

**SCHOOL OF PUBLIC HEALTH
COLLEGE OF HEALTH SCIENCES
UNIVERSITY OF GHANA**



**ADHERENCE TO MULTI-DRUG THERAPY AMONG PATIENTS DIAGNOSED
WITH LEPROSY AT THE QUA IBOE CHURCH LEPROSY HOSPITAL, EKPENE
OBOM, SOUTHERN NIGERIA**

BY

EMAEDIONG IBONG AKPANEKPO

(10746814)

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DECLARATION

I hereby declare that this submission is my own work and that to the best of my knowledge, it contains no material previously published or written by another person nor material, which has been accepted for award of any degree or diploma of any university or other institutions of learning except where due acknowledgement is made in the text.

NAME: **EMAEDIONG IBONG AKPANEKPO**

SIGNATURE: 

SUPERVISOR: **DR. ERNEST KENU**

SIGNATURE:  25th July 2019

DEDICATION

This work is dedicated to my family, for their unflinching support to me throughout the course of this programme.

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LIST OF ABBREVIATIONS

- D:C - Dapson: Creatinine
- QIC - Qua Iboe Church
- HD - Hansen's Disease
- MB - Multibacillary
- MDT - Multi-drug Therapy
- MMAS-8 - 8-Item Morisky Modified Medication Adherence Scale
- NCDC - Nigeria Centre for Disease Control
- NTBLCP - National Tuberculosis and Leprosy Control Program
- NTD - Neglected Tropical Diseases
- PB - Paucibacillary
- QIC - Qua Iboe Church
- SLPB - Single lesion paucibacillary
- TLM - The Leprosy Mission
- WHO - World Health Organization

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ABSTRACT

Leprosy is a special public health problem because of its potential for social consequences and permanent disabilities. The multidrug therapy has been efficacious in the treatment of leprosy, including prevention of disability when initiated early. However, adherence rates to the MDT have been below expectations in Nigeria. The objective of this study was to determine the factors influencing MDT adherence in Qua Iboe Church leprosy Hospital, Southern Nigeria. This was a cross sectional study carried out among 83 patients diagnosed with leprosy within the past two years and taking MDT medication recruited from Qua Iboe Church Leprosy Hospital, Ekpene Obom. The 8-Item Morisky Medication Adherence Scale (MMAS-8) was used to measure adherence. Influencing factors were categorized under personal, condition-related, health system and drug-related factors. The study showed a gourmet adherence rate of 10.8 per cent. Waiting time greater than 3 hours was negatively correlated with good MDT adherence and this was statistically significant. ($p < 0.05$). Improvements in MDT adherence can be achieved by optimizing personal factors, reducing health system barriers and responsive management of adverse drug reaction

CHAPTER ONE

INTRODUCTION

1.1 Background Information

Leprosy is a mycobacterium disease that has persisted as a significant health problem globally. Leprosy occurs when there is an infection with *Mycobacterium leprae* resulting in a chronic granulomatous inflammation in man that affects mostly the peripheral nervous system, skin, eyes, mucous membranes, skeletal framework, and testicular tissues and has a variety of clinical manifestations. (Walker et al, 2007; Graham et al 2010; Polycarpou et al, 2013).

Leprosy is seen as an important public health issue because of the potential it has to cause long lasting disabilities and social complications like stigma and discrimination. The major goals in leprosy control are to halt continuous transmission, treat identified and diagnosed patients, and ensure the development and progression of disabilities does not occur. (Moschella, 2004). There has been major improvements in leprosy treatment since the commencement of multi-drug therapy (MDT) but the global incidence still remains high, and patients still come down with complications associated with leprosy (White et al, 2015).

Nigeria accomplished the elimination target for leprosy in 1998 but there are still areas of high endemic occurrences and the country has been identified as one with a high likelihood of epidemic occurrences (WHO, 2010). 2,835 new cases were reported in 2016 and majority of them were male (60.5%) and multi-bacillary (71.5%) (Daniel et al, 2017).

The reduction in the prevalence of leprosy has not been followed by a fall in the detection rate of new cases, especially in Nigeria. The prevalence of leprosy has not also been accompanied by a fall in the rate of identification of new cases, particularly in Nigeria. The reduction in prevalence has probably been achieved by shortening of the treatment duration and the expulsion of relieved or defaulted patients from the registers, as opposed to a decrease in disease transmission (Britton et al, 2004).

Uptake, adherence and completion of MDT have been identified as important determinants of elimination of leprosy from endemic “pockets” and prevention of relapse (Moschella, 2004). The relationship between poor adherence and treatment outcomes is straightforward. Non-adherence in MDT can occur in instances of reducing the required dose or discontinuing the treatment before completion. Early discontinuation of treatment has a stronger impact on reduced sustained bacteriologic response. There are existing barriers which need to be understood in order to increase MDT adherence in the context of leprosy treatment. These barriers can be classified into personal factors, disease-related factors, health system factors and drug-related factors (Nsagha et al., 2009; Copal, 1976).

1.2 Statement of the Problem

MDT adherence and completion remains the cornerstone of leprosy elimination in endemic regions. The multidrug therapy (MDT) is an efficacious intervention in the treatment of leprosy, especially when initiated early in the disease process. The success of the MDT regimen depends mostly on the quality of health care delivery services and patient adherence to scheduled treatment (WHO, 2010).

Nigeria has achieved good coverage rate for MDT of approximately 100% since 1998. However, the level of adherence and completion of the MDT is unimpressive. The 2015 National Tuberculosis and Leprosy Control Program reports that 3913 new cases of leprosy occurred in Nigeria and only 1,020 (26.1%) started and completed treatment. In Akwa Ibom State (where the QIC Leprosy Hospital serves as a referral center for diagnosed leprosy cases), 77 new cases were detected and 46 (59.7%) out of these undertook and completed treatment in the same year (NTBLCP Report, 2015).

MDT adherence can be influenced by socio-demographic factors, facility factors, service provider factors and drug factors (Nsagha et al., 2009; Copal, 1976). However, it is not yet known whether clinical factors like leprosy classification and disability grade play a role in MDT adherence. These factors serve as potential barriers for adequate treatment and have negative consequences on the clinical outcome of leprosy, especially nerve damage and disabilities.

Poor adherence and completion of the MDT leads to sub-optimal treatment, incomplete cure, persisting infection sources, multi-drug resistance and relapse. Conversely, good adherence would lead to high completion rates, and definitive cure. This would enhance elimination of the disease. [Noordeen, 1995; FAHD, 1995; ILEP, 1998].

1.3 Justification

In many countries who have reported endemicity to leprosy, certain factors have been identified as barriers to MDT adherence. These barriers consequently lead to absent, inadequate and irregular therapy after diagnosis of leprosy. Low adherence to MDT has been linked with incomplete cure, persisting infection sources, multi-drug resistance and relapse.

Conversely, high MDT adherence has enabled certain countries to eliminate leprosy with relatively low levels of endemicity post-elimination. Therefore, identifying the factors that influence MDT adherence among patients diagnosed of leprosy in QIC Leprosy Hospital could help identifying strategies that would be implemented to improve adherence. This would be helpful in the elimination of pockets of endemicity of leprosy.

If the factors influencing the low adherence of MDT in Nigeria (despite good coverage rates) are not determined and curtailed, the pockets of endemicity of the disease would still be persistent and the progress made so far would be thwarted.

1.4 Research Question

What are the factors influencing the adherence of multi-drug therapy (MDT) among patients diagnosed with leprosy in QIC Leprosy Hospital, Ekpene Obom, Southern Nigeria?

1.5 Study Objectives

1.5.1 General Objective

To determine the factors influencing the adherence of MDT among patients diagnosed with leprosy in QIC Leprosy Hospital, Ekpene Obom, Southern Nigeria.

1.5.2 Specific Objectives

1. To determine the level of adherence to MDT among patients diagnosed with leprosy in QIC Leprosy Hospital, Ekpene Obom, Southern Nigeria.
2. To determine personal factors influencing the adherence of MDT among patients diagnosed with leprosy in QIC Leprosy Hospital, Ekpene Obom, Southern Nigeria;
3. To determine condition-related factors influencing the adherence of MDT among patients diagnosed with leprosy in QIC Leprosy Hospital, Ekpene Obom, Southern Nigeria;
4. To determine health system factors influencing the adherence of MDT among patients diagnosed with leprosy in QIC Leprosy Hospital, Ekpene Obom, Southern Nigeria;
5. To determine drug-related factors influencing the adherence of MDT among patients diagnosed with leprosy in QIC Leprosy Hospital, Ekpene Obom, Southern Nigeria

1.6 Conceptual Framework: Factors that may influence MDT Adherence

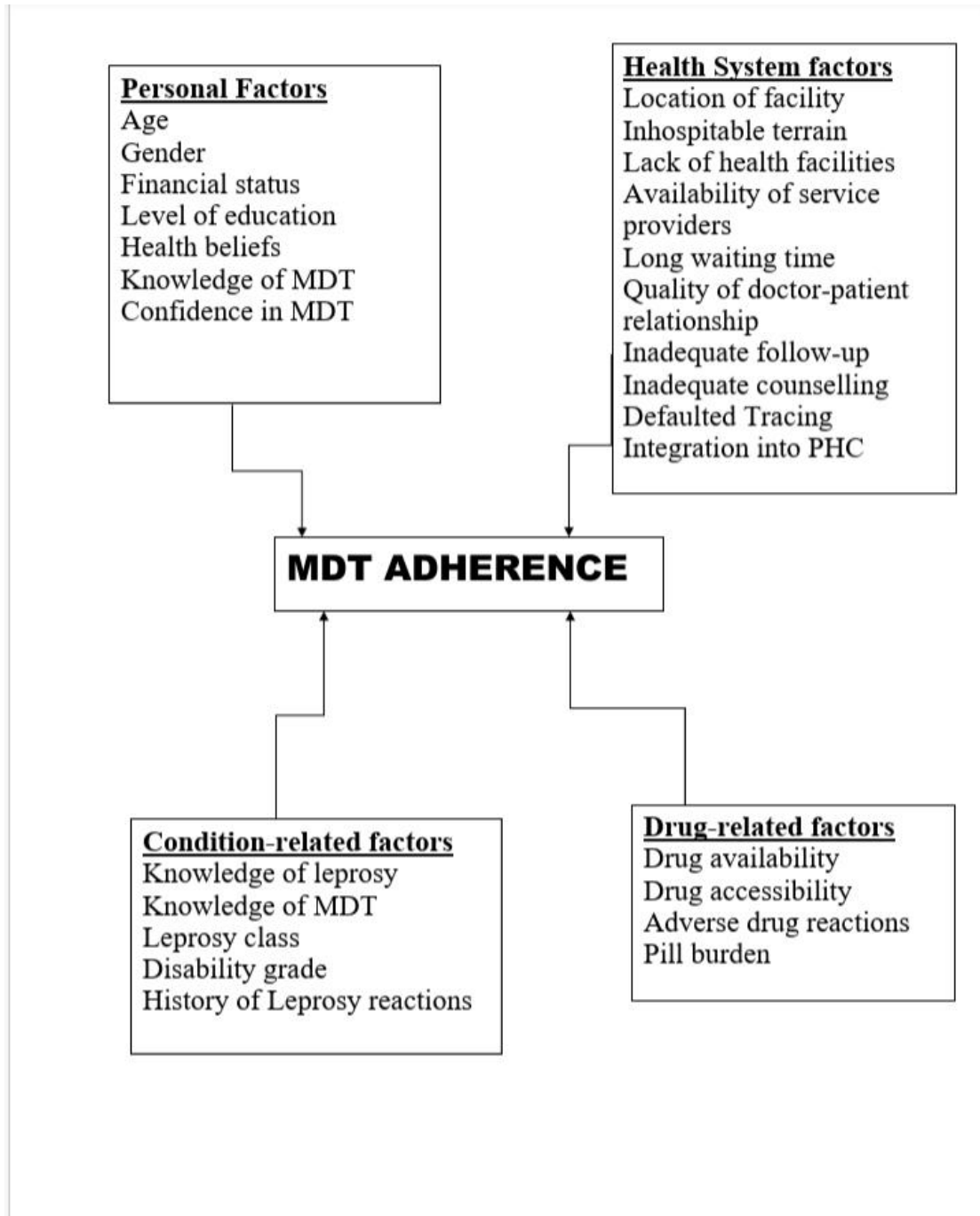


Figure 1.1. Conceptual Framework: Relationship between MDT Adherence and influencing factors

1.7 Narrative

The determinants of MDT adherence can be sorted into four categories: personal factors, condition-related factors, health system factors and drug-related factors.

- Personal factors include gender, age, financial status, marital status, level of education and knowledge of MDT. It has been reported that financial problems which lead to difficulties in making hospital payments and lack of transport funds to the health center have been identified as barriers to MDT adherence (Nsagha et al., 2009).
- Condition-related factors identified were lack of trust in treatment by the patients (because of the relatively long duration of treatment in comparison to other diseases like fever that can be cured within days), lack of knowledge of leprosy treatment, and cultural beliefs that leprosy is incurable (Nsagha et al., 2009; Copal, 1976).
- Health system factors include distance of health facility, registration fee at facility, availability of health facility and living in remote villages, demand for gratification by some health workers, logistics or administrative bottlenecks (which have led to non-availability of MDT in health facilities), lack of health centres in rural areas and shortage of health personnel. (Nsagha et al., 2009; Copal, 1976).
- Drug-related factors are the factors which have an effect on MDT adherence which are due to the ingestion of the MDT regimen. To begin with, the availability and accessibility to the MDT medication are mediating factors in the pathway towards adherence. If the drugs are not available (as at when needed) and accessible, this can lead to infrequent dosing and poor adherence. Also, the MDT regimen routinely involves taking at least 3 drugs for a period

of 6-9 months, if paucibacillary leprosy or a period of 12-18 months, if multibacillary leprosy. Taking this large quantity of drug over such a long period frequently lead to a perception of pill burden by the patients, which has a negative impact on adherence. Finally, unwanted side effects from the leprosy chemotherapy and the presence of adverse drug reactions, further has the potential to worsen MDT adherence because patients may prefer to stop therapy in order to get rid of the unwanted effects.

CHAPTER TWO

LITERATURE REVIEW

2.1. Introduction

This section presents a review of available literature on the subject and topic under consideration.

2.1.0 Literature sources and search strategy

Review of the available literature was done by an internet search. The principal investigator searched through PubMed, the Cochrane Library, Embase and Google Scholar. The following keywords were used in the search: adherence, leprosy, and multidrug therapy. There were no publication or language restrictions.

2.1.0.1 Inclusion criteria

The inclusion criteria for studies included in the review were: (1) Study participants diagnosed with leprosy and taking the MDT Medication. (2) Studies that evaluate socio-demographic, facility, health system and drug factors among leprosy patients. There were no restrictions on sex, race, age, type of leprosy, and publication type.

2.1.0.2 Exclusion criteria

The exclusion criteria were: (1) animal experiments in leprosy drug therapy (2) case reports (3) duplicated literature.

2.1.0.3 Data extraction

Data extraction table was designed beforehand, including sampling methods, sample capacity, basic information of studies, methods and results. The titles, abstracts, and keywords of all records were scanned, and the full articles were identified for further

assessment. After independently searching and screening the studies, the primary investigator extracted and cross-checked the information.

2.1.1 Epidemiology of Leprosy

Leprosy is a granulomatous illness, of a chronic nature, with explicit clinical attributes. It is brought about by the bacillus called *Mycobacterium leprae*, an intracytoplasmic organism that influences (for the most part) the skin and peripheral nervous system (Ministério da Saúde do Brasil, 2013). The principal source of infection in people is transmission patients who are yet to commence treatment. The fundamental setting that encourages the spread of contamination is where contact is consistent. However, close contact with patients who are yet to be treated, will initiate sickness in just 2-5% (Joyce MP, 2012).

Reports from 138 countries in all WHO regions put the estimate of the global prevalence of leprosy at 176176 cases (0.2 cases per 10 000 people), by the end of 2015. The global incidence in 2015 was 211973 (2.9 new cases per 100 000 people). In 2014, 213899 new cases were reported, and in 2013, 215656 new cases (WHO, 2015).

In Nigeria, over 3500 people are identified and diagnosed with leprosy every year with about 25% of them having varying degrees of deformities. A total of 2,835 new cases were reported in 2016 with majority being of the male gender (60.5 per cent) and having multi-bacillary leprosy (71.5 per cent) (Daniel A et al, 2017). Discrimination and stigma against diagnosed persons and communities affected by leprosy in Nigeria is high, due to cultural, religious and superstitions associated with the ailment (NCDC, 2015).

2.1.2 Chemotherapy of Leprosy: The Multi-drug therapy

The pharmacotherapy of leprosy depends on multi-drug treatment (MDT), prescribed by the WHO. In this regimen, leprosy is classified by the quantity of skin lesions into one of three kinds, including multi-bacillary (MB), paucibacillary (PB), and single-lesion PB (SLPB). Multi-bacillary and paucibacillary leprosy patients are treated for 1 year and a half year, separately. The MDT routine comprises of dapsone, rifampicin, clofazimine, ofloxacin, and minocycline. Be that as it may, different anti-leprosy agents, for example, streptomycin (Gelber et al, 1979), clarithromycin (GelberIranmanesh and Murry, 1992), fluoroquinolones (Gelber, Iranmanesh and Murry et al, 1992), and ethionamide (Shepard, 1969) have been demonstrated to be adequate in treating leprosy.

Dapsone was the first successful chemotherapy for the treatment of leprosy. Dapsone supplanted promin, which was utilized prior for the treatment of leprosy (Faget et al., 1943) at a leprosarium in Louisiana, USA. Dapsone represses folic acid synthesis through receptor inhibition and has bacteriostatic effects. Rifampicin has bactericidal effects on the leprosy mycobacterium. This effect was demonstrated tentatively prompting the presentation of rifampicin for the treatment of leprosy during the 1970s. One dose of 1200 mg or a daily dose of 600 mg for 3 days kills the organism in patients, and no further development appeared in mice immunized with patient bacilli (Levy et al 1976). Ofloxacin is a mild bactericidal agent for *Mycobacterium leprae*. Its pharmacological activity against *Mycobacterium leprae* was initially proven by the mouse footpad method in 1986 and thereafter by clinical trials (Saito, et al, 1986; Grosseth et al. 1990).

Clofazimine is recognized to have bactericidal activity against *M. leprae*. The mechanism of action is not completely known; however, a conceivable mechanism

through the binding of GC-rich domains is recommended. It has anti-inflammatory properties and is likewise used to manage type 2 leprosy reactions (Morrison, N.E. et al, G., 1976). Minocycline is another active agent against *M. leprae*. Viability of minocycline against *M. leprae* was affirmed in 1987 (Gelber, 1987). It has bactericidal properties and its pharmacological effect is reinforced when used with other anti-leprosy drugs (Gelber, R.H. et al, 1991).

2.2 Adherence

2.2.1 Concept of Adherence

How patients adhere to a medication or treatment modality as recommended by their service provider is known as adherence, by the WHO (Sabate, 2003). It incorporates the inception and execution of the recommended routine, and cessation of the medicine (Vrijens, S. de Geest et al, 2012). Adherence can either be primary or secondary. Primary non-adherence is the rate with which patients neglect to refill their medicines after it has been prescribed and started (Fischer et al., 2010). Secondary non-adherence happens when recommended drugs are not taken as prescribed (Solomon et al, 2010).

Adherence measures are usually measured as the proportion of the prescribed dose of the medication taken by the patient over a period of time. Certain researchers have re-defined this definition to incorporate information on dose (taking the recommended number of pills every day) and timing (completing the drugs prescribed within a recommended period). For the most part, adherence rates are usually increased among patients with acute and painful disease states, contrasted with those who have chronic states (Jackevicius CA et al, 2002; Cramer J et al, 2003; Haynes RB et al, 2002).

There is no specific agreement on what comprises sufficient adherence. A few researchers recommend rates of more than 80 per cent to be viewed as adequate, while others think about rates of more than 95 percent is necessary for sufficient adherence, especially among patients with life-threatening conditions. Despite the fact that information on adherence are often reported as either adherence or non-adherence, it can shift along a continuum from 0 to (even in excess of) 100 percent, since patients can take more than the recommended measure of drug (Rudd et al, 1988; Pullar T, 1988; Spilker B, 1991).

2.2.2 Methods of Evaluating Adherence

Estimating adherence is important in light of the fact that wrong determination of medication adherence can lead to potentially dangerous problems in research and clinical settings. Therapeutic interventions that were previously esteemed viable might be seen as ineffective and treatment might be superfluously and hazardously escalated (McDonnell et al, 2002; Schiff et al, 2003). Precise evaluations of drug adherence have the potential to give better facts on the results, indicators, and techniques to improve medicine adherence. The choice of a method to evaluate adherence should depend on individual attributes, the objectives of the evaluation and available resources. There is no standard measure of medication adherence and the use of more than one method is usually recommended (McDonnell PJ et al, 2002).

The strategies utilized in the estimation of adherence can be arranged into direct and indirect techniques. Direct measures include directly observed therapy, measurement of concentrations of a drug or its metabolite in blood or urine, and detection or measurement in blood of a biologic marker added to the drug formulation. Direct methodologies are costly, difficult to the service provider, and can be manipulated by

the patient. Notwithstanding, for certain medications, estimating these levels is a usually utilized methods for evaluating adherence.

Indirect proportions of adherence incorporate getting some information about the ease of taking medication; having an assessment of clinical response; number of pills; refill rates for prescriptions; questionnaires; electronic monitoring; measuring biological markers; and medication diary recording (Rudd , Byyny & Zachary et al, 1988; Pullar et al, 1989).

Scrutinizing patient journals (including the patients), and appraisal of clinical reactions are generally simple to utilize, yet scrutinizing the patient can be susceptible to deception and an exaggeration of patient adherence. The utilization of a patient's response to treatment as a measure could be obscured by numerous elements other than adherence to the recommended treatment routine (Cramer JA et al, 1989).

The most widely recognized technique used to quantify adherence, apart from patient questioning, has been pill checks (that is, tallying the pill count that stay in the patient's drug jugs or vials). Despite the fact that the straightforwardness of this technique is appealing to numerous scientists, the strategy is liable to numerous issues, since patients can switch drugs among containers and may dispose of pills before visits so as to give off an impression of being following the routine. Hence, pill tallies ought not be thought to be a decent measure of adherence (Rudd et al, 1988; Pullar et al, 1989).

Medication refill rates are an exact method of determining adherence in a closed pharmacy framework, given that the rates of refill are estimated frequently. A health system that utilizes electronic medicinal records and a closed pharmacy system can furnish the clinician or researcher with promptly accessible data on medication refill

rates that can be utilized to survey adherence and to certify the patient's response to inquiries (Steiner et al, 1997; Lau, de Boer A et al, 1997; Christensen et al, 1997).

Electronic monitoring, administering drops (as on account of glaucoma), or canister activation (as on account of asthma) have been utilized for over three decades (Spector et al , 1986; Norell, 1981; Kass et al, 1984). As opposed to giving week-by-week or month-to-month averages, these devices do not give exact and nitty-gritty bits of knowledge into the conduct of patients in taking drug. They do not record whether the patient really ingested the right medication or right portion henceforth, are indirect measures. Patients may open a holder and not take the prescription, take the off-base measure of drug, or refute the information by setting the medicine into another compartment or take numerous portions simultaneously. However, certain strategies for estimating adherence might be favored in specific instances; hence a mix of techniques boosts exactness (Liu et al, 2001; Turner et al, 2001).

2.2.3 The 8-Item Morisky Medication Adherence Scale (MMAS-8)

The MMAS-8 is an improvement on the MMAS-4 with more sensitivity than the four-item scale reported in 1986. It is viewed as the most usually utilized self-reported technique to decide adherence containing 8 questions having yes/no answers intended to reduce the predisposition of positive reactions from patients' inquiries posed by health professionals, by reverting the responses identified with the adherence behavior (Morisky et al, 2008; Voils, 2011).

Item 1 asks “Do you sometimes forget to take your pills?”; Item 2 asks “People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days you did not take your medicine?”; Item 3 asks “Have you ever cut back or stopped taking your medication without telling your doctor, because you felt worse when you took it?”; Item 4 asks “When you travel or leave home, do you sometimes forget to bring along your medication?”; Item 5 asks “Did you take your medicine yesterday?”

Item 6 asks “When you feel like your illness is under control, do you sometimes stop taking your medicine?”; Item 7 asks “Taking medication every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?”; Item 8 asks “How often do you have difficulty remembering to take all your medications?”. The extent of adherence is assessed by the score gotten from the total of the answers and classified into high adherence, medium adherence and poor adherence (Morisky et al, 2008; Krousel-Wood , 2009).

2.2.4 Adherence to MDT Treatment

Several studies have investigated the determinants of non-adherence to MDT treatment. However, few have studied the issue of non-adherence among patients with leprosy. Notwithstanding this, there is no empirical strategy for estimating adherence and the meaning of adherence differs. Direct ways of measuring adherence include laboratory analysis of blood, urine or other body fluids for the presence of a drug or drug metabolite. Indirect measures include questionnaires, analysis of pharmacy records and pill counts (Bosworth et al, 2006; Nunes et al., 2009)

2.2.4.1 Indirect Measures of MDT Adherence

A commonly used measure of MDT adherence in leprosy is the proportion of MDT default rates. The WHO uses this aberrant measure to distinguish patients who are yet to finish their treatment as planned and as a measure of the quality of leprosy services (WHO, 2015). Patients with PB and MB leprosy must finish their multi-drug therapy (MDT) routine within a maximum time-frame of 9 and 18 months respectively. Patients who don't accomplish this objective are labeled as non-adherent (WHO, 2015).

Pharmacy-related information has additionally been helpful in evaluating MDT adherence. As indicated by the consequences of pill tallies, nine percent of patients with leprosy in Raipur City, India, were observed to be non-adherent (Masih VK et al, 1998). Blister packs have likewise been utilized to gauge adherence and are prescribed by the WHO as an approach to improve MDT adherence (WHO, 2015). As indicated by their treatment records, 40% of patients in Western Sudan did not collect enough drugs to finish treatment (Coebergh JAF et al, 2004).

2.2.4.2 Direct Measures of MDT Adherence

A habitually utilized direct measure of MDT adherence in leprosy treatment is testing urine samples for dapsone, which is taken every day in the course of MDT. The most famous techniques incorporate the dapsone tile test, the dapsone:creatinine (D:C) proportion test and the urine spot test (Naik et al 1994; Naik et al 1990; Irudaya Raj et al, 1983; Ellard, 1995; Bhatnagar et al, 1989; Huikeshoven et al, 1986; van et al, 1991; Balakrishnan, Kumar et al, 1986; Becx-Bleumink, 1992; Yoder et al 1991; Roche et al, 1989; Girdhar et al 1988; Huikeshoven, 1986; Huikeshoven, 1985; Lammers et al, 1995).

Huikeshoven et al. announced that urine spot tests will test negative after roughly three missed doses of dapsone (Huikeshoven H et al, 1986). It was additionally detailed that the D:C proportion test appeared have greater sensitivity than the urine spot test in distinguishing non-adherence. Be that as it may, the urine spot test was said to be more specific and considered the method of choice when rapidity and reproducibility are the major objectives (Bhatnagar P et al, 1989). Different authors have outlined the upsides of the urine spot test - easily performed in field conditions (Weiand D, 2011; Yoder LJ et al 1991) and that results correspond with those of the D:C proportion test (Bhatnagar P et al, 1989; Kumar A et al., 1982; Naik SS, 1984).

Some researchers have utilized the urine spot test in field conditions and greater part report significant degrees of non-adherence among patients with leprosy. In 2009, 13 out of 52 patients (25%) in Hyderabad, India, were observed to be non-adherent as indicated by the urine spot test (Weiand D et al, 2011). Another study led in Kaduna State, Nigeria demonstrated that 20% of 258 patients were non-adherent (Lammers H et al, 1995). In 1991, a study reported that 55 out of 341 (16.1%) outpatients treated in Eastern Nepal were non-adherent (van Trier YD et al, 1991).

In 1989, an investigation reported that 45 out of 337 (13.3%) Nepalese patients were non-adherent (Roche PW et al, 1989). In 1988, a study reported that 45.4% of 366 patients in Agra, India, were noncompliant (Girdhar A et al, 1988). Authors that utilized the dapsona tile test or the D:C ratio test to gauge adherence had comparable outcomes. Utilizing the D:C ratio test, a study in 1993 discovered 82 out of 294 (28%) patients in Mumbai, India, were irregular on dapsona treatment (Revankar CR et al, 1983). In another study in the same geographical area, 65% of patients were non-adherent to treatment on continuous testing with the dapsona tile test (Naik SS et al, 1990).

2.2.5 Factors affecting MDT Adherence

Non-adherence to leprosy treatment is a concern to public health practitioners and has been a significant determinant in keeping up the chain of transmission, advancement of sequelae, handicaps, and resistance to MDT. As indicated by WHO, there are various components prompting poor drug adherence, typically grouped into three classifications: personal factors (patients-related elements, condition-related elements, financial factors, social determinants), treatment factors, and health system factors (Ferreira SMB et al, 2012; Ferreira SMB et al, 2011; Kar S et al, 2010).

2.2.5.1 Personal factors

Age & Gender

Accessible information from research on the relationship between demographic factors and adherence to MDT treatment are opposing. In a research done in Dhanusha, a region of Nepal, it was found that 79.2% of male patients finished treatment, while 34.4% of females did not finish in the predetermined period. The study demonstrated significant associations between MDT adherence and gender (Kar S et al 2010; Silva MCD et al, 2010).

Be that as it may, another study by Heukelbach and colleagues, showed that socio-demographic information, for example, gender, age, and marital status were not related with poor MDT adherence. This study indicated higher rates of non-adherence to MDT treatment in young males (34.4%) when the information was classified by sex. Men demonstrated a difference of around two times (17.6%) contrasted with females of a similar age (Heukelbach J. et al, 2011). The study by Araujo and Oliveira uncovered that most male patients with irregular treatment (48.8%) were distributed in the age group 20-39 years (De Araújo et al, 2005). The study by Trindade and

partners reported a male predominance in non-compliance to leprosy treatment, however, because of the small sample size; the difference was not statistically significant (Trindade LC, 2009).

Marital Status

A similar report by Trinade and colleagues reported that those with noncompliance to the MDT treatment were predominantly unmarried, dissimilar to the findings by Honrado (2008) in which married individuals predominated the proportion of dropout patients (Honrado ER et al, 2008).

Socio-economic Factors

Certain studies have announced that patient practices in connection to MDT treatment are to a great extent impacted by their financial status and level of information (Miranzi et al, 2010; Silva et al, 2012). In a study by Kar and associates, greater part of the MDT treatment defaulters had finished primary education (32.28%), had per capita income between \$7 – 10 (30.71%), and belonged to social class IV (33.86%) and class V (30.71%). This study additionally reported a significant association between the level of education, per capita income per month and financial status, with treatment outcomes (Kar S et al, 2010).

In the Philippines, there was no reported association between financial factors and non-adherence to MDT treatment. Patients who deserted and those who finished treatment belonged to similar income groups (Honrado ER, 2008). In another study performed in a Brazilian region, low salary was not significantly associated with non-adherence to MDT (Trindade LC, 2009). This distinction might be identified with the diverse social settings in the Philippines, Brazil and India.

2.2.5.2 Condition-related Factors

Honrado and partners announced the MDT non-adherence rate among those patients who were not aware of the ailment was significantly higher than the individuals who were aware (44.4% versus 23.6%, separately). Moreover, the likelihood of abandoning the treatment among the unaware individuals was 2.6 times higher than the individuals who were aware of the condition (Honrado ER, 2008).

Another study by Trindade and associates discovered that the quantity of clients who were sufficiently aware of the ailment was marginally higher in the group that finished the normal treatment than the incomplete treatment group (Trindade LC, 2009).

A study by Chalise discovered that approximately 86% of instances of noncompliance have no information about leprosy, around 39% don't know the cause, and just about 14% realized that the infection is brought about by a bacterium or "microorganism". It was additionally revealed that 33.3 percent of non-adherent patients accepted the disease was brought about by spiritual events (Chalise S, 2005). Likewise, greater part (94.7%) of noncompliant cases had a solid conviction that the vanishing of the signs/indications is the main significance of "disease cure". This mirrors a low degree of comprehension of the treatment (Chalise S, 2005).

2.2.5.3 Health system factors

As indicated by scientists from Nova Deli, practically 50% of the patients who resided nearest to the hospitals dropped out of MDT, contrasted with patients who lived far from the hospitals, where about 60% were non-adherent. Patients from outside the region had a fundamentally higher default rates in a wide range of leprosy cases, contrasted with patients who resided close within the centre (Rao PSS, 2008).

Another study in Duque de Caxias did not identify the distance from the patient's residence to the facility as a factor weakening adherence to treatment. The study recommends that if treatment is appropriately done, contextual variables can be limited (Hacker MAVB et al, 2012).

Subsequently, it very well may be set that the patient is bound to be dropout when the habitation is a long way from the treatment center because of movement expenses and time taken. While this is valid, non-adherence rates are additionally high for patients closer to the middle. A few patients may incline toward a spot more distant from the home to stay unknown (Rao PSS, 2008).

2.2.5.4 Drug Factors

Studies have identified other predisposing factors for poor adherence. For instance, the study in the Philippines, 40 percent of patients identified adverse drug effects as the primary driver for not finishing the treatment. These effects were dizziness, headache, queasiness, gastrointestinal uneasiness, and others (Honrado ER, 2008). An examination led by Souza et al. recorded the primary unfavorable drug-related factors that lead to non-adherence: anaemia, agranulocytosis, neuropathy (associated with dapsone), hepatotoxicity (due to rifampicin and dapsone), hyperpigmentation (due to clofazimine). The reactions may begin unexpectedly and cause a wide scope of extraordinary side effects, for example, inflammatory arthritis, erythema nodosum,

fever, neuritis, and paralysis. The health provider must be ready to immediately identify and manage such reactions, utilizing tertiary institutions, if necessary (Souza et al, 2009).

2.2.6 Strategies to Improve Adherence

Methods that can be utilized to improve MDT adherence can be classified into four general classes: patient education; better dosing plans; expanded hours when the facility is open and therefore shorter waiting times; and improved correspondence among doctors and patients. Educational interventions including patients, their relatives, or both can be powerful in improving adherence (Patton K et al, 1997; Ran MS et al, 2003).

Techniques to optimize dosing scheduling can incorporate the utilization of pillboxes to compose everyday portions, rearranging the routine to everyday dosing, and signs to remind patients to take medications. Patients who miss arrangements are regularly the individuals who need assistance to improve their capacity to stick to a medicine routine. Thus, such patients will regularly profit from being assisted in clinic scheduling and “cue dose training” to improve their adherence (Bouvy ML et al, 2003).

Facility booking procedures to optimize adherence incorporate making follow-up visits helpful and proficient for the patient. Delays in patient consultations and issues with transportation can undermine a patient's ability to consent to a drug routine and to keep follow-up arrangements. Mediations that enroll ancillary health care providers such as pharmacists, behavioral specialists and nursing staff can improve adherence (Simoni JM et al 2003).

At last, improving correspondence between the doctor and the patient is a key and viable methodology in improving the patient's capacity to pursue a treatment routine

(Maro EE et al 1997; Ross FM, 1991). Most methods of improving adherence have involved a combination of behavioral interventions and reinforcements in addition to increasing the convenience of care, providing educational information about the patient's condition and the treatment, other forms of supervision and follow-up (Feldman R et al, 1998; Rigsby MO et al, 2000; Zygmunt et al 2002). Successful techniques are complex and laborious, and innovations will need to be developed that are feasible for routine care (Haynes RB et al, 2002). Given the numerous variables adding to poor adherence to a drug, a multi-factorial methodology is required, since a solitary methodology won't be viable for all patients (Cramer JA, 1995; Crespo-Fierro M., 1997).

CHAPTER THREE

METHODS

3.1 Study Design

In this study the quantitative approach was used. A cross-sectional survey design was adopted. The cross-sectional survey was used because the study will be carried out at a single point in time. The study design gathered information on the how patients who are diagnosed with leprosy at the Qua Iboe Church Leprosy Hospital, Ekpene Obom adhered to their MDT regimen and the determining factors. The cross-sectional study design was also used because it is less expensive, ethically safe and simple to use.

3.2 Study Location

The study would be conducted at the Qua Iboe Church Leprosy Hospital in Ekpene Obom Community of Etinan Local Government Area of Akwa Ibom State in Nigeria.

3.2.1 Nigeria

Geographically, Nigeria is located approximately between latitude 4° and 14° North of the Equator; and between longitudes 2° 2' and 14° 30' East of the Greenwich meridian. It is bordered to the north by the Republics of Niger and Chad; to the south by the Atlantic Ocean; to the east by the Republic of Cameroon and to the west by the Republic of Benin. The population is more than 197 million, spread unevenly over a national territory of approximately 923,770 km². Nigeria has the 8th largest national population globally and about a quarter of the total population of all the countries in Sub-Saharan Africa. (UNDP, 2018; CIA, 2013).

3.2.2 Akwa Ibom State

Akwa Ibom is a state in Nigeria with a population of over five million people. It is located in the southern part of the country, lying between latitudes 4°32'N and 5°33'N, and longitudes 7°25'E and 8°25'E. The state is located in the South-South geopolitical zone, and is bordered on the east by Cross River State; west by Rivers State and Abia State; and the south by the Atlantic Ocean and the southernmost tip of Cross River State.

The state was created in 1987 from the former Cross River State and is currently the highest oil- and gas-producing region in the country. The state's capital is Uyo, with population of over 500,000.

3.2.3 Qua Iboe Church Leprosy Hospital, EkpeneObom

This study was carried out at Qua Iboe Church Leprosy Hospital, Ekpene Obom in Etinan Local Government area of Akwa Ibom State of Nigeria. Qua Iboe Church leprosy hospital was established in 1932 in the rural Community of Ekpene Obom as a leprosy settlement in present day Akwa Ibom State by Qua Iboe Mission (QIM). The settlement has evolved over the years into a full-fledged district hospital.

The hospital is presently run under a tripartite agreement between Qua Iboe Church Nigeria (QICN), Akwa Ibom State Government (AKSG) and The Leprosy Mission (TLM). The hospital currently has the following facilities namely: the general outpatient department (GOPD), the inpatient wards, an operating theatre, an eye clinic, a pharmacy unit, a physiotherapy unit as well as an HIV clinic for screening and dispensing of anti-retroviral (ARV) drugs (Idung et al,2014).

3.3 Study Population

Study population comprised of leprosy patients who have been diagnosed or referred to the hospital (after a prior diagnosis of leprosy has been made) in the past 2 years at the QIC Leprosy Hospital, Ekpene Obom, Southern Nigeria.

3.3.1 Inclusion criteria

- Being 18 years or older;
- Being diagnosed of leprosy at QIC Leprosy Hospital;
- Referred to QIC Leprosy Hospital after prior diagnosis elsewhere;
- Diagnosed with leprosy within the past 2 years.

3.3.2 Exclusion criteria

- Treatment completion

3.4 Variables

3.4.1 Dependent variable

Adherence was determined by the 8-Item Modified Morisky Medication Adherence Scale (MMAS-8). It was trichotomized where patients with score less than 3 would be said to have low adherence; score from 3 to <5 would be considered to have medium adherence and those with score 5 and above would be considered to have high adherence.

MMAS-8 scores less than 5 (low and medium) were considered as “poor adherence” while scores greater than 5 (high) were considered as “good adherence”.

3.4.2 Independent variables

Independent variables were defined as personal factors, condition-related factors, health system factors and drug-related factors.

Table 3.1. Dependent and independent variables

Variables	Factors
Dependent variable	MDT adherence
Independent variables	
Personal factors	Gender, age, level of education, occupation, marital status, rural vs urban location, and income level.
Condition-related factors	Awareness of leprosy, awareness of MDT, leprosy class, knowledge of curability of leprosy, disability grade and a history of leprosy reactions.
Health system factors	Location of facility, terrain of facility, presence of registration fee at facility, ready availability of service providers, waiting time, quality of doctor patient relationship, inadequate counseling, and inadequate follow-up
Drug-related factors	Drug accessibility, drug availability, presence of adverse drug reactions, and pill burden.

3.5 Sample Size and Sampling Approach

3.5.1 Sample Size Calculation

Cochran's sample size formula for categorical data was used. Because of the small study population size, a confidence level of 90% and margin of error of (no more than) $\pm 8\%$ was used to determine the minimum sample size.

$$n = \frac{(z)^2 * (p)(q)}{(d)^2}$$

$$n = \frac{(1.645)^2 * (0.2610) (0.7390)}{(0.08)^2}$$

$$n = \frac{0.5219}{0.0064} = 82$$

Where:

n = sample size (82);

z = 90% confidence level (1.645);

p = proportion of MDT adherence (0.2610) from the 2015 National Tuberculosis and Leprosy Control Program Report;

q = proportion of non-adherence to MDT (0.7390);

d = accepted margin of error (0.08).

3.5.2 Sampling Approach

The participants were selected using convenience sampling because the required minimum sample size (82) almost approximated the study population which met the inclusion criteria (83). Participants were interviewed with the study instrument.

3.5.2.1 Training of Interviewers

Data collectors were recruited and trained to administer the study questionnaires in a friendly and professional manner. They were coached on ways to conduct the interviews efficiently to ensure that good quality data was collected. Questionnaires were completed by trained interviewers in a quiet place. Interviewers were not involved with patient treatment and care.

3.5.2.2 Review of Medical Records

Clinical records of the patients from the medical records department were reviewed to confirm the diagnosis of leprosy. After obtaining written informed consent, patients were interviewed using a structured interviewer-assisted anonymous questionnaire.

Information retrieved from the medical records of the patients included: biodata, clinical information (type of leprosy, type of disability grade, and prior history of lepra reactions). The address and phone number in the biodata section of the patient's folder was used to locate the patients at their homes, for those who were not residing on the hospital premises.

The research assistants administered the questionnaires to them at home. For patients who were resident on the hospital premises (due to abandonment by family members), they were located at their hostels and interviewed with the study instrument.

3.5.2.3 Pre-testing and Review of instruments

The study questionnaires were administered first to 5 leprosy patients at the Tuberculosis and Leprosy Hospital, Igbogene, Bayelsa State. The format, comprehension and completion of the questionnaires was assessed and revised accordingly after pre-testing.

3.5.2.4 Quality Control

To ensure the quality of the collected data, the principal investigator reviewed all filled questionnaires daily to correct or address any issue related to them. In addition, data was double-entered to minimize the errors.

3.6 Data Collection Instrument

It consisted of a short introduction explaining why the study was being carried out, and five sections: A, B, C, D, E, and F. Section A comprised of questions concerning socio-demographic information of the respondents. Sections B comprised of questions assessing adherence to MDT. Sections C, D, E and F comprised of questions assessing personal, condition-related, health system and drug-related factors respectively. Open and close-ended questions were used in the questionnaire. The instrument was drafted in English Language.

3.7 Data Processing and Analysis

STATA 15.0 was used for data analysis. Data obtained was examined for correctness, entered into the software and cleaned. It was then coded using numeric values (e.g. gender with options female and male coded as 1=female, 2= male). For categorical data (e.g. socio-demographic data like gender, ethnicity etc), summary tables of counts and percentage were presented with respect to these characteristics. For continuous data, (e.g. age), summary tables of mean and standard deviations were presented. In certain cases, graphical presentations were provided to highlight the level of differences (MDT adherence vs non-adherence). In cases of sparse data (less than 5% observation), to avoid bias on the conduct of analysis, the assessments of respondents in such categories were excluded. Univariate analysis of frequencies was reported for all categorical variables. Chi-square or Fischer's Exact tests was used to determine whether patients differed significantly on adherence and personal, condition-related, health system and drug-related factors and MDT adherence. Logistic regression was used to predict association between MMAS-8 adherence scores and independent variables (gender, age, level of education, occupation, marital status, rural vs urban location, and income level; awareness of leprosy, awareness of MDT, knowledge of curability of leprosy, leprosy class, disability grade and a history of leprosy reactions; location of facility, terrain of facility, presence of registration fee at facility, ready availability of service providers, waiting time, quality of doctor patient relationship, inadequate counseling, and inadequate follow-up; drug accessibility, drug availability, presence of adverse drug reactions, and pill burden). P-value of less than 0.05 was accepted to be statistically significant.

Appropriate diagnostics to ensure that the data satisfied the assumptions, necessary to conduct the logistic regression, was done. The assumptions are as follows:

#1: The dependent variable (MDT adherence) was measured at a nominal level with two categories: good and poor MDT adherence.

#2: The independent variables were continuous, ordinal or nominal.

#3: There was independence of observations and the dependent variable had mutually exclusive categories.

#4: There was no multi-collinearity. Variables that showed multi-collinearity were excluded from the final model

#5: A linear relationship was established between the continuous independent variables and the logit transformation of the dependent variable.

#6: There were no outliers, high leverage values or highly influential points.

3.8 Data Storage/Security and Usage

Hard and electronic copies data were stored in locked file cabinets, and access was limited to the principal investigator and the supervisors of the study.

3.9 Ethical Considerations/Issues

Ethical clearance was sought from the Ethical Review Board of the Akwa Ibom State Ministry of Health and the Ethical Review Committee of the Ghana Health Service before the study initiation.

Approval from study area: Permission was obtained from the Medical Superintendent of the QIC Leprosy Hospital, Ekpene Obom.

Safety Considerations/Risks: The study did not necessitate any invasive procedures to the study participants. However, if some participants felt uncomfortable to answer some

questions, an answer was not mandatory for them. Questions on the study tool were impersonal and non-intrusive.

Voluntary consent: All the study procedures were clearly explained to each study participant to be sure that they understand the topic and to obtain their individual informed consent. The content of the informed consent form was explained when necessary in the local language and then, written consent was obtained from each participant prior to performing any study related procedures. A copy of the informed consent sheet was given to each participant for his/her personal records. The rights and welfare of the participants were protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

Privacy and confidentiality: The name of the study participants as well as their personal information was kept confidential. Access to the research records was limited to the study principal investigator and the study supervisors.

Benefits to participants: Characteristics of the identified non-compliant (if they agreed) was communicated to the health facility to offer them the opportunity to be treated.

Compensation: Participants were not paid anything in the form of material or money for participating in this study.

Declaration of conflict of interests: All investigators declared no competing interests.

CHAPTER FOUR

RESULTS

4.1 Socio-demographic and Clinical Characteristics of Study Participants

The mean age (in years) was 50.3 ± 11.2 years. Most of the respondents were male (51.8%), married (43.4%), and unemployed (68.7%) with secondary level of education (49.4%). Clinically, most people had multibacillary leprosy (56.6%), grade 2 disability (42.2%) with no history of leprosy reactions (56.6%) (Table 4.1).

Table 4.1. Prevalence of MDT Adherence

Adherence level	Prevalence (%)	95% Confidence Interval (%)
Poor adherence	89.2	80.2, 94.3
Good adherence	10.8	5.7, 19.7

4.2 Levels of MDT Adherence Measure among Study Participants

Based on the cut-off points for MDT adherence, 10.8% had good MDT adherence while 89.2% had poor adherence (Table 4.2).

Table 4.2: Socio-demographic and Clinical Characteristics of Respondents

Variable	Frequency (N=83)	Percentage (%)
Age(years); mean±S.D	50.3±11.2	
Gender		
Female	40	48.2
Male	43	51.8
Marital Status		
Single	15	18.1
Married	36	43.4
Divorced	11	13.2
Widowed	21	25.3
Educational Level		
None	7	8.4
Primary	27	32.5
Secondary	41	49.4
Tertiary	8	9.6
Occupation		
Unemployed	57	68.7
Artisan	7	8.4
Trader	16	19.3
Civil Servants	3	3.6
Leprosy Class		
Paucibacillary	36	43.4
Multibacillary	47	56.6
History of Lepra Reactions		
None	47	56.6
Type 1	24	28.9
Type 2	12	14.5
Disability Grade (WHO)		
0	16	19.3
1	32	38.6
2	35	42.2

4.3. Relationship between Personal factors and MDT Adherence

There was a significant relationship between MDT adherence and marital status ($p = 0.03$); educational level ($p = 0.01$) and occupation of respondents ($p = 0.001$), on bivariate association (Table 4.3). However, multivariate regression showed that having tertiary education was associated with 1.85 higher odds of MDT adherence, holding other variables constant, compared to patients with no education (Table 4.7). Regardless, this was not statistically significant.

Table 4.3. Association between Personal Factors and Levels of MDT Adherence

Variable	MDT Adherence(N=83)		P value
	Poor adherence (n=74)	Good Adherence (n=9)	
Age			0.644
30-39	13(86.7)	2(13.3)	
40-49	24(82.8)	5(17.2)	
50-59	17(94.4)	1(5.6)	
60-69	18(94.7)	1(5.3)	
>70	2(100.0)	0(0.0)	
Gender			0.158
Female	38(95.0)	2(5.0)	
Male	36(83.7)	7(16.3)	
Marital Status			0.032
Single	14(93.3)	1(6.7)	
Married	28(77.8)	8(22.2)	
Divorced	11(100.0)	0(0.0)	
Widowed	21(100.0)	0(0.0)	
Educational level			0.008
None	6(85.7)	1(14.3)	
Primary	25(92.6)	2(7.4)	
Secondary	39(95.1)	2(4.9)	
Tertiary	4(50.0)	4(50.0)	
Occupation			0.001
Unemployed	54(94.7)	3(5.3)	
Artisan	7(100.0)	0(0.0)	
Trader	13(81.3)	3(18.7)	
Civil servants	0(0.0)	3(100.0)	

4.4. Relationship between Condition-related Factors and MDT Adherence

Awareness of MDT ($p=0.01$) was significantly associated with MDT adherence. Other condition-related factors were not statistically significant on bivariate and multivariate associations (Table 4.4).

Table 4.4. Associations between Condition-related Factors and Levels of MDT Adherence

Variable	MDT Adherence (N=83)		P value
	Poor adherence(n=74)	Good adherence(n=9)	
Leprosy Class			
Paucibacillary	32(88.9)	4(11.1)	1.00
Multibacillary	42(89.4)	5(10.6)	
History of Leprosy Reactions			
None	41(87.2)	6(12.8)	0.55
Type 1	21(87.5)	3(12.5)	
Type 2	12(100.0)	0(0.0)	
Disability Grade (WHO)			
0	13(81.3)	3(18.7)	0.10
1	27(84.4)	5(15.6)	
2	34(97.1)	1(2.9)	
Awareness of Leprosy			
No awareness of leprosy	15(100.0)	0(0.0)	0.20
	59(86.8)	9(13.2)	
Awareness of MDT			
No awareness of MDT	32(100.0)	0(0.0)	0.01
	42(82.4)	9(17.6)	
Knowledge of Curability of Lep			
No	24(100.0)	0(0.0)	0.05
Yes	50(84.7)	9(15.3)	

4.5. Relationship between Health System Factors and MDT Adherence

Relationship with service providers and being readily attended to by service providers pre-treatment counseling were associated with MDT adherence and it was statistically significant ($p=0.00$) (Table 4.5).

Table 4.5. Associations between Health system factors and Levels of MDT Adherence

Variable	MDT Adherence(N=83)		P value
	Poor adherence(n=74)	Good adherence(n=9)	
Relationship with service providers			
Poor	29(100.0)	0(0.0)	0.00
Fair	12(100.0)	0(0.0)	
Good	17(94.4)	1(5.6)	
Excellent	16(66.7)	8(33.3)	
Readily attended to by service providers			
No	34(100.0)	0(0.0)	0.01
Yes	40(81.6)	9(18.4)	
Pre-treatment counseling	26(100.0)	0(0.0)	0.05
No pre-treatment counseling	48(84.2)	9(15.8)	
Location of facility far from residence	22(81.5)	5(18.5)	0.14
Location of facility close to residence	52(92.9)	4(7.1)	
Waiting time at facility			
30 minutes – 1 hour	11(84.6)	2(15.4)	0.09
1-3 hours	19(79.2)	5(20.8)	
More than 3 hours	44(95.7)	2(4.3)	

4.6. Relationship between Drug-related Factors and MDT Adherence

Adverse drug reactions were significantly associated with MDT adherence (p value =0.001). Pill burden was not significantly associated with MDT adherence (Table 4.6).

Table 4.6. Associations between Drug-related factors and MDT Adherence

Variable	MDT Adherence		P value
	Poor adherence (n=74)	Good adherence (n=9)	
Adverse drug reactions	32(78.0)	9(22.0)	0.001
No adverse drug reaction	42(100.0)	0(0.0)	
Pill burden	18(78.3)	5(21.7)	0.107
No pill burden	56(93.3)	4(0.7)	

4.7 Multiple Regression Model for factors associated with MDT Adherence

On multivariate association, waiting for 30 minutes – 1 hour was associated with a 0.04 higher odds of having MDT adherence, holding other variables constant, compared to patients who wait for 1-3 hours. Based on the p value =0.12, this increase in the odds of MDT adherence is not statistically significant (Table 4.7).

Furthermore, waiting for more than 3 hours was associated with a 0.03 times higher odds of having MDT adherence, holding other variables constant, compared to patients who wait for 1-3 hours. Based on the p value =0.02, this increase in MDT adherence is statistically significant (Table 4.7).

Table 4.7. Multiple logistic regression model for factors associated with MDT Adherence

Variables	Poor adherence	Good adherence	OR (95% CI)	P value	AOR (95% CI)	P value
Age						
30-39	13(86.7)	2(13.3)	1.0		1.0	
40-49	24(82.8)	5(17.2)	1.35(0.30, 5.99)	0.74	1.79(0.17, 18.51)	0.63
50-59	17(94.4)	1(5.6)	0.38(0.04, 3.13)	0.45	0.37(0.01, 9.82)	0.55
60-69	18(94.7)	1(5.3)	0.36(0.04, 2.95)	0.43	0.33(0.01, 7.94)	0.49
Educational level						
None	6(85.7)	1(14.3)	1.00		1.0	
Primary	25(92.6)	2(7.4)	0.48(0.05, 4.11)	0.57	0.13(0.00, 3.94)	0.24
Secondary	39(95.1)	2(4.9)	0.31(0.04, 2.61)	0.37	0.03(0.00, 1.92)	0.10
Tertiary	4(50.0)	4(50.0)	6.00(0.72, 50.2)	0.17	2.00(0.07, 56.4)	0.68
Leprosy classification						
Paucibacillary	32(88.9)	4(11.1)	1.00		1.00	
Multibacillary	42(89.4)	5(10.6)	0.95(0.24, 3.84)	0.95	3.06(0.39, 23.78)	0.28
Waiting time at facility						
30 mins-1 hour	11(84.6)	5(20.8)	0.69(0.15, 3.12)	0.69	0.04 (0.00, 2.18)	0.12
1-3 hours	19(79.2)	2(4.3)	1.00		1.00	
>3 hours	44(95.7)	2(4.3)	0.17(0.04, 0.74)	0.04	0.03(0.00, 0.62)	0.02
Location of facility far						
Location of facility far	22(81.5)	5(18.5)	0.34(0.10, 1.10)	0.13	0.28(0.03, 2.45)	0.25
Location of facility close	52(92.9)	4(7.1)	1.00		1.00	
Pill burden						
Pill burden	18(78.3)	5(21.7)	0.26(0.07, 0.85)	0.06	0.09(0.01, 1.32)	0.08
No pill burden	56(93.3)	4(0.7)	1.00		1.00	

CHAPTER FIVE

DISCUSSION

5.1 Key findings of study

The study showed good MDT adherence rate of 10.8 per cent. Waiting time greater than 3 hours was positively correlated with good MDT adherence and this was statistically significant.

5.2 Comparison of key findings with literature

Majority of patients (89.2%) were found to have poor MDT adherence, while only 10.8% had good adherence. Information on MDT adherence in leprosy patients isn't altogether vigorous in international literature. Be that as it may, in studies done and revealed up until now, the of adherent patients to MDT is comparable to a certain degree - 70% in an study in Cebu, Philippines [Honrado et al, 2008]; 48% in Hyderabad, India [Weiland et al, 2011]; and 57.1% in Brazil [Lira et al, 2012].

This study attempted to investigate the relationship between personal factors and MDT adherence. In this study, however, on multivariate affiliation, personal factors explored were not significantly associated with improved MDT adherence. Accessible information from research published on international literature on the relationship between the demographic variables and adherence to MDT are opposing. In a study done in Dhanusha, a district of Nepal, it was reported that 79.2 per cent of male patients completed treatment, while 34.4 per cent of females did not complete treatment within the predetermined period. The study demonstrated significant associations between MDT adherence and sex (Kar et al, 2010; Silva et al, 2010).

Notwithstanding, another study by Heukelbach and colleagues, demonstrated that demographic information, for example, sex, age and marital status were not related with poor MDT adherence. This study indicated higher rates of non-adherence to MDT treatment in young males (34.4%), when the information was classified by sex. Men demonstrated a difference of around two times (17.6%) contrasted with females of a similar age (Heukelbach J. et al, 2011).

The research by Araujo et al showed that majority of the male patients with incomplete and irregular treatment (48.8%) was dispersed in the age group somewhere in the range of 20 and 39 years (De Araújo RRD et al, 2005). The investigation by Trindade and associates revealed a male predominance in non-compliance to leprosy treatment. Be that as it may, because of the modest number of cases, the difference was not statistically significant (Trindade LC, 2009). A similar report by Trinade and colleagues demonstrated that those with noncompliance to the MDT treatment were prevalently unmarried, unlike what was found by Honrado (2008) in which there was a predominance of married individuals with high dropout rates (Honrado ER et al, 2008).

Certain studies have reported that patient behaviors in relation to drug treatment are largely determined by their socio-economic status and knowledge level (Miranzi et al, 2010; Silva AR et al, 2012). In a study by Kar and colleagues, a greater share of the MDT treatment defaulters had completed primary education (32.28%), had per capita income between \$7 – 10 (30.71%), and belonged to social class IV (33.86%) and class V (30.71%). This study likewise demonstrated a statistically significant association between state of literacy, per capita income per month and socioeconomic status, with treatment outcome (Kar et al, 2010).

In the Philippines, there was no reported association between socio-demographic factors and non-adherence to MDT treatment. Patients who absconded from treatment and those who finished treatment belonged to the same income group (Honrado ER, 2008). In another study performed in Paraíba, a Brazilian state, low salary was not significantly associated with non-adherence to MDT (Trindade LC, 2009). This distinction might be due to the different social contexts in the Philippines, Brazil, and India.

This present study looked to examine the relationship between condition-related variables and MDT adherence. In contrast to other studies, this examination attempted to determine the relationship between leprosy classification, leprosy reactions and MDT adherence. Notwithstanding, there were no significant associations on bivariate and multivariate associations.

A previous study by Honrado and associates revealed that MDT non-adherence rate among those patients who didn't know about leprosy was fundamentally higher than the individuals who were educated (44.4% versus 23.6%, separately). Furthermore, the probability of treatment abandonment among those who were not informed was 2.6 times higher than those who were told the name of his condition (Honrado ER, 2008). Another investigation by Trindade and associates discovered that number of patients who said they had received enough information about the disease during treatment was somewhat higher in the group that completed treatment than the group that did not (Trindade LC, 2009).

A study by Chalise revealed that about 86% of instances of non-adherence have no information about the infection; roughly 39% don't know what caused the sickness; and just about 14% realized that the ailment is brought about by a bacterium or

"microorganism". It was also reported that 33.3 percent of dropout patients accepted that leprosy was brought about by spiritual events or from wrongdoing in previous existences (Chalise S, 2005). Additionally, a larger part (94.7%) of non-adherent cases had a firm conviction that the disappearance of the signs/side effects is the main meaning of disease cure. This mirrors a low degree of comprehension of the treatment (Chalise S, 2005).

This study additionally tried to decide the relationship between health system factors and MDT adherence. On multivariate association, waiting time more than 3 hours was negatively correlated with MDT adherence and this was statistically significant.

According to researchers from Nova Deli, almost half of the patients who lived closest to the hospitals dropped out of MDT, compared with patients who were beyond the hospitals, where about 60% were delinquent. Patients from outside the region had essentially higher default rate in a wide range of leprosy cases, contrasted with patients who live close to the centres (Rao PSS, 2008). Another investigation in Duque de Caxias, and the city of Rio de Janeiro in the period from 1986 to 2008 did not recognize the distance from the patient's residence to the clinic as a factor impairing adherence to treatment. The study suggests that if treatment is properly done, contextual factors can be minimized (Hacker MAVB et al, 2012).

This study sought to determine the relationship between drug-related factors and MDT adherence. On multivariate association, neither adverse drug reactions nor pill burden were significantly associated with MDT adherence but they were negatively correlated with MDT adherence.

In a related study in the Philippines, 40 percent of patient's reported adverse effects as the main reason for not finishing the treatment. These unfavorable side effects were dizziness, migraine, nausea, gastrointestinal distress, and others (Honrado ER, 2008). An investigation led by Souza et al. reported the important side effects that disturb the patient and lead to treatment dropout as iron deficiency, agranulocytosis, neuropathy (related with dapson), hepatotoxicity (due to rifampicin and dapson), hyperpigmentation (due to clofazimine). The reactions may begin acutely and cause a wide scope of serious side effects, for example, joint pain, erythema nodosum, fever, neuritis, and paralysis. The health professional must be ready to promptly recognize and treat such complications, utilizing tertiary services, if necessary (Souza et al, 2009).

5.4 Limitations of the study

This study used a cross sectional design. One important limitation of the cross-sectional nature of the data is that we can neither determine the direction of association between influencing factors and MDT adherence nor can we attribute causality to any effect. There is also possibility of recall bias among the respondents while trying to remember the precise details of their adherence pattern. The present study used a quantitative design. The contexts of MDT adherence cannot be completely explored with this design. A mixed design would be better to help identify and understand these contexts. The study did not explore specific knowledge variables of leprosy or MDT and hence, the extent of knowledge assessment is limited in this study. The sample size for this study was small. This led to wide confidence intervals in certain variables while performing the multiple logistic regression.

CHAPTER SIX

CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

The present study found a MDT adherence rate of 10.8% in QIC Leprosy Hospital Ekpene Obom, Southern Nigeria. Waiting time >3 hours was found to be negatively correlated with MDT adherence. Reducing waiting time and having an improved relationship with service providers are ways of improving MDT adherence.

6.2 Recommendations

Based on the results of the present study, the following recommendations are given:

Patients diagnosed with leprosy: To evolve ways to organize daily dosing of MDT to avoid forgetfulness; to be prompt with clinic visits for MDT re-fills.

Service Providers: To incorporate pre-treatment counselling into their care plan; to improve their communication and relationship with patients diagnosed with leprosy; to evolve health education interventions involving patients' families

Health Facility Managers: To increase the hours when the clinic is open, including evening hours to achieve shorter waiting times; to have clinic scheduling strategies that are convenient for the patient

Researchers: To undertake further research aimed at exploring the contexts of MDT adherence in QIC Leprosy Hospital so as to evolve strategies to improve the gap.

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APPENDICES

APPENDIX A: RESPONDENTS' INFORMATION SHEET

General information

Project Title: Adherence of Multidrug Therapy (Mdt) among Patients Diagnosed with Leprosy in Qua Iboe Church Leprosy Hospital, EkpeneObom, Southern Nigeria

Introduction: I am **EmaediongAkpanekpo**(interviewer), a student of the Department of Epidemiology and Disease Control, University of Ghana pursuing a Master of Public Health Degree Programme. I reside at #73b Aka Etinan Road, Uyo, Akwa Ibom State. My telephone number is +2347039341568 and I study at the School of Public Health, University of Ghana, Legon.

Background/Purpose of Research: Leprosy is a special public health problem because of its capacity to cause permanent disabilities with their social consequences of discrimination and stigma. The three main objectives in controlling leprosy are to interrupt transmission, cure patients, and prevent development of deformities. The treatment of the disease is by a multidrug therapy. Despite treatment, the disease is still being actively transmitted. Many factors can be involved in the persistence of the infection. One of the most important among them is the non-compliance to the treatment.

Nature of Research: This is a cross sectional survey to find out the adherence of the multidrug therapy among patients diagnosed with leprosy in Qua Iboe Church Leprosy Hospital, EkpeneObom.

Participants involvement

Duration/What is Involved: The study will involve answering questions from a questionnaire about adherence of the multidrug therapy. The information you provide will add to knowledge and inform policy about the multidrug therapy and propose some interventions if need be. It would last for two months.

Benefits: Participating in this research would offer the opportunity to assess the adherence of patients diagnosed with leprosy and map out strategies for improvement. The questions on the tool are not compulsory.

Potential Risks: There is a probability that you may feel uncomfortable to answer some questions. In this instance, answers are neither compulsory or mandatory.

Costs: Participating in this study would come at no cost to you.

Confidentiality: No name will be recorded. Your name and identity are not needed in the study. However, the information you are going to provide will be coded and will be treated strictly confidential. You are assured of total confidentiality to the information you will give. Apart from the researcher and supervisor of this research, no one else will have access to information provided whether in part or whole. Data collected will be stored under lock and key then destroyed after a minimum of three years as per research protocol.

Voluntary participation: Participation in this study is voluntary. You are free to answer part or the entire questionnaire. You can choose to withdraw from the study or stop the interview at any time you want. You can also choose not to answer any question(s) you find uncomfortable about. Should you choose not to participate, it will not affect you in any way.

Outcome/feedback: Findings and recommendations would be available at the School of Public Health and it will also be disseminated through a meeting with different stakeholders at the end of the study.

Appropriate alternative Procedures and Treatment: No procedures or treatment would be required in this study

Funding information: This study is sponsored by the WHO/TDR Programme at the School of Public Health, University of Ghana.

Sharing of participants Information/Data: Besides the principal investigator (PI) and supervisor of this research, no one else will have access to information provided whether in part or whole.

Provision of Information and Consent for participants: You would be provided with forms for consent to participate in the study.

Who to Contact for Further Clarification/Questions

If you have any question(s) or further clarification concerning this study and/or the conduct of the researcher and research assistants, please do not hesitate to contact the following;

EmaediongAkpanekpo, School of Public Health, University of Ghana, Legon
emaed.ekpo@gmail.com Tel: +233570318073;

Dr. Ernest Kenu, School of Public Health, University of Ghana. ernestkenu@yahoo.com ;
For further clarification on ethical issues and rights as participants if need be, contact

DR Hannah Frimpong, The ERC Administrator, Research and Development Division,
Ghana Health Service, P.O. Box MB 190, Accra. Email: ghserc@gmail.com
+233302681109

APPENDIX B: CONSENT FORM

STUDY TITLE: Adherence of Multidrug Therapy (MDT) among Patients Diagnosed with Leprosy in Qua Iboe Church Leprosy Hospital, EkpeneObom, Southern Nigeria

PARTICIPANTS' STATEMENT :I acknowledge that I have read or have had the purpose and contents of the Participants' Information Sheet read and satisfactorily explained to me in a language I understand (English/Ibibio/Pidgin). I fully understand the contents and any potential implications as well as my right to change my mind (that is, withdraw from the research) even after I have signed this form.

I voluntarily agree to be part of this research.

Name or Initials of Participant..... ID Code

Participants' SignatureOR Thumb Print.....

Date:.....

INTERPRETERS' STATEMENT :I interpreted the purpose and contents of the Participants' Information Sheet to the afore named participant to the best of my ability in the (English/Ibibio/Pidgin) language to his proper understanding. All questions, appropriate clarifications sort by the participant and answers were also duly interpreted to his/her satisfaction.

Name of Interpreter..... Signature of Interpreter..... Contact Details

Date:.....

STATEMENT OF WITNESS :I was present when the purpose and contents of the Participant Information Sheet was read and explained satisfactorily to the participant in the language he/she understood (English/Ibibio/Pidgin) . I confirm that he/she was given the opportunity to ask questions/seek clarifications and same were duly answered to his/her satisfaction before voluntarily agreeing to be part of the research.

Name:.....

Signature..... OR Thumb Print

Date:.....

INVESTIGATOR STATEMENT: I certify that the participant has been given ample time to read and learn about the study. All questions and clarifications raised by the participant have been addressed.

Researcher's name..... Signature

..... Date.....

APPENDIX C: DATA COLLECTION QUESTIONNAIRE

Question Number	Questions	Var Nat
SECTION A: SOCIO-DEMOGRAPHIC AND CLINICAL INFORMATION		
Q1	Interviewer ID <input type="text"/> <input type="text"/> <input type="text"/>	
Q2	Date <input type="text"/>	
Q3	Name of Respondent	
Q4	Hospital name	
Q5	Sex of Respondent [M] Male <input type="checkbox"/> [F] Female <input type="checkbox"/>	
Q6	Age of Respondent (in completed years) <input type="text"/>	
Q7	Marital Status of Respondent [1] Single <input type="checkbox"/> [2] Married <input type="checkbox"/> [3] Divorced <input type="checkbox"/> [4] Widowed <input type="checkbox"/>	
Q8	Educational level of respondent [1] No formal education <input type="checkbox"/> [2] Primary education <input type="checkbox"/> [3] Secondary education <input type="checkbox"/> [4] Higher education <input type="checkbox"/>	

Q9	<p>Occupation</p> <p>[1] Unemployed</p> <p>[2] Artisan</p> <p>[3] Trader</p> <p>[4] Civil servant</p>	<input type="checkbox"/>
Q10	<p>Have you been diagnosed for leprosy within the past year?</p> <p>[1] Yes</p> <p>[0] No</p>	<input type="checkbox"/>
Q11	<p>Were you prescribed MDT Medication at the health facility?</p> <p>[1] Yes</p> <p>[0] No</p>	<input type="checkbox"/>
Q12	<p>Leprosy Classification</p> <p>[1] Multibacillary</p> <p>[0] Paucibacillary</p>	<input type="checkbox"/>
Q13	<p>History of Leprosy Reactions</p> <p>[2] Type 2</p> <p>[1] Type 1</p> <p>[0] None</p>	<input type="checkbox"/>
Q14	<p>Disability Grade</p> <p>[2] 2</p> <p>[1] 1</p> <p>[0] 0</p>	<input type="checkbox"/>
Q15	SECTION B: MODIFIED MORISKY MEDICATION ADHERENCE SCALE (MMAS-8)	

	<p>Do you sometimes forget to take your medicine?</p> <p>[1] Yes <input type="checkbox"/></p> <p>[0] No</p>	
Q16	<p>People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your medication?</p> <p>[1] Yes <input type="checkbox"/></p> <p>[0] No</p>	
Q17	<p>Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it?</p> <p>[1] Yes <input type="checkbox"/></p> <p>[0] No</p>	
Q18	<p>When you travel or leave home, do you sometimes forget to carry along your medication?</p> <p>[1] Yes <input type="checkbox"/></p> <p>[0] No</p>	
Q19	<p>Did you take your medications yesterday?</p> <p>[1] Yes <input type="checkbox"/></p> <p>[0] No</p>	
Q20	<p>When you feel like your symptoms are under control, do you sometimes stop taking your medications?</p> <p>[1] Yes <input type="checkbox"/></p> <p>[0] No</p>	
Q21	<p>Taking medications every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?</p> <p>[1] Yes <input type="checkbox"/></p> <p>[0] No</p>	
Q22	<p>How often do you have difficulty remembering to take all your medications?</p> <p>Never/rarely ----- 4</p> <p>Once in a while -----3</p> <p>Sometimes-----2</p>	<input type="checkbox"/>

	Usually-----1 All the time-----0	
	SECTION C: CONDITION-RELATED FACTORS	
Q23	Have you ever heard of Leprosy? [1] Yes [0] No	<input type="checkbox"/>
Q24	Have you ever heard of MDT? [1] Yes [0] No	<input type="checkbox"/>
Q25	Do you think leprosy is curable? [1] Yes [0] No	<input type="checkbox"/>
	SECTION D: HEALTH SYSTEM FACTORS	
Q26	Are service providers readily available at the health facility to attend to you? [1] Yes [0] No	<input type="checkbox"/>
Q27	Is the health faciity where you get MDT treatment located far from your residence ? [1] Yes [0] No	<input type="checkbox"/>
Q28	Do you pay a registration fee at the health facility where you receive MDT treatment? [1] Yes [0] No	<input type="checkbox"/>
Q29	How long would you have to wait before being attended to at the facility where you get MDT treatment [3] More than 3 hours [2] 1-3 hours [1] 30 minutes – 1 hour [0] Less than 30 minutes	<input type="checkbox"/>

Q30	<p>How would you describe the nature of the relationship between you and the service providers?</p> <p>[3] Excellent</p> <p>[2] Good</p> <p>[1] Fair</p> <p>[0] Poor</p>	<input data-bbox="1219 293 1337 544" type="checkbox"/>
Q31	<p>Are you adequately counselled about the MDT drugs before/after they are prescribed?</p> <p>[1] Yes</p> <p>[0] No</p>	<input data-bbox="1241 667 1318 775" type="checkbox"/>
SECTION E: DRUG-RELATED FACTORS		
Q32	<p>Are the prescribed MDT drugs available free of charge?</p> <p>[1] Yes</p> <p>[0] No</p>	<input data-bbox="1248 891 1343 1008" type="checkbox"/>
Q33	<p>Do you have adverse reactions when you take the MDT drugs?</p> <p>[1] Yes</p> <p>[0] No</p>	<input data-bbox="1254 1039 1337 1137" type="checkbox"/>
Q34	<p>Do you think the MDT drugs are too much to take at a time?</p> <p>[1] Yes [0] No</p>	<input data-bbox="1267 1227 1356 1308" type="checkbox"/>

GOVERNMENT OF AKWA IBOM STATE OF NIGERIA

Telephone: 085-204091
Telegram: HEALTH

Our Ref:MH/PRS/99/Vol.V/555

Your Ref:



MINISTRY OF HEALTH
IDONGESIT NKANGA SECRETARIAT
BLOCK 8, P.M.B. 1030
UYO

15th January, 2019

Dr. Emaediong Ibong Akpanekpo
School of Public Health,
University of Ghana,
Legon, Ghana.

RE: REQUEST FOR ETHICAL CLEARANCE FOR A RESEARCH

I am directed to convey the approval of the Honourable Commissioner for Health, based on the recommendation of the State Health Research Ethics Committee, to you to carry out a research Project entitled:

"ADHERENCE OF MULTIDRUG THERAPY (MDT) AMONG PATIENTS DIAGNOSED WITH LEPROSY IN QUA IBOE CHURCH LEPROSY HOSPITAL, EKPENE OBOM, SOUTHERN NIGERIA"

This approval is conditional on you seeking and obtaining informed consent of your participants and ensuring their strict confidentiality. While conducting your research, you are not allowed to carry out any invasive procedure on your participants.

Furthermore, you are expected to adhere strictly to the approved research protocol at all times. To this end, you are not allowed to change your approved research protocol without recourse to further consideration and approval of the Honourable Commissioner for Health.

It is important to note that you are also expected to send a copy of the outcome of your research project to the Office of the Honourable Commissioner for Health on completion.

Best wishes.

Yours sincerely,


DR. IBORO E. UDOH
For: Honourable Commissioner

GHANA HEALTH SERVICE ETHICS REVIEW COMMITTEE

*In case of reply the
number and date of this
Letter should be quoted.*



MyRef. GHS/RDD/ERC/Admin/App/19/301
Your Ref. No.

Research & Development Division
Ghana Health Service
P. O. Box MB 190
Accra
GPS Address: GA-050-3303
Tel: +233-302-681109
Fax + 233-302-685424
Email: ghserc@gmail.com
11th July, 2019

Emaediong Ibong Akpanekpo
University of Ghana
School of Public Health
Legon

The Ghana Health Service Ethics Review Committee has reviewed and given approval for the implementation of your Study Protocol.

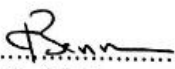
GHS-ERC Number	GHS-ERC 043/04/19
Project Title	Adherence to Multidrug Therapy (MDT) among Patients Diagnosed with Leprosy in Qua Iboe Church Leprosy Hospital, Ekpene Obom, Southern Nigerian
Approval Date	11 th July, 2019
Expiry Date	10 th July, 2020
GHS-ERC Decision	Approved

This approval requires the following from the Principal Investigator

- Submission of yearly progress report of the study to the Ethics Review Committee (ERC)
- Renewal of ethical approval if the study lasts for more than 12 months,
- Reporting of all serious adverse events related to this study to the ERC within three days verbally and seven days in writing.
- Submission of a final report after completion of the study
- Informing ERC if study cannot be implemented or is discontinued and reasons why
- Informing the ERC and your sponsor (where applicable) before any publication of the research findings.
- Please note that any modification of the study without ERC approval of the amendment is invalid.

The ERC may observe or cause to be observed procedures and records of the study during and after implementation.

Kindly quote the protocol identification number in all future correspondence in relation to this approved protocol

SIGNED.....
Dr. Cynthia Bannerman
(GHS-ERC CHAIRPERSON)

Cc: The Director, Research & Development Division, Ghana Health Service, Accra