with tracking and following up on patients who may be lost to follow-up, thus leading to treatment interruptions.

Findings from this study documented that medication-related factors, including medication side effects, complex regimens, co-morbidity, and duration of treatment, negatively influence medication adherence. Evidence from the literature corroborates this finding that patients who experience adverse side effects or take longer to recover might think the drug is ineffective or too much for the body, eventually making them stop their anti-TB treatment (154). The issue of pill burden and medication effect was also prevalent among TB-HIV coinfected patients. Due to the limited staff and the many clients visiting the clinic for services, HCWs had limited or no time to educate and counsel the patient. Training of HCWs on effectively educating and advising the patient could solve these identified problems. TB-HIV coinfected patients faced additional challenges. In Nigeria, TB and HIV services are usually provided in separate clinics in most hospital settings. Patients are forced to visit each clinic one after the other to get treated. This appears time-wasting for some patients as clinic hours interfere with their everyday business, thus leading to treatment interruption. The one-stop clinic, which provides both TB and HIV services, is an intervention that has been explored to address these challenges.

Limitation of findings:

Among the various review articles, particularly those conducted within Nigeria, it was evident that patient adherence levels were primarily determined through self-reporting, leading to overestimation or wrong reporting because patients might not want to say they are not taking their medicine as prescribed. Most of the studies were cross-sectional designs, limiting their ability to assess the long-term adherence patterns of patients.

Most studies were hospital-based, relying on routine clinical data to assess adherence levels. The use of routine clinical data in hospitals can be limited due to inaccurate recording, potentially influencing reported findings and causing either overestimation or underestimation of adherence levels. On the other hand, there were community-based studies conducted in urban or rural areas with small sample sizes, thus limiting the generalisation of their findings to the entire TB population.

Conceptual Framework

The conceptual medication adherence framework (DONUT FRAMEWORK) was instrumental in providing a structured approach to understanding factors influencing medication adherence. The framework outlined five key domains, patient-related, socioeconomic, health system, medical-related, and condition-related factors. Utilizing these domains helped me coherently identify and present the findings, shedding light on factors influencing medication adherence.

While the framework was helpful, it was evident that it was very comprehensive in providing the factors influencing treatment adherence in each domain. However, the framework did not capture certain factors that appeared during the finding to have influenced medication adherence and addressed the study's objective. As a result, these factors, including alternative medication used, were added to the socioeconomic factors, and financing/funding and health policy were added to ensure a thorough analysis. By incorporating these additional factors, the study aimed to offer a more comprehensive and meaningful understanding of medication adherence determinants.

Conclusion:

In conclusion, tuberculosis still poses a severe public health risk in Nigeria, contributing to the high mortality rate in the country. The difficulty of patient adherence to treatment remains despite the availability of free care. The study highlights key factors that affect compliance, including lack of knowledge regarding TB causes and treatment, forgetfulness, harmful lifestyle, perceived well-being, level of education, community stigmatisation and discrimination, lack of social support, traditional medication use, attitude of HCWs, inaccessibility of DOT sites, medication duration, and side effects.

The evidence-based interventions identified from the review, including SMS reminders, CBDOTs, educating and counselling patients, incentive packages, and social support, can aid the Federal Ministry of Health through the NTBLCP in developing targeted strategies to improve TB treatment adherence and reduce the burden of diseases in the country. Effective interventions addressing these factors will be crucial in achieving better treatment outcomes and reducing TB-related mortality rates.

Recommendation:

The Federal Ministry of Health, through the NLTBCP, should ensure that HCWs and counsellors conduct extensive patient education and counselling on the importance of adhering to and completing treatment, correcting the myths and cultural beliefs regarding TB. This can address the issue of lack of knowledge of the diseases.

The Federal Ministry of Health should collaborate with mobile companies operators to scale up, develop and implement an SMS-based reminder system that HCWs may use to remind patients about treatment prescription schedules and their next clinic visit. This address the issue of forgetfulness among patients, especially married couples and workers.

The Federal Ministry of Health, through the NLTBCP, should operationalise the advocacy community sensitisation mechanism (ACSM) by working with local authorities and community influencers, community volunteers, and HCWs to implement a community awareness program, educating community members on the actual cause of the diseases and available treatment. This can address the issue of stigmatisation and discrimination and foster community acceptance.

The Federal Ministry of Health, through the NLTBCP, should collaborate with international non-governmental organisations (NGOs), including Global Fund and World Food Program, to provide an incentive package, particularly for impoverished TB patients. The incentive package will enable patients to afford transportation and food costs.

The NLTBCP and Human Resources for Health should train and post designated TB staff to the DOT sites nationwide. The training should focus on improving the HCWs' knowledge, communication and counselling skills. This can aid them in effectively educating and counselling TB patients and, at the same time, addressing the negative attitude of HCWs.

The Federal Ministry of Health should collaborate with local and international NGOs to strengthen the decentralise community DOT services to reach patients in hard-to-reach communities through trained community volunteers, a mobile clinic, or an outreach program. To reduce the inaccessibility of DOT services and the burden on DOT sites.

The Federal Ministry of Health, through the NLTBCP, should advocate for timely and sufficient disbursement of funds from Federal and local governments to support the implementation of DOT services, including an outreach program, monitoring of staff and tracking of loss-to-follow-up patients.

Research

The NTBLCP should ensure that the adherence module is included in the TB prevalence survey to gain a comprehensive understanding of the actual treatment adherence rates among individuals with TB within the country.

Appendix 1

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