

Adherence to Tuberculosis treatment: challenges and interventions to improve treatment outcomes among patients in the Brong Ahafo Region of Ghana

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55th Master of Science in Public Health/International Course in Health Development

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Adherence to Tuberculosis treatment: challenges and interventions to improve treatment outcomes among patients in the Brong Ahafo Region of Ghana

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

By:

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Declaration:

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The thesis "**Adherence to Tuberculosis treatment: challenges and interventions to improve treatment outcomes among patients in the Brong Ahafo Region of Ghana**" is my own work.

A handwritten signature in black ink, appearing to be 'D. Konka', written over a horizontal line.

Signature:

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Dedication

I dedicate this study to the Konka family especially my lovely wife (Ms. Martha Akua Dansowaa Nimako) and kids (Lois Awinboya Konka and Nathaniel Adabere Konka Jnr) for their moral support, prayers, and sacrifices for me during this long period. I love you so much and God richly blesses you all.

List of abbreviations

TB	Tuberculosis
GHS	Ghana Health Service
CHPS	Community-Based Health Planning and Services
BAR	Brong Ahafo Region
WHO	World Health Organization
NTP	National Tuberculosis Programme
DANIDA	Danish International Development Agency
GF	Global Fund
MDR-TB	Multi-Drug Resistant Tuberculosis
D/RHMT	District/Regional Health management Team
HIV	Human Immune Virus
DOTS	Directly Observed Treatment Short-Course
VU	Vrije University
MoH	Ministry of Health
ART	Anti-Retroviral Therapy
LTFU	Lost to Follow-Up
HRH	Human Resource for Health
GDF	Global Drugs Facility
EWS	Early Warning Systems
LMIS	Logistics Management Information Systems
HTC	HIV Testing and Counseling
VOT	Video Observation Technology
SMS	Short messaging Service
CBDOTS	Community-Based DOTS
HBDOTS	Hospital-Based DOTS
RHD	Regional Health Directorate
CHWs	Community Health Workers

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Glossary

Lost to follow-upⁱ- is a TB patient who did not begin TB treatment or interrupts treatment for two or more consecutive months (1-4).

Directly Observed Treatment Short-Course (DOTS)- is a program whereby a person is given specific training assist by supervising a TB patient to take their daily TB medication at the agreed time, dose and duration (1).

A treatment supporter-is a person chosen by both a TB patient and a health worker to assist the client to complete their treatment by watching him/her take the medication regularly on time throughout the treatment duration (1).

Tuberculosis (TB)- is a disease, which affects primarily the lungs and occasionally other parts of the body, and caused by acid-fast bacilli, called Mycobacterium tuberculosis (1,5).

Adherence to TB treatment-is the ability and willingness of a TB client to abide by an agreed treatment schedule, duration, and appointments between him/her and the clinician (6,7).

Completed treatment-refers to a TB client who has taken all required anti-TB medication at the right time, dose and duration in the absence of bacteriological confirmation or culture at the last month of treatment (4).

Died-a TB patient who dies out of any reason during or before starting the TB treatment (3).

Cured- a pulmonary TB patient confirmed bacteriologically at the start of treatment who became smear or culture negative at the end of treatment or at least on one previous occasion (4).

Treatment success- is the sum of total cases registered for a period that completed treatment plus those that are cured (4).

ⁱ This is a change in practice, which used to be called Default.

ⁱⁱ Poor means the people cannot afford their basic needs like food and other items.

ⁱⁱⁱ The various religions are practiced differently across the whole region

Abstract

Background: Globally, failure in the TB program is largely due to poor adherence to medication. TB treatment success rates in the Brong Ahafo Region (BAR) are below the World Health Organization target of at least 90%, with emerging MDR-TB, which could be due to poor compliance. Death rates, treatment failures, and lost-to-follow-up are worrying. Levels of TB medication adherence challenges in the BAR are unknown.

Objectives: This study sought to identify factors influencing TB medication adherence in the BAR and interventions to promote optimal adherence.

Methodology: The study employed a literature review. The conceptual framework by Roura et al. 2009 was adapted and used for this study.

Findings: The study found that stigma, and discrimination, financial challenges, forgetfulness to take medication, and poor knowledge of TB and its treatment are key factors affecting medication adherence. Suggested evidence-based interventions to address the challenges identified included the use of treatment supporters, psychological counseling, provision of enablers, and using Short Messaging Service as reminders.

Conclusions: Factors such as stigma, and discrimination, poor knowledge on TB and its treatment, and forgetfulness are key factors likely to influence adherence in the BAR, as well as effective interventions which have been implemented elsewhere that could be adopted by the NTP to improve TB medication adherence in the BAR were highlighted.

Recommendations: Developing and promoting enabling environment for TB clients to promote adherence, reduce stigma, and also piloting a package of interventions by the NTP is encouraged.

Keywords: Adherence, TB medication, barriers, facilitators, Ghana.

Word count: 12,921

Introduction

My interest in the TB program dates back to my college level where I was introduced to disease control and prevention methods with a focus on the prevention of communicable diseases. In my first assignment in my first district, I was made a TB coordinator with duties such as liaising with the facilities to find and treat TB patients, carry out contact tracing and investigations as well as requesting for medicines from the regional level for such patients. All these experiences, coupled with my other duties, propelled me to the position of acting Director of health services. I have met many clients who found difficulty completing the TB treatment. Many clients have died in the process including some of our Community-Based Surveillance Volunteers (CBSVs) who contracted the disease. This has reinforced my interest to undertake this study in identifying the challenges those TB clients go through during treatment and review modern and innovative interventions and recommend to stakeholders to implement measures that will help them adhere to the treatment to have a successful treatment outcome.

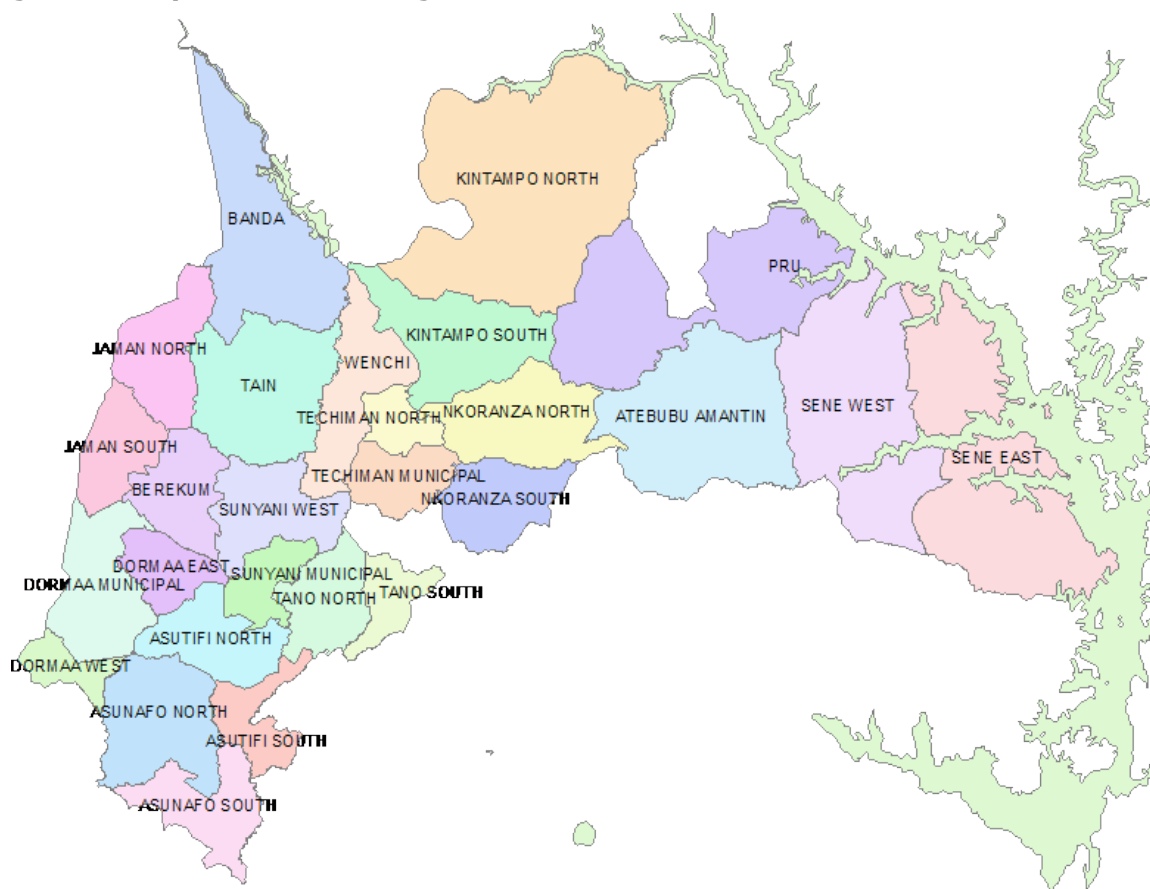
My name is Daniel Konka, a Senior Public Health Officer from the Brong Ahafo Region (BAR), Ghana, and a proud member of the 55th ICHD/MPH 2018-2019. My professional background is disease control and prevention and has been working with the Ghana Health Service since 2002. This study is organized into five main chapters; chapter one talks about the background of the study area as well as a brief of Ghana's health systems and how they are organized. Chapter two explains the issue to be dealt with, as well as the methods that were employed for the thesis. Factors that influence adherence and their innovative interventions cover the results section under chapter three. Chapter four combines the discussion segment as well as major conclusions arising from the various chapters. The final chapter concludes with some recommendations for specific stakeholders to improve TB medication adherence in the BAR.

CHAPTER ONE: BACKGROUND OF BRONG AHAFO REGION (BAR)

1.1 Profile and socio-economic characteristics

The BAR was created in 1959, covering 16.6% of the total surface area of Ghana (8). It's the second-largest region with a 2017 population of 2.7 million. It is made up of 27 Municipals, Metropolitans and District Assemblies (8). Farming is the major occupation with the majority engaged in the production of yams, maize, cassava, and cocoyam, with one of the three largest cocoa production towns in Ghana located there. Few people engage in mining, quarrying, manufacturing, and construction (8). According to the Ghana Statistical Service, the BAR is the 4th poorestⁱⁱ region in the country in 2014 (9) and this has a direct and indirect implication on access to health.

Figure 1: Map of BAR showing various districts.



Source: BAR Health Directorate annual report for 2017 (8).

1.2 Religion and Culture

The predominant ethnic groups are Akan (62.7%), Mole-Dagbon (15.4) and Grusi (4.2%). In terms of religionⁱⁱⁱ, Christianity (70.8%) has the largest followers, followed by Islam (16.1%) and no religion (7.8%) (8). The system of inheritance depends on the type of ethnic group; mostly the Akan practices matrilineal system, whilst the northern part practices the patrilineal system. Polygamy is widely practiced in the region predominantly among the Muslims (8).

ⁱⁱ Poor means the people cannot afford their basic needs like food and other items.

ⁱⁱⁱ The various religions are practiced differently across the whole region

1.3 Education

Education forms a crucial aspect in shaping the value of manpower, as such; educational levels reflect some extent the socio-economic development of a nation or community. Unfortunately, education in the BAR remains low, as 48.5% of the population aged 15 years and older is not literate^{iv}. In terms of having basic education^v, women constitute 16.4% whilst men form 11.4% (10).

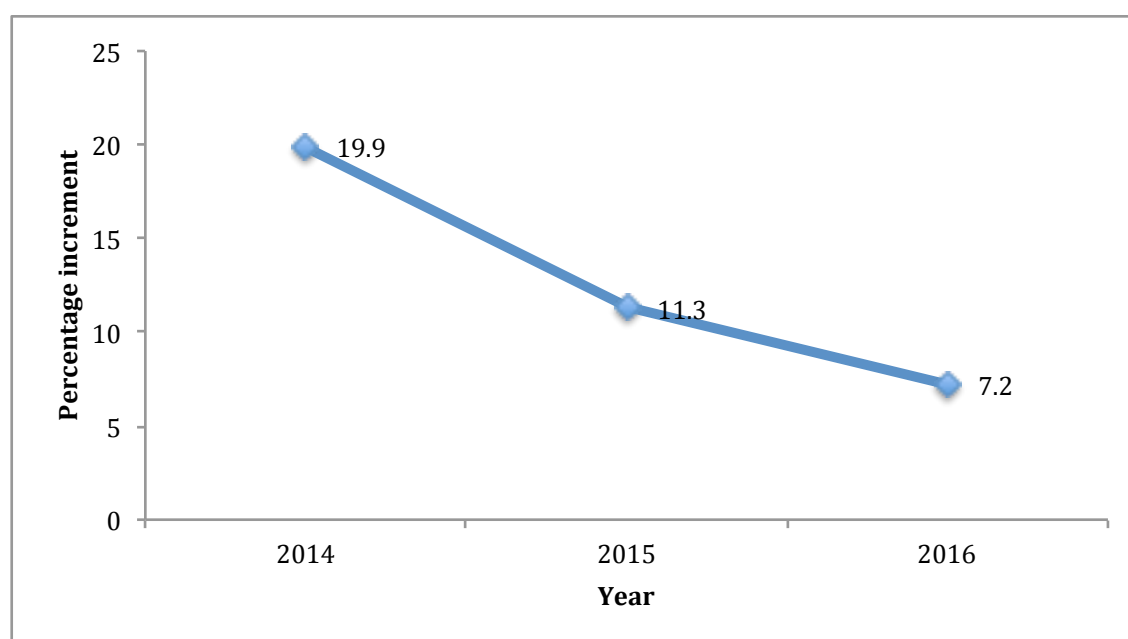
1.4. Health services in the BAR

Health services in the region are organized in the context of the national hierarchy (appendix 1), with both preventive and curative services provided (11). There were a total of 690 health facilities in 2017 made up of 29 hospitals, 83 Health Centers, 43 private Maternity Homes, 423 Community-Based Health Planning and Services (CHPS) zones and 112 clinics (8). The only Regional Hospital serves as a referral facility in the region, and nine districts do not have Hospitals (8).

1.5 Human Resource for Health (HRH)

Ghana is witnessing a gradual decline in its percentage of human resource increments over the years. The doctor to population ratio, however, increased from 1/10,423 in 2010 to 1/8,481 in 2016 (12). The BAR has a total workforce of 6,784 with a doctor-population ratio of 1:13,753 for 2017 (8), which makes it one of the poorly resourced regions in terms of human resource, with the distribution skewed towards the southern part of Ghana (12). According to the Integrated Personnel and Payroll Database, Ghana has a total of 102,019 health staff of all cadres as of 2016; representing a 7.2% increase. The annual workforce increment is shown below.

Figure 2: Total workforce increment (%) in Ghana, 2014-2016.



Source: Ghana Health Service (GHS) 2016 annual report (13).

^{iv} Literate mean people above 15 years old who can read and write.

^v Basic education means having attended a primary school.

1.6 Tuberculosis (TB) Control Activities in the BAR

All districts in BAR have functional TB coordinating units in their management structure (8). An analysis of TB microscopic centers shows that only 38 (5.5%) of the total facilities have functional laboratories that carry out TB microscopy, and the problem is worsened by the few qualified laboratory personnel in the region (8). The region recorded a TB case notification rate of 34.4% for 2017, which is a marginal increase over the 2016 figure of 33.5%. This low case detection rate could be attributable to a lack of qualified staff and proper diagnostic equipment in most of the districts and facilities (8). Additionally, the BAR could not achieve the WHO recommended treatment success rate of 90%, and treatment failures, lost-to-follow-up, and death rates are still a worry in the region (8).

In BAR, all TB cases are diagnosed at health facilities with functional laboratories^{vi}. Cases are then assigned a treatment supporter to supervise the daily treatment at home at the community level. The nearest health facility staff supervises them, and they visit the DOTS center monthly for refills and other routine activities, and there are no special opening hours for TB clients in BAR (8).

^{vi} Facilities with equipment and laboratory personnel that can do TB microcopy

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

2.1 Problem statement

Tuberculosis is an airborne infection caused by the bacilli *Mycobacterium tuberculosis*. The lungs and other parts of the body are affected. Globally, 1.7 billion people were infected in 2017 and persist as a global health problem. There were 1,323,450 cases with 21 deaths per 100,000 populations in 2017 and fueled by the HIV epidemic (5). In Ghana, the notification rate was 54/100,000 populations in 2016 and places much economic burden on the individual, family, community and the nation at large (13). This is about a third and less than the estimated population having the disease, which then means the burden is even much bigger.

The World Health Organization (WHO) has introduced a new strategy to end TB as the Sustainable Development Goals end in 2030. It has three pillars; integrated, patient-focused TB care and prevention, bold strategies, systems to provide support, intensify research and innovation (14). This aims at attaining zero deaths, diseases, and suffering due to TB. The National TB Program (NTP) in Ghana, however, adopted and attained 100% DOTS coverage in 2005 (15).

The WHO defines adherence as "the extent to which a person's behavior-taking medications, following a diet, and/or executing lifestyle changes, corresponds with recommendations from healthcare provider" (6), and this encompasses just taking prescribed pharmaceuticals. Jin J et al (7) also noted that adherence to TB regimen is about the ability and the readiness to abide by the agreed therapeutic regimen.

Globally, there is no golden way for measuring compliance to TB medication; however, some studies look at it in two ways; by directly determining drug levels in blood or drug metabolite levels in urine. This is reliable but expensive and not suitable for the routine TB program, or indirectly by patient's self-report of having taken the pills; by pill count and also when they stick to appointments, though there are limitations (16).

Ghana's adherence strategy currently involves the use of the DOTS under Community-Based Treatment Care. Under this, treatment supporters are chosen together by the health worker and the TB client to monitor their daily doses of treatment at the community level and supervised by the nearest health facility staff (17). WHO targets a TB adherence rate of 90% (14), but a qualitative study conducted by Salify Y et al in 2016 in Ghana recorded an adherence rate of 75% (18). Another cross-sectional study in 2015 revealed a 63% adherence rate among previously treated TB patients (19), but the limitation of this study is that adherence among TB clients using treatment supporters was not stated.

Some studies have noted adherence to the TB regimen as a global problem especially in developing countries where HIV is fuelling the epidemic (5), and the contributing factors as noted include lack of pre-treatment counseling, ignorance about the disease, long distances to treatment centers, not having treatment supporter, and financial constraint (20–23).

2.2 Justification

Failure in the TB program is attributed to poor adherence to therapy in developed and underdeveloped countries including Ghana (24).

Adherence with effective treatment rapidly makes previously infectious patient non-infectious. On the other hand, non-adherence may lead to a prolonged illness with late sputum conversion, to treatment failure or death. Such prolonged treatments result in

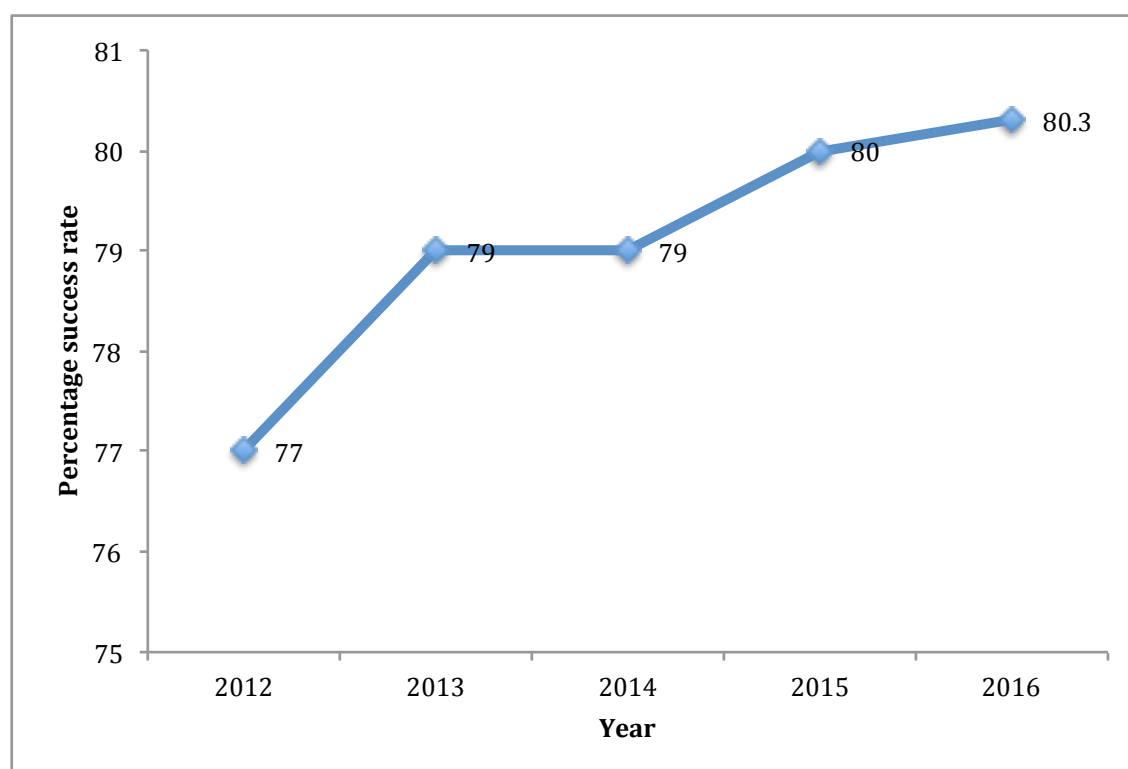
continued transmission in the community. Non-adherence can also lead to persistent and the resurgence of TB, and the development or intensification of drug resistance TB, which is one of the possible risks of incomplete treatment, thereby leading to increased cost to the TB program (25,26).

Multi-drug resistant TB (MDR-TB) is increasing globally, and in Ghana, is estimated to be 0.9% of all new TB cases and 14% of retreatment cases in 2010, and that has increased to 1.5% and 17% respectively in 2017 (27), and all this could be attributable to poor adherence to treatment, thereby representing a significant threat to the NTP's control efforts (28).

Irregular or incomplete treatment and treatment interruptions are a problem in Ghana. Dodor et al recorded a default rate of 13.9% in a study among TB patients in Eastern Ghana in 2001 (20). Even though treatment success rates have improved in the country, death rates are still worrying, with TB and HIV together accounting for 7% of all deaths (29). Also, despite NTP's efforts in ensuring effective DOTS strategy in the country, failure rates have remained about 2% since 2007 (30).

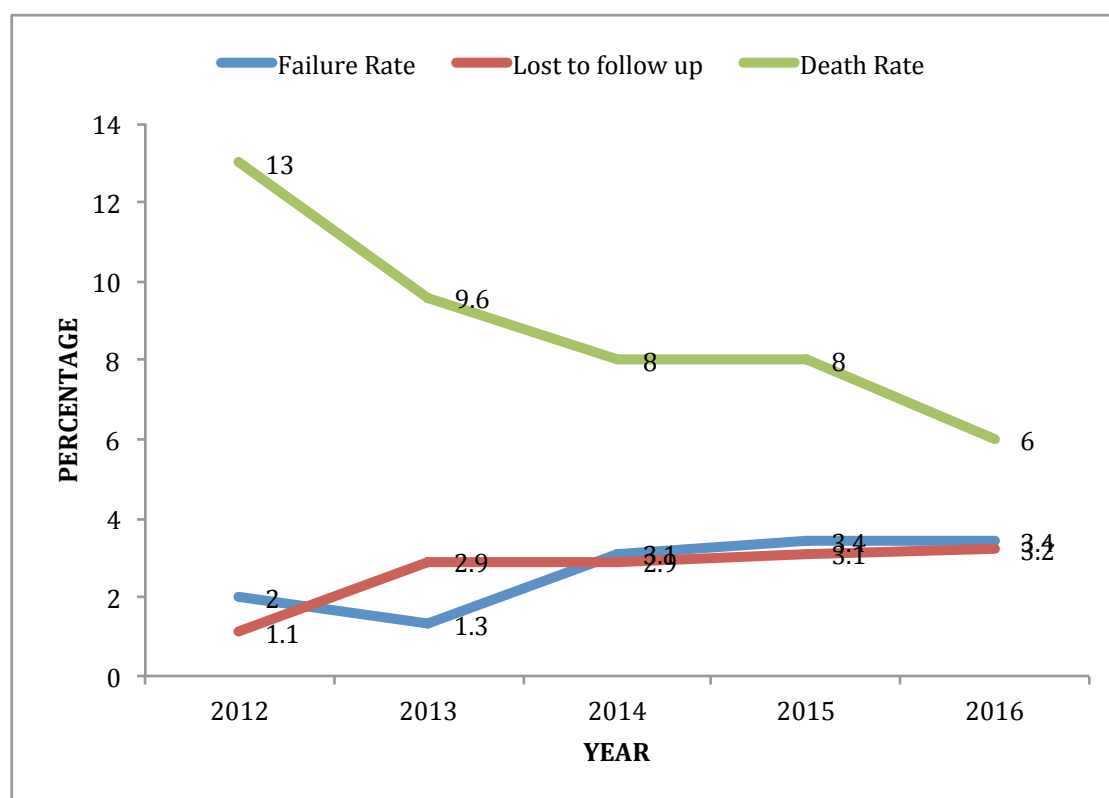
Treatment success rates have remained below the WHO target of 90% over the period in the BAR (Figure 3), with death rates recording 6% just below the national rate of 7% for 2016. There is also a slightly increasing trend of failures and lost-to-follow-up witnessed from 2013 to 2016, and all these could be attributed to poor adherence to TB treatment in the region (8) (Figure 4).

Figure 3: Trend of TB treatment success rates in BAR-Ghana, 2012-2016



Source: Regional Health Directorate (RHD) Annual Report for 2017 (8).

Figure 4: Trend of TB failures, lost to follow up, and death rates in BAR-Ghana, 2012-2016



Source: RHD Annual Report for 2017 (8).

Although failures and default rates are increasing and could have been prevented with proper management, it's plausible to project that death rates among undetected TB cases might be higher. Also, no study has been done in the BAR to identify adherence challenges and strategies to improve TB treatment; hence the focus of this study.

2.3 Objectives

2.3.1 Main Objective

The main objective is to identify challenges in adhering to TB treatment and explore innovative interventions to make recommendations for consideration by policymakers to improve TB treatment outcomes in BAR, Ghana.

2.3.2 Specific Objectives

1. To explore the socio-economic, cultural and individual factors influencing adherence to TB treatment in the BAR.
2. To explore health system-related factors influencing TB adherence in the BAR.
3. To identify current innovative interventions to support adherence and review their effectiveness, applicability, and conditions for successful implementation in the BAR.
4. To make recommendations to Ghana Health Service (GHS), NTP, and other key stakeholders to optimize TB treatment in Ghana.

2.4 Methodology

This was mainly a literature review, which focused on socio-economic, cultural, individual, and health system-related factors that influence adherence to TB medication in the BAR of Ghana. Current innovative interventions for TB adherence and their applicability for successful implementation were also explored. Information from the literature search was put in a table, summarized and grouped by influencing factors and types of interventions. This was then analyzed by comparing, contrasting and also triangulating with different interventions and sources. Both qualitative and quantitative studies were reviewed looking at data collection methods, analysis, and validations to ensure quality, validity, and representative of results from the articles.

2.4.1 Data Bases

Peer-reviewed journals and grey literature relevant to the study were used. A literature search was done using Google Scholar, PubMed, and Vrije University Library databases. Websites such as the GHS, Ministry of Health, Ghana (MoH), WHO and the World Bank were explored. Articles published from 2005 to 2018 were used. Ghana adopted and achieved full DOTS coverage in 2005 and several articles were published on TB adherence which the writer believes are still necessary for the current discussions, hence the extension of the year back to 2005.

2.4.2 Search Terms/inclusion and exclusion criteria

Terms that cover the different potential factors in combination with terms related to treatment adherence and TB were used (Table 1). Only original articles written in English and focusing on factors influencing treatment adherence were used. Randomized-controlled trials, comparative studies, cross-sectional studies, and exploratory studies were included.

Table 1: Search terms

	AND	AND	AND
OR	Tuberculosis adherence Tuberculosis compliance TB adherence TB compliance TB Treatment completion TB treatment outcome TB treatment success	Age Sex Gender Marital status Smoking Alcohol use Cost Poverty Distance Beliefs about TB Beliefs about TB treatment Knowledge about TB Patient beliefs about TB Family support Barriers Stigma and Discrimination Health worker attitude Service delivery factors Waiting time Drugs Accessibility Leadership Governance Health policies	Ghana Lower Middle Income Country Low resource setting Developing Country

		Financing Human resources Video observation technology SMS reminders Pill Count Counselling Enablers package Treatment supporters The pillbox Digital adherence technologies 99DOTS mHealth	
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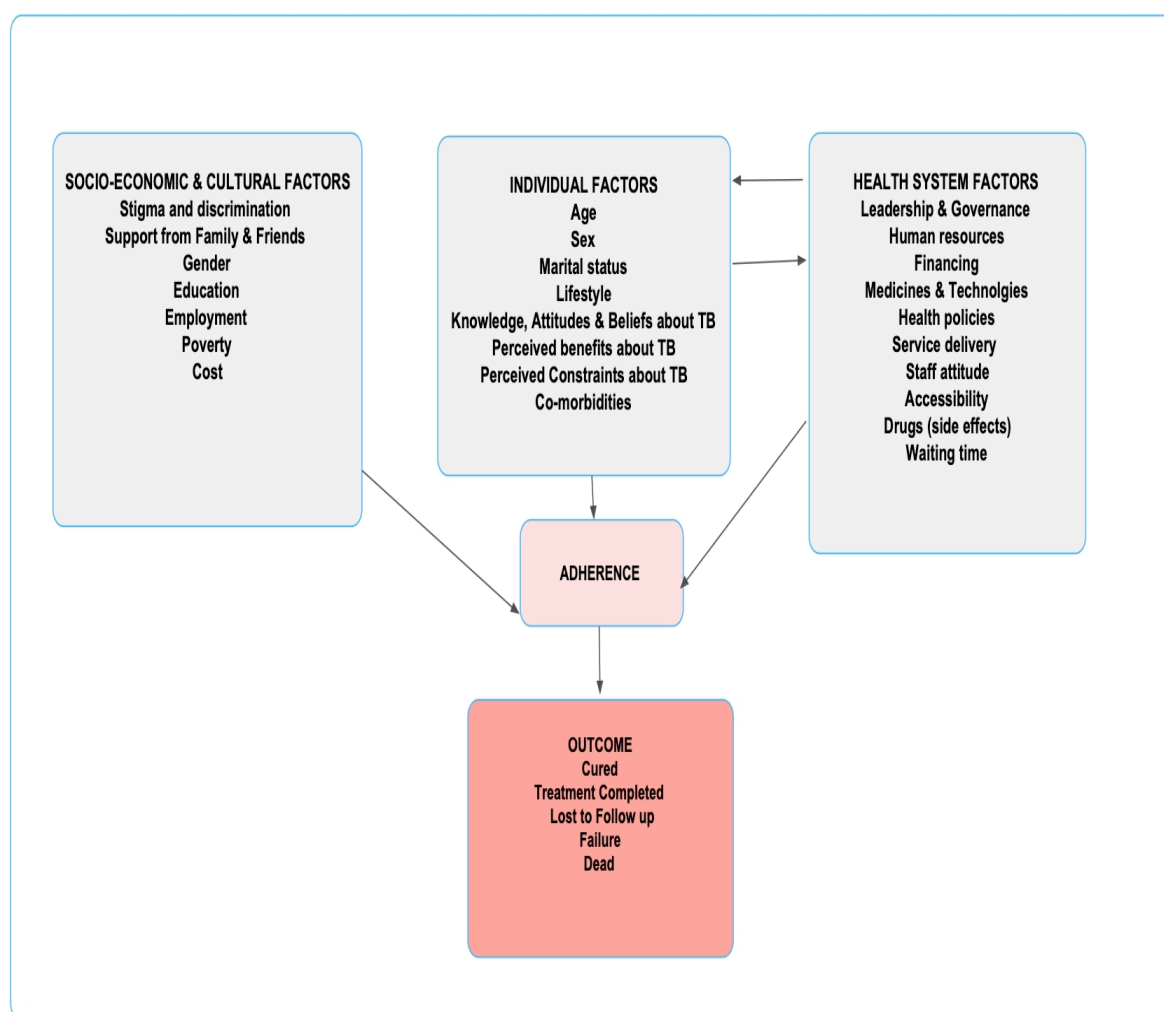
2.4.3 Search Strategy

The initial scanning of titles of documents was done. Abstracts of papers were read and those with information on the factors contributing to adherence included. Snowballing was done to add more relevant articles to the final list.

2.4.4 Conceptual framework for TB medication adherence

The socio-ecological conceptual framework was adapted from Roura et al in their study on antiretroviral treatment (ART) in Tanzania in 2009 (31) (Appendix 4). Though this framework was for ART adherence, it fits my research objectives and could be adapted to search for relevant literature concerning TB adherence. The framework provides a systematic way to look at how the factors relate to influence adherence. Health systems factors such as service delivery, human resources, finance, leadership and governance, medicines & technology, was added to reflect the objectives of this study as the original framework did not cover all. Also, the effect of the causal relationship between the factors and outcome was added to reflect the opinion that disease outcomes are a result of these interactions. The bi-directional connections between the individual and health system factors were added to show how they influence each other. The social context was merged with cultural and economic factors.

Figure 5: Conceptual framework for TB medication adherence^{vii}



Source: adapted from Roura et al 2009 by the author (31).

^{vii} Adapted from Roura et al 2009 conceptual framework by the author

CHAPTER THREE: RESULTS/FINDINGS

Chapter three looks at the findings of the literature reviewed on factors influencing adherence as well as interventions to improve adherence. A total of 18 studies were found on factors influencing adherence in Ghana. Additional 102 studies were retrieved and reviewed from similar countries that met the inclusion criteria, totaling 120 studies on factors influencing adherence as well as interventions to improve adherence, which in my opinion is robust for this study to conclude.

3.1. Individual, cultural, and socio-economic factors

3.1.1. Individual factors

Age

The relationship between age and TB medication adherence is inconclusive. Three studies conducted in Ghana reported different adherence levels: Danso et al (19) reported that older clients complied more to medication than younger clients, whereas Samuel A. et al and Dodor E.A. (2,32) both noted that TB defaulter increase with age, as the aged patients find it difficult adhering to the treatment course. These variations could be due to the study types and the interventions used (Community Vrs Hospital-Based DOT), which require different attendances for treatment. These findings were supported by studies in Tanzania (25), Ethiopia (33,34), Kenya (22), Nigeria (35) and a systematic review by H. Tola et al (36). Other studies, however, found no significant association between age and TB medication adherence (37–39). A prospective cohort study in Mozambique documented a 31.3% incomplete adherence among children less than 3 years with risk factors being migrant mothers and malnutrition [95% CI: 1.4–6.0, $p < 0.05$] (3).

Sex

Sex differences in TB medication adherence have been well documented globally. Norgbe G.K. (1) in his study in eastern Ghana found a less-adherent to TB medication among males 43.5% ($n=69$) as against females 31.1% ($n=61$), whereas Boateng et al also found the male sex to be less-adherent (OR 4.73; 95% CI 2.31– 9.68) (2). However, another study in the Greater Accra region (21) did not find any significant relationship between sex and medication adherence ($p<0.595$). This study was done in a tertiary referral hospital which features cases referred from other health facilities and the results may not be generalizable. This study was supported by a study in Uganda (38) where cases with treatment supporters were assessed. Kigozi et al in their study in South Africa found females to be 40% less likely to default treatment compared to the males (AOR 0.6, 95% CI 0.51–0.71) (40), and many studies have reported males to be less-adherent to TB treatment (40–43).

Marital status

In their cross-sectional study in Eastern Ghana, Danso et al (19) found that though 68% of the never-married complied with their medication against 59% married respondents, there was no significant relationship. Their study is in agreement with a study in Ethiopia that found unmarried to be slightly more adherent (20.3%) than married participants (17.9%) (44). A study conducted in Mogadishu, Somalia, however, found that married TB patients were more likely to have good treatment outcomes. Most TB clients used their spouses as treatment supporters and could be a contributory factor (45). Studies in Kenya (22) and Ethiopia (46) had contrary results as they reported unmarried clients to be associated with poor adherence.

Lifestyle (Alcohol and smoking)

Alcohol and smoking have been documented to be associated with TB medication non-adherence in some studies (19,47,48). Studies in Ghana have described the impact of alcohol consumption and smoking on TB medication adherence (19,49). Danso et al (19) Noted that some clients become involved in alcohol consumption to deal with stress, and forget to take their medication due to intoxication, which then leads to poor adherence. This was supported by studies in Kenya (22,50) and South Africa (48). Some clients who were of the view that some of their family members were involved in smoking and alcohol consumption in the past but never got TB resorted to drinking and smoking despite advice from health workers, which then leads to a relapse. A TB client in a qualitative study in Ghana best explains this assertion:

"I do not believe that drinking alcohol and smoking could cause TB. My grandfather used to smoke and drink alcohol a lot, and yet, he never had TB. I think there is no association between alcohol consumption, smoking habits, and TB" (49).

Alcohol intake is described as a social activity fostering unity, so some clients who are advised by health workers not to drink see that as separation from their peers. They, therefore, interrupt treatment to continue drinking once they feel better (46,51). A study conducted in Uganda noted that those who consume alcohol have the risk of moving and relocating outside the city, providing wrong addresses which then makes it difficult to follow them up (52). Smoking is also noted as a risk factor for default as recorded in a study in South Africa where non-adherent clients who smoked were found to have an increased risk profile, which makes them prone to engaging in risky behaviors without cognizance of the consequences (48). This is supported by some studies (19,36).

Knowledge, attitudes, and beliefs about TB

Knowledge of TB disease transmission greatly influences the beliefs and attitudes towards its treatment and prevention. Studies in Ghana (1,49,53) have documented the interplay between knowledge about TB transmission, causes, treatment, risk factors, etc and medication adherence and this is supported by many studies (34,42,54,55). Tagoe et al found in their study that TB clients with inadequate knowledge about TB, as well as its causes were less likely to comply with treatment (49). Ignorance about TB treatment duration and its effect on adherence has been recorded by many studies (19,36,47,56,57), as some participants that did not understand the duration of treatment stopped taking their medication when they felt better or when they no longer experience symptom (58). The attitude of TB clients towards treatment has a direct bearing on successful completion of treatment (19,56,59). Danso et al noted that the working activities of clients sometimes made them either miss their times to visit health facilities or take medication (19). Forgetfulness (33,47,56,58) is the most cited reason in some studies as reasons for non-compliance whilst others interrupted treatment to attend social gatherings such as weddings and funerals (57). Patients who use herbal medicines during treatment have also been predicted to be non-adherent in a case-control study in Kenya (OR 5.7; 95% CI 1.37-23.7) (22). This was, however, a small study, which may not be generalizable. Studies in Ghana noted that some clients attributed their conditions to witchcraft hence majority went to spiritual/fate-healers for healing, which affected compliance (19,49,53). Myths about TB resulting from curses and punishment from ancestors have been noted in a recent study. A client has this to say regarding the beliefs about TB and its causes:

"When a man and a woman are having sex and the two 'cough on each other' it leads to TB. TB may be as a result of a curse from someone. I suspected my uncle who had a quarrel with me concerning my marriage. So when my condition was not improving, my father and I went to my hometown to really find the root cause of the TB and to perform some rituals" (53)

Belief in TB treatment and subsequent compliance is influenced by knowledge about TB and its causes (53,60,61). Other studies noted that beliefs and use of traditional healing systems were associated with non-adherence, as clients described the system as effective and keep away bad spirit (18,24).

Perceived benefits of TB treatment

The perception of clients on treatment greatly influences their level of adherence to treatment. In their qualitative study in Eastern Ghana, E. Dodor and G. Afenyadu noted that 22% of non-defaulting clients cited that taking the medication and feeling well to take care of their families motivated them to comply to their medication (20). A study in South Africa noted that caretakers of children under five years old mentioned seeing their children flourish and not being hospitalized from the disease as the main motivating factor, as that would have meant daily visits and associated inconveniences (37). Knowledge of the fact that some people have been cured of TB motivated some clients to complete treatment, avoid hospitalization and to provide for their families in studies in South Africa (51,60). A systematic review of qualitative data by Munro et al found that patients adhered to treatment as a result of symptom relief, as they feared becoming ill again (42). Participants with comorbid conditions and who perceived their status to be poor cited the belief in the effectiveness of the medication as the main motivating factor (48). In a qualitative study in South Africa, an adherent TB client had this to say regarding the perceived benefits of TB treatment:

"It was the pain I was feeling, I was in pain and so that is why I thought I should go for treatment I realized nothing else will help me other than the treatment, I have to take my treatment until I complete it. The other thing is I am so scared of really sick people I don't want a person to be so sick that they get pushed around in wheelbarrows and things like that, so that is why it is important for me to get help while I can still walk on my own two feet to get help from the clinic" (51).

Perceived constraint about TB

Many studies have documented work-related issues and their effect on adherence (24,42,51,62,63). A Study in Ethiopia (64) and Munro et al (42) found that people fear to lose their jobs when their status is known by their employers thereby defaulting from treatment. An initial Lost to Follow up (LTFU) client in South Africa during a qualitative study had this to say:

"No I did not start I did not go back to them because of my work schedule because I work from 07:00 till 16:30. There they open from 08:00 until 16:00 and on weekend they are closed..." (51)

Additionally, time off work to attend to treatment (65,66), long distances to treatment centers, clinic opening hours, and other costs associated with treatment (63) mean patients prioritized work over treatment. Munro et al (42) again noted that some patients had difficulty obtaining sick leave for treatment coupled with the fear of requesting for assistance to buy anti TB medications compelled them to prioritize work over treatment (51).

Co-morbidities

Co-morbid conditions and their influence on medication compliance have been noted. Burton et al reported higher non-adherent rates to TB medication among HIV infected patients in Ghana (21). Studies elsewhere have documented co-morbidities and their influence on medication adherence (24,39,41,43). Stigma has been implicated in TB

medication non-adherence, and TB patients infected with HIV were afraid of TB/HIV stigma and this led to the denial of their HIV positive status (40,60). The increased risk of accessing separate clinics for TB and HIV, financial burden on families in terms of travel costs and other expenses, the side effects of TB and HIV drugs, as well as the pill load worsens their problem which forces them to interrupt treatment (35,36,67,68). However, a qualitative study in South Africa did not find any association between co-morbidities and treatment completion (37).

3.1.2. Cultural factors

Stigma and Discrimination

TB is a highly stigmatized disease, which is worsened by misconceptions, taboos, and misunderstanding of the disease in many societies (24,49). TB is called "Nsamanwa"^{viii} in the local Twi^{ix} language, depicting how the disease is stigmatized. Community members, distant family members, health workers as well as friends play a role in stigmatization (18,69). This has led to many clients refusing to disclose their status to friends and family members (24). In a cross-sectional study in Eastern Ghana, 60.3% defaulters mentioned being prevented from mixing with people in their communities which reinforces the magnitude of the stigma attached to the disease (2), and this has led to some clients refusing to take their medications at designated places for fear of being seen (55). In a qualitative study in the Ashanti region of Ghana, a female TB client had this to say:

I made a decision not to tell any of my co-workers because I will be excluded from some activities such as chatting, group eating and others. I did not even inform my head teacher about it... I may be excluded from many things there [at school].' (18)

Many studies have documented the effects of stigma on non-compliance (22,36,44,61,66), with some experiencing job loss when their status was found out by their employers (60). Studies in South Africa (51) and Papua New Guinea (70) however documented that though stigma exists, none of the clients experienced it.

Support from family and friends

The kind of support clients enjoy from family members, friends and the community goes a long way to influence adherence to TB treatment (2,18,20,49,51). Support in the form of money (71), collection of medications on their behalf (42), supervising medication and reminding them of their appointments (66), etc ensures clients complied with treatment. Support systems facilitate or act as barriers to compliance (70), as lack of support leads to clients interrupting treatment (36). A cross-sectional study in Eastern Ghana recorded that clients that received support from family members complied better with treatment than those who did not (2). Another study in Southern Ethiopia found that some clients discontinued treatment because there was no support from the family and community (24), underscoring the importance of social support. Many studies have documented the benefits of support from family and friends in ensuring optimal adherence to treatment (32,37,55,61,64,72,73). In a qualitative study in Ghana, a TB client had this to say:

"It was my aunty and mother who went to the hospital with me when I was weak. They had to stop working to take care of me" (49).

The above statement underscores the importance TB clients attach to support from family members, which helps in complying with treatment.

^{viii} Nsamanwa means 'ghost cough' as it was believed people with TB will eventually die

^{ix} Twi is a language spoken by the Akans, one of the largest ethnic groups in Ghana.

3.1.3. Socio-economic factors

Gender

Some studies conducted in Ghana concluded that male gender is associated with poor adherence to medication (2,19,32), however, a study by Burton et al (21) did not record any association between gender and medication adherence in their retrospective studies in the Greater Accra region of Ghana. Dodor E.A (32) noted in his study that men's role in African homes as breadwinners of the family and the difficulty getting permission from their employers to attend to health facilities for treatments requiring long periods like TB may pose big problems for such individuals as their bosses may not be happy with their constant absents. This finding was supported by a case-control study in Kenya (66). Another case-control study in Botswana also found that men were two times and three times the odds of women to poorly adhere to TB medications respectively (41). However, self-report was used in this survey, which may result in some bias in answering the questions about non-adherence, which was also acknowledged by the authors. Many studies have recorded male gender to be less-adherent (22,36,40,68), and Munro et al (42) mentioned that females however in some countries require permission from their husbands or heads of their households to attend treatment. Studies in Uganda (38) and Equatorial-Guinea (39), however, did not document any connection between gender and TB medication adherence.

Education

Education helps the individual to read, write as well as to be equipped with knowledge on the transmission of diseases. Danso et al (19) found that higher educational attainment was not a significant factor in TB medication adherence contrary to what is reported in most literature (22,44,45), as 89% of clients who had no formal education complied with their TB medication more than those who had some form of education in their study. The sample size was small and cannot be generalized. This finding was however supported by a case-control study in Botswana (41). However, studies in Somalia and Kenya showed that illiteracy influences TB medication adherence (22,45). Educated people know the consequences of poor adherence on survival, as education increases one's awareness about the importance of compliance (74). Higher levels of educational attainment improve communication between health workers and their clients, which then helps them to retain health information on adherence to their medication (75). Other studies reported that illiteracy or lower levels of education are risk factors for non-adherence to TB medication (39,44,68).

Employment

Employment plays a major role in people adhering to TB treatment, as it provides income for the individual to be able to provide necessities in life including food, shelter, and healthcare. The income per month allows the TB patient to pay for supplemental drugs prescribed alongside the TB treatment as well as feed oneself during the treatment period thereby preventing defaulting (20). Unemployed patients, however, have limited financial access to pay for transport cost and other expenses, thereby posing as a barrier to treatment adherence (64). In their study in Eastern Ghana, Danso et al (19) found that three-quarters of TB clients (83%) who were not employed adhered to their medication as compared with those employed as farmers (61%), traders (55%) and artisans (65%). This study was supported by Kulkarni et al (47). It also confirms the assertion that work schedules prevent people from adhering to their medication as they face the choice of their work and treatment (42). Contrary to the above, Kizito et al in a retrospective unmatched case-control study in Kenya reported that patients who are employed are less likely to default from treatment (66). This was supported by Gebreweld et al (55).

Poverty

Poverty, which correlates with one's income and ability to take care of basic needs including feeding, transportation, and drugs, considerably predicts adherence to TB medication. Poverty is noted to contribute to poor medication adherence in Ghana (1,18,19). In a qualitative study at a Hospital in Eastern Ghana, E. Dodor and G. Afenyadu noted that default was significantly associated with financial difficulties and income less than US\$10.5 among TB defaulters (20). This was supported by studies in Kenya (50) and Ethiopia (44) where clients with income less than 10,000 Kenyan Shillings (US\$100) and those in low economic scores respectively were associated with defaulting. Another study in Eastern Ghana found that the odds of defaulting was 4.14 times higher among clients with financial difficulties during treatment (2). This then made some clients miss taking their medication as they had no money to buy food to eat after taking their medications (53). Several studies have recorded the association between poverty and poor adherence to TB medication because of direct and indirect costs associated with taking the medication (22,36,42,48,51,55,64,67,72).

Cost

TB treatment in Ghana is free (49), but other out-of-pocket payments and financial burden faced by clients have been documented to influence adherence (20). Clients normally face financial burden such as transport costs for those staying far away to health facilities for treatment (34,37,55,63). Cost for other supplementary drugs prescribed (20,42,76) as well as other hospital services (24), all contribute to poor adherence, especially for those who are unemployed or cannot afford the payments. A 37-year-old female participant in an in-depth interview in Eritrea had this to say better regarding other costs they encounter:

"I am from Adi Guaedad, I was informed to take medication from Merhano. This means I had to do a one-hour walk daily. I was reluctant because it was difficult and I opted to go to Godaif. It is still a long-distance and, there is lack of transportation. Sometimes I use taxi but it is so expensive. I can't afford it" (55)

Cross-sectional studies in Uganda (77) and Ethiopia (33) however mentioned that the cost of travel did not have any significant association with medication non-adherence, but the studies did not address other non-TB related costs like drugs and other opportunity costs. The studies also relied on self-reports by patients, which could be overestimated.

3.2. Health system factors

Leadership and governance

Strong leadership and governance provide the framework for building a health system that ensures policies exist to provide effective oversight, coalition building, regulation and accountability (78). Leadership and governance are therefore crucial in all spheres of the health system, considering the consequences of weak leadership on health outcomes (79). The GHS is the statutory body entrusted to supervise an equitable, efficient, accessible and responsive healthcare system (80). The NTP with support from the Global Fund (GF) in 2006 started providing the enablers package^x to all TB clients to improve case detection and adherence, though this has not been fully evaluated (69). The MOH/NTP in its strategic plan for 2009 to 2013 also sought to take advantage of the

^x The enabler's package includes cost for transport, food supplements, other medical expenses not covered by the NHIS, and other direct and indirect costs borne by the TB clients.

expanding nature of the private sector in Ghana's healthcare delivery to improve TB activities by ensuring inclusive service provision. This ensures patients that travel for long distances to public health facilities for DOTS can use the facilities of the private facilities to ensure optimal adherence (81). TB diagnosis and treatments are free in Ghana, but there are other direct and indirect costs borne by the clients. The MOH/NTP has collaborated with the parliamentary select committee on health in 2013 to advance insurance coverage for all TB patients for health-related costs other than free anti-tuberculosis treatment to ensure compliance (82). TB/HIV was integrated in 2007 due to the comorbidity of the two diseases (83), and there are coordinating units in all regions and districts (30). Because of the vertical^{xi} nature of the programs, diagnosis, and treatment outcomes are reported in the District Health Information Management Systems (DHIMS)^{xii} and to the respective coordinators to the national level (11,80). This has led to poor coordination at local levels which has indirect consequences on optimal adherence (80). Funding is provided by the GF (84) but this is woefully inadequate and has been dwindling over the years. There are sometimes delays in releasing funds, which interrupt the implementation of certain programs such as training, monitoring, and supervision at the implementation levels (84).

Human resources for Health

HRH is a critical component of the WHO health systems building blocks to attain, sustain and accelerate progress on universal health coverage, yet less attention has been paid in that regard in most developing countries including Ghana (78). Studies have shown evidence of a correlation between the number of health workers and health outcomes, and an adequate health workforce is key to achieve that (85–87). Ghana's skilled health workforce is not up to the required number to meet the global 2035 targets amid increasing TB/HIV burden on the health systems, which, as of 2010 stands at 10.21 per 10,000 populations (88). The human resource data for Ghana and the BAR are presented in table two below.

Table 2: Selected human resource situation for Ghana and BAR, 2017 and 2018 compared.

Type of staff	National Level		Brong Ahafo Region	
	2017	2018	2017	2018
Medical Doctors	3263	3365	226	231
Professional Nurses	48939	52605	4006	4629
Laboratory assistants	812	934	23	25
Pharmacists	570	598	16	18

Source: GHS facts and Figures 2017/District Health Information Management Systems (DHIMS) (12,89).

Ghana's human resource challenges currently include a lack of health worker motivation, poor supervision, migration, and negative attitudes towards work (87). The country is also challenged with the inequitable distribution of health staff to the lower levels and the northern part of Ghana including BAR (12,87). In terms of personnel, there is a relatively higher proportion of professional Nurses than Doctors, Pharmacists and Laboratory assistants across the country, and the large numbers of nursing training

^{xi} Districts have TB and HIV coordinating units at the same place but are coordinated by different officers, with different reporting forms.

^{xii} DHIMS is a web-based platform for recording and reporting real-time data from health facilities in Ghana

schools in the country could influence that (12,87). The training of health professionals is constrained by physical and technical capacity. In-service training is insufficient, ineffective, and health workers often lack the necessary equipment to perform their duties efficiently (87). From my observations working with GHS since 2002, there is staff designated for coordinating TB activities up to the district level, but the challenge has been inadequate staff to coordinate at the sub-district and facility levels which compromises quality and coordination. Most facilities lack critical staff for laboratory and pharmacy services, which means patients are referred to the next level, which poses an extra challenge.

Financing

The financing of TB activities is one of the critical areas to ensure the objectives of the control efforts are achieved. Adequate funds are required to promote access to required services and reduce financial impoverishment associated with accessing TB services (90). Ghana, like any other lower-middle-income country, faces the challenges of insufficient funding and capacity to identify gaps to secure reliable funding (79). The government of Ghana supports the program financially, but GF is the major financier of TB activities since 2003 (91,92). The MOH is the principal recipient of these grants whereas the GHS is the primary implementer of the GF activities. Most of the funding goes into infrastructure, capacity building for health staff, procurement, service delivery, and monitoring and evaluation, as well as providing enablers package to TB clients (92). No study in Ghana and BAR has been found that looked at the role of funding and TB adherence, but a systematic review on domestic and donor financing for tuberculosis care by Floyd K. et al reported that there were impressive cost-effective gains in TB activities with financing support (93).

Medicines and technologies

In Ghana, the Central Medical Stores is responsible for receiving all anti-TB drugs through its supply chain system and distributes to all health facilities through the regional and district stores (8,13). The country is part of the Global Drugs Facility (GDF); hence all TB drugs and Laboratory consumables are supplied by the GDF in collaboration with WHO and Stop TB partnership. They are delivered alongside the scheduled delivery of items to the service delivery points by the respective Regional Medical Stores (RMS) (8,13). The various districts and facilities in the country are challenged by storage space and personnel to effectively manage supply and procurement issues (13). Ghana currently adopted the Early Warning System (EWS), a short messaging service (SMS) data reporting platform that is useful in accessing near-real-time logistics data visibility to prevent the shortage of TB drugs (8,13). There is also the Logistics Management Information System (LMIS), which is a web-based platform for reporting helps to keep track of all anti-TB drugs to avoid stock-outs and expiration in the DHIMS (89). No study has documented the frequency of TB drugs stock-out during the past years in Ghana, or the effects of TB drugs and other logistics shortage on treatment outcome of TB patients in Ghana and BAR.

Health policies

Health policies to increase access to TB diagnostic services, prompt treatment, availability of logistics and care, as well as infrastructure, greatly influence prompt care-seeking, diagnosis, and adherence to medication. The current policy in Ghana, legal support for TB treatment, entreats all patients suffering from TB to be exempted from payment of all fees (84). The Hospital's fees ACT article 2(2) of 1971, which became effective on 19 July 1985, clearly mandates all TB patients to be exempted from payment of all fees (84). There is also a policy to improve access and care by ensuring the integration of TB/HIV services (94,95). In Ghana, TB diagnosis and treatment are

free but there are other hospital charges^{xiii} that are still borne by the patients, which hampers adherence to treatment (42,55,63,76). The NTP is responsible for training, provision of logistics as well as monitoring and evaluation of activities (91). Ghana currently uses the standard TB/HIV clinical guidelines for TB/HIV co-infection management and has been implemented in all districts and health facilities in the country (96). This is to provide a common platform for integration and ensuring the two diseases are tackled holistically.

Service delivery

From the literature, this is discussed under TB/HIV collaboration, integration and quality of care.

TB/HIV integration

TB/HIV service integration is an integral part of the country's response to the two diseases, as advocated by WHO (97), to reduce fragmentation, increase access and improve efficiency and quality of care (83). One of the pillars of the new end TB strategy talks about early diagnosis of TB and advocates for the use of Genexpert machines as the first line of diagnosis of Mycobacterium TB (14), however, the total number of diagnostic centres in the BAR stands at 0.7/100,000 population which is woefully inadequate, with a DOT facility to population ratio of 1:5,357 in 2017 (8). TB/HIV activities are decentralized, with the services available in most private and public health facilities and communities^{xiv} (83). It is expected that all TB clients are offered HIV testing and counseling (HTC) and HIV positive clients enrolled also screened for TB (83,94). Quality of care to TB/HIV patients as well as its management is part of the training standards provided to healthcare workers in the country. Facilities for TB/HIV in the BAR are presented in table three below.

Table 3: Sites providing TB/HIV services in BAR (2016 & 2017) compared.

Site	Cumulative as of December 2016	Cumulative as of December 2017
HTC Sites	214	220
PMTCT Sites	214	220
ART Sites	24	43
DOTs sites	196	224

Source: BAR annual report for 2017 (8).

In Ghana and BAR, ART for people co-infected with TB/HIV is provided as part of basic services (8,83). The benefits of TB/HIV integration in increasing access, reducing mortalities and improving TB cure rates in the country have been documented by some studies (83,94,95). TB/HIV integration provides a one-stop-shop and improves patient's

^{xiii} These include cost for x-rays, other drugs dispensed and other laboratory diagnosis or services apart from sputum microscopy.

^{xiv} Some nurses are assigned to communities where they operate the CHPS concept and offer TB/HIV services.

access to comprehensive care where clients can access both treatments without incurring travel costs (95). A study conducted in Ghana on TB/HIV service integration recorded an increase in TB treatment success rates from 46% to 78%, and lost-to-follow-up and transferred out from 14.3% and 15.3% before integration, to 1.4% and 9.0% post-integration respectively, underscoring the benefits of the integration on TB treatment adherence (83). Studies have documented the benefits of TB/HIV service integration elsewhere (98–100).

Staff attitude

Throughout the treatment period, clients come into contact with healthcare providers and the kind of interactions and relationship between them influences adherence to treatment. Many studies indicated that, poor attitude of service providers (1,2,22,36,42,51,56), such as shouting at clients for not adhering to rules (64), scolding for missing appointments, lack of physical contact (42,49), and lack of opportunity to express their feelings (56) resulted in poor adherence. In a qualitative study in Ghana, a TB patient said this about the attitude of some healthcare workers:

"Some nurses at the ward put on gloves and nose masks when touching [suspecting] the TB patients who are not infectious. It annoys me when a patient's relative is given gloves to wear while washing the patients' clothes. Even a physician would not allow the patient to sit in his consulting room, and the patients should stand outside while the physician sits in his office and talks with the patient through the open door of his office. (49)"

This emphasizes the role healthcare workers play in discouraging TB clients to attend health facilities, which negatively impacts on adherence. A cross-sectional study in Ethiopia found clients to be 4.6 times more likely to be non-adherent due to poor staff attitude (59). This was, however, subject to recall bias and cannot be generalized as non-adherence was assessed according to data taken during the past month, and patients attending hospitals and health posts were excluded respectively. In contrast, some studies noted the positive impact of some health staff that facilitated adherence (20,24,55,61), which shows there are good ones that require commendation. Few studies did not, however, find any significant relationship between staff attitude and adherence to treatment (33,77).

Accessibility

The distance TB clients cover to receive healthcare, the cost of transport, availability, and acceptability of the services, etc. has a direct impact on compliance. Current Ghana's NTP protocol urges health providers to refer clients to the nearest health facility for care (49). Long distances to treatment centers mean clients have to incur transport costs (32,36,37,56,101,102) or walk for long distances (51,63) to access care, and the fact that some clients are poor, unable to do their daily work to earn income, etc compounds the situation limiting their access to care and subsequently compliance (54). The frustrations of some TB clients with regards to distance to health facilities for treatment was evident when an initial LTFU client in a qualitative study in South Africa remarked as follows:

'If you are not fit enough it can even take 3 hours. Too much, everything is a problem there are a lot of defaulters at [] because of the distance they are complaining because it is too far that is why there are so many defaulters' (51).

A study in Eastern Ghana found that 79.6% of defaulters had problems with the distance (1), and E.A. Dodor noted that sometimes clients change vehicles or cross rivers to access care in the same region, and their motivation decreases once they begin to feel better (1,32). This was in agreement with a study in Nepal where 74.2% of clients who took less time to reach the treatment centers complied with treatment (103). Contrary, studies in Uganda (77) and Ethiopia (33) did not find any significant association between distance and non-compliance to treatment. The smaller sample sizes used could result in those variations as well as how the services were organized (facility-based vs community-based DOTS) and might not establish a stronger relationship.

Drugs (side effects)

The side effects, type of regimen and duration of treatment of TB drugs play a critical role in compliance to treatment. Side effects of drugs make some patients believe the treatment was worsening their condition, whilst prolonged treatment duration affects compliance as it interferes with their daily personal activities (55). Side effects commonly experienced by clients included skin rashes, weakness, vomiting, feeling of choking, etc. (51,53). These affect compliance, leads to hospitalization, death or prolonged treatment (49). Danso et al reported in their study that, 17% of the clients complained of the treatment duration and were tempted to abandon their treatment when they felt better (19). In a case-control study in Botswana, side effects were noted as a risk factor for a larger proportion of non-adherent cases (41) but the study did not mention whether clients were on other drugs which could produce side effects other than the TB drugs. Side effects of TB drugs and non-compliance have been reported in many studies (1,22,24,38,41,104,105), whereas the duration of treatment (42,59,64,75) and type of regimen (77) has also been cited as risk factors for poor adherence in some studies.

Waiting time/opening hours

The time patients spend at a health facility receiving care have been documented to contribute to TB medication non-adherence (20,22,37,49,50,52,56,106). Long waiting times spent by clients is a barrier to compliance with treatment (42,50,102,106). It makes clients frustrated and lose productive periods in queues (49). A Study in Ghana and Uganda showed that waiting times are not significantly associated with default (20,77), and these studies may be biased because defaulters may not give an honest answer. Also, reliance on self-reports may not be accurate. However, studies in Kenya (50) and Ethiopia (102) reported waiting times of more than one hour to be associated with non-compliance. Waiting times as reported by researchers ranges from one hour (50) to the whole day (51) in some settings, which contributed to non-compliance. In most cases, opening hours are not convenient too, which pose an extra challenge especially those who are working and fear to lose their job (42).

3.3. Interventions to improve adherence

Video Observation of Therapy (VOT)

This is one of the technologies explored to promote optimal adherence to TB medication in settings challenged with human resources. It involves the use of mobile phones to record videos of clients taking their daily medications either by themselves or their treatment supporters, which are then sent and synchronized into a central server for health workers to view those videos for program purposes^{xv} (107,108). It provides a two-way visual communication over standard phone lines, with clients receiving messages on advice from physicians and motivational messages from recovered clients (108,109). This technology has not been explored in Ghana and BAR, but a prospective

^{xv} For identification of potential defaulters, schedule appointments, and for supervision, and monitoring purposes.

cohort study in Vietnam involving bacteriologically confirmed pulmonary TB patients found that 71.1% took all the required doses, with 87.5% finding it easy to use (110). This is consistent with a study in Kenya where 72.2% preferred the VOT (108). The sample sizes in both studies were small to generalize, and the level of adherence was measured by pill count, which could not be authenticated. VOT has been used in areas to compensate for the health worker shortage (108,111) and improve appointment attendance compared to the conventional DOTs (112). The advantage of the VOT is that it promotes privacy as clients do not need the presence of the health worker, however, patients can feign ingestion or conspire with the treatment supporter to create a false report, and the device also relies on internet connectivity which may not be reliable in some rural settings (107).

Short Messaging Service (SMS)

SMS for TB treatment adherence has been explored in many settings in both developed and developing countries (26,47,113–116). It involves sending automated messages to phones of clients at designated intervals to remind them to take their medication or for appointment schedules. Their use is targeted at improving adherence (26,113), reduce LTFU (117) and increase appointments to health facilities (115). Liu et al found in their systematic review that, SMS led to a TB treatment completion rate increase from 73% to 88% where DOTS is not practiced, and 83% to 96% in areas where DOTS was implemented, showing the combination of SMS with DOTS is effective and could improve adherence (115), whereas Car et al also found that the rate of clinic attendance improved with SMS reminders than no reminders (118). The adherence rate was however not mentioned. Contrary to that, a randomized controlled trial in Cameroon found patients cured at six months were almost similar in both intervention and control groups, although cure rates improved (116). Other studies have recorded no significant difference between the use of SMS to improve adherence and LTFU in comparison with the usual method of care (113,117).

Pill/medicine boxes

Pillboxes or medicine boxes have been explored to monitor patients' adherence to TB medication in some African countries (119,120). It involves pillboxes that are linked to a web-based application that records and sends messages to a central server when opened. (111,119). It, however, sends a reminder message to the phone of the patient only when there is a delay in opening it, and has been recorded to outperform the strategy of the standard DOTS (111). A pilot study in Tanzania found a mean adherence rate of 96.3% among 47 patients for six-month (120). This adherence rate is, however, closer to another prospective single-arm observational study in Tanzania, using the pillbox where a 95% adherence rate was recorded (IQR 94–97%) (121). These studies however employed small sample sizes that cannot be generalized. Liu et al also recorded that use of the pillboxes reduced poor medication compliance by 40%-50% in comparison to the standard care (122) this may be biased as the opening of the pillbox is not synonymous with ingesting the drug. The device is also noted to be associated with low rates of follow up by Alipanah et al in their systematic review of trials and observational studies (26). These devices, however, rely on Internet connectivity and are noted to be difficult to operate in areas without the service (119). It also allows for doses to be recorded once the box is opened even if swallowing is not done (123).

99DOTS/Medication envelopes

99DOTS or the medication envelope is a mHealth innovative intervention that is used to monitor and improve adherence to TB medication (124,125). The drugs are in blister packs wrapped in a customized envelope with a mobile number, which is visible when the drug is taken out. Patients are required to call the toll-free number after taking the drugs. When the patient fails to take the drug, a 'missed' call is placed to the supervisor

who makes a follow up to record and ask for reasons for the missed dose(s) (124,126). This technology has been used in a few countries and found to be effective (124,126,127). In India, a study in Rajkok district recorded an overall treatment adherence rate of 96.03% (126), whereas in Davanagere district in same India, a cross-sectional study found 95% of the clients to be non-adherent with multiple reasons such as phone number was for a relative/neighbor, network problems, side effects and improvement in health, etc (128). The difference could be due to the study types and subjects used, as the latter used only participants with TB/HIV co-infection and the motivation to call the hidden numbers may not be there coupled with stigma. The smaller sample size could also be a contributory factor.

Ingestible sensors

This is one of the digital adherence technologies employed to enhance TB treatment compliance, but its use has not been explored in many African countries. The device contains sensors that are worn on the body and ingested with the tablets, which together verify the ingestion of the TB drug and record the time and date of ingestion (129). The data is then interpreted and sent to a central server which supervisors can use (129,130). In a prospective, non-randomized descriptive study among 30 TB patients, Belknap et al found that the device can correctly identify tablets with the ingestible sensors, poses a low risk to users and has high patient acceptance, with 95% detection accuracy (129). This was a small study with a small sample size that was conveniently selected from two sites and is not generalizable. Au-Yeung et al also noted that using the ingestible sensors appears to provide potential cost savings when used as an alternative to the WHO-recommended continuation phase of treatment (130). The device is reported to provide high sensitivity and specificity (123,129), but patients may not be comfortable with the device as it could lead to stigmatization.

Community-Based DOTS (CBDOTS)

CBDOTS, which involves clients taking their medication at home at the community level, is preferred by many because of perceived stigma from health workers (2,18,69) and long distances to health facilities (32,37,51,102), which many studies have found to hamper treatment adherence (22,36,56,61). The CBDOTS also enables clients to receive more psychological support because of closeness of family and friends as compared with the feeling of loneliness and isolation associated with undergoing the treatment in a health facility (131). It also reduces system costs^{xvi}, makes health facility beds available for other patients and allows individuals to return to their normal work (63). A retrospective cohort study in Eastern Ghana which compared community decentralized TB care to centralized care found that the proportion of clients who defaulted was significantly lower (3.3%) in the decentralized than the centralized (17.7%) (132). The study did not look at other factors that could contribute to default. It was however in agreement with a study in Tanzania where 95% of clients who opted for treatment at the community level under the patient-centered treatment approach adhered to the treatment regimen (25). Similarly, a randomized controlled trial in Nigeria reported an overwhelming superiority of CBDOTS with two months default rate of 2.6% compared with 20% in the Hospital-Based DOTS (HBDOTS) (133). Many studies have documented the importance of CBDOTS in improving adherence and treatment success rates among TB patients (26,134).

Incentives and enablers package

Patient adherence to medications for conditions of long duration, such as TB, is usually challenging and can result in poor treatment outcomes. Enablers to reward good

^{xvi} System costs include the cost of disinfectants, employment of additional staff to reduce workload, etc.

behavior and assist to overcome challenges in assessing care sometimes are given as vouchers, cash or food to improve compliance (135). No study in Ghana has looked at the effects of the enabler's package on patient's adherence to TB treatment although the program is implemented in the country. The package includes the provision of food supplements, payments for hospitalization for other conditions and transport costs for a refill. A prospective non-randomized study in Nigeria found that financial incentives proved effective in improving treatment success rate by 21% and a reduction of 75% LTFU among poor patients as compared to the pre-intervention phase (43). The benefits of the enablers to adherence as well as keeping to clinic appointments is reiterated by a 32- year- old male general health worker as follows:

'The financial support has motivated them; I notice they now come regularly for their follow-up visit and they freely discuss their problems with us' (71)

The study was in agreement with another qualitative study also in Nigeria where cash incentives were beneficial and recorded high uptake of the services among the poor without means of transport to the hospital for drug collection and follow up (71). This was, however, a qualitative study that did not quantify the percentage of clients that reported the benefits of the cash incentives. It's however in contrast to a study in South Africa where economic support in the form of vouchers did not have a significant impact on treatment outcome (136). The low fidelity in the delivery of the voucher recorded could, however, be a confounding factor in that study which was acknowledged by the authors. Systematic reviews of literature found increased compliance rates for Latent TB infection treatment among those who received either a money or methadone incentive (137). It also recorded a reduction in LTFU (138). Food incentives to improve compliance and treatment completion for HIV and TB-DOTS is also recorded (139). The review, however, did not mention whether the nutritional benefit of the food incentive was evaluated or not.

Treatment supporters

The use of treatment supporters considerably improves adherence. Several studies have documented the benefit of using them to ensure optimal adherence to treatment (19,21,66,103,132,134,140). They are given minimal training and assist clients during their treatment by observing clients taking their drugs, collection of drugs, and reporting to health workers, etc (70). A study in Eastern Ghana found high compliance among clients served treatment by their supporters as compared with those without supporters (19), and this was supported by a study in a hospital in Accra, Ghana that also reported that patients who defaulted therapy were significantly more likely to have no treatment supporters (21). This, however, could be biased because during the intensive phase at the hospital most clients are not assigned treatment supporters. Choice of a treatment supporter was also found to correlate with adherence, as clients who had family members or Community Health Workers (CHWs) complied with treatment, as reported by a study in Kenya where clients who utilized CHWs had 83% compliance against 68% that did not utilize CHWs (140). In the United Republic of Tanzania, a study reported that clients with treatment supporters staying far away from their clients are less likely to adhere to treatment (25) especially when they felt better, and non-compliance was reported to be higher (52.5%) among clients that did not meet their treatment supporters in a study in Nepal (103).

Patient counseling and education

Proper counseling and education on the need to adhere to their treatment regimen until completion can promote optimal adherence (49) because some clients stopped their medication because of poor understanding of treatment duration and side effects (53,75). Two systematic reviews by Alipana et al (26) and Stuurman et al (137) found

that education and counseling led to a higher rate of treatment completion and lower rates of LTFU, and Woimo et al reported a three times risk of defaulting among patients who did not get counseling and health information at every visit than those who got the service in their cross-sectional study in Ethiopia (AOR = 3; 95% CI: 1.1–8.4) (76). Counseling and education each time client visits are necessary to reinforce the need to adhere to treatment. A cluster randomized controlled trial in Senegal found an improved patient outcome among patients who received counseling and education as compared with the usual control procedures, and suggested the approach may be used in the context of resource-poor countries (134), whilst similar trials in Ethiopia at endpoint found non-adherent rate of 9.5% among intervention group as against 25.4% in the control group (46) (baseline adherence was 19.4% for both groups). Patient education and counseling to improve adherence and LTFU have been reported in many studies (25,61,104,134), however, studies in Northwest Ethiopia did not find any association between proper counseling and adherence (33). This was, however, a hospital-based cross-sectional study, which may not provide strong evidence about causality.

CHAPTER FOUR: DISCUSSIONS

This part of the thesis discusses factors that influence TB medication adherence and interventions to improve treatment outcomes in the BAR. Firstly, it's worth sharing some thoughts on the quality of studies used in this thesis. As mentioned earlier, no study is done in the BAR on TB adherence. Few studies were conducted in other parts of the country that looked at adherence on a small scale and had limitations such as selection bias and sample size, and the findings cannot be generalized. Most studies in Africa are cross-sectional, and change in adherence levels over time is not known. Adherence is mostly measured by self-report in many studies, which is subject to overestimation. Most of the literature focuses on pill adherence without cognizance of other factors like dietary intake, which are equally important. There are factors such as enablers packages to clients, availability of TB drugs, increased sensitization on the fact that TB is curable if adherence is achieved, etc that have helped patients to adhere to treatment in Ghana.

4.1 Factors influencing TB medication adherence

Though studies were explored to look at the link between age and TB drug adherence, they were inconclusive. Being married is not a contributing factor, but a study in Somalia found that being married is a factor to adhere to treatment with the motivation being getting well to take care of their families. The DOTS program in Ghana requires both clients and health workers to choose a treatment supporter they can trust and rely on, and in most cases are spouses of the clients who will want their partners to get well again to continue their routine activities. The role of the Ghanaian family, therefore, plays a great role in impacting adherence. They support by collecting drugs on their behalf, accompanying them to health facilities as well as supporting them financially, but where that support is lacking impact negatively on adherence. Male sex and gender were found to be less compliant in many studies. In many Ghanaian homes, men are required to work and provide necessities for their families and coupled with work schedules, commitments, and finding work, tend to skip or prioritize work over treatment. Better laws/regulations that prevent discrimination at the workplace must be enforced to ensure they are protected and go through the treatment duration. Lifestyles such as alcoholism and smoking are incriminated in many studies as risk factors for non-adherence. Clients who take alcohol forget to take their medication on schedule due to forgetfulness. In some societies in Ghana, alcohol is said to foster unity, hence clients who are advised against alcohol, will interrupt treatment to be with their social group thereby impacting on adherence. Stigma also plays a role in people drinking because as they become depressed, the best will be to get intoxicated to sleep thereby missing their doses. Some people who drink alcohol smoke alongside, and the two seem interlinked to influence adherence as smokers are found to have a high-risk profile in a study in South Africa where they involve in risky behaviors that predisposes them. Knowledge of TB and its transmission has a direct influence on attitudes, perceptions, and beliefs of the disease. Poor knowledge leads to people ascribing different interpretations to the cause of TB and where to get remedies for its cure, and that influences how people perceive the efficacy of TB treatment. In the Ghanaian context, many cultures believe TB is caused by witchcraft or punishment from ancestors for sins committed, and will always go for other herbal treatments alongside TB medication. Knowledge is also linked to the perceptions about the benefits of TB treatment, as getting well to work and care for their families motivated some people. People with co-morbid conditions are confronted with the dual treatment for TB/HIV, and the number of tablets to swallow per day becomes challenging, making them develop fatigue and resort to other herbal concoctions, which worsens their conditions as a result of the combined drugs. Side effects of drugs also disturb the ability to work, with some complaining of dizziness when they take the drugs without food to eat, this induces clients to stop their medication. Information concerning side effects, related disorders, and the drug-taking schedules and benefits is important and needs to be communicated well during counseling sessions.

Regarding socio-cultural factors, stigma and discrimination have been noted as constant and strong predictors of non-adherence in many studies. They are interlinked with several of the other factors to influence adherence. The resultant community perception of people with TB in Ghana and the associated stigma from family and society increase the fear of people with TB to disclose their status or ask for permission to attend treatment because they fear to lose their jobs. The social stigma makes some clients travel to health facilities far from home to receive treatment and incurring other travel costs thereby interlinking with the financial barriers. In some instances, TB clients are prevented from mixing with people from their communities in Ghana thereby increasing the refusal of people to disclose their status and go for treatment.

Reflecting on the context of Ghana, stigma, and discrimination were found to be the main concerns for TB medication adherence. These factors lead to people resorting to traditional medicines with no social support. TB clients were discriminated against and stigmatized by health workers in some clinics. Some TB clients missed their doses due to forgetfulness and others to attend social activities, reflecting the refusal to take drugs in front of people for fear of stigmatization and discrimination. Stigma and discrimination have an impact on job opportunities and consequently affect the incomes of TB clients, which indirectly affects adherence. TB clients face financial barriers to optimal adherence such as indirect costs, though the TB treatment is free in the country. The anti-discriminatory laws in the country need to be enforced to provide a supportive environment for clients to voluntarily seek appropriate care without prejudice to their work and social belonging.

Among the socio-economic factors, one's educational status is linked with the nature and kind of job, and that influences how they can take care of their families, which also impact on the understanding of TB disease and its treatment as well as long-term adherence to treatment as noted by many studies. A study in Ghana noted that default was associated with clients with less income, which then means they are unable to afford other indirect costs associated with treatment thereby leading to defaulting. Another study found that unemployed people adhered more to treatment than those employed. This could be that employed people have difficulty getting permission to attend to treatment or may lose their jobs when their status is found out. Educational level is found to increase knowledge about TB diseases as well as obtaining and using the information on TB that impacts on optimal adherence. Studies in Kenya and Somalia documented a correlation between literacy and TB medication adherence, but surprisingly a study in Ghana found that 89% of illiterate TB clients adhered more to medication than literates. Hypothetically, this could be because most educated people are employed, and may not have time to go for scheduled appointments so prioritize work over treatment. Secondly, TB is perceived as a disease for the poor, and because of stigma, educated clients find it difficult accessing treatment, and finally, the educated Ghanaian is "sophisticated" and would always look at alternate opinions thereby impacting negatively on adherence.

On the health system factors, the attitude of health workers towards TB patients and its long-term impact on treatment adherence has been documented in many studies. The patient-provider relationship plays a crucial role in optimal adherence. Good communication with service providers helps clients get the needed information about the disease and its treatment, build trust and encourage them to share their challenges with the providers. Long waiting times experienced by clients in health facilities coupled with poor staff attitude combine to have a long-term impact on adherence. The poor staff attitude could be traced to the kind of training given, the low human resource for TB activities, poor motivation, and lack of equipment to work with as witnessed in the country, which then puts pressure on them. Most facilities do not have convenient opening hours for TB clients, which also impacts on adherence. A clinic during evening hours for follow up of TB patients may help people who are employed and fear to lose

their job. Ghana's TB treatment regimen and supply chain are per the WHO and Stop TB partnership guidelines. Though not documented, there are few cases of drug stock-outs in some facilities. The country is currently harnessing technology; the EWS and the LMIS to improve its drug supply chain. Funding for TB activities is inadequate, thereby posing as a challenge and affecting other activities such as human resources, training, supervision, and monitoring, etc., which then affects the quality of services. There is strong TB coordination to the district levels, but there is the need to strengthen leadership at the service delivery levels to improve collaboration and curbing of some of the challenges affecting service delivery.

4.2. Interventions to improve adherence to TB medication

Several interventions have been explored to improve adherence to TB in lower-middle-income countries, which ranges from conventional DOTS to digital adherence technologies. The use of treatment supporters has been advocated in many studies, which could help address the challenge of forgetfulness by clients to take their medications. But the supporters must be carefully chosen, as some clients may not like being supervised especially when the person is not close to them. It may also be challenging and fatigue may set in when the person has other responsibilities. Due to the role of family members in optimizing adherence, the use of peers and spouses, etc as treatment supporters could be beneficial. The CBDOTS, which is preferred to the HBDOTS, is mooted to solve some of the issues concerning staff attitude, stigma, and long distances to health facilities. Together with patient education and counseling, it helps to improve optimal adherence, but again, this requires available and dedicated human resources. The provision of enablers to TB clients in the form of food, cash, and vouchers has been recognized to improve adherence. This helps clients who are poor, unable to afford transport costs as well as feeding, the opportunity to meet those needs and stay adherent to their medication. A study in Nigeria found that financial incentives given to clients improved treatment success rates, but from experience, some clients have been noted to use those financial incentives for alcohol which defeats the purpose of the program, and infidelity on the part of health workers could also affect the program.

VOT, which offers health staff the opportunity to monitor patients take their drugs amid human resource constraint is one of the novel technologies but yet to be explored in many African countries. The device may be preferred by most clients especially those who will not want to be observed taking medication but infringes on the privacy of the individual especially taking videos that are viewed by someone else. The device may also have challenges with poor Internet connectivity in most parts of Ghana, and older people who may not be abreast with technology may find it difficult recording and sending videos. The use of the ingestible sensors provides high sensitivity, specificity, and patient acceptance but also relies on Internet connectivity to synchronize data to the central server. Some clients may find it stigmatizing especially wearing the sensors each time they take their medication, and larger studies are required to evaluate its acceptance and safety. The SMS can resolve some issues regarding forgetfulness to take medication, and its use has been recorded to improve adherence, reduce LTFU, and increase showing up at appointments in many studies. With the growing population of mobile phone users and the extension of the services to most rural parts of Ghana, this technology could be explored, but there is the need to do a feasibility study about its acceptance, willingness to use and cost to NTP. The pillbox, which also has an SMS component, is noted to improve adherence rate of 96.3% in a pilot study in Tanzania. The device may, however, give a false adherence rate, as the opening of the box is not synonymous with taking the drug, but could be effective when combined with sensitive devices like the ingestible sensors, and its cost component needs to be assessed. The 99DOTS is also good in addressing forgetfulness issues like other technologies, but issues about adherence are difficult to authenticate. The patient's cost is zero, although they need to have some credit to be able to use the toll-free numbers, and the cost to

the NTP needs to be considered. This technology has however been used in few studies and recorded an overall adherence rate of 96.03% in a pilot study in India, but this may be a biased patient group that agreed to use the technology and does not mean adherence would improve when implemented on a large scale.

4.3 Effective interventions and their applicability to improve TB medication adherence in BAR

A review of literature showed the proven interventions by Alipana et al. (26), which includes incentives and enablers, psychological interventions, reminders and tracers, patient education and counseling as well as treatment supporters could be used in the BAR to address several of the individual as well as the socio-cultural factors identified in the literature to improve TB treatment outcomes.

These interventions are cost-effective and feasible in resource-poor settings like the BAR. Ghana already has Community-Based Volunteers that assist in healthcare delivery and can be given minimal training to provide most of the services that have human-resource requirements like treatment supporters, educational counseling support and community education to reduce stigma. The use of mobile phones is expanding in BAR and Ghana, and their effectiveness has been documented. The use of text messages as reminders could help improve adherence and overcome forgetfulness to take medication. Based on WHO recommendations on the use of mHealth and evidence from other studies, they can be adopted in BAR and Ghana, however, there is the need to investigate the cost implication to the NTP before its full implementation.

Other interventions like the pillbox, 99DOTS, ingestible sensors, and VOT may not be feasible and applicable in the BAR context. Most of these require Internet connectivity to be able to synchronize data, which is currently a challenge especially in most rural communities in Ghana. Also, the stigma attached to using some of these devices means clients may not be willing to use them. Moreover, other operational costs to the NTP in the midst of dwindling funding makes it not sustainable.

The adapted conceptual framework by Roura et al 2009, for the literature review, though focuses on ART adherence, has been effective in analyzing individual, socio-economic, cultural, and health system factors that are likely to influence TB medication adherence in the BAR.

CHAPTER FIVE: CONCLUSIONS AND RECOMMENDATIONS

This chapter deals with conclusions of the study as well as some recommendations to relevant stakeholders including the NTP for considerations.

5.1 Conclusions

This study identified factors that are likely to influence TB medication adherence in the BAR. From the findings, stigma, and discrimination, financial constraint, lack of knowledge on TB and forgetfulness are highlighted as important barriers. Stigma and discrimination prevented people from disclosing their status because they fear to lose their jobs, thereby leading to poor social support and impacting on adherence. Forgetfulness arises as clients prioritize work above treatment, and also when some patients feel better due to poor knowledge of the need to complete treatment. Lack of knowledge of TB diseases and its treatment leads to people ascribing spiritual definitions to its causes, with some clients resorting to herbal and spiritual treatments alongside TB treatment, which worsens their condition.

Interventions that are evidence-based and could be useful in addressing the main challenges in the BAR were identified. These include patient education and counseling, enablers and incentives, psychological interventions, use of SMS as well as treatment supporters, and these will help address several of the challenges identified. Educational counseling, as well as tracers and reminders, will help address stigma and forgetfulness issues, whereas enablers and incentives, which include financial support, would help clients cope with other indirect costs associated with TB treatment.

5.2 Recommendations

The results of this study recommend the implementation of adherence-enhancing policies and effective interventions, which will address the most important factors likely to influence TB medication adherence in BAR. This can be done by the NTP playing a leadership role, guided by the MoH.

5.2.1 NTP, MoH, and Policymakers

1. The MoH should collaborate with Ghana's Ministry of Justice and the Attorney General to identify key gaps in policy and legal framework affecting TB clients to reduce stigma and discrimination. This will ensure the enforcement of laws such as anti-discriminatory laws at the workplace; ensuring working TB clients have access to treatment without hindrances and make patients aware of their rights and steps to take if their rights are not upheld.
2. A set of adherence interventions tailored towards the Ghanaian and BAR setting should be developed. Support teams for TB medication adherence should be established in all DOTS centers to provide psychological support to TB patients on treatment.
3. Training on a provider-patient relationship and adherence counseling should be provided for service providers, counselors, and peers. This will eventually help in reducing stigma.
4. Collaborating with donors such as the GF, World Food Program, and other agencies to improve and sustain the enablers' package to address financial difficulties faced by TB clients.

5.2.2 District/Regional Health Management Teams (D/RHMT)

1. D/RHMT to ensure they integrate TB activities especially on adherence counseling and ethics in their annual training plans to train requisite staff using the limited resources.
2. There is the need to make TB activities in the communities visible, especially having clinic hours in the evening, this may help those who are employed and fear to lose their jobs have access to treatment.
3. Community Health Officers^{xvii} should be encouraged to integrate TB educational activities in their community outreach programs, this will improve knowledge about TB and reduce stigma in the communities.

5.2.3 Non-Governmental Organizations

1. Integrate adherence support activities such as stigma reduction, peer education into their mainstream activities.
2. Collaborate with peer support groups to improve adherence promotion activities in their communities.

5.3 Areas for further research

Further research should focus on:

- a. How the factors influence TB adherence over time.
- b. Feasibility, cost-effectiveness, and perceptions of TB clients on using SMS to advance adherence in BAR and Ghana before full-scale implementation.

5.4 Study limitations

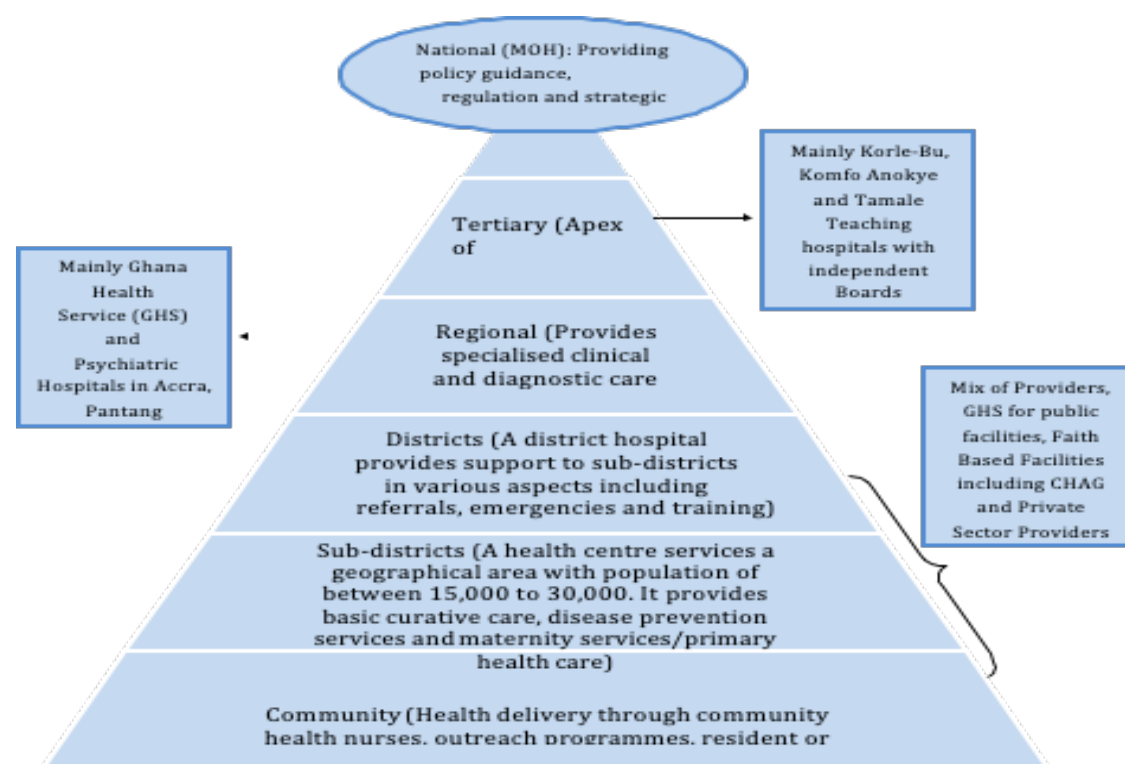
This thesis reviewed published and unpublished literature, but primary data collection would have been ideal to understand the problem and its associated factors vis-à-vis the literature review as the data used may not apply to the current situation. No study has been done in the BAR, and few studies were retrieved from other regions in Ghana which compelled information to be retrieved from other countries outside Ghana, and the possibility of that information been outdated could not be precluded as the health care is dynamic and adapts new policies and plans in the process. Time constraints could not allow for primary data collection.

^{xvii} These are usually nurses who are given specific training in Ghana's CHPS concept to provide preventive and curative services in CHPS zones as part of the Universal Health Coverage.

Appendix 1: Organizational structure of Health systems in Ghana

Ghana's health service is organized into a three-level system: from the national level at the apex, through the regional and district levels but is a five-level system in service delivery: from national, regional, district, sub-district, and CHPS zones as shown by figure seven below (11).

Figure 6: Organizational structure of health services in Ghana.



Source: GHS/District Health Information Management Systems (11).

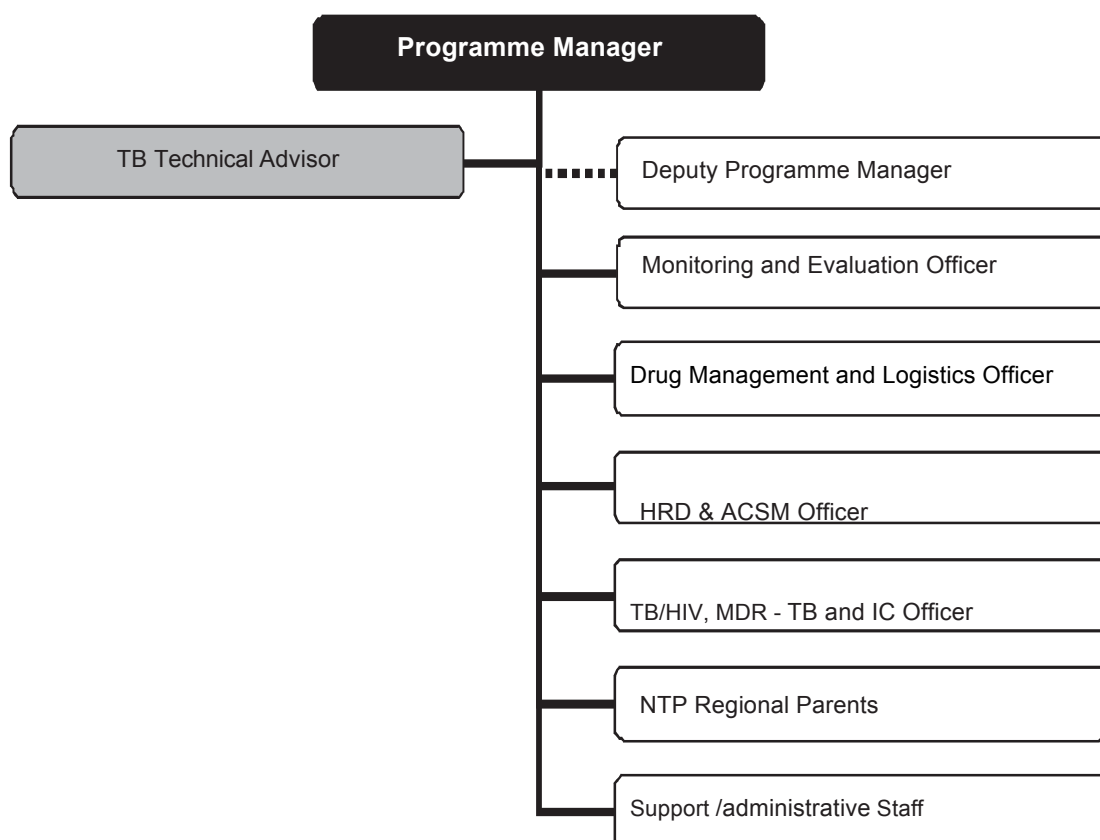
Ghana's health service delivery starts at the community level to the national level to ensure a comprehensive health service delivery package and the addition of private health facilities and other faith-based organizations is to ensure a wider range and access to health care for all (11). The teaching and regional hospitals serve as referral points for the polyclinics and district hospitals, while the polyclinics and hospitals serve as referral points for the health centers and CHPS zones. At the CHPS zones, most of their activities are preventive and refer all cases including obstetric cases to the next level. The MOH is at the top of the pyramid, situated at the national level and headed by a minister with several agencies to fulfill its mandate of making and regulating health policies in the country (141). The GHS, which is headed by a director-general, is composed of ten main divisions, with departments that carry out their main activities of the division (13). The GHS provides about 60% of health services delivery with the rest supplied by Teaching Hospitals, Christian Health Association of Ghana and the private sector. There are other agencies and bodies that regulate the activities of its members in the provision of health services such as the Ghana College of Surgeons and Physicians, Ghana Medical and Dental Council, Ghana Registered Nurses and Midwifery Association, Pharmacy Council, Food and Drugs Authority, the National Health Insurance Authority (142).

The Total Fertility Rate of Ghana for 2016 is 3.9 births per woman which is a reduction in the 2015 figure of 4.0 (143). Life expectancy at birth in years is at 62.7 (63.7 for females and 61.7 for males), a marginal improvement over that of the 2015 figure of 62.4 years (143), and that could be attributed to growth in health care and the economy. The top 5 causes of mortality in the country for 2017 were Stroke, coronary heart disease, Influenza and Pneumonia, malaria and Liver diseases (144), whereas TB was part of the top 10 causes of most deaths and disabilities combined in 2017 (145).

According to WHO, Ghana's Current Health Expenditure (CHE) as a % of Gross Domestic Products reduced from 6% in 2015 to 4% in 2016 with a Total Health Expenditure as % of GDP at 5.9% in 2015 (146). The Domestic General Government Health Expenditure reduced from 9% in 2015 to 7% in 2016, which is nowhere near the Abuja target of 15% (146). Out of pocket payments (OOPs) as a % of CHE increased from 36% in 2015 to 38% in 2016, which could increase financial catastrophe for many families (146). Ghana's Health Insurance Scheme was implemented in 2005, to remove barriers as a result of the user fees and provide equitable universal access to basic health care for the entire population (147). The main sources of financing the insurance scheme are the 2.5% National Health Insurance Levy on goods and services and a 2.5% social security contributions of workers in the formal sector (147). Other sources include money approved for the fund by parliament, accruals from investments by the authority, grants, donations and voluntary contributions, fees charged by the authority and contributions made by its members (147). Pregnant women and children under 18 years who form the greatest % of active members are covered under the scheme (148).

According to the WHO, Ghana has an estimated TB incidence of 152/100,000 populations (5). The notification rate for 2016 was 54/100,000 population, which is a decrease in the previous year's achievement (13). The implementation of critical activities of the NTP is organized within the structure of the health system in Ghana. The NTP is responsible for implementing TB technical activities, which includes planning, budgeting and technical oversight of these activities (141), and headed by a program manager. Funding for TB activities is from the Government of Ghana, DANIDA and the GF (149). Treatment success rates from 2013-2016 have remained at 85%, below WHO's 90% or more target. Notwithstanding its control efforts, the country has seen an increasing trend of MDR TB cases with an incidence of 3.4/100,000 populations in 2017 (150)

Appendix 2: organogram of NTP, Ghana.



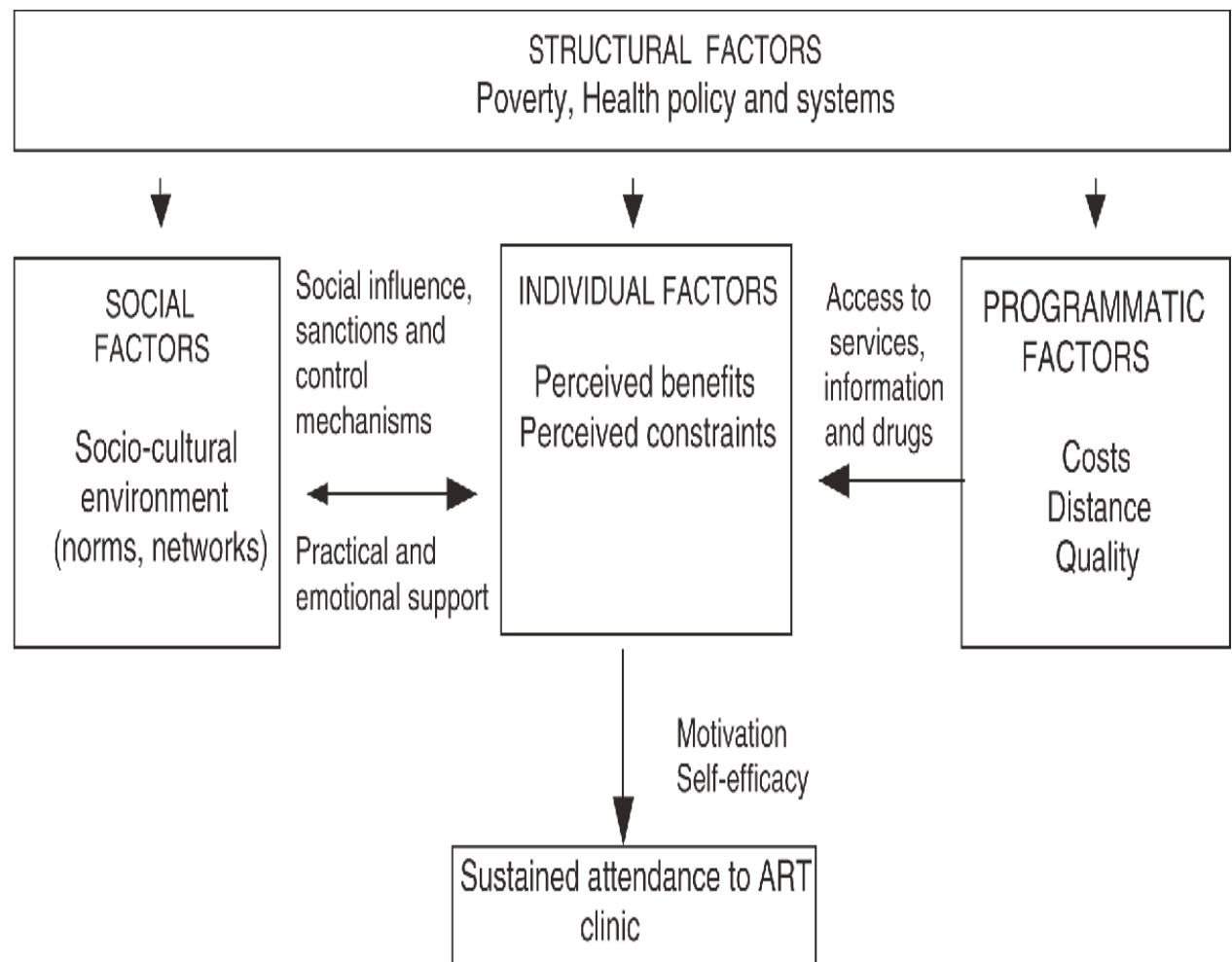
Source: Ghana health sector TB strategic plan 2009-2013 (141)

Appendix 3: Map of Ghana showing various regions



Source: Map of Ghana, Wikipedia (151).

Appendix 4: Conceptual framework for ART adherence



Source: Roura et al, 2009 (31).

REFERENCES

1. Norgbe GK. Factors influencing default rates of Tuberculosis patients in Ghana. *African J Nurses Midwifery*. 2011;13(2):67–76.
2. Boateng SA, Tomako K, Tomako T, Nobuyuki. H. Factors Contributing to Tuberculosis (TB) Defaulter Rate in New Juaben Municipality in the Eastern Region of Ghana. *J Natl Inst Public Heal*. 2010;59(3):291–7.
3. Lopez-Varela E, Sequera VG, García-Basteiro AL, Augusto OJ, Munguambe K, Sacarlal J, et al. Adherence to Childhood Tuberculosis Treatment in Mozambique. *J Trop Pediatr*. 2016;63(August 2016):87–97.
4. World Health Organization. Definitions and reporting framework for tuberculosis-2013 revision. 2014.
5. World Health Organization. Global 2018 TB report. Vol. 69, WHO report. 2018.
6. World Health Organization G. Adherence to long-term therapies. World Health Organization [Internet]. 2003 [cited 2019 Feb 20];1–194. Available from: <https://apps.who.int/iris/bitstream/handle/10665/42682/9241545992.pdf?sequence=1>
7. Jin J, Sklar GE, Min V, Oh S, Li SC. Factors affecting therapeutic compliance: A review from the patient's perspective. *Ther Clin Risk Manag* [Internet]. 2008 [cited 2019 Feb 20];4(1):269–86.
8. Brong Ahafo Regional Health Directorate. 2017 Annual report. Ghana Health Service. Sunyani, B/A; 2017.
9. Ghana Statistical Service. Ghana Living Standards Survey Round 6 (GLSS 6) report [Internet]. Accra, Ghana; 2014 [cited 2019 Jun 27]. Available from: http://www.statsghana.gov.gh/gssmain/fileUpload/Living conditions/GLSS6_Main Report.pdf
10. Ghana Statistical Service. Ghana Demographic and Health Survey 2014 [Internet]. Accra; 2015 [cited 2019 Jun 26]. Available from: <https://dhsprogram.com/pubs/pdf/fr307/fr307.pdf>
11. Ghana Health Service. DHIMS / Standard Operating Procedures for Health Information Management [Internet]. [cited 2019 Feb 21]. Available from: <https://dhims.chimgh.org/dhims/api/documents/wkOgpsPEqtS/data>
12. The Ghana Health Service. The Health sector in Ghana- Facts and Figures 2017. 2017.
13. Ghana Health Service. 2016 Annual Report. Ghana Health Service Reports. Accra, Ghana; 2017
14. WHO. Strategy to end TB [Internet]. 2014 [cited 2019 Mar 10]. Available from: https://www.who.int/tb/End_TB_brochure.pdf?ua=1
15. Ghana Health Service/NTP. Monitoring and evaluation plan for NTP, Accra-Ghana
16. Kaona FA, Tuba M, Siziya S, Sikaona L. An assessment of factors contributing to treatment adherence and knowledge of TB transmission among patients on TB treatment. *BMC Public Health*. 2004 Dec 29;4(1):68.
17. Ghana Health Service / NTP-Accra. Introduction To WHO Stop TB Strategy and TB Control Programme, Accra-Ghana.
18. Salifu Y, Eliason C, Mensah G. 'Ghost' stories: sociocultural factors influencing tuberculosis treatment adherence in Ghana. *Prim Heal Care*. 2016 Dec 29;26(10):34–41.
19. Danso E, Addo IY, Ampomah IG. Patients' Compliance with Tuberculosis Medication in Ghana: Evidence from a Periurban Community. *Adv Public Heal*. 2015;2015:1–6.
20. Dodor EA, Afenyadu GY. Factors associated with tuberculosis treatment default and completion at the Effia-Nkwanta Regional Hospital in Ghana. *Trans R Soc Trop Med Hyg*. 2005 Nov;99(11):827–32.
21. Burton NT, Forson A, Lurie MN, Kudzawu S, Kwarteng E, Kwara A. Factors associated with mortality and default among patients with tuberculosis attending a teaching hospital clinic in Accra, Ghana. *Trans R Soc Trop Med Hyg*. 2011 Dec;105(12):675–82.

22. Muture BN, Keraka MN, Kimuu PK, Kabiru EW, Ombeka VO, Oguya F. Factors associated with default from treatment among tuberculosis patients in Nairobi province, Kenya: A case control study. *BMC Public Health*. 2011 Dec 9;11(1):696.
23. Adejumo OA, Daniel OJ, Otesanya AF, Ashipa T, Adejumo EN, Abdur-Razzaq HA. Factors Affecting Treatment Interruption among TB Patients in Lagos Nigeria: Is There Any Need for Treatment Supporters? *Int J Clin Med*. 2012;7:389–98.
24. Gugssa Boru C, Shimels T, Bilal AI. Factors contributing to non-adherence with treatment among TB patients in Sodo Woreda, Gurage Zone, Southern Ethiopia: A qualitative study. *J Infect Public Health*. 2017 Sep;10(5):527–33.
25. Mkopi A, Range N, Lwilla F, Egwaga S, Schulze A, Geubbels E, et al. Adherence to Tuberculosis Therapy among Patients Receiving Home-Based Directly Observed Treatment: Evidence from the United Republic of Tanzania. *PLoS One*. 2012;7(12):1–7.
26. Alipanah N, Jarlsberg L, Miller C, Linh NN, Falzon D, Jaramillo E, et al. Adherence interventions and outcomes of tuberculosis treatment: A systematic review and meta-analysis of trials and observational studies. Murray M, editor. *PLOS Med*. 2018 Jul 3;15(7):e1002595.
27. World Health Organization. Tuberculosis Country Profile-Ghana [Internet]. [cited 2019 Feb 20]. Available from: https://extranet.who.int/sree/Reports?op=Replet&name=%2FWHO_HQ_Reports%2FG2%2FPROD%2FEXT%2FTBCountryProfile&ISO2=GH&LAN=EN&outtype=html
28. Boakye-Appiah JK, Steinmetz AR, Pupilampu P, Ofori-Yirenkyi S, Tetteh I, Frimpong M, et al. High prevalence of multidrug-resistant tuberculosis among patients with rifampicin resistance using GeneXpert Mycobacterium tuberculosis/rifampicin in Ghana. *Int J Mycobacteriology*. 2016 Jun 1;5(2):226–30.
29. Amo-Adjei J, Awusabo-Asare K. Reflections on tuberculosis diagnosis and treatment outcomes in Ghana. *Arch Public Heal*. 2013 Dec 23;71(1):22.
30. Ghana Health Service / NTP-Accra. Plan to Initiate and Expand Drug Resistant TB Management in Ghana. 2011, Accra-Ghana.
31. Roura M, Busza J, Wringe A, Mbata D, Urassa M, Zaba B. Barriers to Sustaining Antiretroviral Treatment in Kisesa, Tanzania: A Follow-Up Study to Understand Attrition from the Antiretroviral Program. *AIDS Patient Care STDS*. 2009;23(3):203–10.
32. Dodor E.A. Tuberculosis treatment default at the Communicable Diseases Unit of Effia-Nkwanta Regional Hospital: A 2-year experience. *Int J Tuberc Lung Dis*. 2004;8(11):1337–41.
33. Adane AA, Alene KA, Koye DN, Zeleke BM. Non-adherence to anti-tuberculosis treatment and determinant factors among patients with tuberculosis in northwest Ethiopia. *PLoS One*. 2013;8(11).
34. Shargie EB, Lindtjørn B. Determinants of treatment adherence among smear-positive pulmonary tuberculosis patients in Southern Ethiopia. *PLoS Med*. 2007;4(2):0280–7.
35. Ifebunandu NA, Ukwaja KN. Tuberculosis treatment default in a large tertiary care hospital in urban Nigeria: Prevalence, trend, timing and predictors. *J Infect Public Health*. 2012;5(5):340–5.
36. Tola HH, Tol A, Shojaeizadeh D, Garmaroudi G. Tuberculosis Treatment Non-Adherence and Lost to Follow Up among TB Patients with or without HIV in Developing Countries: A Systematic Review. *Iran J Public Health*. 2015;44(1):1–11.
37. van Elsland SL, Springer P, Steenhuis IHM, van Toorn R, Schoeman JF, Marceline van Furth A. Tuberculous meningitis: Barriers to adherence in home treatment of children and caretaker perceptions. *J Trop Pediatr*. 2012;58(4):275–9.
38. Kisambu J., Nuwaha F., Sekandi J.N. Adherence to treatment and supervision for tuberculosis in a DOTS programme among pastoralists in Uganda. *Int J Tuberc Lung Dis*. 2014;18(7):799–803+i.
39. Fagundez G, Perez-Freixo H, Eyene J, Momo JC, Biyé L, Esono T, et al. Treatment adherence of tuberculosis patients attending two reference units in Equatorial

- Guinea. *PLoS One*. 2016;11(9):1–13.
40. Kigozi G, Heunis C, Chikobvu P, Botha S, van Rensburg D. Factors influencing treatment default among tuberculosis patients in a high burden province of South Africa. *Int J Infect Dis*. 2017;54:95–102.
 41. Gust DA, Mosimaneotsile B, Mathebula U, Chingapane B, Gaul Z, Pals SL, et al. Risk factors for non-adherence and loss to follow-up in a three-year clinical trial in Botswana. *PLoS One*. 2011;6(4).
 42. Munro SA, Lewin SA, Smith HJ, Engel ME, Fretheim A, Volmink J. Patient adherence to tuberculosis treatment: A systematic review of qualitative research. *PLoS Med*. 2007;4(7):1230–45.
 43. Ukwaja KN, Alobu I, Gidado M, Onazi O, Oshi DC. Economic support intervention improves tuberculosis treatment outcomes in rural Nigeria. *Int J Tuberc Lung Dis*. 2017;21(5):564–70.
 44. Tola HH, Karimi M, Yekaninejad MS. Effects of sociodemographic characteristics and patients' health beliefs on tuberculosis treatment adherence in Ethiopia: A structural equation modelling approach. *Infect Dis Poverty*. 2017;6(1):1–10.
 45. Ali MK, Karanja S, Karama M. Factors associated with tuberculosis treatment outcomes among tuberculosis patients attending tuberculosis treatment centres in 2016–2017 in Mogadishu, Somalia. *Pan Afr Med J*. 2017;28:1–14.
 46. Tola HH, Shojaeizadeh D, Tol A, Garmaroudi G, Yekaninejad MS, Kebede A, et al. Psychological and educational intervention to improve tuberculosis treatment adherence in Ethiopia based on health belief model: A cluster randomized control trial. *PLoS One*. 2016;11(5):1–15.
 47. Kulkarni P, Akarte S, Mankeshwar R, Bhawalkar J, Banerjee A, Kulkarni A. Non-Adherence of New Pulmonary Tuberculosis Patients to Anti-Tuberculosis Treatment. *Ann Med Health Sci Res*. 2013;3(1):67.
 48. P. N, K. P, J. L, G. M, G. M, B. T. Predictors of tuberculosis (TB) and antiretroviral (ARV) medication non-adherence in public primary care patients in South Africa: a cross sectional study. *BMC Public Health*. 2013;13:396.
 49. Tagoe ET, Agbadi P, Adomah-Afari A. Influential Factors in the Treatment Outcomes of Tuberculosis in Directly Observed Therapy at the La General Hospital in the Greater Accra Region, Ghana. *J Human, Environ Heal Promot*. 2019;4(3):99–105.
 50. Wanyonyi AW, Wanjala PM, Githuku J, Oyugi E, Kutima H. Factors associated with interruption of tuberculosis treatment among patients in Nandi County, Kenya 2015. *Pan Afr Med J*. 2017;28(Suppl 1):11.
 51. Skinner D, Claassens M. It's complicated: Why do tuberculosis patients not initiate or stay adherent to treatment? A qualitative study from South Africa. *BMC Infect Dis*. 2016;16(1):1–9.
 52. Sendagire I, van der Loeff MS, Kambugu A, Konde-Lule J, Cobelens F. Urban movement and alcohol intake strongly predict defaulting from tuberculosis treatment: An operational study. *PLoS One*. 2012;7(5).
 53. Salify Y, Eliason C, Mensah G. Tuberculosis treatment adherence in Ghana: Patient's perspective of barriers and enablers to treatment. *Int J Nurs Midwifery*. 2017;1(2):11–22.
 54. Méda ZC, Lin YT, Sombié I, Maré D, Morisky DE, Chen YMA. Medication-adherence predictors among patients with tuberculosis or human immunodeficiency virus infection in Burkina Faso. *J Microbiol Immunol Infect*. 2014;47(3):222–32.
 55. Gebreweld FH, Kifle MM, Gebremicheal FE, Simel LL, Gezae MM, Ghebreyesus SS, et al. Factors influencing adherence to tuberculosis treatment in Asmara, Eritrea: a qualitative study. *J Heal Popul Nutr*. 2018;37(1):1–9.
 56. Elbireer S, Guwatudde D, Mudiope P, Nabbuye-Sekandi J, Manabe YC. Tuberculosis treatment default among HIV-TB co-infected patients in urban Uganda. *Trop Med Int Heal*. 2011;16(8):981–7.
 57. Nackers F, Huerga H, Espié E, Aloo AO, Bastard M, Etard JF, et al. Adherence to self-administered tuberculosis treatment in a high hiv-prevalence setting: A cross-sectional survey in homa bay, Kenya. *PLoS One*. 2012;7(3):1–8.

58. Tesfahuneygn G, Medhin G, Legesse M. Adherence to Anti-tuberculosis treatment and treatment outcomes among tuberculosis patients in Alamata District, northeast Ethiopia. *BMC Res Notes*. 2015;8(1):1–11.
59. Mekonnen HS, Azagew AW. Non-adherence to anti-tuberculosis treatment, reasons and associated factors among TB patients attending at Gondar town health centers, Northwest Ethiopia. *BMC Res Notes*. 2018;11(1):1–8.
60. Naidoo P, Dick J, Cooper D. Exploring Tuberculosis Patients ' Adherence Programs at a Public Health Site. *Qual Health Res*. 2009;19(1):55–70.
61. M.K. G, G.A. B, J.C. F. Barriers and facilitators of adherence to TB treatment in patients on concomitant TB and HIV treatment: a qualitative study. *BMC Public Health*. 2010;
62. Montagu D. Franchising of health services in low-income countries. *Health Policy Plan*. 2002 Jun 1;17(2):121–30.
63. Birch S, Govender V, Fried J, Eyles J, Daries V, Moshabela M, et al. Does treatment collection and observation each day keep the patient away? An analysis of the determinants of adherence among patients with Tuberculosis in South Africa. *Health Policy Plan*. 2016;31(4):454–61.
64. Sagbakken M, Frich JC, Bjune G. Barriers and enablers in the management of tuberculosis treatment in Addis Ababa, Ethiopia: A qualitative study. *BMC Public Health*. 2008;8:1–11.
65. Ministry of Health. Ghana Health Financing Strategy [Internet]. 2015 [cited 2019 Feb 21]. Available from: <http://www.moh.gov.gh/wp-content/uploads/2016/02/Health-Finance-Strategy-160203045304.pdf>
66. Kizito KW, Dunkley S, Kingori M, Reid T. Lost to follow up from tuberculosis treatment in an urban informal settlement (Kibera), Nairobi, Kenya: What are the rates and determinants? *Trans R Soc Trop Med Hyg*. 2011;105(1):52–7.
67. Tola HH, Garmaroudi G, Shojaeizadeh D, Tol A, Yekaninejad MS, Ejeta LT, et al. The effect of psychosocial factors and patients' perception of tuberculosis treatment non-adherence in Addis Ababa, Ethiopia. *Ethiop J Health Sci*. 2017;27(5):447.
68. Patton GC, Coffey C, Carlin JB, Degenhardt L, Hall W, Lynskey M. Adherence in the treatment of patients with extensively drug-resistant tuberculosis and HIV in South Africa: A prospective cohort study. *BMJ (Clinical Res ed)*. 2002;325(August 2008):1195–8.
69. Dodor EA, Kelly SJ. Manifestations of tuberculosis stigma within the healthcare system: The case of Sekondi-Takoradi Metropolitan district in Ghana. *Health Policy (New York)*. 2010 Dec;98(2–3):195–202.
70. Diefenbach-Elstob T, Plummer D, Dowi R, Wamagi S, Gula B, Siwaeya K, et al. The social determinants of tuberculosis treatment adherence in a remote region of Papua New Guinea. *BMC Public Health [Internet]*. 2017;17(1):1–12. Available from: <http://dx.doi.org/10.1186/s12889-016-3935-7>
71. Ukwaja KN, Alobu I, Mustapha G, Onazi O, Oshi DC. "Sustaining the DOTS": Stakeholders' experience of a social protection intervention for TB in Nigeria. *Int Health*. 2017;9(2):112–7.
72. Takele T, Meaza D, Yemane B, Yigzaw K, Markos A. Long distance travelling and financial burdens discourage tuberculosis DOTs treatment initiation and compliance in Ethiopia: a qualitative study. *BMC Public Health*. 2013;13.
73. Ayisi JG, van't, Hoog AH, Agaya JA, McHembere W, Nyamthimba PO, et al. Care seeking and attitudes towards treatment compliance by newly enrolled tuberculosis patients in the district treatment programme in rural western Kenya: a qualitative study. *BMC Public Health*. 2011;11(1):515–24.
74. Wabe N, Kebede A. Medication adherence and its determinants among patients on concomitant tuberculosis and antiretroviral therapy in South West Ethiopia. *N Am J Med Sci*. 2012;4(2):67.
75. Ndwiga JM, Kikuvu G, Omolo JO. Factors influencing knowledge on completion of treatment among tb patients under directly observed treatment strategy, in selected health facilities in embu county, Kenya. *Pan Afr Med J*. 2016;25:1–8.

76. Woimo TT, Yimer WK, Bati T, Gesesew HA. The prevalence and factors associated for anti-tuberculosis treatment non-adherence among pulmonary tuberculosis patients in public health care facilities in South Ethiopia: a cross-sectional study. *BMC Public Health*. 2017;17(1):1–10.
77. Amuha MG, Kutyabami P, Kitutu FE, Odoi-Adome R, Kalyango JN. Non-adherence to anti-TB drugs among TB/HIV co-infected patients in Mbarara Hospital Uganda: prevalence and associated factors. *Afr Health Sci*. 2009;9 Suppl 1(August):S8-15.
78. World Health Organization (WHO). *Monitoring the building blocks of Health systems: a handbook of indicators and their measurement strategies*. Geneva; 2010.
79. Atun R, Weil DE, Eang MT, Mwakyusa D. Health-system strengthening and tuberculosis control. *Lancet*. 2010 Jun;375(9732):2169–78.
80. Amo-Adjei J, Kumi-Kyereme A, Fosuah Amo H, Awusabo-Asare K. The politics of tuberculosis and HIV service integration in Ghana. *Soc Sci Med*. 2014 Sep;117:42–9.
81. Ministry of Health. *The National Tuberculosis Health Sector Strategic Plan for Ghana (2009-2013)*. Accra; 2009-Ghana.
82. Mauch V, Bonsu F, Gyapong M, Awini E, Suarez P, Marcelino B, et al. Free tuberculosis diagnosis and treatment are not enough: patient cost evidence from three continents. *Natl TB Control Program*. 2013;17(3):381–7.
83. Ansa GA, Walley JD, Siddiqi K, Wei X. Assessing the impact of TB/HIV services integration on TB treatment outcomes and their relevance in TB/HIV monitoring in Ghana. *Infect Dis Poverty*. 2012 Dec 24;1(1):13.
84. Amo-Adjei J. Political commitment to tuberculosis control in Ghana. *Glob Public Health*. 2014 Mar 16;9(3):299–311.
85. Dräger S, Gedik G, Dal Poz MR. Health workforce issues and the Global Fund to fight AIDS, Tuberculosis and Malaria: an analytical review. *Hum Resour Health* [Internet]. 2006 Dec 24 [cited 2019 Jun 17];4(1):23. Available from: <https://human-resources-health.biomedcentral.com/articles/10.1186/1478-4491-4-23>
86. Anand S, Bärnighausen T. Human resources and health outcomes: cross-country econometric study. *Lancet*. 2004 Oct;364(9445):1603–9.
87. Ebenezer Appiah-Denkyira, Christopher H. Herbst, Agnes Soucat, Christopher Lemiere, Karima Saleh. *Toward Interventions in Human Resources for Health in Ghana-Evidence for Health Workforce Planning and Results*. Washington, DC: World Bank; 2013
88. World Health Organization. *Global Health Observatory | By category | Skilled health personnel - Data by country* [Internet]. WHO. World Health Organization; 2010.
89. Ghana Health Service. *Ghana Health Service DHIMS 2*. Accra, Ghana.
90. World Health Organization. *Everybody's business: strengthening health systems to improve health outcomes. WHO's framework for action*. Geneva; 2007
91. Ghana Health Service / NTP-Accra. *National TB Control Programme 2019*.
92. Atun R, Pothapregada SK, Kwansah J, Degbotse D, Lazarus J V. Critical Interactions Between the Global Fund-Supported HIV Programs and the Health System in Ghana. *JAIDS J Acquir Immune Defic Syndr*. 2011 Aug;57:S72–6.
93. Floyd K, Fitzpatrick C, Pantoja A, Raviglione M. Domestic and donor financing for tuberculosis care and control in low-income and middle-income countries: an analysis of trends, 2002–11, and requirements to meet 2015 targets. *Lancet Glob Heal*. 2013 Aug;1(2):105–15.
94. Ghana Health Service / MOH. *Implementation of TB/HIV collaborative activities in Ghana*. Accra; 2007 [cited 2019 Jun 12]. Available from: http://www.ghanahealthservice.org/downloads/TBHIV_Technical_Policy_Guidelines-Ghana.pdf
95. Ansa GA, Walley JD, Siddiqi K, Wei X. Delivering TB/HIV services in Ghana: a comparative study of service delivery models. *Trans R Soc Trop Med Hyg*. 2014 Sep 1;108(9):560–7.

96. Ghana Health Service/NTP. Guidelines for the Clinical Management of TB and HIV Co-infection in Ghana [Internet]. Accra; 2007 [cited 2019 Jun 17]. Available from: <https://www.who.int/hiv/pub/guidelines/ghana.pdf>
97. World Health Organization. WHO policy on collaborative TB/HIV activities. Guidelines for national programmes and other stakeholders. Geneva; 2012. 1–36 p.
98. Coetzee D, Hilderbrand K, Goemaere E, Matthys F, Boelaert M. Integrating tuberculosis and HIV care in the primary care setting in South Africa. *Trop Med Int Heal*. 2004 Jun;9(6):A11–5.
99. Harris JB, Hatwiinda SM, Randels KM, Chi BH, Kanchea NG, Jham MA, et al. Early lessons from the integration of tuberculosis and HIV services in primary care centers in Lusaka, Zambia. *Int J Tuberc Lung Dis*. 2008;12(7):773–9.
100. Sweeney S, Obure CD, Maier CB, Greener R, Dehne K, Vassall A. Costs and efficiency of integrating HIV/AIDS services with other health services: a systematic review of evidence and experience. *Sex Transm Infect*. 2012 Mar;88(2):85–99.
101. Ibrahim LM, Hadejia IS, Nguku P, Dankoli R, Waziri NE, Akhimien MO, et al. Factors associated with interruption of treatment among pulmonary tuberculosis patients in plateau state, Nigeria. 2011. *Pan Afr Med J*. 2014;17:1–8.
102. Zegeye A, Dessie G, Wagnew F, Gebrie A, Islam SMS, Tesfaye B, et al. Prevalence and determinants of anti-tuberculosis treatment non-adherence in Ethiopia: A systematic review and meta-analysis. *PLoS One*. 2019;14(1):1–15.
103. Nepal A, Shiyalap K, Sermsri S, Keiwekarnka B. Compliance with DOTS among tuberculosis patients under community based DOTS strategy in Palpa District, Nepal. *Int J Infect Microbiol*. 2012;1(1):14–9.
104. Mulogo EM, Nahabwe C, Bagenda F, Batwala V. Determinants of treatment completion among rural smear positive pulmonary tuberculosis patients: A cross-sectional survey conducted in south-western Uganda. *Infect Dis Poverty*. 2017;6(1):1–7.
105. Ruru Y, Matasik M, Oktavian A, Senyorita R, Mirino Y, Tarigan LH, et al. Factors associated with non-adherence during tuberculosis treatment among patients treated with DOTS strategy in Jayapura, Papua Province, Indonesia. *Glob Health Action*. 2018;11(1).
106. Nezenega Sahile Z, Gacho Michael H, Tafere Ejigu T. Patient satisfaction on tuberculosis treatment service and adherence to treatment in public health facilities of Sidama zone, South Ethiopia. *BMC Health Serv Res*. 2013;13:110.
107. DiStefano MJ, Schmidt H. mHealth for Tuberculosis Treatment Adherence: A Framework to Guide Ethical Planning, Implementation, and Evaluation. *Glob Heal Sci Pract*. 2016;4(2):211–21.
108. Hoffman JA, Cunningham JR, Suleh AJ, Sundsmo A, Dekker D, Vago F, et al. Mobile Direct Observation Treatment for Tuberculosis Patients. A Technical Feasibility Pilot Using Mobile Phones in Nairobi, Kenya. *Am J Prev Med*. 2010;39(1):78–80.
109. DeMaio J, Schwartz L, Cooley P, Tice A. The Application of Telemedicine Technology to a Directly Observed Therapy Program for Tuberculosis: A Pilot Project. *Clin Infect Dis*. 2002;33(12):2082–4.
110. Nguyen TA, Pham MT, Nguyen TL, Nguyen VN, Pham DC, Nguyen BH, et al. Video Directly Observed Therapy to support adherence with treatment for tuberculosis in Vietnam: A prospective cohort study. *Int J Infect Dis*. 2017;65:85–9.
111. Denking CM, Grenier J, Stratis AK, Akkihal. A, Pant-Pai N, Pai M. Mobile health to improve tuberculosis care and control: A call worth making. *Int J Tuberc Lung Dis*. 2013;17(6):719–27.
112. Ngwatu BK, Nsengiyumva NP, Oxlade O, Mappin-Kasirer B, Nguyen NL, Jaramillo E, et al. The impact of digital health technologies on tuberculosis treatment: a systematic review. *Eur Respir J*. 2018;51(1).
113. Mohammed S, Glennerster R, Khan AJ. Impact of a daily SMS medication reminder system on tuberculosis treatment outcomes: A randomized controlled trial. *PLoS*

- One. 2016;11(11):1–13.
114. Nglazi MD, Wood R, Hussey GD, Bekker L-G, Wiysonge CS. Mobile phone text messaging for promoting adherence to anti-tuberculosis treatment: a systematic review. *BMC Infect Dis.* 2013;13(1):1–16.
 115. Liu Q, Abba K, Alejandria MM, Sinclair D, Balanag VM, Lansang MAD, et al. Reminder systems to improve patient adherence to tuberculosis clinic appointments for diagnosis and treatment -Systematic Review. *Cochrane Database Syst Rev.* 2014;(11):1–59.
 116. Bediang G, Stoll B, Elia N, Abena J-L, Geissbuhler A. SMS reminders to improve adherence and cure of tuberculosis patients in Cameroon (TB-SMS Cameroon): a randomised controlled trial. *BMC Public Health.* 2018;18(1):583.
 117. Hermans S., Elbireer S, Tibakabikoba H, Hoefman BJ, Manabe YC. Text messaging to decrease tuberculosis treatment attrition in TB-HIV coinfection in Uganda. *Patient Prefer Adherence.* 2017;11:1479–87.
 118. Car J, Gurol-Urganci I, de Jongh T, Vodopivec-Jamsek V, Atun R. Mobile phone messaging reminders for attendance at healthcare appointments. *Cochrane Database Syst Rev.* 2012;(12).
 119. Siedner MJ, Lankowski A, Musinga D, Jackson J, Muzoora C, Hunt PW, et al. Optimizing Network Connectivity for Mobile Health Technologies in sub-Saharan Africa. *PLoS One.* 2012;7(9):1–5.
 120. Boogaard J van den, Lyimo RA, Boeree MJ, Kibiki GS, Aarnoutse RE. Electronic monitoring of treatment adherence and validation of alternative adherence measures in tuberculosis patients: a pilot study. *Bull World Health Organ.* 2011;89:632–9.
 121. de Sumari-de Boer IM, van den Boogaard J, Ngowi KM, Semvua HH, Kiwango KW, Aarnoutse RE, et al. Feasibility of Real Time Medication Monitoring Among HIV Infected and TB Patients in a Resource-Limited Setting. *AIDS Behav.* 2016 May 24;20(5):1097–107.
 122. Liu X, Lewis JJ, Zhang H, Lu W, Zhang S, Zheng G, et al. Effectiveness of Electronic Reminders to Improve Medication Adherence in Tuberculosis Patients: A Cluster-Randomised Trial. *PLoS Med.* 2015;12(9):1–18.
 123. Subbaraman R, de Mondesert L, Musiimenta A, Pai M, Mayer KH, Thomas BE, et al. Digital adherence technologies for the management of tuberculosis therapy: mapping the landscape and research priorities. *BMJ Glob Heal.* 2018 Oct 11;3(5):1–16.
 124. Thekkur P, Kumar AM, Chinnakali P, Selvaraju S, Bairy R, Singh AR, et al. Outcomes and implementation challenges of using daily treatment regimens with an innovative adherence support tool among HIV-infected tuberculosis patients in Karnataka, India: a mixed-methods study. *Glob Health Action.* 2019 Jan 4;12(1):1–12.
 125. World Health Organization. Handbook for the use of digital technologies to support Tuberculosis Medication adherence. Geneva; 2017. 1–58 p.
 126. Thakkar D, Kiran GP, Suresh GL. A pilot project: 99DOTS information communication technology-based approach for tuberculosis treatment in Rajkot district. *Lung India.* 2019;36(2):108–11.
 127. Cross A, Gupta N, Liu B, Nair V, Kumar A, Kuttan R, et al. 99DOTS: A low-cost approach to monitoring and improving medication adherence. *ACM Int Conf Proceeding Ser.* 2019;1–12.
 128. Ghatage S, S AM, Aithal SS, B SD, Angadi N. A study on reasons for nonadherence to 99DOTS among HIV-tuberculosis coinfecting patients in Davanagere district, Karnataka. *Int J Med Sci Public Heal.* 2018;(10):1–4.
 129. Belknap R, Weis S, Brookens A, Au-Yeung KY, Moon G, DiCarlo L, et al. Feasibility of an Ingestible Sensor-Based System for Monitoring Adherence to Tuberculosis Therapy. Pai M, editor. *PLoS One.* 2013 Jan 7;8(1):1–5.
 130. Au-Yeung KY, DiCarlo L. Cost comparison of wirelessly vs. directly observed therapy for adherence confirmation in anti-tuberculosis treatment. *Int J Tuberc Lung Dis.* 2012 Nov 1;16(11):1498–504.

131. Verputten M, Kasozi S, Reynolds L, du Cros P, Casas EC, Horter S, et al. "Home is where the patient is": a qualitative analysis of a patient-centred model of care for multi-drug resistant tuberculosis. *BMC Health Serv Res.* 2014;14(1):1–8.
132. Boateng SA, Kodama T, Sata F, Bonsu G, Osawa E. Community-involved strategy to improve tuberculosis (TB) treatment outcomes in Eastern Region of Ghana. *J Natl Inst Public Heal.* 2012;
133. Adewole OO, Oladele T, Osunkoya AH, Erhabor GE, Adewole TO, Adeola O, et al. A randomized controlled study comparing community based with health facility based direct observation of treatment models on patients' satisfaction and TB treatment outcome in Nigeria. *Trans R Soc Trop Med Hyg.* 2015;109(12):783–92.
134. Thiam S, LeFevre AM, Hane F, Ndiaye A, Ba F, Fielding KL, et al. Effectiveness of a Strategy to Improve Adherence to Tuberculosis Treatment in a Resource-Poor Setting-A Cluster Randomized Controlled Trial. *Jama.* 2007;297(4):380.
135. Lutge EE, Wiysonge CS, Knight SE, Sinclair D, Volmink J. Incentives and enablers to improve adherence in tuberculosis. *Cochrane Database Syst Rev.* 2015 Sep 3;(9).
136. Lutge E, Lewin S, Volmink J. Economic support to improve tuberculosis treatment outcomes in South Africa: a qualitative process evaluation of a cluster randomized controlled trial. 2014;15(1):236.
137. Stuurman AL, Vonk Noordegraaf-Schouten M, van Kessel F, Oordt-Speets AM, Sandgren A, van der Werf MJ. Interventions for improving adherence to treatment for latent tuberculosis infection: A systematic review. *BMC Infect Dis.* 2016;16(1).
138. van Hoorn R, Jaramillo E, Collins D, Gebhard A, van den Hof S. The Effects of Psycho-Emotional and Socio-Economic Support for Tuberculosis Patients on Treatment Adherence and Treatment Outcomes - A Systematic Review and Meta-Analysis. *PLoS One.* 2016;11(4):1–27.
139. de Pee S, Grede N, Mehra D, Bloem MW. The Enabling Effect of Food Assistance in Improving Adherence and/or Treatment Completion for Antiretroviral Therapy and Tuberculosis Treatment: A Literature Review. *AIDS Behav.* 2014;18:531–41.
140. Ong'ang'o JR, Mwachari C, Kipruto H, Karanja S. The effects on tuberculosis treatment adherence from utilising community health workers: A comparison of selected rural and urban settings in Kenya. *PLoS One.* 2014;9(2):1–8.
141. Ministry of Health. The National Tuberculosis Health Sector Strategic Plan for Ghana 2009-2013. Accra; 2009-Ghana.
142. Ministry of Health. Ministries and Agencies, Accra-Ghana 2019.
143. The World Bank. Ghana Country Data. [cited 2019 Feb 21].
144. World Health Organization. Health Profile of Ghana-Age adjusted death rate estimates: 2017. [cited 2019 Feb 21].
145. Institute for Health Metrics and Evaluation (IHME). Ghana-Health Metrics and Evaluation. [cited 2019 Feb 21].
146. World Health Organization. Global Health Expenditure Database. 2017 [cited 2019 Feb 21].
147. National Health Insurance Authority-Ghana. National Health Insurance ACT [Internet]. 2012 [cited 2019 Feb 21]. Available from: <http://www.nhis.gov.gh/files/ACT852.pdf>
148. National Health Insurance Authority. NATIONAL HEALTH INSURANCE AUTHORITY 2013 ANNUAL REPORT, Accra-Ghana. 2013 [cited 2019 Mar 13]. Available from: [http://www.nhis.gov.gh/files/2013 Annual Report-Final ver 29.09.14.pdf](http://www.nhis.gov.gh/files/2013%20Annual%20Report-Final%20ver%2029.09.14.pdf)
149. Ministry of Health. The National TB Health Sector Strategic Plan for Ghana, 2015-2020, Accra-Ghana.
150. World Health Organization. Estimates of TB and MDR-TB burden-Ghana [Internet]. 2017 [cited 2019 Feb 21]. Available from: https://extranet.who.int/sree/Reports?op=Replet&name=%2FWHO_HQ_Reports%2FG2%2FPROD%2FEXT%2FTBCountryProfile&ISO2=GH&LAN=EN&outtype=html
151. Regions of Ghana, 2019 [Internet]. Modern Ghana. 2019 [cited 2019 Aug 13]. Available from: <https://www.modernghana.com/news/916140/ghana-now-has-16-regions.html>

