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# Effect of Model of Care and Comorbidities on Multiple-Drug-Resistant Tuberculosis Treatment in Nigeria

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Abstract

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MPH, University of Sheffield, 2009

B. Pharm, University of Lagos, 2005

Doctoral Study Submitted in Partial Fulfillment

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Abstract

Multidrug-resistant tuberculosis (MDR-TB) is a public health problem in several countries such as Angola, India, China, Kenya, and Nigeria. Due to the increasing high burden of MDR-TB, most of these countries do not have adequate capacities to manage MDR-TB patients effectively. This study investigated the effect of model of care; human immunodeficiency virus comorbidity; and demographic factors such as age, gender, and marital status on the treatment outcomes of MDR-TB patients in Nigeria. The study was based on the analysis of secondary data of 402 MDR-TB patients accessed from the data systems of the National Tuberculosis, Buruli Ulcer, and Leprosy Control Program. The theoretical framework for this study was the health belief model. The results of the study showed that treatment outcomes were similar for hospital and community-based models of care. Age was the only factor found to be significantly associated with treatment outcomes; age > than 40 years was a predictor of unsuccessful treatment outcomes among MDR-TB patients at a *p*-value of 0.026. In the multivariate logistics regression analysis, age and model of care were found to be significantly associated with treatment outcomes at *p*-values of 0.043 and 0.048, respectively. Marital status, gender, and HIV comorbidity were not significantly associated with treatment outcomes. Implications of the findings of this study for social change in a health care program include opportunities to help reduce the number of patients on waiting lists for MDR-TB treatment. These strategies may ultimately help to reduce the spread of MDR-TB infection as well as the mortality associated with late treatment.

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# Dedication

This work is dedicated to almighty God who has given me the opportunity to advance in both my study and career. This work is also dedicated to all my public health colleagues both in Nigeria and overseas who work tirelessly to improve the health and quality of life of people globally. I also dedicate this work to my colleagues at the World Health Organization who consistently inspired me to reach out for excellence in all that I do. Your efforts have contributed tremendously to the health of Nigerians.

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Section 1: Foundation of the Study and Literature Review

## Introduction

In this study, I investigated the effect of the model of care and existence of co-morbidities on the treatment outcomes among multidrug-resistant tuberculosis (MDR-TB) patients. MDR-TB has become increasingly prevalent in countries such as China, India, and Nigeria among others (World Health Organization [WHO], 2016). In 2013, 136,000 multidrug/rifampicin resistant tuberculosis (MDR/RR-TB) cases were reported globally; this increased to 153,119 in 2016 and 160,684 cases in 2017 (WHO, 2014, 2018b). In 2016, an additional 110,000 cases rifampicin resistant tuberculosis (RR-TB) cases that were also susceptible to isoniazid were notified globally (WHO, 2017).

The burden of tuberculosis (TB) globally is currently estimated to be 558,000 (WHO, 2018b). Similarly, an estimated 230,000 deaths from MDR/RR-TB were reported in 2017 (WHO, 2018b). Nigeria has remained one of the high burden countries for MDR-TB with an ever increasing trend of the disease from 550 cases detected in 2013 to 798 in 2014; 1,242 in 2015 and 2,286 in 2017 (USAID, 2016; WHO, 2016, 2018a). MDR-TB is defined as *Mycobacterium tuberculosis* strains that are resistant to both isoniazid and rifampicin (Falzon et al., 2011). The increasing trend in the burden of MDR-TB has made it pertinent to increase the capacities of individual high burden countries to manage patients affected by the disease. Against this backdrop, efforts to rapidly scale up the capacities of MDR-TB treatment services are underway in high burden countries such as Nigeria.

In Nigeria, the national guidelines for the management of MDR-TB are in line with WHO guidelines, which recommend ambulatory care to include 8 months of intensive phase in specialized treatment centers and 12 months of continuation in the community (Falzon et al., 2011). The intensive phase comprises daily injections of aminoglycosides as well as oral medications that are toxic and less effective than the medications used to manage drug susceptible TB ( Tanzania Ministry of Health and Social Welfare National Tuberculosis and Leprosy Programme [NTLP], 2013). The continuation phase includes the use of mainly oral medications for 12 months.

Based on review of programmatic reports, Nigeria adopted the complete community care model in 2013; this model of care comprises community or home-based management of MDR-TB from enrollment to end of treatment regimen. More recently, the shorter regimen as stipulated by the latest WHO guidelines were piloted in the country and became a mandatory component of the treatment guidelines in 2018. The shorter regimen includes a 4–6 months intensive phase with a combination of kanamycin, moxifloxacin, prothionamide, clofazimine, pyrazinamide, high-dose isoniazid, and ethambutol, followed by a 5-month continuation phase containing moxifloxacin, clofazimine, ethambutol, and pyrazinamide (Chee et al., 2017).

Currently, countries employ varied models of care, which include hospital-based, ambulatory and complete community-based models of care. The need for scale-up of MDR-TB services raises questions as to the sustainability of the hospital-based model of care which is often inadequate, in resource-limited settings, to meet the demand for treatment services (Salje et al., 2014). The number of bed spaces and staffing required to

enroll and manage MDR-TB patients in such settings often exceed the available resources (Taneja, 2017). In question is also the cost effectiveness of the hospital-based model of care relative to ambulatory and community-based treatment models. These issues are currently relevant to the Nigerian MDR-TB program because of the increasing burden of the disease in the country and the need to ensure a patient-centered approach to the management of MDR-TB patients. Additionally, the ultimate goal of the National TB program is to provide the best quality of TB care in the most effective and efficient manner. Against this background, it is essential that the effect of model of care and other relevant factors such as the existence of co-morbidities, among others, on the treatment outcomes of MDR-TB patients is investigated.

**Potential Positive Social Change Implications**

A major pillar in the international standard for TB care is the emphasis on a patient-centered approach in the management of TB (Mohan, 2007). In line with this, it is critical that policies that impact treatment conditions, quality of care, and outcomes of MDR-TB patients are implemented and evaluated with the aim of ensuring an optimal quality of care that will result in the best outcomes possible for the patients that are being managed. The implications for social change for this study therefore include the possibility of improving the quality of treatment provided to MDR-TB patients by ensuring the scale-up of the optimal and most effective model of care based on empirical evidence. This study includes information about the effect of co-morbidities such as HIV and demographic factors such as age, gender and marital status on treatment outcomes among MDR-TB patients. A deeper understanding of the relationship between these

factors may inform the development of policies and guidelines that can address existing gaps in the quality of care provided to MDR-TB patients. Other implications for social change include more gender-sensitive treatment guidelines, adaptation of specific treatment model for different age categories and special provisions for the management of co-morbidities in MDR-TB control programs.

## Problem Statement

The burden of TB continues to be a public health issue in several countries including Nigeria (WHO, 2017). According to the 2017 Global TB Report, about 10.4 million people were diagnosed of TB out of which 1.7 million people died of the disease (WHO, 2017). The situation is further worsened in countries such as Angola, India, China, Kenya, and Nigeria, among others, where there has been a rise in the incidence of drug resistant strain of the disease (WHO, 2017). MDR-TB remains a major threat to the progress made in the control of the global TB epidemics. The treatment for MDR-TB is expensive, less effective, and more toxic than that of drug susceptible TB (Patel et al., 2016). Hence, there is need for specific actions toward addressing the risk factors associated with the disease while ensuring adequate treatment capacities and quality of care are made available.

In most settings, the treatment of MDR-TB has been provided through centralized and prolonged in-patient care. Several limitations have been associated with this model of care, among which are low retention, high risk of nosocomial infections, high cost of treatment, and high risk of transmission of MDR-TB (Ho, Byrne, Linh, Jaramillo, & Fox, 2017). This gave rise to the ambulatory care model which includes a short stay in the

hospital for about 6–8 months followed by community-based management of the disease (Falzon et al., 2011). WHO recommended the ambulatory care model as the mainstay for MDR-TB treatment (Bassili et al., 2013). This recommendation however requires empirical evidence to support the rapid scale-up of the community-based model of MDR-TB care in settings with huge gaps in MDR-TB case detection and enrollment due to inadequate bed spaces such as Nigeria (Molla et al., 2017; USAID, 2016). Beyond that, it is critical that patients are offered the most effective model of care in terms of patients' treatment and survival outcomes. Similarly, post-implementation evidence is needed in resource-limited settings with regards to the effectiveness of community-based MDR-TB care model.

Since the introduction of the Xpert machine in Nigeria in 2010, there has been a steady rise in the detection of MDR-TB due to the sensitivity of the diagnostic technology (Abdurrahman et al., 2014). Notification of MDR-TB increased from 21 in 2010 to 550 in 2013 and 798 in 2014 (WHO, 2011, 2014, 2015a). The Xpert MTB/RIF is a rapid diagnostic test which detects presence of TB bacilli as well as rifampicin resistance (Kuyinu, Odugbemi, Salisu-Olatunji, & Adepoju, 2018; Mustapha et al., 2015). The detection of rifampicin resistance is usually an indication of MDR-TB because patients that are resistant to Rifampicin are often also resistant to Isoniazid (Kumar, Datta, & Kumar, 2016). Although, there is limited access to the machine due to weak infrastructure at the primary health care facilities, MDR-TB case detection has increased in areas where the machines are situated (Mustapha et al., 2015). This rapid increase in case detection has called for a scale up of the treatment facilities for MDR-TB

cases detected to enable adequate enrollment of patients for treatment. However, a gap in case detection and those that are subsequently enrolled for treatment has remained an issue in the country (USAID, 2016). In response to this gap, the ambulatory care model has been adopted in Nigeria, along with a complete community-based *or out-patient* care model, which means that patients are started and completed on treatment in their local community for a duration of 20 months. The treatment of MDR-TB is complex and costly to both the healthcare system and the affected individuals, hence it is important that effective and cost-efficient models of care are adopted, particularly in resource-constrained settings (Fitzpatrick, & Floyd, 2012; Mitnick et al., 2003). Aside from model of care, other factors such as the existence of comorbidities such as HIV and diabetes have been associated with poor treatment outcomes among MDR-TB patients (Burgos et al., 2018; Wells et al., 2007).

There is evidence to support the effectiveness of the complete community-based model of care (Bassili et al., 2013; Ho et al., 2017; Weiss, Chen, Cook, & Johnston, 2014) in settings other than Nigeria. There are however contextual factors in Nigeria that may affect the delivery of the different models of MDR-TB care. These factors include a generally weak health system and poor government funding of National Tuberculosis Program among others (WHO, 2017). There is limited evidence to establish the relative advantage of community-based model over the hospital-based model. A systematic review that compared the community-based to hospital model of care in Bangladesh, China, Ethiopia, Kenya, India, South Africa, Philippines, Russia, and Uzbekistan showed that community-based model is associated with better treatment outcomes than the

traditional hospital model of care (Williams et al., 2016). However, the quality of the studies included in the systematic review was not robust enough to establish the effectiveness of the community-based model of care in settings other than those investigated (Williams et al., 2016). Considering this, the result may not be generalizable to other high burden countries such as Nigeria. Different variants of community and hospital-based model of care are adopted in different settings, hence results obtained in other countries may not be applicable in all settings (Molla et al., 2017). Additionally, Nigeria's community-based model of care is relatively recent and builds on global rather than local experience. These global settings may not be similar to the Nigerian context.

In a study conducted in Nigeria, in which researchers reviewed treatment outcomes of a cohort of MDR-TB patients managed in treatment centers, researchers recommended the hospital-based model of care as an effective method because it improved treatment adherence (Oladimeji et al., 2014). However, the result of this study is contrary to the findings of similar studies conducted in other MDR-TB high burden countries (Loveday et al., 2015; Williams et al., 2016). In the same study, the association between HIV and treatment outcomes among MDR-TB patients was investigated; however, the results were inconclusive due to inadequate sample size. A similar study conducted in Nigeria, researchers reviewed the treatment outcome of patients managed in the community and reported a low rate of loss to follow up (Mbaave, Igbabul, & Achinge, 2016). This study was limited by a small sample size (40 patients) and the researchers also failed to account for outcomes at the end of the treatment period, instead only considering the outcomes after the intensive period of 8 months. Considering these

gaps in literature, there is need for further investigation to demonstrate the most effective treatment or care model for MDR-TB in resource-limited settings such as Nigeria and to determine how the existence of co-morbidities such as HIV and diabetes, among others, affect treatment outcomes among MDR-TB patients.

## Purpose of the Study

The purpose of this study was to investigate the effect of model of care whether hospital-based or complete community-based model on the treatment outcomes of MDR-TB patients. I also investigated the effect of other factors such as the existence of other diseases such as HIV and demographic factors such as gender, age and marital status on treatment outcomes of MDR-TB patients. The burden of MDR-TB in Nigeria makes it an important public health issue that heavily impacts the quality of life of those affected by the disease (Daniel & Osman, 2011). In light of this fact, the National TB program has adopted the complete community-based management of MDR-TB alongside the ambulatory model of care to increase the treatment capacity to manage MDR-TB patients.

The treatment of MDR-TB is extensive, toxic, and expensive both to the healthcare system and to the individual, hence the need for a systematic evaluation of the effectiveness of existing models of care and some other key variables, such as the presence of comorbidities that may affect the outcome of the treatment. A patient-centered approach to TB management is essential to achieving a positive outcome. Hence, it is critical that policies and treatment guidelines adopted by the National TB programs are tested empirically to establish their effectiveness and appropriateness in the

country's context. A robust understanding of the factors that influence treatment outcomes among MDR-TB patients may be key in reducing the burden and impact of the disease.

The result of this study may provide insights on how treatment outcomes among MDR-TB patients can be improved by addressing some of the identified risk factors that are associated with poor treatment outcomes (see Drobniewski et al., 2002). Most importantly, the result of this study may provide the evidence needed to inform policy changes in the management of MDR-TB patients in Nigeria particularly with regards to the model of care that is adopted and how care is delivered in general. Additionally, the findings of the study may address the existing gap in literature as it relates to the demonstration of the effective model of care that is feasible for managing MDR-TB patients in resource-limited settings like Nigeria.

## Research Questions and Hypotheses

Research Question 1 (RQ1): Is there an association between type of treatment model; hospital or complete community-based, and treatment outcome among MDR-TB patients in Nigeria?

Null Hypothesis ($H_0$1): There is no association between type of treatment model and treatment outcomes among MDR-TB patients in Nigeria.

Alternate Hypothesis ($H_a$1): There is an association between type of treatment model and treatment outcomes among MDR-TB patients in Nigeria.

Research Question 2 (RQ2): Are co-morbidities such as HIV associated with poor treatment outcomes among MDR-TB patients in Nigeria?

Null Hypothesis ($H_0$2): There is no difference in treatment outcomes between patients with co-morbidities and those without in Nigeria.

Alternate Hypothesis ($H_a$2): There is a difference in treatment outcomes between patients with co-morbidities and those without in Nigeria.

Research Question 3 (RQ3): Is type of treatment model associated with survival outcomes among MDR-TB patients in Nigeria?

Null Hypothesis ($H_0$3): There is no difference in survival outcomes between patients enrolled on the two different models of care in Nigeria.

Alternate Hypothesis ($H_a$3): There is a difference in survival outcomes between patients enrolled on the two different models of care in Nigeria.

Research Question 4 (RQ4): Are demographic factors such as age, gender, and marital status associated with treatment outcomes among MDR-TB patients in Nigeria?

Null Hypothesis ($H_0$4): There is no association between demographic factors such as age, gender, marital status, and treatment outcomes among MDR-TB patients in Nigeria.

Alternate Hypothesis ($H_a$4): There is an association between demographic factors such as age, gender, marital status, and treatment outcomes among MDR-TB patients in Nigeria.

## Theoretical Foundation for the Study

The key theoretical framework for this study was the health belief model (HBM). The HBM was originally developed in the 1950s by social psychologists to improve the uptake of free tuberculosis screening program (Hochbaum, 1958). Researchers use the model to explain how health behaviors are shaped by individual factors. The key constructs of HBM include individual factors such as perceived susceptibility, perceived severity to a disease, perceived barriers and benefits to achieving behavior change, and the individual's self-efficacy (Glanz & Bishop, 2010). The HBM focuses on the individual's innate ability to achieve behavior change by targeting the perceptions and beliefs about the disease and emphasizing the benefits that will accrue if behavior change is achieved. Researchers have used the HBM to address public health issues that are driven by negative health behaviors (Glanz & Bishop, 2010). These include smoking, obesity, and HIV, among others. The HBM is therefore applicable to address other health challenges and issues that may be driven by human behaviors. In the case of MDR-TB management, adherence to treatment regimen is a key component of patient management and can impact heavily on the outcome of treatment (Kliiman & Altraja, 2009).

The HBM can be applied to enhance adherence to treatment and is therefore appropriate for explaining the complex pathways between MDR-TB patient enrollment and the outcomes at the end of the treatment period. The model provides a framework that can guide the development of health education programs toward improving treatment adherence (Glanz & Bishop, 2010). For the purpose of this study, I used the HBM to describe the effect of patients' adherence pattern on treatment outcomes and how self-

efficacy influenced these behavioral patterns. Similarly, I applied the model to explain individual variables that acted as modifying factors between treatment enrollment and outcomes. The modifying factors for this study included gender, age, and marital status as shown in Figure 1. Because the main constructs of the health belief model emphasize self-efficacy and self-assessment of risk as enablers of positive behavior changes, it provided a useful framework for describing the actions and policies needed to develop a patient-centered and effective model of care for the management of MDR-TB patients.

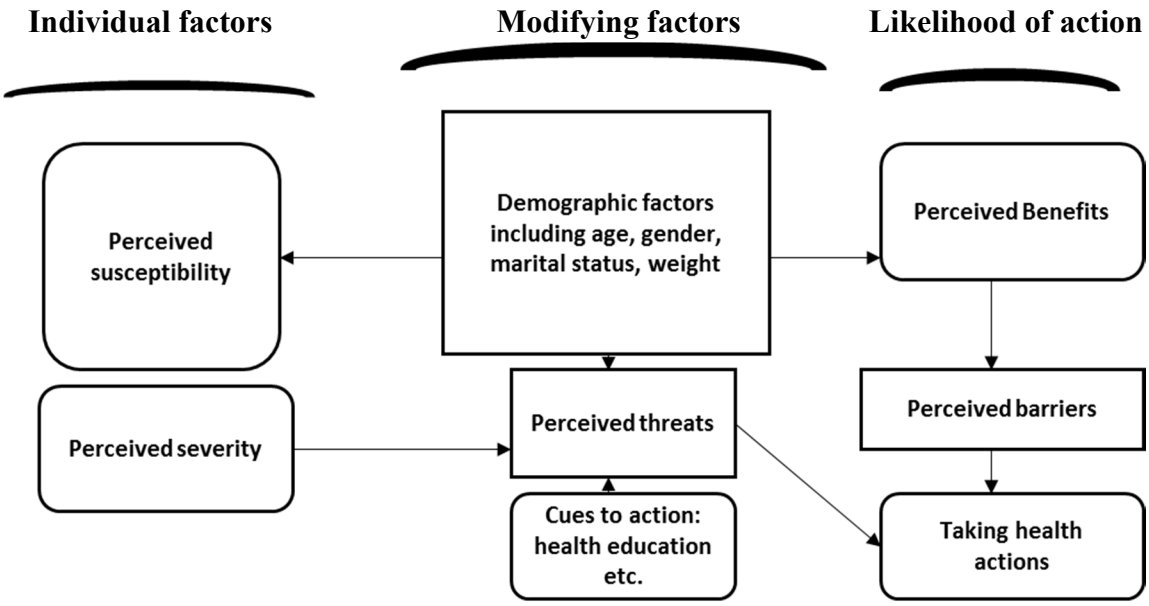


*Figure 1.* Conceptual framework of Health Belief Model. From "Effect of Health Belief Model based intervention on promoting nutritional behaviors about osteoporosis prevention among students of female middle schools in Isfahan, Iran." by M. Ghaffari, A. Esmaillzadeh, E. Tavassoli, & A. Hassanzadeh, 2012, *Journal of Education and Health Promotion*, *1*(1), p. 14.

## Nature of the Study

In this study, I used a quantitative research method. I conducted a register based cross-sectional study of routinely collected National Tuberculosis Program data for the period of January 2013 to December 2014. The dependent variable for the study was the treatment outcome for the MDR-TB patients, which I reclassified as successful or unsuccessful from the many categories of outcomes defined by the TB program (treatment completed, cured, loss to follow up, died, treatment failure). The predictor variables included the model of care, existence of co-morbidities and demographic factors specifically age, gender, and marital status.

I included all clients with complete records of the treatment outcome in the study and prepared a checklist to extract data from patient records. I selected patients' records from the two models of care adopted in Nigeria. I drew the study population from patients enrolled for treatment between 2013 and 2014 through the National Tuberculosis Program. The study included patients managed in the treatment centers using the ambulatory approach and those managed in the communities. I conducted statistical analysis to determine if type of treatment model is a predictor of treatment outcomes among MDR-TB patients in Nigeria. Other predictor variables included the existence of co-morbidities such as HIV and demographic factors such as age, gender, and marital status.

## Literature Search Strategy

The library databases and search engines I used for the literature review included EBSCO, Science Direct, PubMed, MEDLINE, AJOL and PsycARTICLES, PsycINFO,

and CINAHL databases. I also retrieved articles from Google Scholar and useful websites such as those of World Health Organization. I accessed databases through the Walden University Library. The search terms I used included *multidrug resistant, multi-drug resistant, MDR-TB, MDR-TB and treatment models, drug resistant TB, MDR-TB and treatment outcomes, MDR-TB,* and *comorbidities.*

The scope of the literature included papers published from 2010 until 2018 as well as a few papers published before 2010. I included mainly peer-reviewed studies in the literature review, but also included some non-peer-reviewed studies. There is limited current research on the subject area, hence all literature available was included as well as programmatic reports, conference reports, and non-peer-reviewed journals.

## Literature Review Related to Key Variables and Concepts

### Population and Settings

The population of Nigeria is the largest in Africa. As of 2013, it was estimated to be 173 million people across 36 states and the Federal Capital Territory (FCT; (WHO, 2015b). The Nigerian population is fairly young, with a median age of 18 years (National Population Commission & ICF International [NPC & ICF], 2014). The country has a large land mass and a diverse geography with both uplands and lowlands. Nigeria is located on the west coast of Africa between latitudes 4º16' and 13º53' north and longitudes 2º40' and 14º41' east (NPC & ICF, 2014). The country is situated on an estimated 923,768 square kilometers of land extending from the Gulf of Guinea on the Atlantic coast in the south to the borders of the Sahara Desert in the North (NPC & ICF, 2014). The geography boundaries are shared with the republics of Niger and Chad in the

north, the Republic of Cameroon on the east, and the Republic of Benin on the west. Nigeria is divided geographically into the north and the south. There is a further subdivision into six geopolitical zones, namely: the Southwest, South-south, Southeast, Northeast, Northwest, and the Northcentral. The climate of the country is mainly tropical and characterized by the wet southerly winds and the cold, dry, and dusty northeasterly winds. The country has a growing agricultural sector, but the economy is largely dependent on the exportation of crude oil. Nigeria is blessed with a diversity of ethnic groups and cultures. There are over 250 ethnic groups and more than 500 languages (National Population C & ICF, 2014). The main languages are Yoruba, Igbo, and Hausa while English is used to communicate across the different ethnic groups. The majority of the people are either Christians or Muslims.

The country has a weak health system and there is no universal health coverage (PharmAccess Foundation, 2014). Only 6% of the country's GDP is spent on health and healthcare (WHO, 2015b). There are huge disparities in the way healthcare is delivered across the country with the majority of the health workforce being in the southern part of the country (NPC & ICF, 2014).

**MDR-TB profile in Nigeria.** Nigeria is among the highest TB burden countries in the world. In 2017, Nigeria was ranked highest in Africa and fourth in the world for TB burden (WHO, 2016). The country has also been classified as a high burden MDR-TB country. In high-burden settings such as Nigeria, interpatient transmission is the main source of MDR-TB infection (Onyedum, Alobu, & Ukwaja, 2017). The HIV/AIDS epidemics in Nigeria may have also fueled the increasing trend observed in the burden of

MDR-TB in the country as indicated by the results of the 2012 National Drug Resistant Tuberculosis Prevalence survey. Based on the report of the survey, 2.9% of MDR-TB cases were from new TB patients and 14.3% were from previously managed TB patients (Nigeria Federal Ministry of Health, 2012). The growing burden of the disease calls for expansion of the treatment capacities. As at 2014, there were nine functional MDR-TB treatment centers spread across seven states (Avong et al., 2015). Based on a review of the programmatic report, there are currently 15 treatment centers in the country, with 390 Xpert MTB/RIF sites to facilitate early diagnosis of MDR-TB among patients in high risk groups across all the states in the country.

**Challenges of the MDR-TB program in Nigeria.** There are a number of challenges hampering the effective control of MDR-TB in Nigeria. These include weak political will and over-reliance on external funding support for the MDR-TB program (USAID, 2016). Other issues include a weak healthcare system and poor infrastructural capacity to support the diagnosis and management of the disease (Aliyu et al, 2010). Gidado (2018) showed that installation of Xpert MTB/RIF machine which is the first line of diagnosis for MDR-TB in the country requires adequate power supply, laboratory space, and capable staff for the machine to be optimally utilized. However, these requirements are rarely met at the primary health care facilities and most of the secondary and tertiary facilities are unable to provide uninterrupted power supply (Mustapha et al., 2015). Researchers have recommended installation of solar panels; however, this requires a lot of resources which may not be readily accessible through internal funding. Bed spaces for hospital-based management of MDR-TB patients are inadequate and the

community-based model of care is new enough that unresolved issues are hampering rapid scale-up across the states of the country. Other challenges include lack of technical expertise in-country to maintain the Xpert MTB/RIF machines, poor health workers' attitude, high rates of loss to follow up, and an ever increasing gap in cases detected and those enrolled for treatment (Abdurrahman et al., 2014; Isara & Akpodiete, 2015; Mustapha et al., 2015). The gap in case detection and enrollment for care in 2014 was over 370 MDR-TB patients (USAID, 2016). According to USAID (2016), this gap has increased steadily over the years to about 500 MDR-TB patients in 2017.

**MDR-TB treatment guidelines in Nigeria.** The National Guidelines for management of MDR-TB in Nigeria is in line with the WHO's recommended MDR-TB guidelines. The diagnosis of the disease commences with the identification of a presumptive MDR-TB case (Falzon et al., 2011). A presumptive MDR-TB patient may be anyone who has come in contact with a confirmed MDR-TB patient and who shows symptoms of TB, a patient whose AFB result is smear positive when smear is repeated at the end of month three of treatment with anti-TB medications, all previously treated drug-susceptible TB patients, relapse cases, patients receiving treatment after long periods of interruption, other previously treated patients, and persons with unknown history of TB (NTLP, 2013). Persons considered to be vulnerable to MDR-TB include all persons with smear negative AFB result who still show symptoms of TB after 1 week of administration of broad spectrum antibiotics, persons living with HIV virus who present with symptoms of TB, all health care staff who present with symptoms of TB, all children who present with symptoms of TB, and all persons with symptoms suggestive of

extra-pulmonary TB in which specimen could be collected for Xpert MTB/RIF testing such as collection of cerebrospinal fluid (CSF) for examination as in TB meningitis (NTLP, 2013).

Treatment delivery models include the ambulatory model of care as well as the complete community-based model. The ambulatory model entails the initial hospitalization for the 8-month period of the intensive phase while the ambulatory treatment is provided to patients at the nearest TB treatment clinic for the remaining duration of treatment (Falzon et al., 2011). Specialized medical services are also provided to the patient as at when required. The complete community model entails the commencement of patients on treatment in their homes with the assistance of a treatment supporter (NTLP, 2013; Williams et al., 2016). The medications used in the management of MDR-TB include kanamycin or capreomycin, pyrazinamide, cycloserine, levofloxacin, and prothionamide (NTLP, 2013). The newly adopted shorter regimen entails a 4 to 6-month intensive phase of treatment with a combination of kanamycin, moxifloxacin, prothionamide, clofazimine, pyrazinamide, high-dose isoniazid and ethambutol, followed by a 5-month continuation phase containing moxifloxacin, clofazimine, ethambutol, and pyrazinamide (NTLP, 2013). Based on the resistant profile, newer formulations and medications in the same of class of antibiotics can be used.

## National Treatment Protocol

The treatment protocol for MDR-TB in Nigeria is line with the WHO guidelines for treating MDR-TB (Falzon et al., 2011). In the years researchers reviewed for the study, the National MDR-TB treatment protocol entails 6-8 months of intensive phase

with the administration of oral medications and injectable and a 12-month continuation phase with the use of only oral medications. The standardized treatment regimen includes kanamycin or amikacin, levofloxacin, prothionamide, cycloserine, and pyrazinamide (with pyridoxine). All patients are taken through a baseline investigation that tests for kidney and liver functions, audiometry among others. During treatment, patients are monitored monthly using sputum smear microscopy and culture examinations.

**Reporting of Treatment Outcomes for Tuberculosis & Drug-Resistant TB**

Treatment outcome analysis of patients managed for TB including MDR-TB is done using a cohort approach. The cohort review describes the outcome analysis of the group of patients enrolled for treatment over a specific period of time, usually three months. These patients are reviewed at about 6-9 months after completion of treatment. This is to ensure that all patients registered within the cohort period are given the opportunity to complete their treatment and to account for any challenges for data collection and collation. Hence, outcome evaluation for the cohorts of MDR-TB patients registered in 2013 was done between 2014 and 2015 while those registered in 2014 were evaluated between 2015 and 2016. The outcome evaluation is done on a case by case basis and outcome is assigned to each of the patients to complete the patient-level data collected for the treatment period. Upon completion of the cohort review, outcomes are included as a composite of the MDR-TB patient level data.

**Description of existing models of MDR-TB management.** The models of care have different variants across countries; hence comparison of effectiveness as measured by successful treatment outcomes may not be possible. The extent of decentralization

also varies across settings; some countries employ complete community or home-based models of care while many adopt the ambulatory model of care as recommended by WHO whereby patients spend the intensive phase of treatment in the hospitals and the continuation phase is managed in the community (Molla et al., 2017). Researchers agree that there is a need for more empirical evidence from sub-Saharan African countries to support the effectiveness of decentralized model of care in resource-limited settings (e.g., Molla et al., 2017; Schnippel et al., 2015; Weiss et al., 2014). Decentralization of care as described in the literature describes the management of MDR-TB patients in their own homes by involving trained health workers or linking the patients to specific health facilities where their treatment can be monitored and adverse drug reactions managed (Molla et al., 2017). The approach also involves the application of injections by the health workers for models where complete home-based care is implemented. In this case, patients are managed completely in their community as against the ambulatory approach that involves partial hospitalization during the intensive phase of treatment (Burtscher et al., 2016; Molla et al., 2017). Evidence from Ethiopia and South Africa shows some merit in adopting the decentralized or home-based model of care for managing MDR-TB patients (Brust et al., 2012; Loveday et al., 2015; Molla et al., 2017). Favorable treatment outcomes were reported for community-based model of care from similar studies that compared community-based and hospital-based models of care in different settings (Weiss et al., 2014; Williams et al., 2016). Qualitative evidence suggests that patients prefer to be treated at home because of psychosocial support from family members and the fact that they can continue to earn a living (Bieh, Weigel, & Smith, 2017; Burtscher et

al., 2016; Horter et al., 2014) There is also evidence to suggest the association of socioeconomic barriers with hospital-based model of care but not with home-based care model (Horter et al., 2014).

Involvement of community health workers and trained volunteers in the home-based management of MDR-TB patients was recommended in Ethiopia, South Africa, Peru and Myanmar among others (Horter et al., 2014; Molla et al., 2017; Shin et al., 2004; Wai et al., 2017; Weiss et al., 2014; Williams et al., 2016). TB-related stigma has been associated with poor treatment adherence. Community health workers have been found to be relevant in addressing stigma through health education (Molla et al., 2017).

**Evidence to support decentralization of MDR-TB management.** MDR-TB is a major threat to the effective control of the TB epidemics (Brust et al., 2012). The ever-increasing burden of the disease calls for immediate public health responses that can halt its transmission while providing optimal care for those already affected (Molla et al., 2017). There is ample evidence to suggest the need for scaling up MDR-TB treatment services, particularly in high burden countries, to meet the overwhelming rise in case detection (Brust et al., 2012; Loveday et al., 2015; Molla et al., 2017; Taneja, 2017).

Scale up of treatment services in resource-limited settings require innovation and ongoing investigations to determine the optimal model of care. Researchers have found the hospital-based model of care to be unsustainable in the face of the rising burden of MDR-TB incident cases in high-burden countries such as India, Nigeria, China, and South Africa, among others (e.g., Brust et al., 2012; Horter et al., 2014; Salje et al., 2014).

Through a systematic review of the cost effectiveness of models of care in Estonia, Peru, the Philippines, and Tomsk, Fitzpatrick and Floyd (2012) found that outpatient or community-based model of care incurred lower costs than hospital-based or in-patient model of care. Their findings may, however, not be directly applicable to the Nigerian setting due to contextual differences between the African region and the European and Asian settings which were the focus of the study. Musa, John, Habib, and Kuznik (2016), who conducted their study in Nigeria, also confirmed that community-based model of care is more cost effective than the hospital-based model. Bassili et al.'s (2013) systematic review, in which they evaluated the effectiveness of the hospital-based and the ambulatory model of care in a wide range of settings across 22 countries including South Africa, resulted in findings that the hospital-based model was not significantly associated with better treatment outcomes than the ambulatory model.

Considering the limited treatment capacities in many high burden countries and the fact that only 16% of the estimated number of MDR-TB cases among TB diagnosed globally have access to treatment, this finding favors the adoption of the ambulatory model of care (WHO, 2017). This finding provided the evidence that backed the recommendation of the ambulatory model by the World health Organization (Bassili et al., 2013). Also, in a systematic review conducted to determine the effectiveness of decentralized (community-based) model of care in comparison with centralized or hospital-based model of care, researchers found that patients were more likely to have treatment success when treated using the decentralized model (Ho et al., 2017). Ho et al. explained that the better treatment outcome recorded among patients managed using the

decentralized model may be explained by improved adherence as a result of greater social support from family members and wider social networks. The effectiveness of decentralization of MDR-TB care as documented in many resource-constraint settings such as India, South Africa and Ethiopia provided the basis for implementing ambulatory and community-based models of care in countries with similar settings (Brust et al., 2012; Furin et al., 2011; Loveday et al., 2015; Molla et al., 2017; Taneja, 2017). However, lessons learned in countries may be context specific and may not apply in other country settings. Moreover, hospital-based models of care were found to be associated with higher rates of loss to follow up than decentralized models in a few countries (Ho et al., 2017).

**Evidence that supports hospital-based management of MDR-TB.** There are some arguments in favor of hospital-based management of MDR-TB, these include the need to administer and monitor complex, toxic drug regimens and to limit the community spread of drug-resistant TB (Heller et al., 2010). However, many MDR-TB patients are not detected early and therefore remain untreated and infectious long before they are hospitalized, hence, early detection may be a more effective way to contain the spread of the infection than patient isolation in hospitals (Heller et al., 2010; Van Cutsem et al., 2016). In addition, hospital-based models may expose patients and health workers to nosocomial infections (Van Cutsem et al., 2016). In the same vein, MDR-TB patients admitted in hospitals may infect the health workers who relate closely with them in the course of providing care, as well as visiting family members and friends (Luyirika et al., 2012; Van Cutsem et al., 2016). In light of this, infection control strategies are required at

both the health facility and community levels (Heller et al., 2010; Ho et al., 2017). Also, Oladimeji et al. (2014) conducted a study in Nigeria and found lower loss to follow up among MDR-TB patients managed using the hospital-based model of care. Skrahina et al. (2013) conducted in Belarus with similar results, finding higher loss to follow up among MDR-TB patients during the outpatient treatment phase. However, this is contrary to the findings of studies conducted in Peru and South Africa which suggested that hospital-based management of MDR-TB is not associated with improved treatment adherence relative to the community-based model of care (Heller et al., 2010; Mitnick et al., 2003). This may be explained by the social and economic costs associated with hospitalizing MDR-TB patients which may include loss of income and loss of, or reduced social support from relatives and friends (Baleta, 2007; Heller et al., 2010). Also, patients may feel confined in hospital settings and may abscond from treatment as a result of the prison-like feeling of being hospitalized for the duration of MDR-TB treatment (Baleta, 2007).

Management of adverse drug reactions is key to the successful outcome of MDR-TB treatment (Akshata & Chakrabarthy, 2016). This is because of the complexity and toxic nature of the medications used in the management of MDR-TB (Dela, Tank, Singh, & Piparva, 2017). Some have argued that the management of adverse drug reactions associated with MDR-TB treatment may be more effective in hospital settings and this expertise may be lacking under the community-based model of care (Dela et al., 2017; Heller et al., 2010). However, a study that compared the ambulatory and hospital-based model of care indicated that patients managed in the hospital suffered more adverse drug

reactions than the patients managed using the ambulatory model of care (Kalandarova et al., 2016).

**Factors associated with poor treatment outcomes in MDR-TB management.** Several authors have identified predictors of poor treatment outcomes among MDR-TB patients (i.e., Aibana et al., 2017; Kliiman & Altraja, 2009; Li, Ge, Shen, & Wei, 2016; Mohd Shariff, Shah, & Kamaludin, 2016; Schnippel et al., 2015). These predictors include previous treatment history, age greater than 45 years old, sputum smear positive result at time of diagnosis, migrant status, distance from the patient's home to the related TB hospital, and co-morbidities such as HIV and diabetes (Li et al., 2016). Wai et al. (2017) also identified age greater than 55 years old, anemia, and weight less than 45 kg as risk factors for poor treatment outcomes among MDR-TB patients. Another study conducted in Belarus, however, produced results indicating young age, HIV, history of incarceration, unemployment, and homelessness as predictors of poor treatment outcomes among MDR-TB patients (Skrahina et al., 2013). Researchers have also identified diabetes as a predictor of poor treatment outcome (Muñnoz-Torrico et al., 2017). Also, being HIV positive and not on ART was found to be associated with poor treatment outcomes among MDR-TB patients although the sample size of the study was small (Aibana et al., 2017; Kliiman & Altraja, 2009). A similar study conducted in Lesotho demonstrated the effectiveness of managing HIV positive MDR-TB patients using the community-based model of care (Satti et al., 2012). Predictors of successful treatment identified include knowledge about the disease, adherence to treatment and dedicated health workers (Napirah, Wandira, & Aulia, 2017). A study conducted in India to study

the association between gender, marital status and treatment outcome of MDR-TB patients was inconclusive (Patel et al., 2016). This may be due to small sample size and suboptimal study design.

## Operational Definitions

*Ambulatory model of care:* involves in-patient management in the hospital under the close supervision of health workers for the duration of the intensive phase of about 6 months and out-patient management for the rest of the treatment period (WHO, 2014b.

*Complete community or home-based model of care:* involves management of the patients in their home or social settings throughout the duration of treatment (USAID, 2017; Falzon et al., 2011). In the Nigerian context, this involves the use of treatment supporters and linkage to nearby health facilities where injections can be provided and adverse drug reactions and other treatment components monitored closely by the health worker (Mbaave, Igbabul & Achinge, 2016).

*Cure*: treatment completed as recommended by the national policy without evidence of failure and in which three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase (WHO, 2014a).

*Death*: death from any cause (TB or non-TB) during the course of chemotherapy (WHO, 2014a).

*Failure*: treatment terminated or need for permanent regimen change of at least two anti-TB drugs because of lack of conversion by the end of the intensive phase or bacteriological reversion in the continuation phase after conversion to negative, or

evidence of additional acquired resistance to fluoroquinolones or second-line injectable drugs, or adverse drug reactions (WHO, 2014a).

*Loss to follow up:* describes any patient who had interrupted treatment for two consecutive months or more and who never returned for treatment.

*Successful treatment outcome:* refers to a patient being cured or treated.

*Transferred out*: refers to patients transferred out of the country.

*Treatment outcome:* outcomes that include cure, treatment completed, died, transferred out, and loss to follow (WHO, 2014a).

*Treatment completed:* completion of the treatment course without bacteriologic documentation of cure while treatment success is described as those who completed treatment or were cured (WHO, 2014a).

*Unsuccessful treatment outcome:* refers to any result other than cure or treatment, including loss to follow up, death, and treatment failure, but not including transferred out patients, who will not be considered in the analysis.

## Assumptions

For the purpose of this study, I made assumptions that all patient-level data received from the National Tuberculosis and Leprosy Control Program are accurate and complete information of the patients. Furthermore, I assumed that the health workers who collected the data were objective and collected accurate and complete information from the patients without manipulating or entering false data into the data management systems. I also assumed that the patient provided correct information and complete data about the state of their health and the presence of all other diseases they may suffer from.

Also, all patients who died during the MDR-TB treatment were assumed to have died as a result of the disease, regardless of the actual cause. This is line with the definition of death as a treatment outcome in the course of TB treatment (WHO, 2014a). This is a general assumption on the TB program because it is often difficult to determine the cause of death. These assumptions about the quality of the data and the cause of death may have affected the results and inferences made from the study.

## Scope and Delimitations

For the purpose of this study, I employed a quantitative approach without exploring the experiences and perspectives of the patients about the treatment and how this may have impacted the observed treatment outcomes. My investigation was focused on the relationship between model of care and treatment outcomes, in which case, models of care was limited to just community-based and the ambulatory models and did not account for variants that may exist such as some patients that may have to be admitted in hospitals in the course of their treatment due to adverse drug reactions or other causes of illness while being classified as patients managed in the community.

Existence of co-morbidities only included HIV. I did not consider other health conditions such as hypertension, heart diseases, malaria, typhoid, and other common health conditions in the country as part of the investigation. While the scope of the study did not include these illnesses, they may, nonetheless, be associated with the observed treatment outcomes. I did not investigate health workers' attitudes, or the kind of social support provided to the patients, although these factors may have had an effect on the observed treatment outcomes. I included only patients managed in Nigeria between 2013

and 2014. This is because the community-based model of care became fully operational in Nigeria in 2013 and I could not determine when the cohort analysis of patients beyond 2014 would be available at the time I was designing the study.

## Significance, Summary, and Conclusions

The purpose of this study was to develop a better understanding of the factors that result in poor treatment outcomes among MDR-TB patients. The key objective of the study was to determine if the model of care (ambulatory and complete community-based or out-patient), existence of co-morbidities, particularly HIV and other demographic characteristics such as age, marital status and gender, influence the treatment outcomes observed in MDR-TB patients. A robust understanding of the factors that influence treatment outcomes among MDR-TB patients may be key in reducing the burden and negative impact of the disease. The results of this study provided insights on how treatment outcomes among MDR-TB patients can be improved by addressing some of the identified risk factors that result in poor treatment outcomes (see Drobniewski et al., 2002). Most importantly, the results of this study provided evidence necessary to inform policy changes in the management of MDR-TB patients in Nigeria particularly with regards to the model of care that is adopted and how care is delivered in general. Additionally, the findings of the study helped fill the existing gap in literature as it relates to the demonstration of the effective and optimal model of care that is feasible for managing MDR-TB patients in resource-limited settings like Nigeria. The implication for social change is that Nigeria may improve the quality of treatment provided to MDR-TB patients by ensuring that the more effective model of care is adopted. Also, this study

provided information about the effect of HIV and demographic factors such as age, gender, and marital status on treatment outcomes among MDR-TB patients. A deeper understanding of the relationship between these factors may inform the development of policies and guidelines that can address existing gaps in the quality of care provided to MDR-TB patients. Other implications for social change include the possibility of more gender-sensitive treatment guidelines, adaptation of specific treatment models for different age categories, and special provisions for the management of co-morbidities in MDR-TB control programs.

Several factors have been associated with poor treatment outcomes among MDR-TB patients. These factors include model of care, age, gender, existence of co-morbidities such as HIV, and type of social support provided to the patients among others (Li et al., 2016). Researchers have investigated the effect of model of care on treatment outcomes in countries such as South Africa, Ethiopia, India, Peru, among others (i.e., Loveday et al., 2015; Mitnick et al., 2003; Molla et al., 2017; Patel et al., 2016). The results of these studies suggested that community or home-based models of care may be a better treatment option based on the more favorable treatment outcomes observed. Researchers have also used qualitative evidence to support the superiority of the home-based model of care over the hospital-based model of care (Burtscher et al., 2016; Horter et al., 2014). Little empirical evidence has been generated through quantitative methodology, and quantitative studies often have small samples sizes. The quality of a few of these studies was also suboptimal; hence the need for a more robust study methodology to determine the relationship between model of care and treatment outcomes among MDR-TB patients

(Ho et al., 2017; Loveday et al., 2015; Oladimeji et al., 2014). Through the literature review, I only identified a few studies that were conducted in resource limited settings such as Nigeria (e.g., Mbaave, Igbabul, & Achinge, 2016; Oladimeji et al., 2014). Oladimeji et al. (2014) conducted their study in Nigeria before the adoption of the community based model of care and suggested that hospital-based model of care was linked to better treatment adherence. Their evidence was not compelling and was not consistent with the available evidence in literature, such as that from Ho et al. (2017), Loveday et al. (2015), Molla et al., (2017) and Williams et al. (2016). A few studies also assessed the cost effectiveness of the different models of care employed in the management of MDR-TB patients (e.g., Bassili et al., 2013; Fitzpatrick & Floyd, 2012; Musa et al., 2016). The findings of most of these studies showed community-based model of care to be more cost effective than hospital based.

Therefore, through this study, I sought to investigate the relationship between model of care and treatment outcomes among MDR-TB patients in a resource-limited setting and a country with high HIV burden such as Nigeria. The findings of this study provided empirical evidence needed to determine which of the models of care currently employed in Nigeria is more effective to enable the optimization of patients' quality of care. Also, through this study I sought to investigate how the existence of co-morbidities such as HIV interfere with treatment outcomes among MDRTB patients in Nigeria. This is important because of the inherent weaknesses in the country's healthcare system especially lack of universal health coverage and mostly out of pockets expenditures for healthcare (Tadesse, Demissie, Berhane, Kebede, & Abebe, 2013).

Section 2: Research Design and Data Collection

## Introduction

Multidrug resistant tuberculosis (MDR-TB) has become increasingly prevalent in countries such as China, India, and Nigeria, and others (World Health Organization [WHO], 2016). The increasing trend in the burden of MDR-TB has made it necessary to increase the capacities of high-burden countries to manage patients affected by the disease. The burden of MDR-TB in Nigeria makes it an important public health issue that impact heavily on the quality of life of those affected by the disease (Daniel & Osman, 2011).

In light of this fact, the National TB program has adopted the complete community-based management of MDR-TB alongside the ambulatory model of care to increase the treatment capacity to manage MDR-TB patients. Against this backdrop, there is an urgent need for the rapid scale-up of MDR-TB treatment services in high burden countries such as Nigeria. Currently, there are limited studies to establish the effectiveness of community-based model of care for MDR-TB patients in Nigeria. Through this study, I sought to demonstrate the effect of the model of care and existence of co-morbidities such as HIV on treatment outcomes among MDR-TB patients.

The treatment of MDR-TB is extensive, toxic, and expensive both to the healthcare system and to the individual hence the need for a systematic evaluation of the effectiveness of existing models of care and some other key variables, such as the presence of comorbidities that may affect the outcome of the treatment. A patient-centered approach to TB management is essential for achieving a positive outcome.

Hence, it is critical that policies and treatment guidelines adopted by the National TB programs are tested empirically to establish their effectiveness and appropriateness in the country's context. A robust understanding of the factors that influence treatment outcomes among MDR-TB patients may be key in reducing the burden and impact of the disease.

The results of this study may provide insights on how treatment outcomes among MDR-TB patients can be improved by addressing some of the identified risk factors that are associated with poor treatment outcomes (see Drobniewski et al., 2002). Most importantly, the result of this study may provide the evidence needed to inform policy changes in the management of MDR-TB patients in Nigeria particularly with regards to the model of care that is adopted and how care is delivered in general. Additionally, the findings of the study may address the existing gap in literature as it relates to the demonstration of the effective model of care that is feasible for managing MDR-TB patients in resource-limited settings like Nigeria.

In the previous section, I described the existing evidence in literature that compares the different models of care, their effect on treatment outcomes of MDR-TB patients, other predictors of successful or unsuccessful treatment outcomes. In the previous section, I also described the scope of the study, the operational definitions of the dependent and independent variables, and the assumptions and limitations of the study.

## Research Design and Rationale

For the purpose of this study, I employed a quantitative approach to investigate the effect of model of care whether hospital-based or community-based on treatment outcomes of MDR-TB patients. Other researchers have employed both qualitative and qualitative approaches to investigate and explore the effect the model of MDR-TB care has on the patients and their treatment outcomes (e.g., Bieh et al., 2017; Brust et al., 2012; Ho et al., 2017; Horter et al., 2014; Loveday et al., 2015; Molla et al., 2017; Williams et al., 2016). In this study, I employed a cross-sectional design to investigate the factors that are associated with poor treatment outcomes among a retrospective cohort of MDR-TB patients. Factors I investigated included model of care, existence of other diseases (specifically HIV), age, gender, and marital status.

A qualitative approach was not suitable for this study because it would not have provided the information needed to determine the empirical association between treatment outcomes and the factors or variables that are being investigated. It may however have provided insight into the perspectives of the patients and health workers. For instance, Bieh et al. (2017) conducted a study in Port Harcourt, Nigeria to explore the perspectives of patients and health workers on the hospital-based model of care. I determined that the retrospective cohort design was suitable for this study because of my desire to investigate the degree of association or relationship between treatment outcomes among MDR-TB patients, model of care, and other key predictor variables. A

randomized control design would have been most suitable to determine causality and therefore provide the highest level of evidence to support the best model of care for MDR-TB (see Akobeng, 2005). However, I utilized secondary data for this study; therefore, it was impossible to randomly assign persons to different types of treatment. For this reason, I chose the retrospective cohort design. The dependent variable was the treatment outcome, which I classified into two broad categories, successful and unsuccessful. I also considered survival outcomes after treatment whether dead or alive as another dependent variable in the data analysis. The independent or predictor variables included model of care, existence of co-morbidities, age, gender, and marital status. I conducted several bivariate analyses in order to determine the association between the dependent variable and predictor or independent variables. Additionally, I conducted multivariate analyses for each of the combination of variables to establish whether the group of two variables formed a more significant predictor than one variable alone (see Rencher, 2012).

The scope of this study did not include the effect of adverse drug reactions on treatment outcomes. Due to time constraint, I did not validate the secondary data used for the analysis in the field for correctness and completeness. I assumed that the data quality control mechanisms of the National Tuberculosis, Buruli Ulcer and Leprosy Control Program (NTBLCP) were optimal and that the data were entered correctly and completely at the point of collection. I managed missing information at the analysis stage.

## Methodology

The study was based on the analysis of secondary data. The data were accessed from the NTBLCP. I collected the data through the institutions' electronic data management system referred to as the e-TB manager. I exported the data to an excel template and then transferred to SPSS version 24 for analysis. Extraction of patient-level information was done serially until the calculated sample size was achieved. I excluded patients with no treatment outcome computed at the time of the study from the analysis. I also excluded patients with incomplete information and those under the age of 6 years from the analysis. It was impossible to determine the model of care applied per patient through this electronic management system, hence I triangulated the extracted patient-level data with state-level data collected by the state's TB program that managed the patients. In order to achieve this, I contacted the state program managers through the Monitoring and Evaluation Manager of NTBLCP to verify the model of care applied for each of the patient included in the study. I deidentified the information of the patients at the point of transmission by the states and NTBLCP. I accomplished the deidentification mostly via emails to enable the transmission of verifiable data regarding the model of care to which patients were enrolled.

## Population

The study population include MDR-TB patients who were enrolled for treatment in Nigeria between 2013 and 2014. I chose this period because the community management of MDR-TB commenced fully in Nigeria in 2013 hence data for this period enabled a comparison between the two models of care that is currently being employed to

manage MDR-TB patients in Nigeria (see Mbaave, Igbabul & Achinge, 2016). I did not include years after 2014 in the study because the treatment of MDR-TB before the commencement of the shorter regimen in 2017 took an average of 20 months. For this reason, the cohort analysis, including the outcome of treatment which is the dependent variable I intended to evaluate, may not have been be available for patients managed in Nigeria after 2014 at the time I was conducting this study. The estimated number of new MDR-TB patients in 2014 was 21,000, of which only 800 cases were detected and about 50% enrolled in treatment (USAID, 2016). The number of patients enrolled for treatment in 2013 was similar to the figure reported for 2014 (USAID, 2016). All MDR-TB patients were eligible except children from the age of 6 years and lower. I did not include children because of factors that can affect their treatment outcomes that I did not consider in this study. These factors included lack of sufficient evidence for optimal dosing and treatment duration for children and the paucibacillary nature of the MDR-TB in children, which may result in a faster clearance of the bacteria than in adults (see Ettehad, Schaaf, Seddon, Cooke, & Ford, 2012).

## Sampling and Sampling Procedures

For the purpose of this research, I employed a convenience sampling approach. I collected secondary data from patients from states across Nigeria. I then extracted the data serially until I reached an adequate number that met the sample size requirement calculated for the study. The sampling frame included all MDR-TB patients managed in Nigeria between 2013 and 2014 who were older than 6 years and who were treated using either the hospital-based model or the community-based model. I excluded patients who

were enrolled in treatment after 2014 from the study. I also excluded patients whose treatment outcomes were not known at the time the study was being conducted. The secondary data I used for this study represented the routinely collected patient-level data of MDR-TB patients managed in Nigeria in line with the National TB treatment guidelines, which align with WHO guidelines for management of MDR-TB (see Falzon et al., 2011). I entered data routinely in both hard and electronic form for all patients enrolled in treatment. For the purpose of this study, I accessed the electronic data through the e-TB manager. I contacted the National Tuberculosis and Leprosy Control unit, which is part of the department of Public Health under the Ministry of Health, for permission to access the secondary data. I shared letters and held meetings to discuss the objective of the study. The Head of the Monitoring and Evaluation of the unit agreed to allow me to use the data by signing an agreement form.

## Sample Size Calculation

In this study, I sought to determine the empirical relationship between five independent variables and two dependent variables. The independent variables were model of care whether hospital-based or community-based, existence of co-morbidities, specifically, HIV and gender, age, and as marital status. The dependent variables were treatment and survival outcomes, which I dichotomously classified for the purpose of this study. I classified the treatment outcome broadly into two categories of successful or unsuccessful outcomes, while I classified survival outcome as dead or alive. I applied logistics regression as the statistical analysis to determine the predictive relationship between the independent variables and the dependent variables. Using G*Power 3.1.9.2, I

calculated sufficient sample size for the study with an alpha of 0.05, power of 0.8, and a moderate effect size (odd ratio = 1.43) using a two-tailed test (Erdfelder, FAul, Buchner, & Lang, 2009). The effect size was based on a similar study conducted in South Africa to compare the effect of model of care on treatment outcomes (see Loveday et al., 2015).

In this study, 1549 patients were prospectively enrolled on either community or hospital-based MDR-TB care. The settings of the study may not be exactly similar to the Nigerian context; however, the study design was robust and the sample size adequate to suggest a reliable result. The required sample size computed for determining the empirical validity for logistics regression with more than four predictor variables is a minimum of 392 patients.

The power level, alpha, and effect size I chose for this study are the minimum required to determine the predictive relationship between the independent variables and the dichotomous dependent variable and it is consistent with the sample size applied in reliable literatures (e.g., Erdfelder et al., 2009; Ho et al., 2017).

## Instrumentation and Operationalization of Constructs

I used secondary data for this study. I originally collected the data using routine data collection tools. I employed no instrument during the data collection process; therefore, review of reliability and validity of instrumentation was not necessary.

## Operationalization

Treatment outcome is the dependent variable for this study. According to WHO definitions, treatment outcomes include cure, treatment completed, died, transferred out, loss to follow (WHO, 2014). Cure is defined as treatment completed as recommended by

the national policy without evidence of failure and three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase (WHO, 2014a). Completed describes completion of the treatment course without bacteriologic documentation of cure. Failure is defined as treatment terminated or need for permanent regimen change of at least two anti-TB drugs because of lack of conversion by the end of the intensive phase or bacteriological reversion in the continuation phase after conversion to negative, or evidence of additional acquired resistance to fluoroquinolones or second-line injectable drugs, or adverse drug reactions (ADRs) (WHO, 2014a). Transferred out describes patients transferred out of the country. Death is defined as death from any cause (TB or non-TB) during the course of chemotherapy (WHO, 2014a). Loss to follow up is used to describe any patient who had interrupted treatment of two consecutive months or more and who never returned for treatment. For the purpose of this study, treatment outcome will be classified into two broad categories, successful and unsuccessful. Cured and treatment completed will be considered as successful outcomes while other outcomes will be considered as unsuccessful, including loss to follow up, death and treatment failure. Transferred out patients will not be considered in the analysis.

The key independent variable for this study was model of care. There are two categories, ambulatory or hospital-based model and the complete community or home-based model of care. The ambulatory model is defined by WHO as models that involve in-patient management in the hospital under the close supervision of health workers for the duration of the intensive phase of about 6 months while complete community or home-based model of care involves management of the patients in their home or social

settings throughout the duration of treatment. This may involve visits to nearby health facilities for management of adverse reactions where necessary. Other dependent variables investigated in the study include the presence of co-morbidities or other diseases which in this study is defined as patients who are HIV positive in addition to having MDR-TB. This variable was treated as a dichotomous variable defined as co-morbid or not co-morbid. Demographic characteristics such as gender, age and marital status were also investigated. Marital status was classified as single or married, age was classified as below and equal to 40 years and above 41 years of age in line with the findings from literature review (Li et al., 2016). Gender was classified as males and females.

## Data Analysis Plan

I exported all data for the analysis into SPSS version 24 for Windows, which is the software I used for data analysis. I cleaned the data by ensuring that all necessary data elements were available. I attempted to retrieve all missing information; however, I did not include patients with missing or incorrect information on treatment outcome. I developed a data dictionary to define all the variables and how they were labelled or recoded for analysis. I recoded the data to prepare the data for analysis. I recoded age into age below or equal to 40 years and age above 41 years. I recoded marital status into single and married only; I recoded all divorced, separated, or widowed patients into the single category. I classified the outcome or dependent variable as successful and unsuccessful. I developed a data table to list all the dependent and independent variables

and their levels of measurement. For ease of interpretation of the results of the analysis, I recoded continuous variables such as age into categorical variables.

## Research Questions and Hypotheses

RQ1: Is there an association between type of treatment model; hospital or complete community-based, and treatment outcome among MDR-TB patients in Nigeria?

$H_0$1: There is no association between type of treatment model and treatment outcomes among MDR-TB patients in Nigeria.

$H_a$1: There is an association between type of treatment model and treatment outcomes among MDR-TB patients in Nigeria.

RQ2: Are co-morbidities such as HIV associated with poor treatment outcomes among MDR-TB patients in Nigeria?

$H_0$2: There is no difference in treatment outcomes between patients with co-morbidities and those without in Nigeria.

$H_a$2: There is a difference in treatment outcomes between patients with co-morbidities and those without in Nigeria.

RQ3: Is type of treatment model associated with survival outcomes among MDR-TB patients in Nigeria?

$H_0$3: There is no difference in survival outcomes between patients enrolled on the two different models of care in Nigeria.

$H_a$3: There is a difference in survival outcomes between patients enrolled on the two different models of care in Nigeria.

RQ4: Are demographic factors such as age, gender, and marital status associated with treatment outcomes among MDR-TB patients in Nigeria?

$H_0$4: There is no association between demographic factors such as age, gender, marital status, and treatment outcomes among MDR-TB patients in Nigeria.

$H_a$4: There is an association between demographic factors such as age, gender, marital status, and treatment outcomes among MDR-TB patients in Nigeria.

I conducted descriptive analysis for each of the variables. These included frequencies, percentages, mean, mode, and median. I conducted the inferential analysis using logistics regression, using both bivariate and multivariate analysis to test each of the hypotheses. I determined the association between the dependent and each of the categorical independent variables using chi-square analysis. The level of significance was defined at 0.05 and the decision rule was to reject the null hypothesis if $p$ was greater than 0.05. I calculated the odds ratio at each bivariate analysis using a confidence level of 95%. The inferential statistics included hypothesis testing and the determination of the predictive relationship between the independent and dependent variables. If $p$-value was less than 0.05, I rejected the null hypothesis and confirmed the association between the predictive variables and the treatment outcomes among MDR-TB. I determined the effect size or the strength of the association using the value of the odds ratio. At the multivariate level of analysis, I included all the predictor variables in the model and used the adjusted odds ratio to determine which of the variables has the highest effect on treatment outcomes among MDR-TB patients. Potential confounders may be included in the analysis based on existing evidence in the literature. A key confounder that should have

been tested is the weight of the patient at the onset of treatment and type of smear at the beginning of treatment whether positive or negative (Kliiman & Altraja, 2009; Milanov et al., 2015). However, these variables were difficult to collect retrospectively. I tested conditions of linearity and multicollinearity to determine the appropriateness of the logistics regression as the method of analysis (see Field, 2009).

## Inferential Statistics

I determined the overall significance of the logistic regression by examining the classification table, the display of the incorrect and correct classifications of the outcome variable. In addition, I used chi- square goodness of fit test to test the appropriateness of model. I used Wald statistic to determine the significance of each of the independent variables (Sperandei, 2014). Logistics regression analysis yields a model result that enables the prediction of the relationship between the dependent variable and the predictor variables by calculating the effect of each explanatory or dependent variables on the odds ratio of the observed event of interest which in this case is a successful treatment outcome and survival at end of treatment. The model summary provides the -2 Log Likelihood statistic which measures how poorly the model predicts the decisions, a small statistic indicates a good model (Sperandei, 2014). I used the Snell $R^2$, Cox and Nagelkerke $R^2$ to determine the percentage of variance in the dependent variable that is explained by the predictor or independent variable (see Field, 2009). Also EXP (B) value shows the increase in odds from one unit increase in the selected variable (Field, 2009).The omnibus result gives the outcome of the test of significance (Field, 2009). For the purpose of this study, *p*-value was set at 0.05. The decision rule was that the null

hypothesis is rejected, and the alternative accepted at *p*-values lower than 0.05. I set unsuccessful treatment outcome as the reference variable; hence, I interpreted results as the odds of having an unsuccessful treatment outcome as predicted by the explanatory or independent variable.

## Threats to Validity

The sampling method did not include randomization, and this may have introduced selection bias as a result of the convenient sampling technique. This method may affect the internal validity of the results; however, I addressed this problem by ensuring that samples selected were diverse and came from different states in the country. External validity relates to the generalizability of the study findings to the general population (Creswell, 2012). I addressed issues relating to external validity by ensuring that the study was adequately powered and by limiting the interpretation of the findings of the study to the Nigerian setting. My use of secondary data for the analysis may introduce issues with the reliability of the data used because data quality cannot be improved at the point of use. I have stated these limitations in the study. Construct validity describes the appropriateness of the theoretical framework to the nature of the study (Creswell, 2012). I addressed construct validity by ensuring that the key constructs of the behavioral theory applied in this study were well aligned to each of the hypotheses tested in the study. I employed no instrument for data collection in this study because I used secondary data; therefore, measurement errors due to instrumentation are not applicable and did not affect the validity and reliability of the results.

## Ethical Procedures

I obtained permission to use secondary data from the institution responsible for management of tuberculosis patients, which is the National Tuberculosis, Buruli Ulcer and Leprosy Control Program. This permission took the form of a data agreement form that enabled unlimited access to the database of patient-level information of MDR-TB patients in the country. I anonymized and de-identified all patient information to ensure confidentiality. I managed the data with utmost discretion and stored them securely in electronic format using password protected laptops. Data dissemination also ensured that patient-level information was de-identified in order to ensure patient confidentiality. I met other IRB requirements of Walden University appropriately.

## Summary

In this section, I described the research design and methodology I employed in the study. I applied a quantitative method. The population of interest were MDR-TB patients treated in Nigeria between 2013 and 2014. The study design was cross-sectional in nature. The patient-level data I used was, however, the retrospective cohort information of the patients that have concluded MDR-TB treatment. The predictor variables I investigated included model of care, existence of co-morbidities, gender, age, and marital status, while the dependent variable was treatment and survival outcomes, which are dichotomous in nature. I applied SPSS version 24 statistical software and used logistics regression as the method of analysis. Analysis included both descriptive and inferential analysis and I did inferential statistics at the bivariate and multivariate levels. The power

level was 80% and the *p*-value was set at 0.05 at 95% confidence level. In the next section, I will describe the results of the data analysis.

Section 3: Presentation of the Results and Findings

## Introduction

The purpose of this study was to investigate the effect of model of care whether hospital-based, ambulatory or complete community-based model on the treatment outcomes of MDR-TB patients. I also investigated the effect of other factors such as the existence of other diseases such as HIV and demographic factors such as gender, age, and marital status on treatment outcomes of MDR-TB patients. The burden of MDR-TB in Nigeria makes it an important public health issue that has a heavy impact on the quality of life of those affected by the disease (Daniel & Osman, 2011). In light of this fact, the National TB program has adopted the complete community-based management of MDR-TB alongside the ambulatory model of care to increase the treatment capacity to manage MDR-TB patients.

The treatment of MDR-TB is extensive, toxic, and expensive both to the healthcare system and to the individual; hence, the need for a systematic evaluation of the effectiveness of existing models of care and some other key variables, such as the presence of comorbidities that may affect the outcome of the treatment. A patient-centered approach to TB management is essential for achieving a positive outcome. Itis critical that policies and treatment guidelines adopted by the National TB programs are tested empirically to establish their effectiveness and appropriateness in the country's context. A robust understanding of the factors that influence treatment outcomes among MDR-TB patients may be key in reducing the burden and impact of the disease. The result of this study may provide insights on how treatment outcomes among MDR-TB

patients can be improved by addressing some of the identified risk factors that are associated with poor treatment outcomes (see Drobniewski et al., 2002). Most importantly, the result of this study provided the evidence needed to inform policy changes in the management of MDR-TB patients in Nigeria particularly with regards to the model of care that is adopted and how care is delivered in general. Additionally, the findings of the study addressed the existing gap in literature as it relates to the demonstration of the effective model of care that is feasible for managing MDR-TB patients in resource-limited settings like Nigeria.

## Research Questions and Hypotheses

RQ1: Is there an association between type of treatment model; hospital or complete community-based, and treatment outcome among MDR-TB patients in Nigeria?

$H_0$1: There is no association between type of treatment model and treatment outcomes among MDR-TB patients in Nigeria.

$H_a$1: There is an association between type of treatment model and treatment outcomes among MDR-TB patients in Nigeria.

RQ2: Are co-morbidities such as HIV associated with poor treatment outcomes among MDR-TB patients in Nigeria?

$H_0$2: There is no difference in treatment outcomes between patients with co-morbidities and those without in Nigeria.

$H_a$2: There is a difference in treatment outcomes between patients with co-morbidities and those without in Nigeria.

RQ3: Is type of treatment model associated with survival outcomes among MDR-TB patients in Nigeria?

$H_0$3: There is no difference in survival outcomes between patients enrolled on the two different models of care in Nigeria.

$H_a$3: There is a difference in survival outcomes between patients enrolled on the two different models of care in Nigeria.

RQ4: Are demographic factors such as age, gender, and marital status associated with treatment outcomes among MDR-TB patients in Nigeria?

$H_0$4: There is no association between demographic factors such as age, gender, marital status, and treatment outcomes among MDR-TB patients in Nigeria.

$H_a$4: There is an association between demographic factors such as age, gender, marital status, and treatment outcomes among MDR-TB patients in Nigeria.

Section 3 is divided into three subsections. The introduction contains a brief summary of research purpose, questions, and hypotheses. The result section includes a detailed explanation of the outcomes of both the descriptive and inferential statistical analysis. The results are organized by the research questions and hypothesis. Figures and tables are also included in the result subsection.

## Data Collection of Secondary Data Set

The data of MDR-TB patients are collected routinely at the facility and LGA level. Trained health workers who act as LGA tuberculosis and leprosy supervisors are responsible for the collation and reporting of TB and MDR-TB data for their respective LGAs. At the facility, there are trained health workers who are responsible for the primary collection of the patient level data using treatment cards and treatment registers. They are referred to as DOTS providers. Each of the states also have personnel designated as MDR-TB focal persons who are responsible for the coordination of the management of all MDR-TB patients in the state under the leadership of the state tuberculosis and leprosy program control manager. The data flow is such that the DOTS providers collect the patient level information which is collated by the LGA TB supervisor. Most states have a monthly meeting where the MDR-TB data are reviewed for accuracy and completeness. The MDR-TB data are entered into the electronic platform which is the e-TB manager by the MDR-TB focal person for the state. There are currently 28 treatment centers for MDR-TB in the country; these are facilities for the centralized management of MDR-TB patients and usually have patients transferred in from other states. For such facilities and because of the huge number of patients managed at that level, the patient level information is collated by a designated data officer and entered directly into the e-TB manager. The National Tuberculosis, Leprosy and Buruli Ulcer Control Program have a mechanism for data review and validation. This includes regular onsite data verification to facilities and LGAs, data quality assessments and a

quarterly data review meeting at the state level and for the six geopolitical zones in the country.

## Results

The final study included 402 patients selected from the population of MDR-TB patients managed in the country between 2013 and 2014. Of these patients, 137 (34%) are females and 262 (66%) are males. The gender of three of the patients included in the study could not be retrieved. There were more males in the sample than females in the study sample. This is consistent with the pattern of the gender distribution of TB patients in accordance with the findings of the prevalence survey conducted in the country in 2012 and routine program data (National Tuberculosis and Leprosy Control Program, 2012). The mean age of study participants was 33.98 years (standard deviation of 11.634). Of the 402 patients, five (1.3%) were aged 7–14 years, 76 (19.5%) were aged 15–24 years, 143 (36.7%) were aged 25–34 years, 95 (24.4%) were aged 35–44 years, 46 (11.8%) were aged 45–54 years, 18 (4.6%) were aged 55–64 years and seven (1.8%) were aged 65 years and over. Of the patients whose information about age was included in the analysis, 297 (76.2%) of them were aged 40 years and below while 93 (23.8%) of them were aged 41 and above. The age of 12 of the patients included in the study could not be retrieved. Of the 402 patients included in the study, 213 (56.5%) were married, 154 (40.8%) were single, eight (2.1%) were widowed, one (0.3%) was divorced and one (0.3%) was cohabitating but not married. Table 1 summarizes the sociodemographic characteristics of the study sample.

Table 1

*Frequency Distribution of Demographic Characteristics of Study Sample*

| Variable | Count (*N*) | Percentage |
|---|---|---|
| **Age (years)** | | |
| 7-14 | 5 | 1.3% |
| 15-24 | 76 | 19.5% |
| 25-34 | 143 | 36.7% |
| 35-44 | 95 | 24.4% |
| 45-54 | 46 | 11.8% |
| 55-64 | 18 | 4.6% |
| 65 & over | 7 | 1.8% |
| Total | **390** | **100%** |
| **Gender** | | |
| Male | 262 | 65.7% |
| Female | 137 | 34.3% |
| Total | **399** | **100** |

Table 1 (cont.)

*Frequency Distribution of Demographic Characteristics of Study Sample*

| Variable | Count (N) | Percentage |
|---|---|---|
| **Marital Status** | | |
| Married | 213 | 56.5% |
| Single | 154 | 40.8% |
| Widowed | 8 | 2.1% |
| Divorced | 1 | 0.3% |
| Cohabitating | 1 | 0.3% |
| Total | **377** | **100** |

The age distribution of the study population reflects the distribution in the general population as described by the prevalence survey conducted in 2012. The age groups 25–44 have the highest frequencies, as shown in Figure 2, thereby supporting the findings of the survey that the working age groups are the hardest hit by TB. This also partially explains the age cut-off point of 40 years that was used in the logistics regression analysis. Additionally, I applied this cut-off because it provided a midpoint between the study population mean age of 34 years and the cut-off point of 45 years as seen in the literature review.

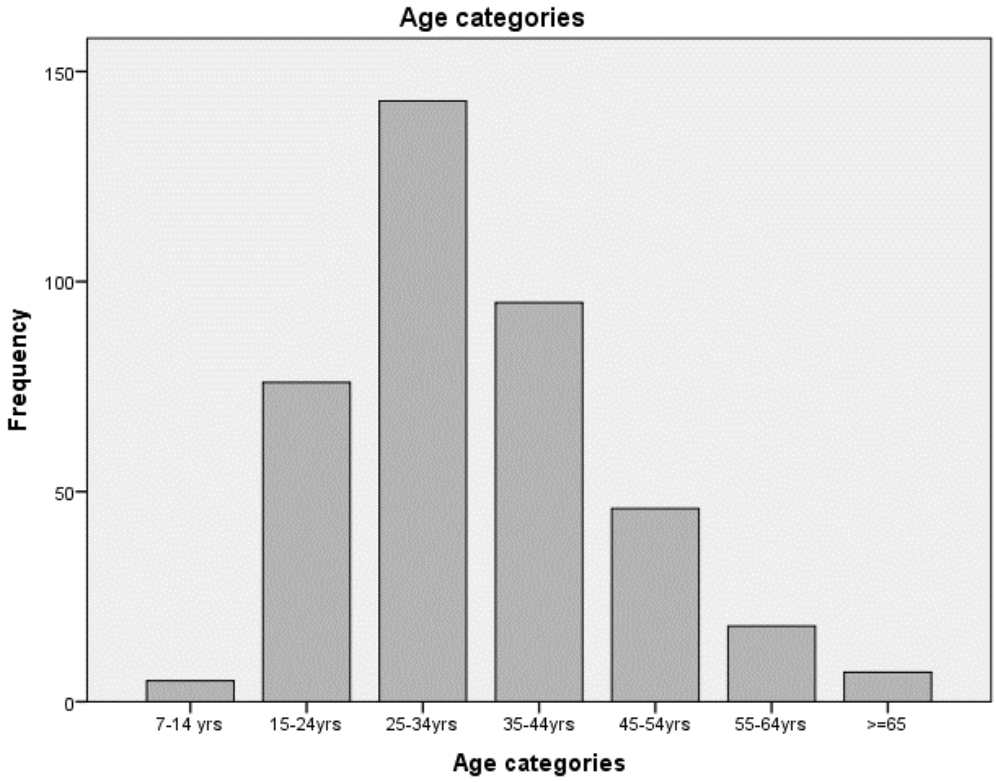


*Figure 2.* Distribution of study population by age-groups.

**Patient Distribution by Model of Care**

Of the 402 MDR-TB patients included in the study, 188 were managed in the community and 214 were managed using the hospital-based or ambulatory model of care as shown in Figure 3.

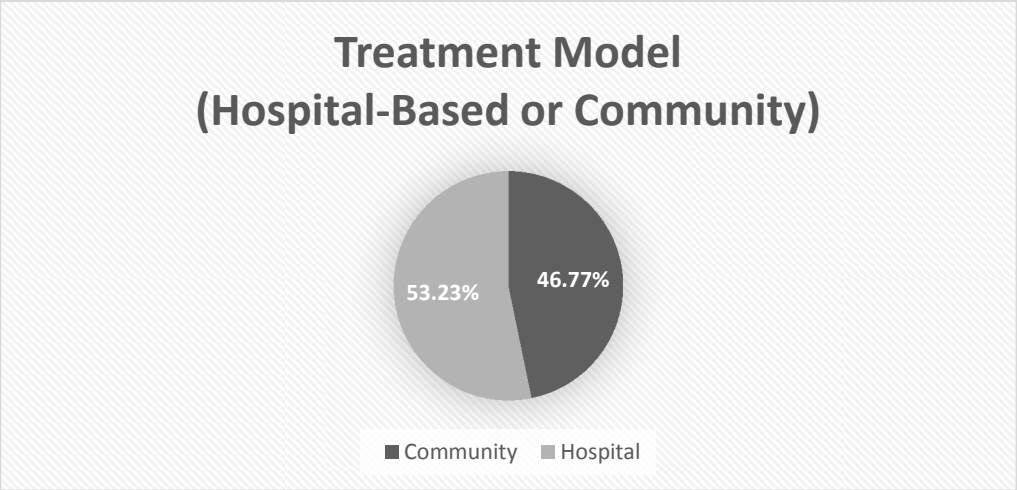


*Figure 3.* Distribution of model of care.

**Distribution of Co-morbidities among Sample Population**

The sample population included 402 MDR-TB patients. Of the 402 patients, 356 were HIV negative, 42 were HIV positive and the HIV status of four of the patients were unknown. It was difficult to retrieve information of other comorbidities that affected the patients particularly diabetes. Table 2 shows the distribution of co-morbidities among the sample population.

Table 2

*Presence of Co-morbidities*

| | Count (N) | Percent | Valid Cumulative Percent |
|---|---|---|---|
| HIV Negative | 356 | 89.4% | 89.4% |
| HIV Positive | 42 | 10.6% | 100 |
| Missing | 4 | 1 | |
| Total | 402 | 100 | |

**Treatment Outcome Reported for Sample Population**

Of the 402 MDR-TB patients who were included in the analysis, 176 (43.8%) completed treatment, 149 (37.1%) were cured, 47 (11.7%) died, 2 (0.5%) failed treatment and 28 (7%) were lost to follow up. The treatment outcome was recoded into successful and unsuccessful outcomes with all cured and completed classified as successful outcomes and all other categories categorized as unsuccessful treatment. After recoding, 325 (80.8%) of the MDR-TB patients had successful treatment outcomes while 77 (19.2%) had unsuccessful treatment outcomes.

Adherence to treatment was investigated by reviewing the number of patients who were lost to follow up in terms of their age category, gender, marital status and the model of care they were enrolled in before they defaulted. Of the 28 MDR-TB patients who were lost to follow up, 17 (60.7%) were enrolled for care in the community while 11 (39.3%) were managed in the hospital before they defaulted. Based on gender distribution, 6.6% (9) of the female MDR-TB patients and 7.3% (19) of the male MDR-TB patients were lost to follow up respectively. Based on marital, 14 of the patients were married while 11 of them were single, the marital status of the three of those lost to follow up was unknown. Based on age distribution, the age group with the highest proportion (14.3%) of patients who were lost to follow up were 65 years and above. This was followed by patients aged 55 years and above and then by patients between the ages of 45 to 54 years. None of the persons aged between 7 to 14 years were lost to follow up. Table 3 gives a summary of the distribution of the patients who were lost to follow up by age, gender, marital status, presence of HIV as a comorbidity and model of care.

Table 3

*Distribution of Patients Lost to Follow Up*

| Variable | Loss to follow up | N | % (Number lost to follow up/N*100) |
|---|---|---|---|
| **Age (years)** | | | |
| 7-14 | 0 | 5 | 0 |
| 15-24 | 4 | 76 | 5.3 |
| 25-34 | 6 | 143 | 7.7 |
| 35-44 | 4 | 95 | 6.3 |
| 45-54 | 4 | 46 | 8.7 |
| 55-64 | 2 | 18 | 11.1 |
| 65 & over | 1 | 7 | 14.3 |
| Total | **28** | | |
| **Gender** | | | |
| Male | 19 | 262 | 7.3 |
| Female | 9 | 137 | 6.6 |
| Total | **28** | | |

Table 3 (cont.)

*Distribution of Patients Lost to Follow Up*

| Variable | Loss to follow up | N | % (Number lost to follow up/N*100) |
|---|---|---|---|
| **Marital Status** | | | |
| Married | 14 | 214 | 6.5 |
| Single | 11 | 163 | 6.7 |
| Total | **25** | | |
| **Model of Care** | | | |
| Community | 17 | 188 | 9 |
| Hospital | 11 | 214 | 5.1 |
| Total | **28** | | |
| **Co-morbid HIV** | | | |
| HIV Negative | 23 | 356 | 6.5 |
| HIV Positive | 5 | 42 | 11.9 |
| Total | **28** | | |

## Bivariate Analysis

### Research Question 1

The first research question for this study was as follows: Is there an association between type of treatment model; ambulatory or complete community-based, and treatment outcome among MDR-TB patients in Nigeria? The null hypothesis was that there is no association between type of treatment model and treatment outcomes among MDR-TB patients in Nigeria. The alternate hypothesis was that there is an association between type of treatment model and treatment outcomes among MDR-TB patients in Nigeria. I tested the association between model of care and treatment outcome using chi-square analysis. I classified model of care into two categories, namely hospital and community-based models of care. I broadly classified treatment outcomes into successful and unsuccessful outcomes. Successful outcomes included patients that completed treatment and those that were cured while unsuccessful treatment outcomes included those whose treatment failed, those who died, and patients that were lost to follow up and therefore did not complete the treatment. Both variables are categorical and independent of each other hence the conditions for using chi-square analysis were met. The outcome of the analysis showed a Pearson chi-square statistics test value of 1.607 and a *p*-value of 0.205. The outcome of the analysis showed that out of the 188 (46.77%) patients who were managed in the community, 147 (78.2%) had a successful treatment outcome while 41 (21.8%) had an unsuccessful treatment outcome. Out of the 214 (53.23%) patients who were managed in the hospital using the ambulatory approach, 178 (83.2%) had a successful treatment outcome while 36 (16.8%) had an unsuccessful treatment outcome.

The *p*-value of 0.205 is higher than 0.05 hence the null hypothesis was not rejected. This result indicates there is no sufficient evidence to establish that there is a difference in treatment outcomes between patients who were treated using the hospital-based model of care and those treated in the community. The odds of having a successful treatment when enrolled in the community model of care relative to the hospital-based model is 0.725, approx. 1. This value further supports the result of the hypothesis test that indicates inadequate evidence to reject the null hypothesis that there is no difference between the two models of care with regards to treatment outcomes. Table 4 shows the result of the cross tabulation for model of care and treatment outcome.

Table 4

*Association between Model of Care and Treatment Outcome*

| Treatment model | Treatment outcome | | Total |
|---|---|---|---|
| | Successful N (%) | Unsuccessful N (%) | |
| Community | 147 (78.2%) | 41 (21.8%) | 188 |
| Hospital | 178 (83.2%) | 36 (16.8%) | 214 |
| Total | 325 | 77 | 402 |

*p=0.205*

**Research Question 2**

The second research question was as follows: Are co-morbidities such as HIV associated with poor treatment outcomes among MDR-TB patients in Nigeria? The null hypothesis stated that there is no difference in treatment outcomes between MDR-TB patients who have HIV as a co-morbid condition and those who do not. The alternate hypothesis stated that there is a difference in the two groups. I coded the independent variable into presence of HIV as a co-morbid condition, yes or no. Both variables are categorical and independent of each other hence the conditions for using chi-square analysis were met. The outcome of the analysis showed a Pearson chi-square statistics test value of 1.657 and a *p*-value of 0.198. The outcome of the cross-tabulation showed that out of the 356 (89.4%) patients who were HIV negative, 292 (82%) had a successful treatment outcome while 64 (18%) had an unsuccessful treatment outcome. Out of the 42 (10.6%) patients who were HIV positive, 31 (73.8%) had a successful treatment outcome while 11 (26.2%) had an unsuccessful treatment outcome. The *p*-value of 0.198 is higher than 0.05 hence the null hypothesis was not rejected. This result indicated that there is no sufficient evidence to establish that there is a difference in treatment outcomes between patients who were HIV positive and those without HIV comorbidity. The odds of having a successful treatment when HIV negative relative to having HIV as a comorbidity is 1.619. This shows a slightly higher odd of having a successful treatment outcome for HIV negative patients, but the difference observed is not statistically significant. Table 5 shows the result of cross-tabulation of treatment outcome and HIV status.

Table 5

*Association between Co-morbidities and Treatment Outcome*

| Treatment outcome | Presence of co-morbidities | | Total |
|---|---|---|---|
| | HIV negative N (%) | HIV positive N (%) | |
| Successful | 292 (82%) | 31 (73.8%) | 323 |
| Unsuccessful | 64 (18%) | 11 (26.2%) | 75 |
| Total | 356 | 42 | 398 |

$P = 0.198$

**Research Question 3**

The third research question was as follows: Is type of treatment model associated with poor survival outcomes among MDR-TB patients in Nigeria? The null hypothesis was that there is no difference in survival outcome among patients enrolled in the two model of MDR-TB care in Nigeria. The alternate hypothesis was that there is a difference in survival outcomes among patients enrolled in either community or hospital-based model of care. The dependent variable is survival outcome, which I defined as dead or alive at the end of the MDR-TB treatment regimen. I classified patients who died from any cause during the course of the treatment as dead and those who were alive at the end of the treatment period as alive. I classified the survival outcome into two categories of dead or alive. The outcome of the analysis showed a Pearson chi-square statistics test value of 0.208 and a *p*-value of 0.649. The outcome of the cross-tabulation showed that

out of the 188 (46.77%) patients who were enrolled under the community model of care, 166 (88.3%) survived while 22 (11.7%) died before the end of the treatment period. Out of the 214 (53.23%) patients who were enrolled under the hospital-based model of care, 192 (89.7%) survived, while 22 (10.3%) died before the end of the treatment period. The *p*-value of 0.649 is higher than 0.05 hence the null hypothesis was not rejected. This result indicated that there is no sufficient evidence to establish that there is a difference in survival outcomes between patients who were enrolled on the hospital-based model of care and those managed in the community. The odds of surviving the MDR-TB treatment regimen when enrolled in the community relative to the hospital model of care were 0.865, approx. 1. This underscores the result of the hypothesis testing which indicates insufficient evidence to reject the null hypothesis that there is no difference in survival outcomes between patients enrolled in the two models of care. Table 6 shows the result of cross-tabulation of model of care and survival outcomes.

Table 6

*Association between Treatment Outcome Model and Survival Outcome*

| Survival outcome | Treatment model | | Total |
|---|---|---|---|
| | Community N (%) | Hospital N (%) | |
| Alive | 166 (88.3%) | 192 (89.7%) | 358 |
| Dead | 22 (11.7%) | 22 (10.3%) | 44 |
| Total | 188 | 214 | 402 |

$p$=0.649

**Research Question 4**

The fourth research question was as follows: Are demographic factors such as age, gender and marital status associated with poor treatment outcomes among MDR-TB patients in Nigeria? The null hypothesis was that there is no association between demographic factors such as age, gender, marital status and poor treatment outcomes among MDR-TB patients in Nigeria while the alternate hypothesis was that there is an association between demographic factors such as age, gender, marital status and poor treatment outcomes among MDR-TB patients in Nigeria. I analyzed age in its natural state as a continuous variable using logistics regression and I also recoded it into a categorical variable with the two categories, age equals or is less than 40 years and age is greater than 41 years. I recoded marital status into single and married; I recoded all those who were divorced, widowed, or separated as single and those who were married or

cohabitating as married. I recoded with the objective of capturing the essence of having a partner living in the household as the patient. I classified gender as males and females. I applied chi square analysis to determine the association between age and treatment outcome, marital status and treatment outcome, and gender and treatment outcome.

**Age and Treatment Outcome**

The result of the logistics regression analysis showed an odds ratio of 1.027 (95% C1: 1.006-1.049) at a *p*-value of 0.013 This *p*-value is less than 0.05 therefore the null hypothesis was rejected. Age is therefore a good predictor of the outcome of MDR-TB treatment. The older the MDR-TB patient, the higher the chances of having an unsuccessful treatment outcome and for every one-unit increase in age, the odds of having an unsuccessful treatment outcome increases by about 3%. The outcome of the chi-square analysis for the recoded age variable showed a Pearson chi-square statistics test value of 4.967 and a *p*-value of 0.026. The outcome of the cross-tabulation showed that out of the 297 (76.2%) patients who were aged 40 years and below, 248 (83.5%) had a successful treatment outcome while 49 (16.5%) had unsuccessful treatment outcome. Out of the 93 (23.8%) patients who were aged 41 years and above, 68 (73.1%) had successful treatment outcome while 25 (26.9%) had unsuccessful treatment outcome. The *p*-value of 0.026 is lower than 0.05 hence the null hypothesis was rejected. This result indicates that there is an association between age and treatment outcomes among MDR-TB patients. The odds of having a successful treatment when aged 40 years and lower relative to age 41 years and above is 1.861. This shows higher odds of having a successful treatment outcome for the younger age group, about 86% more than the

patients aged 41 years and above. The observed difference is statistically significant, and it is in consonance with the result of the logistics regression analysis. Table 7 shows the result of cross-tabulation of age and treatment outcomes.

Table 7

*Association between Age and Treatment Outcome*

| Treatment outcome | Age | | Total |
|---|---|---|---|
| | 1-40yrs N (%) | >=41yr N (%) | |
| Successful | 248 (83.5%) | 68 (73.1%) | 316 |
| Unsuccessful | 49 (16.5%) | 25 (26.9%) | 44 |
| Total | 297 | 93 | 390 |

$p$=0.026

**Gender and Treatment Outcome**

The outcome of the chi-square analysis showed a Pearson chi-square statistics test value of 0.186 and a *p*-value of 0.666. The outcome of the cross-tabulation showed that out of the 262 (65.7%) patients who are male, 215 (82.1%) had a successful treatment outcome while 47 (17.9%) had unsuccessful treatment outcome. Out of the 137 (34.3%) patients who are female, 110 (80.3%) had successful treatment outcome while 27 (19.7%) had unsuccessful treatment outcome. The *p*-value of 0.186 is higher than 0.05 hence the null hypothesis was not rejected. This result indicates that there is no sufficient evidence to establish that there is an association between gender and treatment outcomes

among MDR-TB patients. The odds of having a successful treatment when male relative to female is 1.123. This shows a slightly higher odd of having a successful treatment outcome for males, however, the observed difference is not statistically significant. Table 8 shows the result of cross-tabulation of gender and treatment outcomes.

Table 8

*Association between Gender and Treatment Outcome*

| Treatment outcome | Gender | | Total |
|---|---|---|---|
| | Female N (%) | Male N (%) | |
| Successful | 110 (80.3%) | 215 (82.1%) | 325 |
| Unsuccessful | 27 (19.7%) | 47 (17.9%) | 74 |
| Total | 137 | 262 | 399 |

*p = 0.186, N=399*

**Marital Status and Treatment Outcome**

The outcome of the chi-square analysis showed a Pearson chi-square statistics test value of 0.000 and a *p*-value of 0.993. The outcome of the cross-tabulation showed that out of the 214 (56.8%) patients who are married, 176 (82.2%) had a successful treatment outcome while 38 (17.8%) had unsuccessful treatment outcome. Out of the 163 (43.2%) patients who were single, 134 (82.2%) had successful treatment outcome while 29 (17.8%) had unsuccessful treatment outcome. The *p*-value of 0.993 is higher than 0.05, hence the null hypothesis was not rejected. This result indicates that there is no sufficient

evidence to establish that there is an association between marital status and treatment outcomes among MDR-TB patients. The odds of having a successful treatment when married relative to being single is 1.002. This shows similar odds of having a successful treatment outcome for the married and single patients. Similarly, when gender was adjusted by marital status, the odds of having an unsuccessful treatment outcome was similar for both single males and females with an odds ratio of 1.074 at a *p*-value of 0.8 which shows no statistical significance. Table 9 shows the result of cross-tabulation of marital status and treatment outcomes.

Table 9

*Association between Marital Status and Treatment Outcome*

| Treatment outcome | Marital status | | Total |
|---|---|---|---|
| | Married N (%) | Single N (%) | |
| Successful | 176 (82.2%) | 134 (82.2%) | 310 |
| Unsuccessful | 38 (17.8%) | 29 (17.8%) | 67 |
| Total | 214 | 163 | 377 |

*P=0.993 Note: N=377*

## Multivariate Analysis

I included all the independent variables tested at the bivariate level in a logistics regression model to determine the association between them and the dependent variable, which is treatment outcome. I determined the significance of the logistic regression model by reviewing the classification table, which displayed the percentage accuracy of the model. In addition, I used the Hosmer Lemeshow goodness of fit test to test the appropriateness of model. Both tests showed a fairly accurate model with a classification value of 81.9% and a Wald statistics value of 125.945 for the fully adjusted model that included all the independent variables. The independent variables included in the model were model of care, gender, marital status, age, and presence of HIV as a co-morbidity. The outcome of the logistics regression analysis showed that model of care and age were predictors of treatment outcomes. At the bivariate analysis, the association between model of care and treatment outcome was not statistically significant; however, after adjusting for age, gender, marital status, and the presence of HIV as a co-morbidity, model of care was found to be a predictor of treatment outcome. The result of the logistics regression showed that an odds ratio of 1.737 (95% C1: 1.004, 3.007) for patients enrolled in community having an unsuccessful treatment outcome relative to the patients managed in the hospital at a *p*-value of 0.048. This *p*-value is less than 0.05, hence the observed difference is not likely to be due to chance. This result suggests that patients managed in the community are 74% more likely to have an unsuccessful treatment than patients managed in the hospitals. For age, the result of the analysis showed an odds ratio of 1.948 (95% C1: 1.021, 3.716) for patients aged 41 years and

above to have an unsuccessful treatment outcome relative to the younger age category of 40 years and younger, at a *p*-value of 0.043. This result shows that patients 41years and above are 95% more likely to have an unsuccessful treatment outcome relative to patients aged 40 years and below. Marital status, gender, and presence of co-morbidity, specifically HIV, were not significantly associated with treatment outcome. Similarly, gender adjusted by marital status was not significantly associated with treatment outcome. Therefore, based on the findings of this study, married males were just as likely to have successful treatment outcomes for MDR-TB as their single counterparts and the same applied for the females. Table 10 shows the summary result of the fully adjusted logistics regression model.

Table 10

*Result of Multivariate Binary Logistics Regression Analysis*

| Description | B | S.E. | Wald | df | Sig. | aOR | 95% C.I. for OR | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Lower | Upper |
| Age | .667 | .330 | 4.089 | 1 | .043 | 1.948 | 1.021 | 3.716 |
| Marital status | -.201 | .302 | .444 | 1 | .505 | .818 | .452 | 1.478 |
| Gender | .139 | .292 | .228 | 1 | .633 | 1.149 | .649 | 2.035 |
| Presence of comorbidities (HIV) | -.158 | .496 | .102 | 1 | .750 | .854 | .323 | 2.255 |
| Treatment model | .552 | .280 | 3.896 | 1 | .048 | 1.737 | 1.004 | 3.007 |

*Model of care and age were predictors of treatment outcome with p-values less than 0.05. Reference categories are hospital model of care, age=/>40 years, male, single and HIV+.*

## Summary

In this section, I presented the results of the analysis of the MDR-TB patient level data, which included age, gender, marital status, presence of HIV as comorbidity, and model of care whether community or hospital-based as independent or predictor variables. Treatment outcome and survival outcomes were the dependent variables. At the bivariate level, I found only age to be associated with treatment outcome while at the multivariate level, I found model of care to be a predictor of treatment outcome after adjusting for gender, age, marital status, and presence of HIV as a comorbidity. The analysis showed the importance of age when managing MDR-TB patients and suggests that patients enrolled in communities may have a higher likelihood of having unsuccessful treatment when older.

In the next section of this dissertation, I will discuss the findings of my analysis with reference to similar published studies. I will apply the Health Belief Model to improve treatment adherence amongst MDR-TB patients.

Section 4: Application to Professional Practice and Implications for Social Change

## Introduction

The burden of TB has become a public health issue in countries such as China, India, and Nigeria, among others (World Health Organization [WHO], 2016). The huge burden of TB in these countries has made it pertinent to increase their respective capacities to manage MDR-TB patients. Nigeria has grappled with one of the highest burdens of MDR-TB, which has had a negative impact on the quality of life of those affected by the disease (Daniel & Osman, 2011). In light of this fact, the National TB program has adopted a complete community-based management of MDR-TB alongside the ambulatory model of care to increase the treatment capacity to manage MDR-TB patients. In the face of this expansion of treatment capacities, there has been limited empirical evidence to establish the effectiveness of the community-based model of care for MDR-TB patients in Nigeria. This study sought to demonstrate the effect of the model of care and existence of co-morbidities such as HIV on treatment outcomes among MDR-TB patients.

## Summary of Findings

A total of 402 MDR-TB patients were included in the analysis. There were 137 (34.3%) females and 262 (65.7%) males. This shows a preponderance of males that is in consonance with the gender distribution reported in the national prevalence survey conducted in 2012 and routine programmatic data. The distribution of the patients in terms of treatment model was fairly equal with 184 (46.8%) enrolled on the community model of care and 214 (53.2%) managed in the hospitals. The age group of 25–44 years

accounted for 61% (238 out of 390) of the sample population with known age, this formed the majority followed by the age group 15–24 years which formed 19.5% of the sample population with known age. The least represented age groups are seven to 14 years and 65 years and above which accounted for only 1.3% and 1.8% of the sample population respectively. The sample population also showed a fairly even distribution of marital status with 213 (56.5%) of the patients being married and 154 (40.8%) being single. Other categories for marital status include divorced patients (one, 0.3%), widowed (eight, 2.1%) and cohabitating but married (one, 0.3%). 356 (89.4%) of the patients were HIV negative while 42 (10.6%) were people living with HIV. The status of 4 of the patients was unknown.

In this study, I focused on investigating the effect of model of care on treatment outcome among MDR-TB patients. I also reviewed other factors that may affect treatment outcome such as age, gender, marital status, and presence of HIV as a comorbidity. At the bivariate level, I did not find model of care to be a predictor of treatment outcome as the difference observed between the two models in terms of treatment outcomes were not statistically significant. I found age to be significantly associated with treatment outcome at a *p*-value of 0.026. Patients 40 years and younger were found to be 1.86 times more likely to have a successful treatment outcome compared with patients aged 41 years and above. Presence of HIV as a comorbidity as well as marital status and gender were not significantly associated with treatment outcome. The outcome of the survival outcome analysis showed that model of care was not significantly associated with survival outcome (*p*-value=0.865). At the multivariate

level, age and model of care were found to be significantly associated with treatment outcomes. Age at a *p*-value of 0.043, is a predictor of treatment outcome with patients aged 41 years and above having 1.948 more odds of having an unsuccessful treatment outcome relative to patients aged 40 years and below. Model of care is a predictor of treatment outcome with patients enrolled in the community being 1.737 times more likely to have an unsuccessful treatment outcome than patients managed using the hospital-based approach (*p*-value of 0.048).

In this study, I addressed four key research questions, which are as follows.

RQ1: Is there an association between type of treatment model; hospital or complete community-based, and treatment outcome among MDR-TB patients in Nigeria?

RQ2: Are co-morbidities such as HIV associated with poor treatment outcomes among MDR-TB patients in Nigeria?

RQ3: Is type of treatment model associated with survival outcomes among MDR-TB patients in Nigeria?

RQ4: Are demographic factors such as age, gender, and marital status associated with treatment outcomes among MDR-TB patients in Nigeria?

## Interpretation of the Findings

### General Issues

There were more MDR-TB patients aged 25–44 years (61%) in the study population. More males than females were affected by MDR-TB based on the sample population, 65.7% While females were only 34.3%. This gender distribution suggests a male preponderance in the burden of MDR-TB. The percentage of the MDR-TB patients

who were HIV positive was 10.6%. In Nigeria, the proportion of TB patients with HIV comorbidity is 19.1% (Adejumo, Daniel, Otesanya, Adegbola, & Femi, 2017). This statistic suggests that while the country may have achieved great strides in reducing the burden of TB/HIV co-infection, the National TB Program may be missing a lot of TB cases among people living with HIV (Adejumo et al., 2017). The low detection rate among this group may not be unrelated to the difficulties that abound with TB diagnosis in people living with HIV. This is due to their poor immune response to the presence of the mycobacterium tuberculosis which often makes it difficult to detect the organism in their sputum, hence many of them present as smear negative TB (Adejumo et al., 2017). There are newer and more sensitive diagnostics now such as the TB-LAM which can detect TB in urine samples of people living with HIV (WHO, 2015c). This development along with the policy to commence antiretroviral therapy in all TB HIV co-infected patients may address the difficulties in diagnosing TB among this key population (Ministry of Health Nigeria, 2010).

The findings of this study suggest that MDR-TB patients with HIV co-morbidity were not particularly at risk of poorer treatment outcomes compared to their HIV negative counterparts. This can be explained by the fact that all MDR-TB patients with HIV co-morbidity are all placed on antiretroviral therapy in line with the national TB/HIV guidelines (Ministry of Health Nigeria, 2010).

**Treatment Model and Treatment Outcomes**

The result of the analysis investigating the relationship between model of care and treatment outcome showed that community model of care had a slightly higher proportion

of patients with unsuccessful treatment outcome (21.8%) compared to the hospital-based approach (16.8%). The result was however not statistically significant with a *p*-value of 0.205. At the multivariate level, the result was statistically significant at a *p*-value of 0.048 and an adjusted odds ratio of 1.737 (95% C1: 1.021, 3.716). This result suggests that the two models of care for managing MDR-TB patients in Nigeria, community and hospital may lead to similar treatment outcomes among MDR-TB patients. This is in agreement with Bassili et al. (2013)'s findings, which showed that community treatment model is an optimal model for treating MDR-TB patients. This finding also suggests that the National TB program in Nigeria has deployed the model effectively and addressed the challenges that are often associated with community model of care for MDR-TB. These challenges include difficulty in managing adverse drug reactions in the community and long distance to health facilities in case of complications, amongst others (Weiss et al., 2014).

Adjusting for age and marital status, the hospital model appeared to lead to higher rates of successful treatment outcomes than the community model. Higher proportion of the MDR-TB patients managed in the hospital (83.2%) had successful treatment outcome relative to the community model (78.2%). These similar treatment success rates among the two models of care corroborates the findings of Weiss et al. (2014) and Kalandrova et al. (2016) which indicated that community model of care for MDR-TB patients is comparable to the hospital-based model of care in terms of the treatment outcomes of the patients. Also, the Cox et al. (2014), Loveday et al. (2015), Williams et al. (2016), and Taneja (2017) found favorable treatment outcomes when MDR-TB patients were

managed in the community in countries like South Africa, Swaziland and China, among others.

This is, however, contrary to the findings of Oladimeji et al. (2014), in which the authors suggested that patients managed in the hospital may have better treatment compliance as indicated by the zero loss to follow up reported by the study. The design of the study was descriptive and did not compare treatment compliance between patients enrolled in the hospitals versus those managed in the community. The similar treatment outcomes seen for the two models of care underscores the support systems built into the community MDR-TB management program which includes the use of treatment supporters and the extensive social and psychosocial support provided to the MDR-TB patients by family members and loved ones (USAID TB CARE II, 2017). Managing MDR-TB patients in their natural environment as against the confinement of the hospital environment may have contributed to improved treatment outcomes. This corroborates the findings of Bieh et al. (2017), who highlighted the psychological trauma and health provider-related discrimination suffered by MDR-TB patients when managed using the hospital-based model of care.

Researchers have also found the community model of care to be more cost-effective than the hospital approach and all of these advantages of the community approach combine to make it a more practical option for managing MDR-TB patients (Fitzpatrick & Floyd, 2012; Musa et al., 2016). Also, the Loveday et al. (2014) suggested that there is a relationship between health system performance and treatment outcomes of patients managed using the decentralized or community model of care. Health systems

performance in this context were measured using a combination of factors which include availability of motivated health staff, uninterrupted supply of medications, effective laboratory systems to support treatment monitoring, integration of MDR-TB, and HIV services, among others. The TB program in Nigeria is supported by the Global Fund, USAID, and other partners; therefore, in spite of the inadequacies of the health systems in general, measures have been put in place by the supporting agencies to address key gaps in the health systems (NTLP, 2013). These include provision of financial support to MDR-TB patients to cover nutritional needs and transportation costs to the hospitals where needed, technical support to ensure optimal functionality of the logistics and supply chain of anti-TB medications in the country and support for regular quality assurance reviews of the laboratory systems, among others. With these mechanisms in place, it is safe to state that the community model of care showed similar treatment outcomes to the hospital-based approach because it was implemented in the context of a relatively effective health performance system.

**Age and Treatment Outcomes**

I found age to be significantly associated with treatment outcome. My analysis suggested that the older the patient, the more likely that patient was to have an unsuccessful treatment outcome. For every one unit of age, the likelihood of having an unsuccessful treatment outcome increased by 1.027. Based on the results, patients aged 41 years and above have higher odds of having an unsuccessful treatment outcome. This result supports Wai et al.'s (2017) and Li et al.'s (2016) findings that older age ranging

45–55 years and above was a predictor of poor treatment outcomes among MDR-TB patients.

This finding is incongruent with the finding of Skrahina et al. (2013), who found that younger age was associated with poor treatment outcome among MDR-TB patients at a *p*-value of 0.24. The result of this study is in line with existing evidence that old age is associated with poorer health outcomes (i.e. Deeks, Lombard, Michelmore, & Teede, 2009). Older patients may have other health conditions that predispose to poor treatment outcomes when managed for MDR-TB. These comorbidities may also lead to drug-to-drug interactions that may reduce the efficacy of the drugs used for managing MDR-TB. It was however not possible to investigate the effect of other comorbidities that may have resulted in poorer treatment outcomes among the older MDR-TB patients in this study.

The finding that old age is a predictor of poor treatment outcome has significant implications for the design and implementation of MDR-TB program in Nigeria. It is particularly important when making decisions on the model of care patients with which to manage MDR-TB patients. Policies and guidelines that are tailored to account for the vulnerability of the older patients when undergoing MDR-TB treatment should be developed. Specific support and age-sensitive program designs need to be instituted as a deliberate response of the National TB Program to the needs of the older MDR-TB patients.

**Gender and Treatment Outcomes**

I did not find any significant relationship between gender and treatment outcome. Male patients were just as likely to have successful treatment outcomes as their female

counterparts. This finding is similar to that of Patel et al. (2016), who found that there was no sufficient evidence to suggest an association between gender and treatment outcome. This is contrary to the finding of Skrahina et al. (2013), who found that the male gender was a predictor of poor treatment outcomes among MDR-TB patients at a *p*-value of 0.001.

The results of this study show a contrary finding to the general tendencies for men to have poorer health seeking behavior than women and for women to play the role of the healthcare gatekeepers in families (see Deeks et al., 2009; Ostlin, Eckermann, Mishra, Nkowane, & Wallstam, 2006). Also, there are biological differences between males and females that lead to differentials in health outcomes as measured using life expectancies, with women generally having longer life expectancies than their male counterparts (Vlassoff, 2007). Some have, however, argued that biological differences alone cannot account for the health disparities observed between males and females considering the fact that gender is constructed socially (Ostlin et al., 2006). Hence, social and economic factors also explain the gender-related difference observed in health (Ostlin et al., 2006). While many health interventions have been accused of being gender blind, it appears that there is no sufficient evidence for gender-related disparities in treatment outcomes among the MDR-TB patients I investigated in this study. The similarity in treatment outcomes observed between the male and female MDR-TB patients in this study may be due to confounding variables such as the quality of psychosocial support available to patients as well as the use of treatment supporters which in the case of males may be mostly females. Female treatment supporters may have assisted the male patients to comply to treatment

and this may have masked the poor health seeking behavior that is often associated with the male gender. It is, however, important to explore the possibilities of such gender-related inequities in outcomes in future studies, with particular reference to treatment compliance.

**Marital Status and Treatment Outcomes**

The study results did not show any significant relationship between marital status and treatment outcome. Married patients were just as likely to have successful treatment outcomes as their unmarried counterparts. This was similar to Patel et al.'s (2016) findings that no statistically significant relationship between marital status and treatment outcomes existed among MDR-TB patients in India. While Lund (2006) suggested that living alone was associated with poorer health outcomes, the possibilities of other external factors such as social and economic factors confounding the observed association have not been fully explored. However, there are reasons to explain the better health outcomes in persons cohabitating with partners, including the emotional satisfaction of having someone to turn to in times of ill-health and psychosocial support provided by partners that may improve treatment compliance (Robards, Evandrou, Falkingham, & Vlachantoni, 2012). It is important to note that the quality of such living arrangements and relationships also matter in terms of the effect on health and in this case, treatment outcome of MDR-TB patients. Partners may not be supportive of treatment. In extreme cases, gender and domestic violence may even worsen treatment compliance thereby leading to poor treatment outcomes (Robards et al., 2012). In light of this fact, it is important to explore the impact of marital relationships and living

arrangements on treatment outcomes among MDR-TB patients while taking into account factors such as quality of relationship, economic situation, religion and the presence of other social networks and support systems.

**Presence of HIV as a Comorbid Condition and Treatment Outcomes**

The study findings did not show any significant relationship between HIV comorbidity and treatment outcome. People living with HIV patients were just as likely to have successful treatment outcomes as those HIV negative. These findings corroborate the findings of Satti et al. (2012) that effective management of HIV with the use of antiretroviral therapy (ART) resulted in similar treatment outcomes among co-infected and HIV negative patients. The result of this study is however contrary to the finding of Skrahina et al. (2013) that presence of HIV was a predictor of unsuccessful treatment outcomes. Aibana et al. (2017) and Kiliiman & Altraja (2009) similarly suggested that HIV comorbidity and not being on ART were associated with poor treatment outcomes among MDR-TB patients. The findings of this study suggest that the National TB program may not be doing so badly when it comes to managing TB/HIV co-infected patients and the adoption of the policy to place all TB/HIV co-infected patients on ART in 2010 may have impacted positively on the treatment outcomes among MDR-TB patients as suggested by the findings of this study (Ministry of Health Nigeria, 2010).

**Model of Care and Survival Outcomes**

The findings of the study show that model of care is not significantly associated with survival outcomes; therefore, patients enrolled in the community have an equal chance of surviving the MDR-TB treatment regimen as patients managed in the hospital.

This finding corroborates the findings of Heller et al. (2010), Ho et al. (2017), and Taneja (2017), all of whom indicated favorable survival outcomes among patients managed in the community. However, the results of this study are incongruent with the findings of Loveday et al. (2015), who found lower survival rates among patients managed in the community. The reasons for the observed similarity in survival outcomes are similar with those stated for model of care and treatment outcome. Effective decentralization of MDR-TB care using the community model of care appears to influence survival outcomes positively because patients are managed in their natural environment and have access to psychosocial support from family members and other social networks (Loveday et al., 2015). Also, as stated by Bieh et al. (2017), health worker-related discrimination of MDR-TB patients may be associated with poor treatment outcomes. This negative external factor is mitigated when patients are managed in the community and may be responsible for the optimal survival outcomes in the community. Reducing the indirect costs related to hospital admissions may reduce the catastrophic costs associated with MDR-TB treatment thereby leading to lower stress levels for the patients (Fitzpatrick & Floyd, 2012). Additionally, while patients confined in the hospitals may be expected to have lower rates of follow up compared to those managed in the community, it appears that the National TB program's provision of psychosocial support, through treatment supporters, may have mitigated the risk of treatment default associated with community or home-based care in general. These treatment supporters are often family members or healthcare workers who are trained to support the patient psychologically throughout the treatment period.

**Analysis and Interpretation of Findings in Context of HBM**

The HBM was originally developed to improve uptake of tuberculosis screening services, therefore it has the essential characteristics to address the issues related to social stigma and other factors that are barriers to the uptake of TB services. HBM is applicable for improving MDR-TB treatment outcomes particularly with regards to treatment adherence. The modifying factors of HBM in the context of MDR-TB management in this study include age, gender and marital status. These factors may have some level of influence on the way the patients perceive their susceptibility to an unsuccessful treatment outcome if treatment compliance is not achieved. Age greater than 40 years was found to be significantly associated with unsuccessful treatment outcome. It is however not clear from this study if the poorer treatment outcomes seen among patients older than 40 years is related to poor treatment adherence. Marital status was not associated with treatment outcomes, therefore single persons, the widowed and others who may not live with civil partners or "spouses" were not more likely to comply to MDR-TB treatment compared to their married counterparts. However, treatment adherence using loss to follow up as a proxy appears to be better among the married population. This may be explained by the fact that the presence of a significant other or a civil partner o may provide the psychosocial support needed by the patients to adhere to MDR-TB treatment especially if the partner is empowered to support treatment. Gender was also found not to be significantly associated with treatment outcomes, however there was a higher proportion of loss to follow up among males. This is in consonance with

existing evidence which suggests that males have poorer health seeking behavior which may also reflect in the way they comply to treatment regimens (Vlassoff, 2007).

In addition, the findings of the study showed that 28 (7%) of the patients were lost to follow up with loss to follow up being used a proxy to describe treatment non-compliance among the MDR-TB patients. Of these, the greater proportion were the patients in the community model of care relative to the hospital model. The highest rate of loss to follow up was seen amongst the patients aged 55 years and above and the lowest rate was seen among patients aged 7−14 years. Males were more likely to be lost to follow up than females. The proportion of patients that were lost to follow up was also different for the married patients, with married patients having a marginally lower proportion compared to the single patients. For HIV status, people living with HIV have higher proportion of loss to follow up compared to HIV negative patients. This result is similar to the finding of a study conducted in Nigeria which suggests that loss to follow up was associated with being HIV co-infected (Ifebunandu & Ukwaja, 2012). The explanation provided for this is the pill burden of taking ARVs as well as anti-TB medications, side effects from both medications as well as the need to access care for both diseases in different health facilities (Ifebunandu & Ukwaja, 2012). These are potential barriers to treatment adherence for MDR-TB patients with HIV as a co-morbidity. A similar study stated that with adequate counselling, TB patients with HIV co-infection may have improved treatment adherence (Amuha, Kutyabami, Kitutu, Odoi-adome, & Kalyango, 2009). It is therefore important that MDR-TB programs include counselling sessions for patients with HIV co-morbidity to address issues such as pill

burden, side effects of the medications and the stress associated with seeking care for both diseases, among others.

These findings may be applied to inform the health education programs to address the factors that will impact negatively on treatment adherence. Also, based on the finding that age is a predictor of treatment outcomes, it is important to develop campaigns and health education programs that are age-sensitive. These health education programs should target the characteristics of the older population that may act as barriers to treatment compliance. Similarly, the health education programs will be informed by the core constructs of HBM which include self-efficacy to comply to MDR-TB treatment, personal perception of risk, perceived severity of MDR-TB, perceived threat of having unsuccessful treatment outcomes when treatment adherence is not achieved and on the other side, the perception of health benefits if treatment adherence is achieved. I will apply HBM to emphasize the negative consequences of poor treatment adherence and to develop messages that are targeted toward addressing the probable factors that may likely lead to poor treatment compliance. According to the findings of this study, these include being single, being male, older age, enrolled on community model of care and having a positive HIV status.

The behavioral patterns that are related to poor treatment adherence may also be easy to decipher as well as the barriers to treatment adherence based on the characteristics of the patients. Family support from a close partner may be responsible for the better adherence seen in the married group relative to the single patients, however, support systems can be tailored to address this social need. The MDR-TB program currently

employs the use of treatment supporters and this can be emphasized particularly for the single patients. Also, this may inform the need to prioritize family members as treatment supporters and to design special health education programs for them such that they are also aware of the benefits of treatment adherence and the negative consequences of not adhering to the MDR-TB treatment regimen.

A study identified key barriers to treatment adherence among TB patients in general across several settings including Nigeria, they include smoking, male gender, feeling better, long distance to health facility, social stigma, lack of social support, alcohol use, being on ARV, lack of knowledge among others (Tola, Shojaeizadeh, & Garmaroudi, 2015). Based on the findings of this study, it is critical that potential barriers to treatment adherence are overcome by designing interventions that are targeted at the patients that are more likely not to adhere to treatment. The focus of the interventions should be to heighten their perceived personal risk of unsuccessful treatment outcome by describing the negative consequences of non-compliance and emphasizing the benefit of compliance which is having a successful treatment outcome. The threat-based approach can be used during counselling sessions by sharing the stories of patients who died due to poor treatment compliance. Considering that a key construct of the HBM is the individual's self-efficacy which in this case describes the MDR-TB patient's innate ability to comply to treatment, emphasis should be placed on building the patient's capacity to address both individual and environmental factors that may deter treatment adherence. Hence, with due consideration to the model of care a patient is enrolled in, adequate health education should be provided to ensure treatment adherence. Similarly,

such health education packages should be tailored to address individual patient's needs and risk factors for poor treatment compliance.

## Limitations of the Study

For this study, I employed a retrospective cohort design; hence, it was difficult to collect information on potential confounding factors that may have led to the associations or lack thereof, that I observed in the results of the study. Similarly, issues with data completeness and accuracy are usually not easily addressed when using a retrospective cohort design; hence, for this study, I excluded incomplete records from the analysis. Also, it was difficult to differentiate patients who died as a result of MDR-TB from those who died from other causes. In addition, I used a quantitative approach without the qualitative method, meaning I was not able to explore the experiences and perspectives of the patients about the treatment and how this may have impacted the observed treatment outcomes. In my investigation, I focused on the relationship between model of care and treatment outcomes, limiting models of care to just community-based and ambulatory models, which may not have accounted for variants that may exist such as some patients that may have to be admitted in hospitals in the course of their treatment due to adverse drug reactions or other causes of illness while being classified as patients managed in the community.

Existence of co-morbidities only included HIV. I did not investigate the effect of having diabetes as a co-morbidity because it was difficult to retrieve the diabetes status of the patients as diabetes tests and results are not included in the routine data collected on the National TB program. I also chose not to consider all other health conditions such as

hypertension, heart diseases, malaria, typhoid and other common health conditions in the country due to this gap in routine data collection on the program. While the scope of the study did not cover these illnesses, they may, nonetheless, be associated with the observed treatment outcomes. I did not investigate health workers' attitude and the kind of social support provided to the patients in this study in spite of the fact that these factors may have effect on the observed treatment outcomes. I included only patients managed in Nigeria between 2013 and 2014 in this study. This is because the community-based model of care became fully operational in Nigeria in 2013 and the cohort analysis of patients beyond 2014 was not readily available as at the time this study was conducted.

## Recommendations

The findings of this survey provided insight into how model of care, demographic factors such age and gender, marital status and HIV comorbidity affect treatment outcomes among MDR-TB patients. Based on the results of the study, community model of MDR-TB treatment compared favorably with the hospital-based approach; hence, I recommend a rapid scale up of the community model in states with high burden of TB to meet the high demand for MDR-TB. Older and other high risk patients may be considered strictly for the hospital-based model of care.

The findings of this study were based on the analysis of secondary data; I was unable to provide the reasons behind the associations or lack thereof that I observed between the variables I investigated in relation to MDR-TB treatment outcomes. Against this backdrop, qualitative studies using in-depth interviews to explore patients' perspectives on their treatment experience for both the community and the hospital-based

model of care are essential for many reasons. Key among these reasons is the need to better understand the contextual factors relating to health worker's attitude, direct and indirect costs associated with MDR-TB treatment and how they impact on the patients' lives, and more importantly how patients are affected by the adverse events associated with MDR-TB treatment and how they navigate the difficult period of undergoing MDR-TB treatment. Also, it is critical to understand the reasons behind the patterns of treatment default observed in this study and why the behavior may be modified by age, gender, marital status, model of care and presence of HIV comorbidity. A deeper understanding of the reasons for non-adherence to treatment will provide the insights needed to design effective programmatic interventions that can address the barriers to treatment compliance. Overall, more qualitative evidence is needed to refine existing policies and guidelines for managing MDR-TB in Nigeria toward a more patient-centered approach to treatment.

This study should provide the baseline for further explorative investigation to understand the contextual factors that affect MDR-TB treatment outcomes as well as the pathway between treatment enrollment and completion and how they interface with individual, organizational and societal factors that modify behaviors during the treatment period. Furthermore, in line with the findings of this study, it is critical to further investigate the association between age and treatment outcomes as well as how the presence of other comorbidities such as diabetes, hypertension and other morbidities associated with old age may have confounded the association between age and treatment outcomes.

## Implication for Professional Practice and Social Change

The findings of this study show that management of MDR-TB patients in communities results in similar treatment outcomes as the hospital-based approach. This study provides the empirical evidence needed to support the rapid expansion of the community model of care for MDR-TB management in Nigeria

### Professional Practice

The findings of this study show the need for continuous review of programmatic responses to disease control especially when managing difficult diseases such as MDR-TB. It is important that policies are backed by local empirical evidence that captures the country-level experience and context. This will support the implementation of effective health interventions that are tailored toward addressing factors that may affect the quality of treatment available to MDR-TB patients. I based this study on the analysis of secondary data collected as part of the routine data collected through the M&E system of the National TB program. In line with this, it is essential that programmatic data that are collected routinely are reviewed quantitatively to identify key factors that may be associated with quality of treatment and patients' outcome. This approach provides a cost-effective way to synthesize the evidence needed to improve the way health programs, which in this context is MDR-TB management, are implemented.

Similarly, the findings of this study showed that patients managed in the hospital have similar treatment outcomes as those managed in the community. This is an indication that the National TB program has effectively deployed the newer model of care which is the community-based approach to manage MDR-TB patients. There are

many programmatic challenges that abound with managing MDR-TB patients in the community. They include adverse drug events and reactions to the toxic second line drugs for managing MDR-TB, ensuring optimal infection control practices when patients are managed in their homes, among others. Considering all these challenges, the similarity in treatment success rates for the two models of care is a good development and provides the empirical evidence needed to support the rapid scale-up of community management of MDR-TB patients. It is, however, critical, when considering the patient-centered approach to TB management, to ensure that the selection of the model of care to be employed per patient is given careful consideration with regards to living circumstances, age, other co-morbidities, among other factors.

**Positive Social Change**

The findings of this study showed that while treatment outcomes between the two models of care may be similar, old age is a predisposing factor for poor treatment outcome. In line with the international standard for TB care which emphasizes a patient-centered approach to TB management, it is critical that this factor is given full consideration when designing and implementing MDR-TB care. MDR-TB programs in Nigeria should therefore be robust enough to accommodate the peculiar issues associated with old age that may predispose to poor treatments. Similarly, this study can form the basis for developing a special treatment package for patients aged above 40 years. This package may include health education, social support from family and non-family members as well as counseling sessions with health workers to ensure treatment adherence and early identification of adverse drug events. Other implications for social

change may be the need to review the existing guidelines and policies for managing MDR-TB patients in line with the findings of this study. Such changes may include the need for age-specific management approaches. Similarly, rapid and urgent scale up of community model of care in all the states in the country is recommended to address the gap in MDR-TB case detection and enrollment for care. By ensuring that all MDR-TB patients have access to immediate care, the country stands a better chance to curb the spread of primary MDR-TB infection and to reduce the high morbidity and mortality rates associated with the disease.

The findings of this study may also be useful toward developing effective health education programs that are tailored toward addressing the probable factors that may predispose to non-adherence at the individual and societal levels.

## Conclusion

The findings of this study suggest that the outcomes of treatment for patients managed in the community are fairly similar to those managed in a hospital. Also, age was shown to be significantly associated with treatment outcomes with older patients having more likelihood of a poor treatment outcome than their younger counterparts. These key findings provide the empirical evidence needed to rapidly and urgently expand the community-based model of MDR-TB care in Nigeria. Considering that the health systems of the country are already overwhelmed with other infectious diseases such as HIV/AIDs and other non-communicable diseases, the expansion of community model of care may reduce the burden MDR-TB places on the health facilities. Also, community model of care has been found to be a cost-effective approach to managing MDR-TB care;

hence, deploying more patients for community management after a careful review of their health conditions and social support systems may free up costs that can be used to treat more MDR-TB patients and, possibly, address other health issues. Summarily, all the findings of this study should inform policy changes that will ultimately improve the quality of care provided to MDR-TB patients in Nigeria.

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