A literature review on the contributing factors influencing Medication Adherence to Treatment in Type 2 Diabetes Mellitus in Nigeria

Martha Chioma Ebuenyi

Nigeria.

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By

Martha Chioma Ebuenyi
Nigeria

Declaration:

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

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LIST OF ABBREVIATIONS

ADA	American Diabetes Association
DALYs	Daily Adjusted Life Years
DM	Diabetes Mellitus
FMoH	Federal Ministry of Health
HICs	High Income Countries
IDF	International Diabetes Federation
LMICs	Low and Middle-Income Countries
NCDs	Non communicable Diseases
NHIS	National Health Insurance Scheme
NIDDM	Non-Insulin Dependent Diabetes Mellitus
OHA	Oral Hypoglycemic Agent
UN	United Nations
WHO	World Health Organization

DEFINITION OF TERMS

Adverse Drug Reaction:

An appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product (Edwards and Aronson, 2000).

Adherence:

The extent to which a person's behaviour – taking medication, following a diet,

and/or executing lifestyle changes, corresponds with agreed recommendations

from a health care provider(World Health Organization, 2003a).

Polypharmacy:

Regular daily consumption of multiple medications as well as the use of high-risk medications and questionable dosing(Golden et al., 1999)

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To my ICHD/ MPH classmates, you guys were phenomenon

Finally, to my darling husband and kids, my parents and siblings, you all made me stronger. God bless you and I love you all.

DEDICATION

The thesis is dedicated to my father in law Late Mr. Theophilus Ebuenyi and to my uncle Late Mr. Thaddeus Nkemnakwu

Introduction

As a pharmaceutical scientist my job is to discover, manufacture, supply and dispense medications for the healthcare needs of the population. My desire for this literature review on medication adherence in Type 2 diabetes mellitus derives from my interest in health promotion, policy, intervention and research.

My Pharmacy school and internship experience revealed the dearth of health services, provision of effective medication use and education and limitations to the utilization of available health care especially in chronic diseases. Although as a private citizen and health professional I could make a difference, I yearned for an opportunity to affect health at a population level through research. The experiences and challenges of my work environment reawakened my interest in NCDs especially on medication use.

Globally, effective management of T2DM (Type 2 diabetes mellitus) still remains a challenge for all persons involved in the management of the disease. The intersection between NCDs and medication adherence interests me and presents a responsibility for the pharmacist and public health professional. This responsibility extends from medication production, distribution to administration. Therefore, to prevent premature morbidity and mortality that could result from non-adherence in T2DM, and to also understand what encourages medication adherence, the overall objective of the study is to explore the factors that influence medication adherence in Type 2 Diabetes Mellitus. The findings of the review will encourage recommendations for appropriate and effective interventions to policy makers and stakeholders to improve medication adherence in Type 2 Diabetes in Nigeria.

The thesis is divided into 5 chapters.

- Chapter one gives background information about Nigeria, an overview of the

health care system, information about Type 2 diabetes mellitus(T2DM), diagnosis and treatment, existing policies on non-communicable disease (NCDs) including nutritional guidelines, prevention and control strategies.

- Chapter two includes the problem statement, justification, objectives and methodology for the study
- Chapter three presents the results/findings from the literature review of literature on contributing factors influencing medication adherence in T2DM.
- Chapter four discusses the findings in the available literature analyses
- Chapter five presents the conclusion and recommendations for policy review and/or change based on the findings and discussion.

"Cancer, diabetes, and heart diseases are no longer the diseases of the wealthy. Today, they hamper the people and the economies of the poorest populations even more than infectious diseases. This represents a public health emergency in slow motion."

Ban Ki-Moon, Former United Nations Secretary-General

Abstract

Background: Type 2 Diabetes Mellitus (T2DM) the most common form of Diabetes Mellitus (DM) is primarily managed through life style modification and/or oral hypoglycemic agents (OHA) and insulin. Patients are expected to adhere to treatment to prevent complications resulting to premature morbidity and mortality. Therefore, identifying the contributing factors that influence medication adherence (MA) in T2DM is important.

Objective: To explore the factors that influence MA in T2DM from the literature, in order to make recommendations for MA in T2DM in Nigeria**.**

Method: Review of literature for studies identifying contributing factors that influence MA in T2DM in Nigeria. The holistic model by Jaam et al. was applied as a guide to analyze findings from the included literature.

Result: The patient, disease (T2DM), medication, healthcare professional, health care institution and societal related factors were identified. The major influence on MA identified were complexity of regimen, cost of medication, use of herbal remedy, side effects of medications and poor patient- health professional interaction.

Conclusion: Medication adherence in T2DM is essential, to prevent complications resulting to premature morbidity and mortality. However, an appraisal of the literature on contributing factors influencing MA in T2DM reveals a dearth in data on other vital factors influencing MA in the model.

Recommendations: Further research on the prevalence of T2DM in Nigeria and influence of the multidisciplinary health system and society on MA, a review of national policies on diabetes care in healthcare facilities, national health insurance scheme and drug regulations**.**

Keyword: type 2 diabetes mellitus, medication adherence, patient, Nigeria.

Word count: 11, 440

CHAPTER ONE: BACKGROUND INFORMATION

This chapter provides information about Nigeria. It gives vital information about the geography, demography, sociocultural, educational status, health indicators and healthcare system structure.

1.1. Geography

Nigeria officially referred to as the Federal Republic of Nigeria is a sub Saharan country located in the Western region of Africa. It is bounded by the Atlantic Ocean in the south, Niger Republic and Chad in the north, Benin republic in the west and Cameroun in the east(Federal Ministry of Health, 2008). Nigeria is divided into six geo-political regions (see figure 1), with a total of 36 states and Abuja as the federal capital territory. The country has a total of 774 Local Governments Areas (LGA) with a total mass of 923,768sq km2(Federal Ministry of Health, 2008).

Figure 1: Map of Nigeria showing the geopolitical zones (Umaru Yusuf, 2018).

1.2. Demography and population

Nigeria occupies the 7th position on the world population list with over two hundred million inhabitants; and commonly known as the most populous black nation (Federal Ministry of Health, 2008). The male population is higher than the female population. There is a preponderant young population with the median age of median age of 19.7years.

1.3. Socio-cultural and economic situation

There are 3 major ethnic groups in Nigeria and over 350 minor ethnic communities (Federal Ministry of Health, 2008). The official language is English however, over 500 local languages including Hausa, Yoruba, and Igbo are spoken(Federal Ministry of Health, 2008). Most people practice Christianity, Islam and Traditional religion. The central and southern region is predominantly occupied by Christians and traditional religion practitioners while Islam is largely practiced in the northern region.

There is presence of crude oil which is the main source of revenue for the government which is not considered labour intensive, and a non-oil economy which is still relatively weak. However, in 2018 about a quarter of the Nigerian workforce was unemployed, and close to another 20 percent were under-employed (The World Bank, 2019).

- **Education**

The 2010 National Bureau of Statistics approximated the literacy level of Nigerian adults to be 56.9%. However, the level of literacy varies depending on sex (male 65.1% and female 48.6%) and on location (urban 74.6 % and rural 48.7%)(UNESCO, 2012). Also, the 2008 National demographic health survey reported a higher literacy level in the southern part of Nigeria respectively as 90.9% in males and 79.6% in females against 63.3% in males and 30.5% in females in the northern part(Federal Ministry of Health, 2008).

1.4. Health status and epidemiological profile

While the majority of the morbidity and mortality in Nigeria is still attributable to communicable diseases (CDs) including human immunodeficiency virus/acquired immune-deficiency syndrome (HIV/AIDS), tuberculosis (TB), malaria and diarrhea; Nigeria however experiences a double burden of disease due to its demography and epidemiological transition, resulting in an increasing DALYs(disability-adjusted life years) lost due to NCDs (World Health Organization, 2014). The increasing prevalence of NCDs including diabetes mellitus, cardiovascular diseases and cancer has led to high morbidity and mortality(World Health Organization, 2014), (World Health Organization, 2010, World Health Organization, 2014). Life expectancy in Nigeria is 53.2 years, 53.8 years and 52.6 years for females and males respectively, with population growth rate of 3.2% and fertility rate of 5.7 births per woman (Federal Ministry of Health, 2008).

1.5. National healthcare system

The federal ministry of health is the main body in charge of the healthcare system headed by a minister of health. The three different tiers of healthcare include primary, secondary and tertiary healthcare institutions (Ademiluyi and Aluko-Arowolo, 2009). Health services are delivered through private, orthodox and traditional facilities. The first point of call is the primary health centre. These Centres are for prevention and treatment of conditions like malaria, fever or cold and provision of health education, and promotion and diagnosis of chronic diseases including T2DM, however, referrals are made to the other higher tiers (Ademiluyi and Aluko-Arowolo, 2009).

The secondary health centre provides preventive and treatment services involving some complex cases, however further complicated cases are referred to the tertiary specialist hospitals. General hospitals and comprehensive health centres (some are owned by private

individual(s) or groups of individuals) are examples of secondary health facilities (Ademiluyi and Aluko-Arowolo, 2009).

The highest tier is the tertiary health institution which is also called specialist/teaching hospitals. These institutions handle complex health problems/cases through referrals from lower healthcare facilities including general hospitals or on direct admission. Tertiary healthcare facilities have sections including accident and emergency unit, diagnostic unit, in patient wards units, outpatient consultation and treatment units. There is presence of skilled staff for every unit. Some of the institutions are university-based, and termed Teaching hospitals. This implies that they conduct research and provide findings and strategies for health policies (Ademiluyi and Aluko-Arowolo, 2009).

The government has made several reforms to increase the provision of health to the Nigerian people, however, only about 43.3% have access to healthcare (Omoruan et al., 2009). This is largely due to the fact that 55% of the populace live in rural settlements against 45% in the urban dwellings(Welcome, 2011). It is also pertinent to mention that the private health institutions provide close to 70% of the health care, as against only 30% by the government (Omoruan et al., 2009, Eneji et al., 2013).

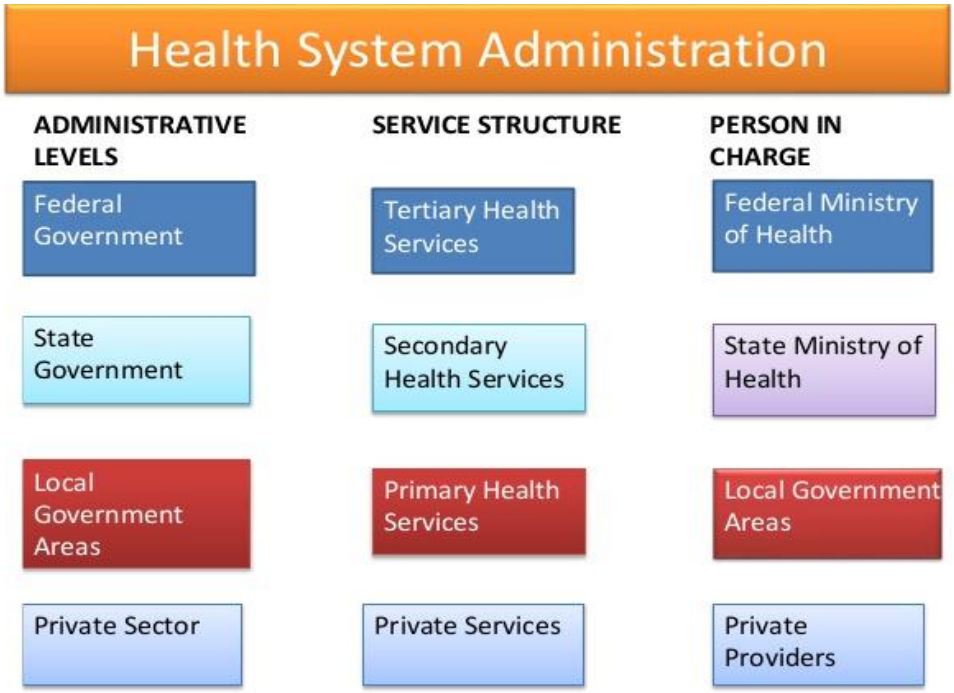

Figure 2 Organizational structure of the Nigeria healthcare system (Williams Uzoma, 2017)

1.6. Prevention and control of NCDs

In low and middle income countries (LMICs) including Nigeria, dietary change has been linked to social and economic transition (Popkin, 2004). This socio-economic transition may lead to both negative and positive dietary changes that have implications for metabolic diseases like diabetes (Popkin, 2004). Consumption of fatty foods or other high-fat condiments is compensating for the reduction in staple food and this could as a result of socio-economic challenges, urbanization and ignorance(Federal Ministry of Health Nigeria, 2014). Furthermore, the increased consumption of energy and fats when accompanied with a sedentary lifestyle and decreased physical activities can result in obesity(Chaput et al., 2011). Hence, a combination of both socio-economic challenges,

lifestyle management, urbanization and ignorance about the right combination of food makes diabetes prevention and management difficult (Federal Ministry of Health Nigeria, 2014).

Dietary control is very important in T2DM, and recommendations for a healthy consumption plan for NCDs prevention, control and management has been reviewed extensively(Federal Ministry of Health Nigeria, 2014). The healthy eating practices for T2DM is almost the same or slightly different from what the general population is advised to practice. The inclusion of fruits and the practice of eating proportioned quantities as well as regular exercise which is a very important factor is advised (Federal Ministry of Health Nigeria, 2014). People are advised to brisk walk and avoid sedentary lifestyles, sedentary lifestyle is a predisposing factor to T2DM and T2DM can be worsened in the presence of obesity (World Health Organization, 2004).

The federal ministry of health introduced the national nutritional guideline on non-communicable disease prevention, control and management in October 2014 (Federal Ministry of Health Nigeria, 2014). The guideline provides vital information and knowledge on good nutrition which is a very practical aspect in the prevention and management of NCDs (Federal Ministry of Health Nigeria, 2014, Foundation, 2017), (Diabetes and NCDs in Nigeria, 2017).

In May 2013, the federal ministry of health developed the national policy and strategic plan of action on prevention and control of non-communicable diseases. The policy seeks to create awareness, control, early detection and subsequent prompt management or referral of NCDs(Federal Ministry of Health Nigeria, 2014).

Furthermore "Nigeria is a signatory to the 2011 United Nation (UN) political declaration on the prevention and control of NCDs and the World Health Assembly of May 2013 Global Action Plan for the prevention and control of NCDs 2013-2020, and the 2030 agenda for sustainable development goals adopted by member states of the United Nations in September 2015 specifically included the reduction of premature deaths from NCDs" (Diabetes and NCDs in Nigeria, 2017). Policies abound and expected to lead to prevention and control of NCDs if they are implemented, therefore, more effort is needed in generating reliable national data on implementation of national policies and strategies concerning NCDs (Diabetes and NCDs in Nigeria, 2017).

Management (including prevention activities and treatment) of T2DM in Nigeria occurs at all levels of care (primary, secondary and tertiary), however, specialist care is usually provided from the secondary level (Ademiluyi and Aluko-Arowolo, 2009).

CHAPTER TWO: PROBLEM STATEMENT, JUSTIFICATION, OBJECTIVES, METHODOLOGY AND CONCEPTUAL FRAMEWORK

2.1. Introduction

Diabetes mellitus(DM) a chronic disease condition, is a group of diseases characterized by high levels of blood glucose as a result of defective insulin secretion or regulation (American Diabetes Association, 2013).

Type 2 Diabetes mellitus also referred to as acquired or non-insulin-dependent diabetes mellitus (NIDDM) occurs when there is a deficiency or resistance of the hormone insulin which is responsible for regulating the level of glucose in the blood (American Diabetes Association, 2013, Tuomilehto et al., 2001). Type 2 diabetes mellitus (T2DM) which is the most common form of Diabetes mellitus can result from one's own body system or from unknown processes, however, a majority of the population with T2DM is of an immune-mediated origin (Rother, 2007). This form of T2DM, can be asymptomatic for some years, hence diagnosis of the disease often results due to associated complications or through incidental blood or urine glucose test. The risk of T2DM increases with increasing age, obesity or overweight, living in urbanized settings, a sedentary lifestyle and genetics(Chen et al., 2012)**.** These risks factors are increasing in LMICs, hence the increase in the prevalence of T2DM (World Health Organization, 2004).

Typical signs and symptoms of diabetes include: increased thirst (polydipsia), frequent urination, (polyuria) weight loss and polyphagia (increased hunger), while itchiness, fatigue, recurrent vagina infections, blurred vision and peripheral neuropathy are often present at diagnosis (Vijan, 2010). However, some individuals experience no symptoms in the early stage of the disease (Force, 2006).

Characteristics	Type 2 Diabetes Mellitus
Onset (Age)	Commonly ≥ 40
Type of onset	Gradual
Nutritional status	Usually obese
Clinical symptoms	Often asymptomatic
Endogenous insulin	Present, but relatively ineffective
Insulin therapy	Required in about 20- 30% of patients
Hypoglycemic drugs	Clinically indicated
Diet	Mandatory with or without drug

Table 1 features of Type 2 Diabetes Mellitus (World Health Organization, 1999)

2.2. Diagnosis of T2DM

The international diabetic federation recommends(IDF) the WHO 1990 criteria as standard for screening and diagnosis of diabetes (Force, 2006, World Health Organization, 2011).

2.3. Treatment and management of Type 2 Diabetes Mellitus

To properly control T2DM oral medication or insulin which is injected is used (Rodbard et al., 2009), however, there exist a range of self-management practices including diet and exercise to improve glyceamic control.

The different antidiabetics used in Nigeria to manage T2DM are: Biguanides, Sulphonylureas

Alpha-Glucosidase inhibitors, Dipeptidyl peptidase 4 (DPP-IV) inhibitorsDPP-4 inhibitors, Human insulin, NPH insulin, Insulatard, Premixed (30/70), Insulin glargine, Insulin lispro (Ogbera and Ekpebegh, 2014)

2.4. Problem statement

According to the International Diabetes Federation (IDF), globally about 382 million people had diabetes in 2013(Lee et al., 2007). In the year 2000, the prevalence of the diabetic population of all ages was 2.8% and the prevalence is expected to increase to about 4.4% in 2030. This is a rise from 171 million diabetics in 2000 to 366 million in 2030. The report further emphasized that this increase will occur in low and middle income (LMICs) including those in sub-Saharan Africa. Specifically in Nigeria, an estimated 1.7million people have Diabetes, and this number will triple in 2030(Wild et al., 2004). The high prevalence can be attributed to both genetic and environmental factors which includes: socioeconomic status, aging, sedentary lifestyle, obesity and diet.

Type 2 Diabetes Mellitus (T2DM) accounts for about 90% of cases of DM (Wild et al., 2004). The burden of T2DM has continued to increase globally, and a high burden of the disease is seen in LMICs (World Health Organization, 2004), with increase in urbanization, lifestyle and diet change.

In Nigeria, there is a dearth of prevalence data for T2DM (Mbanya et al., 2010), however prevalence rates of 0.65% in rural Mangu (Northern), 6.8% in urban Port Harcourt (South south) and as high as 11.0% in urban Lagos (Southwest) have been documented (Chinenye and Ogbera, 2013).

Some complications of T2DM include diabetic nephropathy, diabetic retinopathy, ketoacidosis and diabetic neuropathy and these complications could be long term, leading to disability and in some cases(premature) death (World Health Organization, 1999).

To successfully manage T2DM, to prevent these short and long-term complications and death, adequate blood glucose level control is essential. According to the international diabetes federation, three levels of care including standard care, minimal and

comprehensive care are essential to effectively manage diabetes (Force, 2006).These levels of care include glucose control through oral therapy and lifestyle management(diet and exercise)(Force, 2006). However, for a better clinical outcome, the patient is expected to actively participate in an array of management plan which includes drug therapy (Akinkugbe, 1997). These drugs are usually administered through the mouth (insulin is administered underneath the skin in some persons with T2DM), at specific times of the day, hence it is essential to adhere to treatment guidelines.

However, adherence to medications especially in long term (chronic) diseases is challenging, and research has shown that adherence levels is about 50% in High income countries (HICs) (World Health Organization, 2003b). According to the World Health Organization, medication adherence is "the degree to which the person's behavior corresponds with the agreed recommendations from a healthcare provider "(World Health Organization, 2003a). In the event of poor adherence practices, the patients will not benefit from their drug regimen, compromising the effectiveness of treatment which could result in increased healthcare costs (drugs), healthcare facility use (hospitalization), and reduced quality of life and ultimately premature morbidity and mortality (Sokol et al., 2005, Lau and Nau, 2004).

Poor adherence to long-term therapies is critical and thus an important issue in the quality of life and health economics especially in LMICs, with a dearth of health resources and inequities in access to health care(World Health Organization, 2003a).

Some of the factors that influence medication adherence are multifaceted and they include: Patient related factors such as age, sex, comorbidities, socioeconomic status, educational level, the drug related factors such as regimen complexity and side effects,

healthcare system related factors including drug availability and accessibility to healthcare(Rubin, 2005, Horton, 2008).

A study conducted in Uyo eastern Nigeria, reported that uncontrolled diabetes accounted for 62.1% of the total admissions of patients with Diabetes. About 18.7% had hyperglycemic emergencies and mortality rate was 30.3% of these population(Unadike et al., 2013). Another study in Ilorin (north central Nigeria) showed that mortality was higher in patients that presented with hypoglycemia, followed by hyperglycemic emergencies, although a majority of these patients were managed on oral hypoglycemic agents(combination of sulphonylureas and biguanides) (Chijioke et al., 2010), suggesting medication adherence was neglected.

2.5. Justification

Effective drug therapy management is essential in T2DM to ensure better clinical outcomes including reduced risks of complications and related premature and preventable morbidity and mortality (Chijioke et al., 2010, Morgan et al., 2000, Andersson and Svärdsudd, 1995). Therefore, adherence to oral hypoglycemic agents is critical, however factors including provider patient relationship and the level of information provided, the social economic status of the patient, availability and cost of the medications, the presence of comorbidities and accessibility of healthcare facilities all influence medication adherence (Grant et al., 2002, Yang et al., 2009, Walker et al., 2006).

The WHO report on adherence to long-term therapies: evidence for action. highlights that "having well-designed interventions targeting medication adherence may have far greater outcomes on the population's health than interventions with the medical treatment"(World Health Organization, 2003a). The report also stressed the need to initiate interventions to

encourage effective drug administration/use. While medication treatment can have immediate effects on a disease condition, WHO experts emphasizes that maintaining medication practices is vital; however, medication adherence in chronic diseases like T2DM remains a challenge (Cramer, 2004) especially in LMICs like Nigeria.

Nonetheless, these interventions for improved adherence would provide a meaningful positive effect by preventing risk factors through primary prevention and unwanted clinical outcomes through secondary prevention(World Health Organization, 2003a).

As a Pharmacist and healthcare provider, I play a vital role concerning medication use for effective treatment and expected clinical outcomes. This thesis aims to contribute to the existing knowledge gap regarding factors influencing medication adherence in T2DM in Nigeria. It is pertinent to identify these factors and the role they play in medication adherence, so as to implement appropriate interventions and strategies to improve medication adherence in T2DM in Nigeria.

2.6. Objectives

2.6.1. General Objectives

The overall objective of the study is to explore the factors that influence medication adherence in Type 2 Diabetes Mellitus from original studies in order to recommend appropriate interventions to policy makers and stakeholders to improve medication adherence in Type 2 Diabetes in Nigeria.

2.6.2. Specific Objectives

- To identify the disease related and drug related factors in T2DM that influence medication adherence.

- To identify the patient related and the societal factors that influence medication adherence in T2DM in Nigeria.
- To identify the healthcare provider and health system related factors influencing medication adherence in T2DM.
- To make recommendations to policy makers and stakeholders on interventions or strategies to improved medication adherence in T2DM in Nigeria.

2.7. Methodology

The thesis study is a literature review of original studies on contributing factors influencing medication adherence in T2DM in Nigeria.

2.7.1. Search strategy

Online search in PubMed, Scopus, African Journal Online databases, Cochrane library and Google scholar search engine. Also, database of the Federal ministry of health Nigeria, WHO and International Diabetes Foundation (Africa region), were searched. To limit publication and selection bias and aiming to attaining a robust review, search was extended to conference abstracts and reports from the International Diabetes Foundation. The Boolean operators "OR" and "AND" were used as strategy to search for contributing factors influencing medication adherence in T2DM.

Search terms included: "Factors" OR "Barriers" OR "Determinants" OR "Motivators" OR "Facilitators" AND" Influence" OR" Affect" OR" Impact" AND "Medication" OR "Drug" OR" Hypoglycemic agent" OR" Pharmaceutical Preparation" OR" Treatment" OR "Agent" OR "Adherence" OR "Nonadherence" OR "Compliance" OR "Noncompliance" OR" Concordance" AND "Diabetes" OR "Type 2 Diabetes Mellitus" OR" Blood glucose" OR "Hyperglycemia" OR" "Noninsulin Dependent". Search terms were modified for each database, and references of identified studies was checked (refer to annex 1).

2.7.2. Inclusion criteria

The following inclusion criteria were used to answer the research objectives of the literature review. Only original research studies in the English language between 2005 to 2019 were included in the literature review. This period was chosen because it marked an upsurge in research related to medication adherence in type 2 diabetes (an initial search was done from the period 1990 to 2005, however, there was deficiency of studies in medication adherence in T2DM in Nigeria).

Included studies identified at least one contributing factor according to the medication adherence framework (Jaam et al., 2017) that influence medication adherence in T2DM in Nigeria. The studies included adult patients from age 18years, diagnosed with T2DM and receiving medications (Pharmacological interventions) for at least one month. The included studies were all done in public health institutions and included some patients with comorbidities.

2.7.3. Exclusion criteria

Studies that did not specify the type of diabetes mellitus in their research. Any T2DM medication adherence study that combined other study participants having other medical conditions. Intervention studies were excluded as the review is not about evaluating the effectiveness of an intervention and bias could not be ruled out. Also, studies that involved persons below 18years were excluded.

2.7.4. Conceptual framework

A holistic conceptual framework model was identified during literature review and used to describe the identified factors that influence medication adherence in diabetes (Jaam et al., 2017). The model is suitable as it identifies factors ranging from the disease to the patient related factors, health provider and health system factors, and the drug medication

to societal related factors in medication adherence. These factors have all been identified in different descriptive studies including chronic disease management and is displayed in Figure 3 below (Jaam et al., 2017).

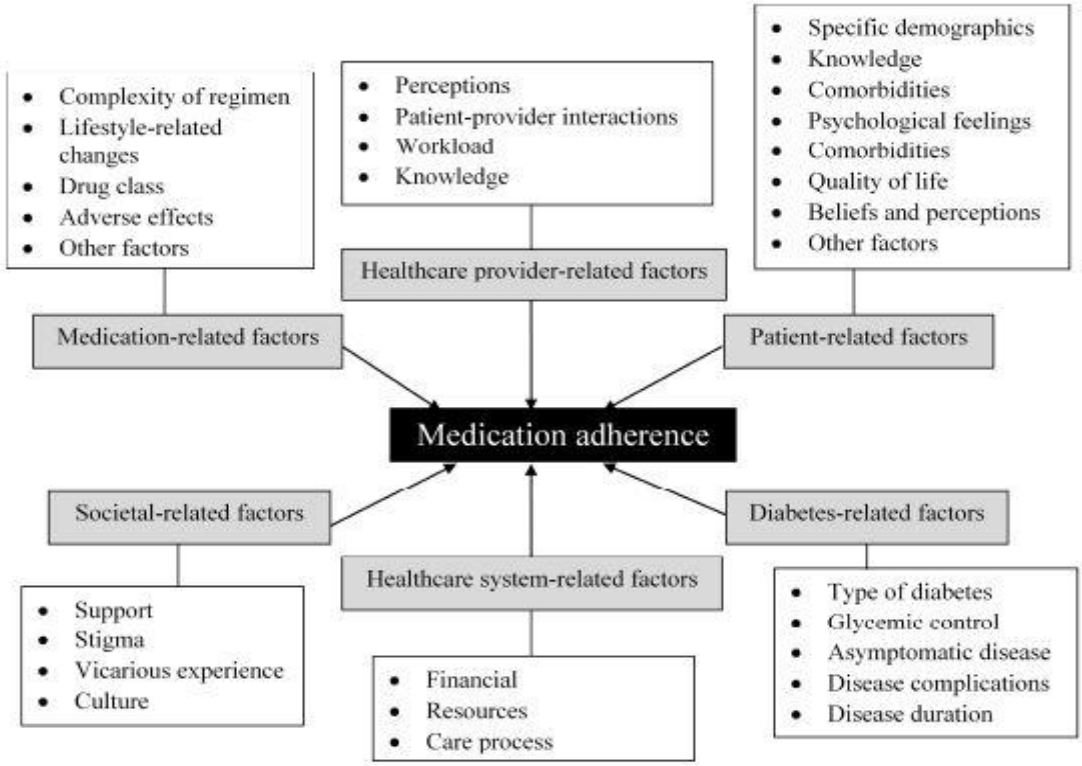

Figure1: A core conceptual framework on factors associated with medication adherence in diabetes

Figure 3. Holistic conceptual framework model

a. Medication related factors influencing medication adherence in T2DM

These factors relate to the drugs used in treatment of T2DM. Aside from lifestyle modification in T2DM, patients receive oral hypoglycemic agents(medications), insulin and in some cases a combination of the two (Tziomalos, 2017). These medications are used at different quantities and at different times of the day depending on each individual

treatment. Some factors associated with these medications include: side effects, size, quantity, drug form and frequency of administration(Polinski et al., 2013).

b. Disease(diabetes) related factors influencing medication adherence in T2DM

Type 2 diabetes require long term treatment and this can be a demotivating factor for the individual. Also, the effect of glycemic control can present with complications including glaucoma, diabetic nephropathy, hyperglycemia, ketoacidosis and diabetic foot ulcer can influence that can affect medication adherence. Also, the disease affects the daily adjusted life years (DALYs)of the individual and quality of life, hence an individual's economic status is affected**.** Furthermore, medication adherence can be influenced when the disease is asymptomatic.

c. Patient related factors

The patient is a key factor in medication adherence; therefore, it is very important to look at factors relating to the patients including demographic, socio cultural beliefs and perceptions, educational level, financial status and knowledge about T2DM (Brundisini et al., 2015). There is also the presence of comorbidities and the quality of life of the patient including their mental and psychological status that could result to unintended adherence practices (Nam et al., 2011). Furthermore, the delay of start of treatment and patient fear of administering the medication(in the case of insulin use) affects medication adherence(Brundisini et al., 2015).

d. Societal related factors influencing medication adherence in T2DM

The society is the immediate environment of the patients with T2DM hence it is important to identify the norms and cultures in Nigeria as regards T2DM. Issues such as stigma due to the disease (the need for diet change) and its complications(such as glaucoma, diabetic

foot ulcers resulting to amputation), availability of a social support system to encourage treatment(including the immediate family members). Also, societal practices concerning the practice of traditional alternative medicines and the specific diet consumed in the societal that could potentiate a drug food interaction.

e. Healthcare provider related factors influencing medication adherence in T2DM

The healthcare providers consist of all health professionals responsible for the T2DM patient. It is important for the healthcare provider to have the required knowledge of treatment guidelines in T2DM to provide effective care. Their attitude and communication skills while providing care is also important. Also, the defined roles and shared decision making amongst all participating healthcare professionals revolves around overall patient satisfaction and improvement. The healthcare providers perception about medication adherence and his bias on the ability of patients to strictly adhere to treatment regimen (Polinski et al., 2013). Further the workload of the healthcare professional plays a role on the presentation of findings to the patients concerning the disease and subsequent treatment plan.

f. Health system related factors influencing medication adherence in T2DM

The health system affects the medication adherence of individual with T2DM through the cost of appointments and prescribed medications, availability of healthcare providers and duration of care, having alternatives of medications (having a variety of brands) and shorter to moderate waiting times. Furthermore, the option of insurance and what is covered by the insurance companies, copayment plans (if it exists and who is liable). Also,

important is the accessibility of the healthcare institution and the monitoring and follow up procedures.

Limitations of the Study

There is no prevalence data for T2DM in the general population in Nigeria, included studies only had prevalence data for specific geographical areas. Another limitation is the inclusion of English language only articles.

CHAPTER THREE: STUDY RESULTS/FINDINGS

3.1. Introduction

The result section provides evidences from identified studies to address the objectives of the study. The chapter explains finding, based on the literature review on the contributing factors influencing medication adherence in T2DM in Nigeria. The influence the factors related to the medication, patients, healthcare provider, disease and society have on medication adherence in T2DM will be analyzed.

The literature search identified 16 studies on contributing factors influencing medication adherence in Nigeria.

The included studies were both case control and cross-sectional studies (observational studies). The south-western region had the highest number (9) of studies followed by the south-eastern region (5) and lastly the south-south (2). Some excluded studies were also conducted in some of the above regions and the northern regions. These studies did not indicate the specific type of diabetes mellitus (in this case T2DM) and some studies in addition to T2DM patients. The included studies were conducted at the different tiers of public health institutions in urban (most tertiary public health institutions are located in urban areas), suburban and rural settings.

Study participants were both male and female between 18 to 85years, with T2DM and treatment initiated at least 2weeks after diagnosis. All studies included outpatients' participants. The educational level of participants was from no formal education to basic education (primary and secondary) and tertiary levels and a mix of both female and male from 18years. Tables 2 and 3 provide a summary of key characteristics of all the included studies for the review.

Table 2. Summary of findings of identified studies on contributing factors to medication adherence in T2DM

Author / Year	Study Design	Location/ Region	Study population	Residency	Drug regimen	Findings
Kazeem et al. 2008	Cross sectional	Ibadan (southwest)	200 patients with T2DM Female /male	Urban	OHA monotherapy OHA combination therapy OHA + Insulin	Lack of finance, side effects and perceived inefficacy of prescribed medications were associated with medication adherence
Adisa et al. 2013	Cross sectional	Ibadan/ Ile ife (southwest)	176 patients with T2DM Male/ female	Urban	OHA monotherapy OHA combination therapy Insulin	Medication adherence and subsequent glycemic control improved in patents Prescribed more than four medications.
Idongesit et. al. 2015	Cross sectional	Calabar, (south south)	303 patients with T2DM Female/male	Urban		Limited access to care, forgetfulness, high cost of medications, low educational level, complexity of regimen, poor patient–provider communication including lack of trust in the provider and depression
Nwaokoro et al. 2014	Cross sectional	Owerri (southeast)	30 patients with T2DM Female/male	Urban	OHA monotherapy OHA combination therapy OHA + Insulin	Fear of hypoglycemia and feeling better influenced medication adherence
Onyeanusi et al. 2015	Cross sectional	Ituku Ozalla (southeast)	250 patients with T2DM	Rural		Patients having higher level of education of education had better medication adherence
Iloh et al. 2012	Cross sectional	Umuahia (southeast)	120 patients with T2DM Female/male	Urban		Financial difficulties influenced medication adherence
Adisa et al. 2009	Cross sectional	Ibadan (southwest)	121 patients with T2DM Female/male	Urban		Patients identified that dosage omission, cost of medication and forgetfulness influenced medication adherence
Awodele et. al. 2015	Cross sectional	Lagos (southwest	152 patients with T2DM Female/male	Urban	OHA combination therapy	Affordability of medications, patient age and gender influenced adherence to medication.
Adisa et al 2014	Cross sectional	Ibadan/ Ile ife (southwest)	176 patients with T2DM Male/ female	Urban		Knowledge, attitudinal and practices barriers influenced medication adherence.

Table 3. Summary of findings of identified studies on contributing factors to medication adherence in T2DM

Author / Year	Study design	Location/ Region	Study population	Residency	Drug regimen	Findings
Fadare et.al. 2015	Cross sectional	Ado-Ekiti (southwest)	123 patients with T2DM Female/ Male	Urban	OHA monotherapy OHA combination therapy Insulin monotherapy	Lack of family support, treatment cost, high pill burden, inadequate medication information, unavailability of medication, cultural and religious beliefs and inadequate information.
Adisa et al. 2017	Cross sectional	Ibadan (Southwest)	200 patients with T2DM Female/male	Urban		Patients desired family, governmental and non-government social support and financial support to improve medication adherence
Iloh et al. 2016	Cross sectional	Umuahia (Southeast)	120 patients with T2DM Female/male	Urban		Treatment satisfaction influenced medication adherence
Oyewole et al. 2015	Cross sectional	Warri (south south)	350 patients with T2DM Female/male	Urban		Use of alternative traditional medicine (herbs), lack of awareness on the seriousness of the disease.
Adisa et. al. 2011	Cross sectional	Ibadan (southwest)	114 patients with T2DM Female/male	Urban	OHA monotherapy OHA combination therapy Insulin monotherapy	Physician mode of communication during patient-physician interaction and financial constrain influenced medication adherence
Ogbonna et. al. 2014	Case control **(**Retrospective)	Nnewi (southeast)	399 patients with T2DM Female/male	Urban	OHA monotherapy OHA combination therapy Insulin monotherapy	Polypharmacy due to comorbidity resulted to drug therapy problem (nonadherence)
Ajibola et al. 2018	Cross sectional	Ibadan / Ijebu Ode (southwest)	110 0 patients with T2DM Female/male	Urban	OHA monotherapy OHA combination therapy	Adequate counseling time, insurance package, monthly income and cost of medication influenced medication adherence

3.2 Contributing factors influencing medication adherence in Type 2 diabetes mellitus in Nigeria

a. Medication related factors influencing medication adherence in T2DM

The form in which a medication is presented and/or administered plays an important role in medication adherence, this can be a potential barrier or enabler to adherence in treatment. Medication T2DM is very vital and to a large extent determines the outcome of the disease. The medication related factors affecting medication adherence have been highlighted by the holistic framework. The medication related factors identified from included studies will be explained below.

- **Complexity of regimen**

Treatment in T2DM usually requires the administration of one or more oral hypoglycemic medications, or in combination of the OHA and or prescribed with insulin. In Nigeria, biguanides and sulphonylureas are the most common OHA prescribed, and only about one in every five persons receive insulin separately or in addition (Chinenye et al., 2012). In chronic disease, the level of adherence to regimen is often reduced especially in complex drug use(Jackson et al., 2015) especially when lifestyle changes is required (Brown and Bussell, 2011).

Type 2 diabetes mellitus has a chronic progressive nature , meaning that there is a possibility for a person diagnosed with T2DM to take medications for life (García-Pérez et al., 2013). These often comes with, complications of the medication regimen which can change over time. The patient may at first require a monotherapy regimen and subsequently a combination later on.

Fadare et al. identified the effect of high burden of medication use and medication adherence. The patients were often confused especially when they had to administered

their number and time of administration (Fadare et al., 2015), and they suggested that this leads to confusion about the names of the medications, the purpose for each medication, forgetfulness to administer the OHA and when administered at the wrong time its potential for interactions with other medications (Fadare et al., 2015)

Interestingly, , Adisa et al. concluded from their study that prescribing more than four medications in T2DM is linked to enhanced adherence and subsequent glycemic outcome (Adisa and Fakeye, 2013).

- **Cost of the medication**

The cost of medication for T2DM affects a patient's ability to adhere to their medication regimen. A patient on a monotherapy plan will only need to purchase a particular drug, but a therapy consisting of a combination of drugs will require more cost. Some of the included studies identified cost of medication as a major factor influencing medication adherence to treatment in T2DM (Yusuff et al., 2008, Jackson et al., 2015, Adisa and Fakeye, 2013, Pascal et al., 2012, Ajibola and Timothy, 2018, Awodele and Osuolale, 2015, Fadare et al., 2015).

The study by Kazeem et al. conducted in a tertiary public health care institution in Ibadan, southwestern Nigeria identified cost of the medication as a major factor influencing medication adherence (Yusuff et al., 2008). About 86% (171) of the study population were prescribed OHA while a combination of insulin and OHA was prescribed in 14% (29) of the study population. The cost of OHA for a month on average for a patient was between $4.8–$38.4(600–4800 naira). The socioeconomic status of the study participants was not mentioned in the research; however, it was stated that the access to OHA appeared to be restricted by economic limitations. Based on the National minimum daily wage of $2, an

average patient with T2DM will require 11.5days of work to pay for anti-diabetic medications (Yusuff et al., 2008) and being a low income setting; about 70% of its citizenry live below the poverty line (Federal Ministry of Health, 2008).

In another study conducted in two major urban cities in the south southern part of Nigeria, participants identified the cost of OHA as a major factor influencing adherence to treatment in T2DM (Jackson et al., 2015). The study included participants from various socioeconomic classes where 34.3% (104) were civil servants, about 27.7% (84) retired, 94 (31.0) persons were self-employed, 13% (4.3) unemployed, 4 (1.3%) were students and 4(1.3) from the clergy. Furthermore, about 37.3% of the study population earned below 30,000 naira/month (Jackson et al., 2015). The findings of this study was that the cost of OHA in the treatment of T2DM influence medication adherence and this is consistent with other studies that identified the role of cost of medication in adherence behaviours in T2DM (Bailey et al., 2012).

Furthermore, Awodele et al. assessed the patients views on the cost of medication used for the treatment of T2DM and its influence on adherence (Awodele and Osuolale, 2015). The study had a greater number of females (110) than males (42) and a majority of this population were either engaging in petty trade or unemployed (Awodele and Osuolale, 2015)**.** About 105 patients (69.0%) said they could only purchase incomplete doses of their OHA due to high cost of medication, however 47 patients (31.0 %) could buy could afford to purchase complete doses of prescribed medications at once**.** The patients reported that their inability to purchase medications due to cost of medication was a mitigating factor affecting medication adherence(Awodele and Osuolale, 2015, Fadare et al., 2015)**,** and this is crucial in patients medication adherence especially in chronic

disease like T2DM as treatment period is long term(Ponnusankar et al., 2004, Bailey et al., 2012).

- **Drugs class**

The major groups of medications used in T2DM are OHA and insulin. The most commonly prescribed OHA are biguanides (metformin), thiazolidinedione also called glitazones (pioglitazone), sulfonylurea (first and second generation including chlorpropamide and glyburide), meglitinide (repaglinide), Alpha glucosidase inhibitor (acarbose) and insulin (Insulin lispro and Insulin glargine). In the included studies

metformin, glibenclamide, glimepiride and Chlorpropamide were the most common prescribed OHA(Yusuff et al., 2008, Awodele and Osuolale, 2015, Fadare et al., 2015, Adisa et al., 2009). However, the included studies did not specifically identify the influence of drug class on medication adherence, but in a systematic review injection-related concerns were identified in insulin-naive patients as barriers to medication adherence in T2DM compared to patients with prior insulin experience (Polinski et al., 2013).

- **Adverse effects of medication**

According to the WHO "Adverse Drug Reaction (ADR) is a part of adverse drug effect, a response to a drug which is undesirable or unintended and noxious, occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for the modification of physiological function"(World Health Organization, 2002). Also side effect is "unintended effects that occur at regular doses and are related to the properties of the drug"(Edwards and Aronson, 2000).

As explained earlier, the biguanide (metformin) is the most commonly used OHA, and widely accepted as a first-line monotherapy treatment in T2DM (Adisa and Fakeye, 2013).

Metformin is sufficient as a monotherapy and in combination with nearly every other OHA including glibenclamide, glimepiride, chlorpropamide, glipizide, glyburide, pioglitazone, vildagliptin, rosiglitazone, repaglinide and sitagliptin for T2DM**.** Metformin has superior efficacy in glucose lowering and reducing diabetes-related complications when compared to other OHA in T2DM treatment, however similar to other drug agents, it has some side effects associated with its use. The most common side effects caused by metformin are gastrointestinal and about 10-25% patients initiating metformin report diarrhea, nausea, cramps or bloating and indigestion. Metformin does not normally cause weight gain, but could result to weight loss in some cases, however to minimize these side effects, treatment is best initiated with low doses and tittered over days to weeks.

Sulphonylureas and biguanides were the most prescribed OHA documented in some of the included studies (Yusuff et al., 2008, Nwaokoro et al., 2014), and patients reported hypoglycemia, headache, cough, insomnia and erectile dysfunction as side effects that affected medication adherence (Yusuff et al., 2008). According to the study, hypoglycemia resulted due to the use of twice daily dose of glibenclamide in 69% of the study population(Yusuff et al., 2008). Nwaokoro et al. also reported that 40% T2DM patients mentioned the fear of hypoglycemia affected medication adherence(Nwaokoro et al., 2014).

b. Diabetes related factors influencing medication adherence in T2DM

Type 2 diabetes mellitus is the most common form of diabetes, especially in individuals above 40years in Nigeria. Management of the disease can be challenging especially due to the disease related factors like the duration of the disease, complications that could arise from glycemic control and the diabetes type in this case T2DM.

- **Disease duration**

Pharmacological and nonpharmacological management is very important in T2DM. These practices are essential to manage the chronic nature of the disease and also prevent complications. However, with prolonged duration of diabetes, patients' attitude towards coping with the disease could reduce on the long run. Hence, influencing their belief concerning the effectiveness of medications, and subsequent reduction in administration of OHA.

A study by Adisa et al. identified that a large number of the study participants (80.0%) who have disease duration between 1-10 years had knowledge, attitude and practice barriers compared to a proportion of 20.0% having the disease between 11-20 years(Adisa and Fakeye, 2014).

- **Disease nature and complications**

Diabetes as a metabolic disorder requires drug and non-drug therapy, however in event of treatment (medication use) certain complications could result. This can be as a result of partial adherence or nonadherence to treatment routine and regimen. Effective drug therapy is essential to reduce the risk of complications including diabetic ketoacidosis, cardiovascular comorbidities, hyperglycemia, athlete foot(resulting to lower limb amputation), erectile dysfunction in men and glaucoma among others(Stratton et al., 2000, Alberti and Zimmet, 1998, Zheng et al., 2018, DeFronzo et al., 2015).

Furthermore, it is also important to state that T2DM can remain asymptomatic for many years while diagnosis is often as a result of associated complications or incidental urine or blood glucose test. The asymptomatic nature of the disease could influence medication

adherence, as medication use will be based on ones feeling and not necessarily about the disease symptoms(Brundisini et al., 2015).

However, these factors were not documented in the included studies.

- **Glycemic control**

Achieving glycemic control equals balancing of the blood glucose level and involves lifestyle modifications like physical activity, diet and medication use. Glycemic level of > 6.1 mmol/L (110 mg/dL) and <7 mmol/l (126mg/dl) is essential in to prevent hypo or hyper glycemia(World Health Organization, 1999). Some studies reported good glycemic control(Adisa et al., 2011, Fadare et al., 2015).

- **Disease type**

Type 2 diabetes mellitus is the commonest form of diabetes in Nigeria. The literature review is focused on T2DM because of the nature of medication use and how it affects adherence. As explained earlier, patients receive OHA either as a monotherapy of combination including insulin, or insulin alone therapy. However, no study Identified how this disease type (T2DM) specifically affect medication adherence, although studies cited few references where disease length was documented as barrier to optimum treatment participation.

c. Patient related factors influencing medication adherence in T2DM

The patient remains one of the major factors in medication adherence in T2DM and so many issues revolves around the patient. A T2DM diabetic patient is someone who has been diagnosed recently over a period of time. For this literature review, a T2DM patient is someone who has been diagnosed and treatment initiated (OHA or insulin) for at least a month. Long term diseases like T2DM encourages self-management practices including

medication adherence. Therefore, it is important to identify influences from the side of the patient that can affect their medication adherence.

- **Comorbidities (presence of another disease)**

The presence of another disease(s) generally represents a barrier to medication adherence in T2DM(Brundisini et al., 2015). A typical co-morbidity in T2DM is hypertension, with prevalence as high as 75% in the diabetic population and may be preexisting at diagnosis or before diagnosis of T2DM (Huri and Wee, 2013). As a result of these patients receive more drug therapy to effectively manage these conditions simultaneously, hence posing a threat to medication adherence. Another frequent comorbid disease experienced in T2DM is depression, which is usually unrecognized and untreated, and can influence medication adherence in Diabetes (Katon, 2008). Furthermore, due to these conditions patients are administered multiple drug therapies (polypharmacy).

A study by Ogbonna et al. identified drug related problems (including medication non adherence), in comorbid elderly patients receiving more drug medication (Ogbonna et al., 2014). The study also identified the role of polypharmacy as a result of comorbidities in drug medication non adherence.

Furthermore, hypertension was the most frequent documented comorbid with T2DM(Yusuff et al., 2008, Ogbonna et al., 2014).

- **Knowledge level of disease**

Patients Knowledge about the disease and medication use to a large extent will affect their participation in treatment management. Health providers have identified patients' lack of sufficient knowledge about T2DM and medication use as a major link to poor medication adherence (Brundisini et al., 2015).

A study reported a lack of knowledge for use of specific prescribed medications, disregard for administration instructions (due to ignorance), inability to identify medications with same brands and administering both afterwards, dosage omission (waiting for refill at appointment) and purchase of fake or counterfeit medicines as knowledge barriers influencing medication adherence (Adisa and Fakeye, 2014).

- **Specific demography**

The studies documented similar sociodemographic characteristics including sex, age, employment status, educational qualification, and marital status. In some included studies medication adherence in T2DM was higher in patients who had educational qualifications from secondary education up till tertiary education (Adisa et al., 2009, Onyeanusi, 2015, Jackson et al., 2015, Emmanuel and Otovwe, 2015), contrary to another study (Adisa and Fakeye, 2014), in employed persons or retired civil servants compared to the self-employed (Fadare et al., 2015, Ajibola and Timothy, 2018), in married patients compared to singles (Adisa et al., 2009) and a comparable medication adherence profile in both sexes (Adisa et al., 2009).

The population of patients with higher level of education was consistent, as most studies were conducted in urban dwellings.

Onyeanusi et al, in their study conducted in a suburban part of the southeastern region, documented that older patients, experienced medication nonadherence, also inferring that a majority of the study participants where ≥ 56 years (Onyeanusi, 2015). However, contrary to this finding, older participants in a study by Awodele e.t al, in the southwestern region had better medication adherence profile compared to the younger group, implicated

the presence of a scheme that provides free drugs (limited quantities) for older patients(Awodele and Osuolale, 2015).

- **Perceptions and Beliefs**

A patient belief could be influenced by their immediate environment or just as a result of personal experience. This can be related to perceptions concerning the efficacy of medications or a feeling of wellness and concludes medication use were unnecessary. Also, cultural belief about the efficacy of traditional practices including herbal remedy use, a bias concerning medications from the hospital could result.

More so, some religious affiliations in Nigeria forbid the use of medications due to imbibed doctrines or when these medications are manufactured with forbidden substances.

A study by Kareem et. al documented that about 13.8% T2DM patients administered local herbal remedies because they perceived the prescribed OHA was ineffective (Yusuff et al., 2008).

Another study reported patients administered herbal concoction, perceiving the prescribed medicines were ineffective and also because the herbal remedies were readily accessible (Emmanuel and Otovwe, 2015).

- **Psychological feelings**

Depression is a common comorbid in T2DM, if unidentified or untreated could influence the psychological stability that is necessary for medication adherence inT2DM (Gonzalez et al., 2007). Fear from the disease condition and complications, phobia for drug administration, self-esteem issues and motivation are important psychological factors to identify.

Two studies identified forgetfulness as a major factor for medication nonadherence(Adisa et al., 2009, Jackson et al., 2015). Forgetfulness in this context was non intentional, however if they had better understand on the importance of medication use in T2DM, they would find ways to create reminders as motivators to encourage timely drug administration whenever necessary.

- **Quality of life of patient**

The quality of life of a patient with T2DM is a very important factor in medication adherence. The social status, physical status (presence or absence of disability or complications), mental and psychological status affects the overall quality of life in T2DM management plan. Findings including depression, financial constrain and side effects of medications were influences that could impact the quality of life of T2DM patients and eventual medication adherence, however these findings are documented in other appropriate sections. More so, the studies did not specifically link these factors to quality of life in T2DM.

d. Societal related factors influencing medication adherence in T2DM

The Nigerian society having very diverse ethnic group has different indigenous traditional and social cultural practices. There are variations on how each society will either influences, affect or support a person of people who have certain disease conditions; however, the level of education and exposure of the individual are import determinants. The society consists of the immediate family of the T2DM patient, including spouse, children other family members and others citizens.

- **Support from spouse and family**

Family provides significant support in diabetes management (Patterson, 2002), and these support could be financial, social, in medication administration or emotional support. It has been established that social support improves medication adherence (DiMatteo, 2004), hence It is essential for patients to ask for support and families reciprocate as required in T2DM management.

A study in the south western part of Nigeria, assumed that the communal practice in Nigeria had an influence on medication adherence in T2DM as over 70% of study participants earn as low as NGN N50,000 (USD $303) monthly, and spends about NGN N6556.60 (USD $39.70), which is a large portion of their monthly earnings. However, the study did not outline the supposed financial assistant from to patients from family members (Fadare et al., 2015).

Another study revealed that social support was the most received form of support from family members, and this led to a significant improvement in therapy adherence (Adisa et al., 2017). Patients also reported they received support from government and non-governmental organizations (NGO) which they also desired and preferred, however, they desired financial support the most which was more functional for them, considering a majority of the study participants are over the age of 60years with comorbid hypertension (Adisa et al., 2017).

- **Culture**

Culture, "is the way of life and of a group of people, living in a said community". Cultural practices include the food, diet, lifestyle and treatment practices in a community. The country Nigeria with a population of over 200million people have very diverse cultures. The analyses on the influence of culture on medication adherence in T2DM will be described based on the culture of the region where the finding was discovered. More importantly, cultural backgrounds can influence a patients choice to seek medication and even when they do, can affect the relationship s/he would have desired to have with the healthcare professionals (Brundisini et al., 2015).

The most obvious cultural influence on medication adherence identified was the use of traditional herbal remedies, either to replaced already prescribed medication or as an adjunct to treatment (Emmanuel and Otovwe, 2015, Adisa et al., 2009). These findings were however described under other suitable/appropriate influencing factors in this result sections.

- **Food, Diet and lifestyle**

There is currently an evolution from healthy to unhealthy nutrition in Nigeria and this is similar to most LMICs. This could be partly attributed to swift urbanization, globalization and improved socioeconomic status of Nigerians influencing lifestyle and eating habits (Federal Ministry of Health Nigeria, 2014). These has led to overweight and obesity which is a predisposing risk factor for NCDs including T2DM (Federal Ministry of Health Nigeria, 2014).

A majority of the included studies were conducted in the south western part of Nigeria, and reported lifestyle practices included the use of alternative therapy in the form of herbal

medications, smoking and drinking. However, the link between these lifestyle practices and its influence on medication adherence were not directly identified in individual study results.

- **Alternate therapy/natural remedies**

The use of alternative therapy also referred to as traditional medicine is a common practice in the vast majority of the population in Nigeria (Ogbera et al., 2010). These concoctions are made from leaves, bark of trees mixed with some other ingredients and soaked in alcohol or water. Remedies are prepared by individuals or are purchased from either a vendor or a traditional medicines practitioner. The practice of the use of these concoctions is common in the southwestern and south-south regions (Fakeye et al., 2008). These preparations have been documented to interact with medications and can might result to some adverse or side effects, unfortunately, there is a dearth of data concerning this phenomenon.

some studies specifically reported on the use of herbal medications, and patients stated they believed it was more efficacy for therapy than prescribed medications which was perceived ineffective (Emmanuel and Otovwe, 2015, Yusuff et al., 2008).

- **Stigma**

The attitudes of others (people) concerning a disease condition or the mode of medication administration of medication can influence medication adherence. Stigma could result to resentment and concealment of (Emmanuel and Otovwe, 2015) disease condition which may influence clinical outcomes(Harper et al., 2018). There is also self-stigmatization which could occur due to the other complications from diabetes (Kato et al., 2016) or the presence of obesity.

A study reported that medication adherence was influenced due to fear of stigmatization (Adisa and Fakeye, 2014).

- **Vicarious experience**

A previous personal or non-personal experience on the use of medication (to include side effects, administration difficulty or financial obligations) may influence a patient's participation in therapy management. These experiences can also be imaginative. However, no studies reported on this potential factor identified in the framework.

e. Health provider related factors influencing medication adherence in T2DM

Healthcare providers (all healthcare professionals responsible for the clinical outcomes of T2DM patient) are important and reliable source to provide therapy and information for the management of T2DM**.** They provide information about the disease, treatment recommendations and follow up, however they identify patient- related factors that could affect treatment plants included cultural and communication barriers, patient's literacy levels, any distrust in the provider and medication adherence challenges.

- **Healthcare provider patient interaction**

At this stage in the health system process (concerning medication), the healthcare providers vital information through counselling on medication purchase, administration (when and how) what to expect (side effects) and storage (how and where to keep medications). This interaction has been established to impact medication adherence in diabetes care(Brown and Bussell, 2011).

Idongesit et al. reported that patient–provider communication influenced medication adherence in T2DM (Jackson et al., 2015). Some patients indicated poor and ineffective

communication, a lack of trust and having a negative attitude towards the health care provider influenced MA to medications. The study finding is consistent with some studies about Patient- health provider communication and its influence on medication adherence (Ibrahim et al., 2010, Sleath et al., 2000).

Health care providers manner of approach during consultation and dispensing , influenced medication adherence (Abdulazeez et al., 2014). The findings revealed nonadherence was partly due to health providers attitude and instructions for medication administration was unclear (Abdulazeez et al., 2014).

Furthermore, patients expressed lack of trust in the healthcare provider resulting to them not confiding in the healthcare providers about challenges they faced concerning medication use.

- **Knowledge of the health care professional**

Health care professionals are expected to provide up to date concise disease and drug information to patients. The pharmacist provides pharmaceutical care. In Nigeria, pharmacists are expected to upgrade their knowledge through the mandatory continuing professional development program (MCPDP). The program enables the pharmacist and other health care professionals to keep abreast of current trends and practices in Pharmaceutical care. Post graduate education and research participation is highly recommended. Medical doctors, nurses and medical laboratory scientists also have continuous development programs incorporated in their practice.

Furthermore, when the level of knowledge of a healthcare professional is questionable, a setback in clinical outcomes target (glycemic control) might occur

Furthermore, it is important for the healthcare provider to be up to date with treatment guidelines (including glycemic targets, initiating treatment, when to change or discontinue a medication amongst others). However, no study specifically reported on the knowledge of the healthcare professional.

- **Workload**

In the Nigerian healthcare system, 40hours a week is the standard work hours excluding call duty hours, which can be all throughout the night, few hours after normal work hours or throughout weekend. This is the same for all healthcare professionals, however there is usually a lack of staff. There is currently an outflow of Nigerian trained healthcare professionals to either western Europe, united states of America or to Asia. There has also been incessant strikes and protests striking poor and pay with high burden of workload and discouraging working conditions.

A study discovered that only about 20% of patients discussed their medication non adherence to healthcare providers and they mentioned lack of privacy and a reduced consultation /counselling time as the major influences. Suggesting the length of time and quality of consultation/counselling was suboptimal (Yusuff et al., 2008).

- **Healthcare providers perception of T2DM**

The perception of the healthcare provider concerning the severity of the disease is important because this can affect the level of care provided. Also, what is the self-efficacy of the health care providers providing care and do they feel they have the capacity to influence the patients who need care.

However, there is a dearth of data on the healthcare providers perceptions on the factors that influence medication adherence in T2DM in Nigeria.

f. Healthcare system related factors influencing medication adherence in T2DM

The healthcare system in Nigeria as explained earlier has three major tiers, the primary, secondary and tertiary. Diabetes prevention, control and care are incorporated in all tiers of the healthcare system. However, due to issues such as human resource and funding, there exist deficiencies in the care process. Also, insurance policies, availability of diagnostic and treatment tools, drugs and other resources, flexible treatment guidelines and cost, visit duration and access to healthcare facilities affect medication adherence in T2DM.

- **Healthcare process**

The internal medicine department is responsible for coordinating the diagnostic, treatment and management of T2DM in secondary and tertiary health care institution. In primary health centres, patients visit the general out patients department, the outpatient department also exist in higher tiers of health care facilities. The endocrinologist is the specialist that provides healthcare services to T2DM. The patients are directed to either the laboratory or pharmacy department, depending on their medical needs.

The above is the standard procedure describing the outpatient activities in a healthcare facility in Nigeria, however as a hospital Pharmacist, I have experienced deviations from this normalcy.

- **Available resources at the healthcare institution**

The government provides the healthcare funds in public health institutions, however, there is usually a lack of resources and frequent strike actions by medical staff for nonpayment of salaries. This scenario could be linked partly to the Nigerian budget allocation for health,

which is lower than what is recommended by the WHO. This will result to lack of resources including human, medication, transportation and translators to interpret information and instructions.

A study by Idongesit et al. in 2 tertiary health care facilities linked the problem of limited access to health care facility and reduced medication adherence. The research further highlighted the need for functional primary health centre to reduce the problem of limited access to seek healthcare.

Furthermore, while availability of translators, transportation, medications and treatment guidelines were highlighted in the model as a health system factor influencing medication adherence, however no study included findings on their influence on medication adherence T2DM.

- **Financial issues**

The Nigerian government formally launched the NHIS in 2006 to address healthcare needs of the Nigerian population including improving accessibility to medications and healthcare services (Chernew et al., 2008), however, the scheme currently is available for people employed in the formal sectors of the country's economy (Onoka et al., 2014). The NHIS has a policy that covers some OHA (mostly generic brands), and no insulin. Interestingly, in chronic disease management, over two thirds of the amount spent on treatment are for drug medications(Onwujekwe et al., 2012).

A study by Ajibola et. al, to determine the influence of insurance (National Health Insurance Scheme, NHIS) on medication adherence in T2DM in Nigeria was conducted in two public health institutions in the south western part of Nigeria. About 61.8% (68) of the study participants were uninsured and 42 (66.7%) insured (Ajibola and Timothy,

2018). The study further reviewed that more of the uninsured patients 51 [75.0%] were self-financed and medication adherence in the insured population was higher than in the uninsured.

The difference in medication adherence could however be linked to the difference in cost of medications between the two groups of study participants(Ajibola and Timothy, 2018).

- **Treatment costs.**

Every patient that visits the hospital is expected to get registered and receive a hospital card. Records of every visit and appointments are recorded on this card. Depending on the health care institutions, treatment fees (consultation fees) are almost nonexistent, however, laboratory and medication cost are payed by the patient. As discussed above, all insured patients get a health care coverage, depending on the package offered by the NHIS.

CHAPTER 4: DISCUSSION

4.1 Discussion

The aim of this study was to explore the contributing factors that influence medication adherence in Type 2 Diabetes Mellitus based on studies in Nigeria. This section will focus on the main factors that influenced medication adherence in order to recommend appropriate interventions to policy makers and stakeholders to improve medication adherence in T2DM management in Nigeria.

Based on the conceptual framework by Jaam et al. (Jaam et al., 2017) six major clusters of factors that influence medication adherence in diabetes management were identified. These factors include Medication related factors, Diabetes related factors, Patient related factors, Societal related factors, Healthcare system related factors, and Health provider related factors. The identified factors may operate as either facilitators or barriers to medication adherence in T2DM. Their effects although interrelated were also distinct in how they affect adherence to diabetic medication. These factors are identical to those documented in a qualitative meta-synthesis and systematic review on medication non adherence in diabetes conducted in Canada and USA (Capoccia et al., 2016, Brundisini et al., 2015).

- **Medication related factors**

The main medication related factors that influenced patient's medication adherence are the complexity of the medication regimen, the cost of the medication, and the adverse effects associated with the medications. Some studies included in this review identified complex dose regimen as a barrier to medication adherence. This is contrary to the findings of another study, demonstrating that medication adherence to regimen is inversely correlated to the number of OHA prescribed. This findings however, could be connected to

the fact that participants adhered to prescribed medications as they perceived the number of medications signified the severity of disease condition, and importantly, they are older (above 60 years of age) and a majority of these study group had tertiary education(which could have influence their medication adherence), compared to the younger adults that received less than four medications and a small proportion of them having tertiary education. (Adisa and Fakeye, 2013) Nevertheless, The findings on adherence in multiple medication use amid older people with T2DMare are corroborated by other studies (California Healthcare Foundation/American Geriatrics Society Panel in Improving Care for Elders with Diabetes, 2003, Bethel et al., 2007).

Studies were unanimous in demonstrating that the higher the cost of the medication, the higher the non-adherence to the medications. A report from a high income country documented cost related non adherence to diabetic medications and also for other non-communicable diseases (Bhuyan et al., 2017).

From my own clinical practice experience, T2DM patients complained about the cost of medications and often asked for a reduction in prescribed quantity, also in the NHIS pharmacy of the tertiary institution, a majority of the medications required for T2DM are not covered by the insurance. More so, when T2DM medications that are covered by the NHIS are unavailable in the hospital, the patients are required to purchase their medications from pharmacies outside the hospital. This however puts a financial challenge on the patients, as they have to pay out of pocket.

Furthermore, the patients usually have to purchase other types of drug medications, as T2DM might not be the only disease condition they have.

The adverse effects of the medications were also noted predictors of medication adherence. The fear of hypoglycemia which was common in patients on glibenclamide were noted to discourage the use of the medications. This finding is supported by studies from both low- and high-income settings. Also, from experience, patients often complained about stomach discomfort and diarrhea. Proper counselling offers patients information on what to expect and what to do to minimize these effects, relating the importance of patient provider relationship

- **Disease related factors**

The nature of the disease is also an important factor in medication adherence. The disease is some patients presents with other comorbidity. Also, the issue of knowledge attitude and practice is very important. Patients who had the disease for a longer period (longer than 10years) had better knowledge about their condition and how and why they have to adherence to medications. However, the included studies did not report enough data on the disease related factors that influence medication adherence.

- **Patient related factors influencing medication adherence in T2DM**

The patient's psychological wellbeing, educational and socioeconomic level and belief about their condition influenced medication adherence. As reiterated earlier, a patient who is unemployed or on a lower economic level will find it difficult purchasing the required medication.

Many patients in the included studies, reported the use of alternative medicines as they perceived the prescribed medications where not effective. This can also be linked to the patient's psychology as regards the disease and drug use, sadly, they most likely don't mention this to the healthcare providers.

Furthermore, patients who had higher levels of education adhered more when compared with those with little or no educational qualification. It is vital for a patient to be able to read and understand administration instructions to effectively administer their medication.

- **Healthcare provider and health system related factors**

Effective patient's health care provider relationship was identified as an influence to medication adherence. The patients mentioned they needed to trust the health care provider to be able to communicate effective. The patients also identified counselling time and quality affected their medication adherence. This can be partially traced to the workload of health care providers in Nigeria. Diabetes care is provided at all levels of care, however, patients usually by pass these lower levels, thereby congesting the tertiary institutions. It is important to state that all the included studies were conducted in secondary and tertiary institutions.

- **Societal related factors**

Furthermore, factors such as support from the government and family members influenced medication adherence. Patients mentioned when family members are in the know about their conditions, they can effectively communicate with them and it affects how they respond to medication use. Also, Social support from the government and non-governmental organizations was identified as an influence on medication adherence.

It is important to state that the included studies were primarily about the patients (T2DM) views or perspectives on what influences their medication adherence, and not from health care providers or the society. Noticeably, only one study was conducted in a rural setting (University teaching hospital). Patients in this study were largely non-adherent on account

of their poor social economic status and ignorance of the usefulness of antidiabetic medications. Overall, this study reveals the complexity of adherence related factors and the effect of the social political environment on medication use.

Hence, further research is encouraged to vividly understand the vicious cycle of adherence in a variety of T2DM population.

- **The holistic framework**

The holistic framework provided a comprehensive model in medication adherence, indicating patient, medication, disease, health professional, health care institution and societal influence on medication in diabetes. However, the review is on T2DM and some aspects in the framework were not applicable to the findings of the included studies. The is partly due to the nature of available research in Nigeria, hence the need for more and comprehensive research to include the multifactorial capacities and organization factors influencing medication adherence in T2DM management.

4.2. Limitations of the study

It is important to point out the limitations of this review:

- The included studies do not give a representation of all the regions in the country.
- The methodology used for the review (limitations on time frame for studies).
- Some studies did not document the drug regimen of study participants
- The included studies were conducted in secondary and tertiary health institutions, T2DM care is provided at all levels of care.
- The level of adherence reported in some included studies were not documented in this review.

- The framework included sections of possible influences from the healthcare providers perspectives about medication adherence in T2DM, however, the included studies only reported the patient's perspective about influential factors on medication adherence.

CHAPTER 5: CONLUSION AND RECOMMEDATIONS

This chapter includes the conclusion which is a summary of the findings and recommendations based on these findings.

5.1. CONCLUSION

Medication adherence remains a key challenge in T2DM management in Nigeria, as it is in other parts of the world. It requires a multifactorial approach which might be presented with some difficulties. The review provided evidence of contributing factors influencing medication adherence in T2DM in the Nigerian setting, using the holistic framework.

Medication adherence is pertinent to overall T2DM management. Notably, patients had considerable level of adherence, however, factors such as cost of medications, complexity of regimen, side effects of medications, poor interaction with healthcare provider and use of alternative herbal treatments were common influences identified amongst study participants.

Aside from the fact that the patient is presented with challenges in managing their health, it was evident from the findings that there is a dearth of data on the role the healthcare professionals, health care institution and the society play in medication adherence in T2DM. Findings from such research will enable stakeholders develop and strategize interventions for improved medication adherence in T2DM, which may prevent premature morbidity and mortality due to complications from T2DM.

5.2. RECOMMEDATIONS

Stakeholders include the Federal Ministry of Health (Republic of Nigeria), National agency for food and drug administration and control, Medical and dental council of Nigeria (MDCN), Pharmacist council of Nigeria (PCN), Nursing council of Nigeria (NCN), National Health Insurance Scheme (NHIS). To make an impact in medication adherence in T2DM in Nigeria,

a stronger commitment is from all stakeholder is vital and through a multidisciplinary approach involving healthcare professionals, health planners, researchers and policy makers, medication adherence can be improved.

Therefore, the following are recommendations based on the findings in the study:

Federal government, Health care professionals (other stakeholders)

a. The role of research in health care management cannot be overemphasized. Hence, I recommend further research to:
    - Address dearth of prevalence data on T2DM and NCDs, in health management information systems (HMIS).
    - Countrywide research including all political regions to unravel individual and regional specific differences in T2DM adherence.
    - To identify health care professional, healthcare institutions and societal influences on medication adherence in T2DM.
b. Specific training for healthcare professionals to include best practices in medication adherence management. This will emphasis strategies to manage T2DM effectively.
c. Also, a review of the NHIS policy is recommended. An affordable coverage package to include more generic brands of medication in T2DM management and revising the treatment guidelines for T2DM treatment in public healthcare institutions
d. Reduction in the outflow of health care professionals from Nigeria through policies and strategies to retain them. This will reduce the workload of health care workers.
e. Creating and encouraging a multifactorial approach to management of T2DM, to include health care professionals from different disciplines. This will provide psychological, emotional and otherwise needs of T2DM patients.

f. insurance policies to include self-employed T2DM patients.

- Government (National Agency for Food Drug Administration and Control (NAFDAC))
- Introduction of policies to encourage production or importation of variety of medications used for T2DM management. This will help the patient get variations and affordable medication options and reduced cost. Also, complexity of regimen through administration of multiple medications can be reduced through production or importation of fixed dose combinations.

Reference

ABDULAZEEZ, F. I., OMOLE, M. & OJULARI, S. L. 2014. Medication compliance amongst diabetic patients in Ilorin, Nigeria. *IOSR Journal of Dental and Medical Sciences. 2014; 13 (3): 96,* 99.

ADEMILUYI, I. A. & ALUKO-AROWOLO, S. O. 2009. Infrastructural distribution of healthcare services in Nigeria: An overview. *Journal of geography and regional planning,* 2**,** 104-110.

ADISA, R., ALUTUNDU, M. B. & FAKEYE, T. O. 2009. Factors contributing to nonadherence to oral hypoglycemic medications among ambulatory type 2 diabetes patients in Southwestern Nigeria. *Pharmacy Practice,* 7**,** 163.

ADISA, R. & FAKEYE, T. O. 2013. Effect of number and type of antidiabetes medications on adherence and glycemia of ambulatory type 2 diabetes patients in southwestern Nigeria. *Pharmacy practice,* 11**,** 156.

ADISA, R. & FAKEYE, T. O. 2014. Treatment non-adherence among patients with poorly controlled type 2 diabetes in ambulatory care settings in southwestern Nigeria. *African health sciences,* 14**,** 1-10.

ADISA, R., FAKEYE, T. O. & FASANMADE, A. 2011. Medication adherence among ambulatory patients with type 2 diabetes in a tertiary healthcare setting in southwestern Nigeria. *Pharmacy Practice,* 9**,** 72.

ADISA, R., OLAJIDE, O. O. & FAKEYE, T. O. 2017. Social support, treatment adherence and outcome among hypertensive and type 2 diabetes patients in ambulatory care settings in Southwestern Nigeria. *Ghana medical journal,* 51**,** 64-77.

AJIBOLA, S. S. & TIMOTHY, F. O. 2018. The Influence of National Health Insurance on Medication Adherence Among Outpatient Type 2 Diabetics in Southwest Nigeria. *Journal of patient experience,* 5**,** 114-119.

AKINKUGBE, O. 1997. Non-communicable Diseases in Nigeria: National Survey (Final Report) on Hypertension, Coronary Heart Disease, Diabetes mellitus, Haemoglobinopathy, G6PD Deficiency and Anaemia National Expert Committee on Non-Communication Disease. *Federal Ministry of Health and Social services. Lagos*.

ALBERTI, K. G. M. M. & ZIMMET, P. F. 1998. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Provisional report of a WHO consultation. *Diabetic medicine,* 15**,** 539-553.

AMERICAN DIABETES ASSOCIATION 2013. Diagnosis and classification of diabetes mellitus. *Diabetes care,* 36**,** S67-S74.

ANDERSSON, D. K. & SVÄRDSUDD, K. 1995. Long-term glycemic control relates to mortality in type II diabetes. *Diabetes care,* 18**,** 1534-1543.

AWODELE, O. & OSUOLALE, J. A. 2015. Medication adherence in type 2 diabetes patients: study of patients in Alimosho General Hospital, Igando, Lagos, Nigeria. *African health sciences,* 15**,** 513-522.

BAILEY, G. R., BARNER, J. C., WEEMS, J. K., LECKBEE, G., SOLIS, R., MONTEMAYOR, D. & POPE, N. D. 2012. Assessing barriers to medication adherence in underserved patients with diabetes in Texas. *The Diabetes Educator,* 38**,** 271-279.

BETHEL, M. A., SLOAN, F. A., BELSKY, D. & FEINGLOS, M. N. 2007. Longitudinal incidence and prevalence of adverse outcomes of diabetes mellitus in elderly patients. *Archives of Internal Medicine,* 167**,** 921-927.

BHUYAN, S. S., SHIYANBOLA, O., KEDIA, S., CHANDAK, A., WANG, Y., ISEHUNWA, O. O., ANUNOBI, N., EBUENYI, I., DEKA, P. & AHN, S. 2017. Does cost-related medication nonadherence among cardiovascular disease patients vary by gender? Evidence from a nationally representative sample. *Women's Health Issues,* 27**,** 108-115.

BROWN, M. T. & BUSSELL, J. K. Medication adherence: WHO cares? Mayo Clinic Proceedings, 2011. Elsevier, 304-314.

BRUNDISINI, F., VANSTONE, M., HULAN, D., DEJEAN, D. & GIACOMINI, M. 2015. Type 2 diabetes patients' and providers' differing perspectives on medication nonadherence: a qualitative meta-synthesis. *BMC health services research,* 15**,** 516.

CALIFORNIA HEALTHCARE FOUNDATION/AMERICAN GERIATRICS SOCIETY PANEL IN IMPROVING CARE FOR ELDERS WITH DIABETES, C. 2003. Guidelines for improving the care of the older person with diabetes mellitus. *Journal of the American Geriatrics Society,* 51**,** 265-280.

CAPOCCIA, K., ODEGARD, P. S. & LETASSY, N. 2016. Medication adherence with diabetes medication: a systematic review of the literature. *The Diabetes Educator,* 42**,** 34-71.

CHAPUT, J. P., KLINGENBERG, L., ASTRUP, A. & SJÖDIN, A. M. 2011. Modern sedentary activities promote overconsumption of food in our current obesogenic environment. *Obesity reviews,* 12**,** e12-e20.

CHEN, L., MAGLIANO, D. J. & ZIMMET, P. Z. 2012. The worldwide epidemiology of type 2 diabetes mellitus—present and future perspectives. *Nature reviews endocrinology,* 8**,** 228.

CHERNEW, M. E., SHAH, M. R., WEGH, A., ROSENBERG, S. N., JUSTER, I. A., ROSEN, A. B., SOKOL, M. C., YU-ISENBERG, K. & FENDRICK, A. M. 2008. Impact of decreasing copayments on medication adherence within a disease management environment. *Health Affairs,* 27**,** 103-112.

CHIJIOKE, A., ADAMU, A. & MAKUSIDI, A. M. 2010. Mortality patterns among type 2 diabetes mellitus patients in Ilorin, Nigeria. *Journal of Endocrinology, Metabolism and Diabetes of South Africa,* 15**,** 79-82.

CHINENYE, S. & OGBERA, A. 2013. Socio-cultural aspects of diabetes mellitus in Nigeria. *Journal of Social Health and Diabetes,* 1**,** 015-021.

CHINENYE, S., ULOKO, A. E., OGBERA, A. O., OFOEGBU, E. N., FASANMADE, O. A., FASANMADE, A. A. & OGBU, O. O. 2012. Profile of Nigerians with diabetes mellitus–Diabcare Nigeria study group (2008): Results of a multicenter study. *Indian journal of endocrinology and metabolism,* 16**,** 558.

CRAMER, J. A. 2004. A systematic review of adherence with medications for diabetes. *Diabetes care,* 27**,** 1218-1224.

DEFRONZO, R. A., FERRANNINI, E., GROOP, L., HENRY, R. R., HERMAN, W. H., HOLST, J. J., HU, F. B., KAHN, C. R., RAZ, I. & SHULMAN, G. I. 2015. Type 2 diabetes mellitus. *Nature reviews Disease primers,* 1**,** 15019.

DIABETES AND NCDS IN NIGERIA 2017. Perspectives, Challenges & the Way Forward.

DIMATTEO, M. R. 2004. Social support and patient adherence to medical treatment: a meta-analysis. *Health psychology,* 23**,** 207.

EDWARDS, I. R. & ARONSON, J. K. 2000. Adverse drug reactions: definitions, diagnosis, and management. *The lancet,* 356**,** 1255-1259.

EMMANUEL, O. O. & OTOVWE, A. 2015. Patterns of adherence to management among patients with type 2 diabetes mellitus in South-South Region of Nigeria. *Journal of Social health and Diabetes,* 3**,** 115-119.

ENEJI, M. A., DICKSON, V. J. & ONABE, B. J. 2013. Health care expenditure, health status and national productivity in Nigeria (1999-2012).

FADARE, J., OLAMOYEGUN, M. & GBADEGESIN, B. 2015. Medication adherence and direct treatment cost among diabetes patients attending a tertiary healthcare facility in Ogbomosho, Nigeria. *Malawi medical journal,* 27**,** 65-70.

FAKEYE, T. O., TIJANI, A. & ADEBISI, O. 2008. A survey of the use of herbs among patients attending secondary-level health care facilities in Southwestern Nigeria. *Journal of herbal pharmacotherapy,* 7**,** 213-227.

FEDERAL MINISTRY OF HEALTH 2008. National Demographic and Health Survey Final Report. *online*

FEDERAL MINISTRY OF HEALTH NIGERIA 2014. National Nutritional Guideline On Non-Communicable Disease Prevention, Control and Management

FORCE, I. C. G. T. 2006. Global Guideline for Type 2 Diabetes: recommendations for standard, comprehensive, and minimal care. *Diabetic medicine,* 23**,** 579-593.

FOUNDATION, W. D. 2017. Diabetes and NCDs in Nigeria - Perspectives, Challenges and the Way Forward,. *online*

GARCÍA-PÉREZ, L.-E., ÁLVAREZ, M., DILLA, T., GIL-GUILLÉN, V. & OROZCO-BELTRÁN, D. 2013. Adherence to therapies in patients with type 2 diabetes. *Diabetes Therapy,* 4**,** 175-194.

GOLDEN, A. G., PRESTON, R. A., BARNETT, S. D., LLORENTE, M., HAMDAN, K. & SILVERMAN, M. A. 1999. Inappropriate medication prescribing in homebound older adults. *Journal of the American Geriatrics Society,* 47**,** 948-953.

GONZALEZ, J. S., SAFREN, S. A., CAGLIERO, E., WEXLER, D. J., DELAHANTY, L., WITTENBERG, E., BLAIS, M. A., MEIGS, J. B. & GRANT, R. W. 2007. Depression, self-care, and medication adherence in type 2 diabetes: relationships across the full range of symptom severity. *Diabetes care,* 30**,** 2222-2227.

GRANT, R. W., CAGLIERO, E., MURPHY-SHEEHY, P., SINGER, D. E., NATHAN, D. M. & MEIGS, J. B. 2002. Comparison of hyperglycemia, hypertension, and hypercholesterolemia management in patients with type 2 diabetes. *The American journal of medicine,* 112**,** 603-609.

HARPER, K. J., OSBORN, C. Y. & MAYBERRY, L. S. 2018. Patient-perceived family stigma of type 2 diabetes and its consequences. *Families, Systems, & Health,* 36**,** 113.

HORTON, E. 2008. Can newer therapies delay the progression of type 2 diabetes mellitus? *Endocrine Practice,* 14**,** 625-638.

HURI, H. Z. & WEE, H. F. 2013. Drug related problems in type 2 diabetes patients with hypertension: a cross-sectional retrospective study. *BMC endocrine disorders,* 13**,** 2.

IBRAHIM, N. K. R., ATTIA, S. G., SALLAM, S. A., FETOHY, E. M. & EL-SEWI, F. 2010. Physicians' therapeutic practice and compliance of diabetic patients attending rural primary health care units in Alexandria. *Journal of Family and Community Medicine,* 17**,** 121.

JAAM, M., AWAISU, A., IBRAHIM, M. I. M. & KHEIR, N. 2017. Factors influencing medication adherence in diabetes mellitus: Developing a holistic conceptual framework model. *Research in Social and Administrative Pharmacy,* 30**,** 1e7.

JACKSON, I. L., ADIBE, M. O., OKONTA, M. J. & UKWE, C. V. 2015. Medication adherence in type 2 diabetes patients in Nigeria. *Diabetes technology & therapeutics,* 17**,** 398-404.

KATO, A., FUJIMAKI, Y., FUJIMORI, S., ISOGAWA, A., ONISHI, Y., SUZUKI, R., YAMAUCHI, T., UEKI, K., KADOWAKI, T. & HASHIMOTO, H. 2016. Association between self-stigma and self-care behaviors in patients with type 2 diabetes: a cross-sectional study. *BMJ Open Diabetes Research and Care,* 4**,** e000156.

KATON, W. J. 2008. The comorbidity of diabetes mellitus and depression. *The American journal of medicine,* 121**,** S8-S15.

LAU, D. T. & NAU, D. P. 2004. Oral antihyperglycemic medication nonadherence and subsequent hospitalization among individuals with type 2 diabetes. *Diabetes care,* 27**,** 2149-2153.

LEE, H., SEO, J., YU, M., UH, S.-T. & HA, H. 2007. Radical approach to diabetic nephropathy. *Kidney International,* 72**,** S67-S70.

MBANYA, J. C. N., MOTALA, A. A., SOBNGWI, E., ASSAH, F. K. & ENORU, S. T. 2010. Diabetes in sub-saharan africa. *The lancet,* 375**,** 2254-2266.

MORGAN, C. L., CURRIE, C. J. & PETERS, J. R. 2000. Relationship between diabetes and mortality: a population study using record linkage. *Diabetes care,* 23**,** 1103-1107.

NAM, S., CHESLA, C., STOTTS, N. A., KROON, L. & JANSON, S. L. 2011. Barriers to diabetes management: patient and provider factors. *Diabetes research and clinical practice,* 93**,** 1-9.

NWAOKORO, J., OKOKON, B., NWAOKORO, A., EMEROLE, C., IBE, S., ONWULIRI, V., OPUTA, R. & CHUKWUOCHA, U. 2014. Problems associated with treatment compliance among type 2 diabetic patients at a tertiary health institution in Nigeria. *African Journal of diabetes medicine,* 22.

OGBERA, A., DADA, O., ADELEYE, F. & JEWO, P. 2010. Complementary and alternative medicine use in diabetes mellitus. *West African journal of medicine,* 29.

OGBERA, A. O. & EKPEBEGH, C. 2014. Diabetes mellitus in Nigeria: The past, present and future. *World journal of diabetes,* 5**,** 905.

OGBONNA, B., EZENDUKA, C., OPARA, C. & AHARA, L. 2014. Drug therapy problems in patients with Type-2 Diabetes in a tertiary hospital in Nigeria. *Int J Innov Res Dev,* 3**,** 494-502.

OMORUAN, A., BAMIDELE, A. & PHILLIPS, O. 2009. Social health insurance and sustainable healthcare reform in Nigeria. *Studies on Ethno-Medicine,* 3**,** 105-110.

ONOKA, C. A., HANSON, K. & HANEFELD, J. 2014. Towards universal coverage: a policy analysis of the development of the National Health Insurance Scheme in Nigeria. *Health policy and planning,* 30**,** 1105-1117.

ONWUJEKWE, O., HANSON, K. & UZOCHUKWU, B. 2012. Examining inequities in incidence of catastrophic health expenditures on different healthcare services and health facilities in Nigeria. *PloS one,* 7**,** e40811.

ONYEANUSI, C. G. 2015. *Effect of family support on medication adherence and glycemic control of type 2 diabetes outpatients in a tertiary hospital in south-eastern Nigeria.*

PASCAL, I. G., OFOEDU, J. N., UCHENNA, N. P., NKWA, A. A. & UCHAMMA, G.-U. E. 2012. Blood glucose control and medication adherence among adult type 2 diabetic Nigerians attending a primary care clinic in under-resourced environment of eastern Nigeria. *North American journal of medical sciences,* 4**,** 310.

PATTERSON, J. M. 2002. Understanding family resilience. *Journal of clinical psychology,* 58**,** 233-246.

POLINSKI, J. M., SMITH, B. F., CURTIS, B. H., SEEGER, J. D., CHOUDHRY, N. K., CONNOLLY, J. G. & SHRANK, W. H. 2013. Barriers to insulin progression among patients with type 2 diabetes: a systematic review. *The Diabetes Educator,* 39**,** 53-65.

PONNUSANKAR, S., SURULIVELRAJAN, M., ANANDAMOORTHY, N. & SURESH, B. 2004. Assessment of impact of medication counseling on patients' medication knowledge and compliance in an outpatient clinic in South India. *Patient education and counseling,* 54**,** 55-60.

POPKIN, B. M. 2004. The nutrition transition: an overview of world patterns of change. *Nutrition reviews,* 62**,** S140-S143.

RODBARD, H., JELLINGER, P., DAVIDSON, J., EINHORN, D., GARBER, A., GRUNBERGER, G., HANDELSMAN, Y., HORTON, E., LEBOVITZ, H. & LEVY, P. 2009. Statement by an American Association of Clinical Endocrinologists/American College of Endocrinology consensus panel on type 2 diabetes mellitus: an algorithm for glycemic control. *Endocrine practice,* 15**,** 540-559.

ROTHER, K. I. 2007. Diabetes treatment—bridging the divide. *The New England journal of medicine,* 356**,** 1499.

RUBIN, R. R. 2005. Adherence to pharmacologic therapy in patients with type 2 diabetes mellitus. *The American journal of medicine,* 118**,** 27-34.

SLEATH, B., CHEWNING, B., SVARSTAD, B. & ROTER, D. 2000. Patient expression of complaints and adherence problems with medications during chronic disease medical visits. *Journal of Social and Administrative Pharmacy,* 17**,** 71-80.

SOKOL, M. C., MCGUIGAN, K. A., VERBRUGGE, R. R. & EPSTEIN, R. S. 2005. Impact of medication adherence on hospitalization risk and healthcare cost. *Medical care***,** 521-530.

STRATTON, I. M., ADLER, A. I., NEIL, H. A. W., MATTHEWS, D. R., MANLEY, S. E., CULL, C. A., HADDEN, D., TURNER, R. C. & HOLMAN, R. R. 2000. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *Bmj,* 321**,** 405-412.

THE WORLD BANK 2019. The World Bank in Nigeria.

TUOMILEHTO, J., LINDSTRÖM, J., ERIKSSON, J. G., VALLE, T. T., HÄMÄLÄINEN, H., ILANNE-PARIKKA, P., KEINÄNEN-KIUKAANNIEMI, S., LAAKSO, M., LOUHERANTA, A. & RASTAS, M. 2001. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *New England Journal of Medicine,* 344**,** 1343-1350.

TZIOMALOS, K. 2017. Barriers to insulin treatment in patients with type 2 diabetes mellitus. Taylor & Francis.

UMARU YUSUF 2018. Map of the Six Geopolitical Zone in Nigeria showing total number of registered voters.
UNADIKE, B., ESSIEN, I., AKPAN, N., PETERS, E. & ESSIEN, O. 2013. Profile and outcome of diabetic admissions at the University of Uyo Teaching Hospital, Uyo. *International journal of medicine and medical sciences,* 5**,** 286-289.
UNESCO 2012. Action Plan Nigeria.
VIJAN, S. 2010. In the clinic. Type 2 diabetes. *Annals of internal medicine,* 152**,** ITC31-15; quiz ITC316.
WALKER, E. A., MOLITCH, M., KRAMER, M. K., KAHN, S., MA, Y., EDELSTEIN, S., SMITH, K., JOHNSON, M. K., KITABCHI, A. & CRANDALL, J. 2006. Adherence to preventive medications: predictors and outcomes in the Diabetes Prevention Program. *Diabetes care,* 29**,** 1997-2002.
WELCOME, M. O. 2011. The Nigerian health care system: Need for integrating adequate medical intelligence and surveillance systems. *Journal of pharmacy & bioallied sciences,* 3**,** 470.
WILD, S., ROGLIC, G., GREEN, A., SICREE, R. & KING, H. 2004. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes care,* 27**,** 1047-1053.
WILLIAMS UZOMA 2017. Health Systems Administration in Nigeria.
WORLD HEALTH ORGANIZATION 1999. Definition, diagnosis and classification of diabetes mellitus and its complications: report of a WHO consultation. Part 1, Diagnosis and classification of diabetes mellitus. Geneva: World health organization.
WORLD HEALTH ORGANIZATION 2002. The importance of pharmacovigilance. Safety monitoring of Medicinal products.
WORLD HEALTH ORGANIZATION 2003a. Adherence to long-term therapies: evidence for action.
WORLD HEALTH ORGANIZATION 2003b. *Diet, nutrition, and the prevention of chronic diseases*, World Health Organization.
WORLD HEALTH ORGANIZATION 2004. Diabetes action now: an initiative of the World Health Organization and the International Diabetes Federation.
WORLD HEALTH ORGANIZATION 2010. *World health statistics* World Health Organization.
WORLD HEALTH ORGANIZATION 2011. Use of glycated haemoglobin (HbA1c) in diagnosis of diabetes mellitus: abbreviated report of a WHO consultation. Geneva: World Health Organization.
WORLD HEALTH ORGANIZATION 2014. Global status report on noncommunicable diseases World Health Organization.
YANG, Y., THUMULA, V., PACE, P. F., BANAHAN III, B. F., WILKIN, N. E. & LOBB, W. B. 2009. Predictors of medication nonadherence among patients with diabetes in Medicare Part D programs: a retrospective cohort study. *Clinical therapeutics,* 31**,** 2178-2188.
YUSUFF, K. B., OBE, O. & JOSEPH, B. Y. 2008. Adherence to anti-diabetic drug therapy and self management practices among type-2 diabetics in Nigeria. *Pharmacy World & Science,* 30**,** 876-883.
ZHENG, Y., LEY, S. H. & HU, F. B. 2018. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nature Reviews Endocrinology,* 14**,** 88.

Annex 1: Summary of search strategy

STUDY OBJECTIVE	SOURCE	KEY WORDS

The overall objective of the study is to explore the factors that influence medication adherence in Type 2 Diabetes Mellitus from original studies in order to recommend appropriate interventions to policy makers and stakeholders to improve medication adherence in Type 2 Diabetes in Nigeria.	• Pub med • Scopus • African Journal Online databases • Cochrane library • Google scholar • Database of the Federal ministry of health Nigeria • WHO data base • International Diabetes Foundation (Africa region) • References of identified studies • Conference abstracts	Motivator Facilitators Impact Adherence Nonadherence Compliance Noncompliance Concordance Diabetes Type 2 Diabetes Mellitus Patients Society Health system Health care provider
1. To identify the disease related and drug related factors in T2DM that influence medication adherence in Nigeria.		Blood glucose Medication Hyperglycemia hypoglycemia Side effects Disease duration Regimen Cost
2. To identify the patient related and the societal factors that influence medication adherence in T2DM in Nigeria.		Socio economic status Demography Comorbidity Stigma support
3. To identify the healthcare provider and health system related factors influencing medication adherence in T2DM.		Cost Workload Knowledge Available resources Access Healthcare provider