INTERVENTIONS TO PROMOTE ADHERENCE TO TREATMENT AMONG ADULT PATIENTS WITH TUBERCULOSIS: EVIDENCE-BASED NURSING

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ABSTRACT

Tuberculosis (TB) is a major public health problem of global proportions including Bangladesh. Regardless, a large number of TB patients discontinue treatment. This leads to increased transmission of tubercle bacilli, as well as morbidity and mortality rates in at community and national levels. Effective interventions need to be identified to promote treatment adherence.

The objective of this study was to summarize current evidence-based interventions to promote treatment adherence among adult patients with TB. The PICO framework was used as a guideline to search for relevant studies in the electronic database sources of the Mahidol University library system. The author searched for systematic reviews published in English from 2010 to 2016. After the search, the author selected eight systematic reviews. All of the studies were appraised by the guidelines proposed by Melnyk and Fineout-Overholt (2015). Based on the aforementioned evidence, it is asserted that direct observe treatment (DOT) alone is unable to promote TB treatment adherence. Rather, a combination of other interventions with DOT is required. The interventions combined with DOT include the following: i) case management with DOT; ii) triad-model program with DOT; iii) intervention package with DOT. However, education and counselling interventions are effective strategies for enhancing treatment adherence. Moreover, reminder systems are also successful interventions for promoting adherence to TB treatment and clinic appointments. Reminder types should be included with these strategies. Telephone calls and letters can be used before a scheduled appointment as a pre-appointment reminder. To the contrary, letters or home visits can be used as default reminders after a missed appointment.

Finally, the author suggests that recommendations be used to develop clinical practice guidelines on interventions promoting adherence to treatment among adult TB patients in the clinical setting of Bangladesh. Further research should be conducted to evaluate intervention effectiveness in promoting treatment adherence among TB patients.

KEY WORDS: TB PATIENTS / INTERVENTIONS / ADHERENCE TO TREATMENT / EVIDENCE-BASED NURSING.

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CHAPTER I
INTRODUCTION

1.1 Background and significance of the clinical problem

Caused by Mycobacterium tuberculosis, tuberculosis (TB) is a major public health problem worldwide. TB remains one of the major causes of mortality due to a single infectious agent (Deliu & Manea, 2014). When TB bacillus is expelled into the air by the coughs or sneezes of an infected person, anyone who inhales the air containing the TB germ may become infected (M'Imunya, Kredo, & Volmink, 2012). TB can cause considerable social and economic interruption and a series of serious effects that impede national development (Cai et al., 2015). TB patients also suffer from several physiological, psychological and financial problems (Aggarwal, 2010). The incidence of this disease increases daily due to the increased number of patients infected with human immunodeficiency virus (HIV), bacterial resistance to drugs, increased global travel with immigration, rising numbers of homeless and drug abusers (Knechel, 2009). From the perspective of serious infection, TB control and prevention is a main concern for public health (Cai et al., 2015). The severity of TB disease is minimized by applying different types of interventions to improve patients' adherence to treatment (Clark, Karagoz, Apikoglu-Rabus, & Izzettin, 2007).

Adherence, which means following the instructions of health care providers regarding prescribed treatment (M'Imunya et al., 2012), is the main way to complete TB treatment (Balbay, Annakkaya, Arbak, Bilgin, & Erbas, 2005; Clark et al., 2007). A major impediment to global TB control is non adherence to treatment (Boogaard et al., 2012). Poor adherence may lead to increased rates of treatment failure and relapse with further increases in the transmission rates of TB bacilli, latent TB, active and multi-drug resistance TB (MDR TB) in the community and escalating mortality and morbidity rates (Liu et al., 2014).

Approximately one third of the global population is infected with TB (WHO, 2012). According to a global TB report in 2015, the global totals for new TB

cases were higher than in previous years (WHO, 2015a). The world Health Organization (WHO, 2015a & 2014a) reported an increase in TB incidence from 9.0 million to 9.6 million new cases. Among the estimated 9.6 million new cases, 58% were from the WHO's South-East Asian Region (SEAR). According to a WHO report, global TB prevalence rose from 12 million to 13 million during 2012 to 2014. In addition, TB related mortalities increased from 1.3 million to 1.5 million during the same period of time and the number of new cases of MDR-TB increased from 0.45 million to 0.48 million during 2012 to 2014 as reported by the WHO (WHO, 2015a, 2014a & 2013).

Bangladesh has been found to have a high TB and MDR-TB burden nationwide (WHO, 2015b). Annually, approximately 0.08 million people are found to die from TB in Bangladesh (WHO, 2014a). According to the WHO in 2012 to 2014, the TB incidence cases increased from 225 to 227. And from 2013 to 2014, the TB prevalence increased from 402 to 404, respectively. In addition, since 2012 to 2014, TB-related deaths increased from 45 to 51 correspondingly per 100,000 people in Bangladesh (WHO, 2015a, 2015b & 2014b). Moreover, since 2012 to 2015 the estimated number of MDR-TB cases increased from 0.0042 million to 0.0048 million (WHO, 2015a, 2015b & 2014b). The population of Bangladesh is highly dense coupled with poor sanitation posing risks for TB. Some barriers such as inadequate management and information about TB treatment services, shortage of caregivers for TB patients, time constraints and stigmas are also associated with TB. Diagnostic and treatment costs also contribute to the economic burdens of TB patients. Financial problems are listed as the top factor hindering TB treatment (Bam, Bhatt, Thapa, Dossajee, & Angdembe, 2014). The above statistics indicate that Bangladesh remains at high risk for TB infection and active TB disease.

Risk factors for TB: Awareness about the factors that increase the risk for TB infection and TB disease is essential. The risk factors for TB are as follows:

1) Age and gender: All age groups are susceptible to TB but the diseases mostly affect adults (Hargreaves et al., 2011; WHO, 2015c). Persons over 65 years of age are at greater risk for TB than other age groups due to low immunity and reactivation of the disease (Knechel, 2009). In addition, people aged 20 to 40

years are also at greater risk for TB (Shetty, Shemko, Vaz, & D'Souza, 2006). Due to frequent social contact, men may also represent a high risk group for TB (Hargreaves et al., 2011; Ndungu, Revathi, Kariuki, & Ng'ang'a, 2013).

2) People with medical conditions: Due to the conditions of the disease, the immune system in people with medical conditions would be weakened. As a result, tubercle bacilli enter the body and TB disease may be developed. Thus, HIV is a notable cause of the threat for TB (Meda et al., 2013; WHO, 2015c). Furthermore, patients with diabetes mellitus are associated with this disease (Hargreaves et al., 2011; WHO, 2015c). Similarly, chronic kidney disease and organ transplants also accelerate the progression of TB (Knechel, 2009; Lee et al., 2013). In addition, chronic obstructed pulmonary disease may develop in active TB (Chu et al., 2014; Lee et al., 2013).

3) Close proximity to infectious persons: Health care providers are associated with a greater risk for developing TB disease (CDC, 2016). Similarly, persons living in a TB patient's house are at also high risk for exposure to TB (Kirenga et al., 2015; Tornee et al., 2004).

4) Low socioeconomic status: Low socioeconomic status is a major cause for the progression of TB disease. In association of poverty and undernourishment may develop weak immune system for causing TB disease. Even persons with low body mass index or malnutrition status are higher risk group of TB (Hargreaves et al., 2011; WHO, 2015c). Beside these unemployment (Ndungu et al., 2013), homeless people (CDC, 2016; MacNeil, Lobato, & Moore, 2005), and low level of education are helpful for TB progression (Hargreaves et al., 2011; Ndungu et al., 2013). Moreover, over-crowding increases the risk of disease transmission by decreasing the degree of air space that is shared resulting increased exposure to TB (Hargreaves et al., 2011; Meda et al., 2013). By the same way, indoor air pollution (Hargreaves et al., 2011; Narasimhan, Wood, MacIntyre, & Mathai, 2013) and poor ventilation (Hargreaves et al., 2011) also pose risk to develop TB disease.

5) Substance abuse: Various type of **s**ubstance abuse are associated with developing TB such as tobacco smoking (Hargreaves et al., 2011; WHO, 2015c), alcohol consumption (Hargreaves et al., 2011; Lee et al., 2013) and

drug users, these habits directly impairs host defense mechanisms and immune functions that exposed to risk for TB (Hargreaves et al., 2011; Ndungu et al., 2013).

All of these risk factors help to progression of TB disease, which impacts not only the patients' but also family members, friends and community people.

Impacts of TB: The impact of TB on individuals is often not only physical health, but also psychological, social, and economic well-being (Ananthakrishnan, Jeyaraj, Palani, & Sathiyasekaran, 2012).

1) Physical impact: TB greatly affect on physical health (Rashmi, Prasad, & Chand, 2014). Major reason of morbidity and mortality globally is TB (Somma et al., 2008). A greater number of HIV infected people also died worldwide due to TB disease (Sullivan, 2010). TB disease affects lungs and others part of the body such as brain, kidney, spine, bone and skin (M'Imunya et al., 2012). Due to severity of illness and side effects of TB drugs, patients cannot perform daily activities and maintain job (Arbex, Varella, Siqueira, & Mello, 2010).

2) Psychological impact: TB is one of the causes of psychological burden (WHO, 2000). Social exclusion, feelings of rejection and stigma these all are affects on patients' psychology (Somma et al., 2008). When patients initially diagnosis with TB disease they feel hopelessness, fear and overflowing regarding their treatment regimens and take care their family members. Due to pressure of family members TB patients bound to change their daily living style such as separate bed for sleeping, eating separately. Additionally, family members, friends and community people do not have a good attitude with TB patients. Patients are also worry about his loss of work or job, due to TB disease. As a result, patients suffer from low self steam, anxiety and depression (Morris et al., 2013).

3) Social impact: The impact of TB can be surrounded all levels of society (Sullivan, 2010). Due to fear of disease transfer to family member, friends and community people they ignored and do not interact with TB patients (Morris et al., 2013). TB patients confronted different separation and rejection from families and society. Especially female TB patients face variety of worse situation of TB associated stigma than males, potentially resulting in divorce or separation.

Cultural belief also burden on patients' personal life and they unable to meet responsibilities for their family work (Somma et al., 2008).

4) Economical impact: Economical condition of TB patients is one of the problems due to disease conditions. TB patients cannot continue their work or education because of their infectiousness, long period of treatment regimen and side effects of the treatment. As a result, they lose of their earning source. Unemployment condition affects on family and overall economy (Morris et al., 2013). Stigma is closely associated with economical impact of TB patients (Somma et al., 2008). TB patients are absent average 3-4 months of work. In addition, due to social discrimination, rejection, stigma and TB morbidity loss of 8 to 20% annual income in treatment cost and 20 to 30% annual income in lost wages. Mortality also associated with the loss up to 15 years of income (Sullivan, 2010).

It can be concluded that all above impacts create great burden not only the patients but also the family members and community people which possible to minimize by adherence to TB treatment.

Adherence to TB treatment: According to WHO (2003), adherence has defined as "the extent to which a person's behavior- taking medication, following a diet, and or executing lifestyle changes, corresponds with agreed recommendations from a health care provider". In particularly, taking medication also includes seeking medical attention, filling prescriptions, taking medication appropriately, attending follow-up appointments. The Centers for Disease Control and Prevention (CDC) stated that adherence to treatment means patients should follow all recommended treatments in a whole treatment period (CDC, 2012).

Adherence is essential not only for patients but also for societies and countries to prevention and control of TB infection (Carlsson, Johansson, Eale, & Kaboru, 2014). It may improve control and surveillance of TB; decrease the rates of TB on national and even global scales. However, about 20–50% of TB sufferers interrupted treatments by their own decisions (Hsieh et al., 2008). Adherence associated with treatment taking behaviors, feature of the treatments, activities of the health care providers, socio-economic, cultural and environmental factors (Gebremariam, Bjune, & Frich, 2010). Adherence can be assessed by the treatment

completion rate, cure rate and success rate (Hsieh et al., 2008; Suwankeeree & Picheansathian, 2014). Besides that, attendants of scheduled follow up visits also used to measure adherence (Clark et al., 2007).

From above descriptions it can be concluded that adherence related with various factors and are measured by diverse parameters.

Factors related to adherence to TB treatment: Various types of factors including health service, personal, and social context factors influence treatment taking behavior as follows (Munro et al., 2007; Widjanarko, Gompelman, Dijkers, & Werf, 2009).

1) Health service factors: Several health services provided to TB patients may create barriers to and facilitators for adherence to TB treatment. The financial constraints of both patients and health organizations are one of the major problems causing non adherence (Munro et al., 2007). Due to a shortage of funds, hospitals cannot provide enough food to admit patients. Moreover, patients cannot arrange food from outside by themselves. Therefore, they are unable to stay in hospitals. As a result, patients become non-adherent to treatment (Boogaard et al., 2012; Munro et al., 2007). Furthermore, other costs such as hospital stay, medications, reviews of x-rays, and transportation costs also influence adherence (Boogaard et al., 2012; Munro et al., 2007; Widjanarko et al., 2009).

In addition, adequate information about treatment and disease, health education and reminder cues; ensure supervision of drug intake and the provision of financial support can facilitate patients in improving adherence (Widjanarko et al., 2009). Some health facilities also depend on distance between clinic and residential areas as well as availability of transport (Munro et al., 2007; Widjanarko et al., 2009). Moreover, poorly accessible and poorly equipped health facilities, long waiting times, long queues, inadequate privacy and inconvenient times also negatively influence adherence (Munro et al., 2007).

2) Personal factors: Different personal factors such as patients' knowledge, attitudes, beliefs and motivation about illness and wellness regarding TB and treatment influence adherence to TB treatment. These factors help to create barriers or facilitators for treatment behaviors. Moreover, substance abuse

creates barriers to adherence (Boogaard et al., 2012; Munro et al., 2007; Widjanarko et al., 2009). Treatment adherence depends on patients' physical and psychological conditions. Patients usually make decisions to stop treatment when they feel better than before (Munro et al., 2007; Widjanarko et al., 2009). The negative consequences of treatment act as barriers to adherence, while patients' positive perceptions about treatment create adherence to treatment regimens (Munro et al., 2007).

3) Social context: Social context influences treatment adherence behaviors. Family and community members and health care providers may provide emotional support for TB patients and help patients to complete treatment. In opposite, family and community members may have negative perception to TB patients. However, family and social support can help patients to overcome barriers and adhere to treatment regimens. In this situation, community-based TB programs and close participation of community members or volunteers can help patients improve adherence to treatment (Munro et al., 2007).

Although adherence is essential to completion of TB treatment, some factors affect treatment taking behavior and contribute to the development of non-adherence. Moreover, these barriers should be minimized through effective interventions and skilled management by healthcare providers.

Interventions to improve adherence to TB treatment: Health care providers play an important role in TB management by helping patients improve adherence and completion of TB treatment. Health care providers could take initiative in ensuring patients' health services and treatment, minimizing medical side effects and protecting patients from non-adherence.

Health care providers can complete the following activities to ensure the health services of patients: 1) evaluate patients and create treatment plans; 2) ensure treatment based on DOT guidelines, provide helpful education for patients and key persons; 3) develop effective clinical approaches for suitable appointment times, maintenance records and pharmacy services; 4) help patients keep appointments and communicate with them with easy language; 5) offer incentives and enablers to improve adherence and also arrange health or social welfare services; 6) if needed,

make referrals to better service agencies; 7) build reliable relationships with TB patients (CDC, 2012).

Health care providers can provide treatment for patients with both latent and active TB. Latent TB treatment consists of four treatment regimens for a period of nine months. The primary phase of treatment for active TB disease is two months followed by options for the continuing phase at four or seven months for a total of six or nine months. The drugs commonly used for latent TB are isoniazid (INH), rifampin (RIF), and Rifapentine (RPT). On the other hand, drugs for active TB include INH, RIF, ethambutol (EMB), and pyrazinamide (PZA) (CDC, 2011).

Patients suffer from various types of TB drug side effects. Health care providers must inform the patients about the side effects and teach them how to manage. Frequent TB drug-related side effects are as follows: the side effects of INH are nausea, vomiting, epigastric pain, anxiety, peripheral neuropathy and clinical hepatitis after taking INH. For RIF, the side effects include nausea, anorexia, abdominal pain, perspiration, dizziness, headaches, hemolytic anemia, vasculitis and septic shock. Common side effects of EMB are decreased visual acuity, nausea, vomiting, headaches, dizziness, skin rash, arthralgia and fever. For PZA, the adverse effects are nausea, vomiting, anorexia, pruritus, and kidney failure (Arbex et al., 2010). General adverse effects of RPT are nausea, vomiting, dizziness, rash, diarrhea, hyperuricemia (Temple & Nahata, 1999).

Due to inadequate access to health care, poor relationships with health care providers and side effects of drugs develop non-adherence among TB patients (CDC, 2012). Health care providers can manage and overcome barriers with their knowledge and skills. Moreover, health care providers could apply various types of interventions based on patients' conditions and local situations to minimize the aforementioned problems and improve adherence to TB treatment.

Bangladesh is a low income country where the majority of the population lives in rural areas with low socioeconomic status. Bangladeshi TB patients do not take treatment regularly due to their personal, health service and socio-economical conditions. Even though Bangladesh has applied DOT program to control and prevention for TB since many years ago, many problems still happen such as continuous increase of the new TB cases and the death rate (WHO, 2015a, 2015b &

2014b)). Furthermore, MDR-TB case also increased unexpectedly (WHO, 2015a, 2015b & 2014b). These reflect that various interventions or strategies should be combined with DOT to promote patients' adherence to TB treatment.

1) Direct observation treatment (DOT): TB control and prevention strategy involves DOT, an approach that ensures medication adherence among TB patients. A health care provider acts as a DOT observer or supporter to ensure the medication adherence of patients (Karumbi & Garner, 2015). DOT may be performed by a health care provider or someone selected by the health care providers and the patient for this purpose called a DOT supporter (Munro et al., 2007). Regular follow-up on patients' treatment could contribute to the adherence of TB sufferers (Hsieh et al., 2008). Although implementation of DOT is difficult, less successful, requires more resources and funds. DOT alone cannot provide solutions for poor adherence to TB treatment (Karumbi & Garner, 2015). Most of the time DOT, is not feasible for patients due to rigid rules and regulations. As a result, patients cannot follow all of the instructions for DOT (Munro et al., 2007).

2) DOT combined with other interventions: No intervention alone is always successful at improving adherence to treatment for TB infection, and that includes DOT, which provides no guarantee for routine use of the strategy in developing countries to improve cures and treatment completion for TB disease (Suwankeeree & Picheansathian, 2014). Numerous studies have recommended that supplementing and thereby intensifying the DOT program with other interventions or strategies could be employed to promote adherence to treatment among adult patients with TB (Clark et al., 2007). Interventions can include education, long-term follow-ups and home visits through the health care provider (Hsieh et al., 2008). In addition, other interventions can be applied to improve treatment adherence among TB patients, especially education and counselling (M'Imunya et al., 2012) with reminder systems (Liu et al., 2014; Liu et al., 2010).

It can be concluded that various types of interventions or strategies can improve adherence to TB treatment. However, effective interventions or strategies should be identified. Those effective interventions should also be applicable to improve adherence to treatment among adult patients with TB in the clinical setting of Bangladesh.

1.2 Clinical problem of the study

TB is a significant health concern in Bangladesh. The author has experienced working at Chest Disease Hospital, a tertiary care and referral level hospital. Approximately 9 million people are dependent on this hospital and the incidence rate of TB patients escalates daily.

Based on the situation in Bangladesh, most TB patients have no knowledge about the disease, treatment and complications. Furthermore, the majority of TB patients live in rural areas. The economic conditions of the patients are not good. Due to ignorance about TB, patients do not take drugs routinely and do not come to hospital follow-up and diagnostic tests as advised by health care providers. TB patients must visit healthcare centers more than once a week for treatment. Thus, they are unable to continue their work. As a result, they lose income. Transportation costs create additional burden for TB patients. Moreover, health care providers have limited knowledge about TB management, while family members, community residents and health care providers may have negative perception with TB patients. For the aforementioned reasons, patients do not continue treatment while concealing the disease and developing non-adherence to treatment.

Due to the shortages of resources and fund health care providers in Bangladesh, the country is unable to properly implement all DOT instructions. Sometimes DOT is not feasible for patients due to long distance from health care facilities. Furthermore, patients feel difficulty in following the stringent requirements for DOT. Therefore, other effective interventions or strategies may be more useful and effective in improving adherence to TB treatment in Bangladesh.

For these reasons, the author would like to review the best available evidence and summarize the contents regarding effective interventions to promote adherence to TB treatment. Consequently, the evidence-based interventions will help improve adherence to treatment among adult patients with TB in Bangladesh.

1.3 Purpose of the study

The purpose of this study was to summarize current evidence-based interventions to promote adherence to treatment among adult patients with TB and draw conclusion on recommendations based on the evidence obtained.

1.4 Expected benefits of the study

1.4.1 Health care providers will gain current evidence for interventions to guide practice in promoting adherence to treatment among adult patients with TB in Bangladesh.

1.4.2 The hospital will have current evidence for interventions to improve care processes and patient outcomes by promoting adherence to treatment among adult patients with TB in Bangladesh.

CHAPTER II
METHODOLOGY

The study reviewed evidence related to “interventions for promoting adherence to treatment among adult patients with tuberculosis”. The author searched for related evidence based on searching strategy. Each of the evidence obtained by the search was apprised for quality and feasibility by considering the setting and conditions of health care resources as well as the preferences and values of patients. In this chapter, the author describes the searching strategy, appraisal methods and levels of evidence as follows:

2.1 Search Strategy

The author searched for evidence on interventions from systematic reviews for promoting adherence to treatment among adult patients with TB by employing the following search strategy:

2.1.1 Search framework: The author searched and selected evidence on interventions to promote adherence to treatment among adult patients with TB by using the PICO framework (Melnyk & Fineout-Overholt, 2015) as detailed below:

P (Population) = Adult patients with tuberculosis
I (Intervention) = Interventions
C (Comparison) = None
O (Outcome) = Adherence to tuberculosis treatment

2.1.2 Scope of the search: Evidence on interventions for promoting adherence to treatment among adult patients with TB in hospital and community settings were sought be using keywords, databases and types of evidence to find out the best available evidence as follows**:**

1) Keywords used in the search according to the PICO framework: To obtain valid evidence, the author selected the scope prescribed by the PICO framework and searched for relevant key words aimed at finding the best evidence. For each PICO component, the author used diverse synonyms and linked the terms with "OR", then located citations relevant to the entire PICO component by linking with "AND".

P (Population) = Pulmonary tuberculosis patients
TB patients
Patients with tuberculosis
Tuberculosis

I (Intervention) = Intervention
Strategy

C (Comparison) = None

O (Outcome) = Adherence to TB treatment
Treatment adherence
Adherence to treatment
Treatment compliance

2) Databases/sources used for the search: The author used the following electronic databases/sources of Mahidol University Library system for searching:

a) The Cochrane Database of Systematic Reviews,
b) Joanna Briggs Institute Systematic reviews Database,
c) The Cumulative Index to Nursing and Allied Health (CINAHL),
d) Ovid Full Text,
e) Pro Quest Nursing,
f) Pub Med,
g) Science Direct,
h) Google Scholar and
i) Springer Link.

The author also conducted a manual search from reference lists of evidence.

3) Type of evidence: The author searched for systematic reviews acquired from full-text evidence published in English from 2010 to 2016. Since there are a number of intervention studies related to this study with a variety of study designs, the author selected only systematic reviews because of these evidence are mostly composed of RCTs and other experimental studies that are good quality and updated evidence.

2.2 Appraisal method and levels of evidence

After searching for evidence related to interventions for promoting adherence to treatment among adult patients with TB, the author assessed the evidence obtained by using the following method and identifying the levels of evidence.

2.2.1 Evidence appraisal method: The author evaluated all evidence by following the guidelines proposed by Melnyk and Fineout-Overholt (2015) to ensure the validity, reliability and applicability of the evidence. The collected evidence was appraised on the basis of the following three questions:

i) Are the results of the review valid?

When the systematic reviews were appraised, clear explanations were considered concerning the databases accessed in terms of the searching years, strategies and search terms used. Other considerations included the following: 1) whether the inclusion criteria for the studies were kept in the analysis; 2) whether the data in the evidence were extracted by using a standard method regarding target population, sample size, program provider, program content, intervention components, processes, and outcomes; 3) whether or not the quality assessment method of the studies was done by at least two independent members of the team; 4) whether or not the systematic review was reported clearly in terms of how the study was conducted and what criteria were used for evaluation. A clear description of the basis for quality assessment should be indicated in the review.

ii) What were the results?

The results of any evidence depends on accuracy, honesty, consistency, achievement and repeatability to ensure that anyone can perform the same experiment by using similar equipment, conditions and achievement of exactly the same outcome. A systematic review provides a clearer synopsis of the effects of interventions from many individual studies. The effectiveness of the interventions in a synopsis statistic compared throughout the study.

iii) Will the results help in caring for patients?

During the time of the review the following three critical questions were the key points to consider: 1) whether the populations in the study are similar to the patients for whom care will be provided or not; 2) whether the benefits are greater than the risk of interventions or not; 3) whether the interventions are feasible for application in the clinical setting or not; 4) and whether the patient and family members prefer the interventions or not.

2.2.2 Levels of evidence: The studies were identified for their strength of evidence. The evidence were classified in six levels as narrated in the following table (Melnyk & Fineout-Overholt, 2015)**:**

Table 2.1 Levels of Evidence:

Level of Evidence	Source of Empirical Evidence
Level I	Evidence from a systematic review or meta-analysis.
Level II	Evidence obtained from randomized controlled trials (RCTs).
Level III	Evidence obtained from controlled cohort studies.
Level IV	Evidence from uncontrolled cohort studies.
Level V	Evidence from case studies and case series, qualitative studies and descriptive studies, evidence-based practice (EBP) implementation and qi-projects.
Level VI	Evidence from the expert opinion.

CHAPTER III
FINDINGS

The search results and summary of evidence are described in this chapter in relation to promoting adherence to treatment among adult patients with TB. The details are described as follows:

3.1 Search results

The author searched for evidence from different electronic databases and websites through the Mahidol University library system. After searching, the author collected the best available evidence on interventions for promoting adherence to treatment among adult patients with TB and published in English from 2010 to 2016. A total of fourteen evidence were found. All are systematic reviews and eight evidence were selected for analysis. The other six evidence were excluded, because the population, outcomes of the interventions, research design and year of publication did not match the present study. The eight selected evidence are listed as follows:

Table 3.1 List and levels of the selected evidence

Evidence No.	Authors , Year and Title	Type of Evidence	Level of Evidence
1.	Karumbi & Garner, 2015. Directly observed therapy for treating tuberculosis (review).	Systematic Review	Level –I
2.	M'Imunya et al., 2012. Patient education and counselling for promoting adherence to treatment for tuberculosis (review).	Systematic Review	Level –I
3.	Liu et al., 2014. Reminder systems to improve patient adherence to tuberculosis clinic appointments for diagnosis and treatment (review).	Systematic Review	Level –I
4.	Liu et al., 2010. Reminder systems and late patient tracers in the diagnosis and management of tuberculosis (review).	Systematic Review	Level –I
5.	Lutge**,** Wiysonge, Knight, & Volmink, 2012. Material incentives and enablers in the management of tuberculosis (review)	Systematic Review	Level -I
6.	Nglazi, Bekker, Wood, Hussey, & Wiysonge, 2013. Mobile phone text messaging for promoting adherence to anti-tuberculosis treatment: A systematic review	Systematic Review	Level -I
7.	Suwankeeree et al., 2014. Strategies to promote adherence to treatment by pulmonary tuberculosis patients: A systematic review.	Systematic Review	Level –I
8.	Wright, Westerkamp, Korver, & Dobler, 2015. Community-based directly observed therapy (DOT) versus clinic DOT for tuberculosis: A systematic review and meta-analysis of comparative effectiveness.	Systematic Review of meta-analysis	Level –I

3.1.1 Brief summary of the selected evidence

Evidence No. 1

Title: Directly observed therapy for treating tuberculosis (review).

Author / Year: Karumbi & Garner, 2015.

Publication source: *Cochrane Database Systematic Reviews,* 3.

Objective: To assess DOT compared to self-administered therapy (SAT) and several forms of DOT in people on the treatment of active TB or on prophylaxis to prevent active disease.

Methodology: The design of this study was systematic review. The investigators searched various databases such as MEDLINE, LILACS, Cochrane infectious diseases group specialized register (CIDG), EMBASE to select studies. The investigators used key words such as tuberculosis and DOT from the meta-Register of controlled trials (mRCT) as search terminology and checked the reference lists of studies included. The investigators then conducted experiment authors and organizations to identify relevant studies. Next, the inclusion and exclusion criteria were applied and nine full-text RCTs and two cluster-RCTs with 5,662 patients were selected. These studies were published in all languages and published until 13 January 2015. Two reviewers extracted and checked the data. The reviewers also contacted the research authors to obtain unclear or missing data for clarification. Any discrepancies were resolved through discussion. The quality of the evidence was evaluated by the Grading Recommendations, Assessment, Development and Evaluations (GRADE) approach**.** The investigators synthesized the data by Review Manager 5 and also used risk ratio (RR) and confidence interval (CI) 95% to assess the effects of the interventions.

Findings: This review found no significant differences in TB cure and treatment completion between the SAT & DOT groups (RR 1.08, 95% CI 0.91 to 1.27 and RR 1.07, 95% CI 0.96 to1.19). The review also found no significant difference between DOT at home by family members or CHWs with DOT by health workers at health facilities in cure and treatment completion (RR 1.02, 95% CI 0.88 to 1.18 and RR 1.04, 95% CI 0.91 to 1.17). Generally, DOT did not provide a solution to low adherence in TB treatment. Cure and treatment completion were low in both the SAT and DOT groups, but the DOT was not able to improve cure and treatment completion.

Appraisal: The results of this review were valid, because the review clearly described the search strategies to find relevant studies, including databases, years of searching, search terms, languages and selection criteria of included studies. The study contained individual RCTs and cluster-RCTs. This review properly completed data extraction, methodological quality assessment and data synthesis. The results of this study were not statistically and clinically significant for DOT, but the CI was precise. Moreover, the author can apply these results in the author's clinical setting, because the populations are similar to the author's study population and all clinically important outcomes are measured. The benefits of the intervention are greater than the risks, and the intervention is feasible in the author's clinical setting.

Evidence No. 2

Title: Patient education and counselling for promoting adherence to treatment for tuberculosis (review).

Author / Year: M'Imunya et al., 2012.

Publication source: *Cochrane Database of Systematic Reviews,* 5.

Objective: To assess the outcomes of education and counselling or both, in people on active and latent TB therapy, on treatment completion and cure.

Methodology: The design of this study is a systematic review. The reviewers searched various databases such as LILACS, Cochrane central register of controlled trials (CENTRAL), EMBASE, MEDLINE to select studies by using key words such as adherence, education, TB, and counselling from mRCT as search terminology. The investigators then checked the reference lists of the studies included and contacted the research authors and organizations to identify relevant studies. The reviewers applied inclusion and exclusion criteria and selected three full-text RCTs with 1,437 patients. These studies were published in all languages from 25 April 2007 to 13 January 2015. The reviewers extracted data and used a pre-designed data extraction form. If the study findings were unclear or missing, the researchers contacted the research authors for clarification. Any differences in opinion were resolved through discussion. The quality of the evidences was evaluated by screens of eligibility, methodological quality and data extraction**.** The reviewers synthesized

the data by Review Manager 5 and also used RR and CI 95% to assess the effects of the interventions.

Findings: This review indicated that people who received latent TB treatment, education had higher treatment completion in intervention group (24%) than those in the control group (12%) (RR 1.94, 95% CI 1.03 to 3.68). Regardless, the treatment completion rates were low for both groups. Moreover, **e**ducation or counselling interventions improved adherence to treatment for latent TB. However, the benefits vary depending on the character of the intervention and setting.

Appraisal: This review clearly described the search strategies to find relevant studies including databases, years of searching, search terms, languages and selection criteria of the studies included. The study contained RCTs. This review properly completed data extraction, methodological quality assessment and data synthesis. Thus, the review results should be considered as valid. The results of this study were clinically significant and CI was precise. In addition, the author can apply these results in the author's clinical setting, because the population is similar to the population studied. Furthermore, all clinically important outcomes are measured. The benefits of the intervention are greater than the risks, and the intervention is feasible in the author's practice setting.

Evidence No. 3

Title: Reminder system to improve patient adherence to tuberculosis clinic appointments for diagnosis and treatment (review).

Author / Year: Liu et al., 2014.

Publication source: *Cochrane Database of Systematic Reviews,* 11.

Objective: To assess the results of reminder systems on adherence to TB diagnosis, clinic appointments and prophylaxis or treatment & their results on treatment outcomes.

Methodology: The design of this study is a systematic review. The reviewers searched various databases such as the cumulative index of nursing and allied health (CINAHL), CENTRAL, LILACS, CIDG, EMBASE, and MEDLINE to select studies by using key words such as tuberculosis, reminder or compliance from mRCT as search terminology. The reviewers also checked the reference lists of

included studies and contacted the research authors and organizations to identify relevant studies. Two reviewers applied the inclusion and exclusion criteria, and selected seven published full-text RCTs and two quasi-RCTs with 4,654 patients. These studies were published in all languages and covered up to 29 August 2014. Two reviewers extracted the data and used a data extraction form. The investigators contacted the research authors to obtain missing data for clarification. Any differences in opinion were resolved through discussion and the quality of each evidence was assessed by the GRADE approach. The reviewers synthesized the data by Review Manager 5 and also used RR and 95% CI to assess the results of the strategies.

Findings: This review stated that the people who received active TB treatment pre-appointment reminder phone-calls increased clinic attendance and treatment completion (RR 1.32, 95% CI 1.10 to 1.59 and RR 1.14, 95% CI 1.02 to 1.27). Similarly, the default reminders also increased both clinic attendance and treatment completion (RR 5.04, 95% CI 1.61 to 15.78 and RR 1.17, 95% CI 1.11 to 1.24). In addition, the people who received prophylactic TB treatment with pre-appointment phone-calls increased clinic attendance and three monthly phone-calls or nurse visits increased final clinic visits {(RR 1.30, 95% CI 1.07 to 1.59) and 93% vs. 65%}. However, people undergoing TB screening with pre-appointment phone-calls and take home reminder cards did not have increased rates of return to clinic for skin test result. This review focused on pre-appointment reminder phone-calls and default reminders, both of which are sensible strategies for TB. Moreover, the interventions have small but potentially significant benefits.

Appraisal: The results of this review were valid, because the review clearly described the search strategies to find relevant studies including the databases, years of searching, search terms, languages and selection criteria of included studies. The study contained RCTs and quasi-RCTs. This review also properly completed data extraction, methodological quality assessment and data synthesis. The results of this study were statistically and clinically significant and CI was precise. Thus, the author can apply these findings in the author's clinical setting, because the population is similar to the population studied and all clinically important outcomes were measured. The benefits of the interventions are greater than the risks, and the interventions are feasible in the author's clinical setting.

Evidence No. 4

Title: Reminder systems and late patient tracers in the diagnosis and management to tuberculosis (review).

Author / Year: Liu et al., 2010.

Publication source: *Evidence-Based Child Health: A Cochrane Review Journal, 5,* 1206-1245.

Objective: To evaluate the outcome of reminder systems and late patient tracers on fulfillment of diagnostics, treatment initiation in people referred for curative or prophylactic TB, completion of treatment in people initiating curative or prophylactic TB, and cures in people treated for active TB.

Methodology: The design of this study was a systematic review. The reviewers searched various databases such as MEDLINE, CIDG, CINAHL, EMBASE, LILACS and CENTRAL to select the studies by using key words such as tuberculosis, reminder or compliance with mRCT as the search terminology. The reviewers also checked the reference lists of included studies and contacted the research authors & organizations to identify relevant studies. Two reviewers applied inclusion and exclusion criteria and selected seven published full-text RCTs and two quasi-RCTs with 5,257 participants. These studies were published in all languages until June 2008. Two reviewers extracted the data and used an appropriate data extraction form. The reviewers contacted research authors to supply missing data to clarify issues. Any discrepancies were resolved through discussion. The reviewers synthesized the data by Review Manager 5 and also used RR and 95% CI to assess the results of the strategies.

Findings: This review found late patient tracers by posting letter reminders to increase the rates of treatment completion and clinic appointments compared with no late patient tracers (RR 0.44, 95% CI 0.24 to 0.83 and RR 0.53, 95% CI 0.34 to 0.83). Home visits plus health education significantly decreased fail to return rates for treatment on scheduled appointment compared with no late patient tracers at 3.8% vs. 17.5% (RR 0.21, 95% CI 0.11 to 0.43). Reminders by automated telephone significantly increased the rates of scheduled appointment attendance at prophylaxis and treatment clinics, but there was no significant difference between the groups with and without reminders groups in the diagnosis clinic (RR 0.72, 95% CI

0.58 to 0.89 and RR 0.69, 95% CI 0.56 to 0.86 but RR 0.94, 95% CI 0.79 to 1.12). This review specified that three studies were late patient tracers and five out of six studies involved reminders that were helpful in increasing adherence to TB treatment and clinic appointments.

Appraisal: This review clearly described the search strategies to find relevant studies including the databases, years of searching, search terms, languages and selection criteria of included studies. The study contained RCTs and quasi-RCTs. This review also properly completed data extraction, methodological quality assessment and data synthesis. Hence, the review results were valid. The results of this review were statistically and clinically significant and CI was precise. Consequently, the author can apply these results in the author's clinical setting, because the population is similar to the population studied, and all clinically important outcomes are measured. The benefits of the interventions are greater than the risks, and the interventions are feasible in the author's practice setting.

Evidence No. 5

Title: Material incentives and enablers in the management of tuberculosis (review).

Author / Year: Lutge et al., 2012.

Publication source: *Cochrane Database of Systematic Reviews*, 1.

Objective: To assess the outcomes of material incentives in people on diagnostic testing and receiving prophylaxis or curative treatment for TB.

Methodology: The design of this study was a systematic review. Reviewers searched various databases such as EMBASE, LILACS, MEDLINE, CIDG, science citation index and CENTRAL to select studies. The reviewers used key words such as tuberculosis, compliance, incentives, adherence, and cash transfer from mRCT as search terminology. The reviewers also checked the reference lists of the studies included and contacted the research authors and organizations to identify relevant studies. Two reviewers applied the inclusion and exclusion criteria and selected eleven published full-text RCTs. These studies were published in all languages until 22 June 2011. Two reviewers extracted the data and used a data extraction form. Any disagreements were resolved through discussions and agreement

between the two reviewers. The quality of each evidence was appraised by the GRADE approach. The reviewers synthesized the data by Review Manager 5 and also used RR and 95% CI to assess the results of the intervention.

Findings: The results of this review indicated that people who received active TB treatment with material incentives had no significantly improved long-term adherence and completion of treatment (RR 0.98, 95%CI 0.86 to 1.12). However, the people who were on prophylaxis TB with material incentives improved initiation and completion rates in some settings (RR 1.58, 95% CI 1.27 to 1.96 and RR 1.79, 95% CI 0.70 to 4.58). Moreover, for people who were on TB diagnosis, incentives might have increased return rates on test results (RR 2.16, 95% CI 1.41 to 3.29). However, this review stated no sufficient evidence for improved long-term adherence and completion of treatment for latent or active TB.

Appraisal: The results of this review were valid, because the study clearly described the search strategies for finding relevant studies including the databases, years of searching, search terms, languages and selection criteria for the studies included. The study contained RCTs. This review properly completed data extraction, methodological quality assessment and data synthesis. The results of this study were not statistically or clinically significant for improving adherence to treatment. These results are not applicable or feasible for the author's clinical setting.

Evidence No. 6

Title: Mobile phone text messaging for promoting adherence to anti-tuberculosis treatment: A systematic review.

Author / Year: Nglazi et al., 2013.

Publication source: *Bio-Medical Central Infectious Diseases, 13*(566).

Objective: To evaluate recent evidence on the efficiency of SMS interventions in promoting patients' adherence to TB treatment.

Methodology: The design of this study was a systematic review. The reviewers searched electronic databases such as EMBASE, CINAHL, PubMED, and CENTRAL as well as the WHO library databases and conference proceedings to select studies. The reviewers used text words and medical subject headings as search terminology. The reviewers also checked the reference lists of included studies and

contacted the research organizations to identify relevant studies. Two reviewers applied the inclusion and exclusion criteria and selected one published full-text RCT and three non-RCTs. These studies were published in all languages until 15 February 2013. Two reviewers extracted the data and used an appropriate data extraction form. Any differences were resolved through discussions and agreement. The reviewers assessed the quality of each evidence by the GRADE approach. The reviewers synthesized the data by Review Manager 5.2 and also used RR and 95% CI to assess the results of the intervention.

Findings: This review stated that SMS interventions did not significantly improve adherence to TB treatment compared to SAT. Furthermore, similar findings were discovered in cure and success rates compared to DOTS {(RR 1.49, 95% CI 0.90 to 2.42) and (cure 62.35% vs. 66.4% & success 72.94% vs. 69.4%) but SMS reminders increased the rates of clinic attendance on scheduled days compared to standard care (RR 1.56, 95% CI 1.06 to 2.29). One the other hand, DOTS plus SIMpill reminders increased cure and smear conversion rates compared to DOTS when patients delayed opening pill bottles (cure RR 2.32, 95% CI 1.60 to 3.36 and smear conversion RR 1.62, 95% CI 1.09 to 2.42).This review found SMS interventions to be potentially beneficial for use in improving patients' adherence to TB treatment. However, there is a shortage of high quality data.

Appraisal: The results of this review should be cautioned. The quality of the studies included in the review is questionable with high risk for bias. Although the review clearly described the search strategies for finding relevant studies including databases, years of searching, search terms, languages and selection criteria of the studies included, the study contained RCTs and non-RCTs with high risk for bias. The results of this study were not statistically or clinically significant in improving adherence to TB treatment. Thus, the results are not applicable or feasible in the author's practice setting.

Evidence No. 7

Title: Strategies to promote adherence to treatment by pulmonary tuberculosis patients: A systematic review.

Author / Year: Suwankeeree et al., 2014.

Publication source: *International Journal of Evidence-Based Healthcare, 12,* 3-16.

Objective: To assess and analyze the best existing evidence investigating the usefulness of strategies for improving adherence to treatment in patients with newly diagnosed pulmonary TB.

Methodology: The design of this study was a systematic review. Reviewers searched various databases such as CINAHL, EMBASE, Cochrane Library, PubMed, Science Direct and Thai thesis databases to select studies by using key words such as adherence, treatment completion, completion rate and cure rate, DOTS and DOT as search terminology. The reviewers also checked the reference lists and bibliographies of the studies included and contacted the research organizations to identify relevant studies. Two reviewers screened all of the studies and selected ten published full-text RCTs and eight quasi-RCTs. These studies were published in all languages during1990 to 2010. Two reviewers extracted the data and used data extraction tools. The investigator entered the data into software for analysis. Any differences in opinion were resolved through discussions and quality was assessed by standardized critical appraisal tools. The reviewers synthesized the data by Review Manager 5.2 and used RR and 95% CI to assess the effects.

Findings: This review found that people who had been newly diagnosed as pulmonary TB patients, DOT increased cure and success rates but did not increase completion rates in comparison to those who received SAT (cure 76% vs. 67% and success 84% vs. 67% but completion was 7.7% vs. 7.8%). Similarly, people who were new TB patients on treatment with DOTS by a case manager had significantly improved completion and success rates in comparison to those who received traditional case management and those who did not receive any strategy (96.9 vs. 68.6 vs. 68.6, $p = 0.007$ and 93.7 vs. 68.6 vs. 68.6, $p = 0.023$)**.** In addition, patients on TB treatment with an intensive tried-model program had significantly improved success and cure rates in comparison to those in the comparison group (96.0 vs. 84.9%, $p = 0.057$ and 95.3 vs. 78.9% $p = 0.02$). New TB patients on treatment with intervention package can have better treatment success rates than those receiving routine TB care (RR 1.18, 95% CI 1.03 to 1.34). Moreover, this review indicated that beneficial

evidence found from the DOT combined with other interventions or strategies for improving adherence to TB treatment.

Appraisal: The results of this review were valid, because the review clearly described the search strategies for finding relevant studies including the databases, years of searching, search terms, languages and selection criteria of the studies included. The study contained RCTs and quasi-RCTs. This review also properly completed data extraction, methodological quality assessment and data synthesis. Most of the results of this review were statistically and clinically significant and CI was precise. Therefore, the author can apply the results in the author's clinical setting, because the population is similar to the population studied, and all clinically important outcomes are measured. The benefits of the intervention are greater than the risks, and the interventions are feasible in the author's clinical setting.

Evidence No. 8

Title: Community-based directly observed therapy (DOT) versus clinic DOT for tuberculosis: A systematic review and meta-analysis of comparative effectiveness

Author / Year: Wright et al., 2015.

Publication source: *Bio-Medical Central Infectious Diseases, 15*(210).

Objective: To assess the usefulness of community-based (CB) DOT performed by community health care workers (CHWs) or community volunteers (CV) in treatment success and loss to follow up compared with clinic DOT.

Methodology: The design of this study was a systematic review of meta-analysis**.** The investigators searched databases such as MEDLINE through OvidSP, PubMed, EMBASE through OvidSP, PreMEDLINE and also checked the reference lists of identified studies by using key words such as community networks, community health services, DOT and tuberculosis as search terms. Two investigators completed the selection of criteria and selected one full-text RCT and seven non-RCTs. These studies were published in all languages until 9 July 2014. The investigators autonomously extracted the data. Differences in evidence selection and data extraction were resolved through discussions. The quality of each study was assessed by the GRADE approach. The researchers synthesized the data with Review Manager

Version 5.3 and also used 95% CI, odds ratio (OR), heterogeneity (I^2) to assess the results of the intervention.

Findings: This review found the people who received TB treatment to have CB DOT with significantly increased success rates in comparison to clinic DOT (OR 1.54, 95% CI 1.01 to 2.36, p = 0.046, I^2 84%). No statistical significance variation was found between CB DOT and clinic DOT in the follow-up (OR 0.86, 95% CI 0.48 to 1.55, p = 0.62, I^2 83%). Finally, this review indicated that CB DOT can achieve higher treatment success than clinic DOT.

Appraisal: The results of this review should be cautioned. The study contained one RCT and seven non-RCTs. The reviews clearly described the search strategies to find relevant studies including databases, years of searching, search terms, languages and selection criteria for the studies included. The reviews properly completed data extraction, methodological quality assessment and data synthesis; hence, the results are valid. The results of this study are statistically and clinically significant. The author can apply these results in the author's clinical setting, because the author's patients are similar to the population studied, and all clinically important outcomes are measured. The benefits of the interventions are greater than the risks, and the interventions are feasible in the author's practice setting.

Table 3.2 Collective Table of Evidence

No.	Authors/Year/ Title and Source of Publication	Type of Evidence and Level	Population/ Outcomes Measurement	Methodology	Outcomes/Results
1.	Karumbi & Garner, 2015. Directly observed therapy for treating tuberculosis (review). *Cochrane Database of Systematic Reviews*, 3.	Systematic Review. Level –I	Nine individual RCTs and two cluster-RCTs with 5,662 patients. Outcomes measured by cure and treatment completion rates.	1) Search methods: Searched databases, meta-register of controlled trials (mRCT), checked the reference lists for the evidence, contacted related researchers and organizations. 2) Study selection: Published full text RCTs and cluster-RCTs in all languages until 13 January 2015. DOT intervention compared to SAT in people who received active or prophylactic treatment for TB to prevent active TB. 3) Data extraction and quality assessment (QA): Done autonomously by two reviewers who contacted the authors regarding unclear and missing data to clarify assessed quality by the GRADE approach; resolved differences in opinion by discussion. 4) Data analysis: Used Review Manager 5, risk ratio (RR) and 95% confidence interval (CI).	This review found DOT to not provide a solution to low TB treatment adherence. TB cure and treatment completion was low in both SAT & DOT groups. 1) No significant differences were found between the SAT and DOT groups in cure and treatment completion (RR 1.08, 95% CI 0.91 to 1.27 and RR 1.07, 95% CI 0.96 to1.19). 2) No significant differences were found between DOT by family members or community health workers at home to DOT by health workers at health facilities in cure and treatment completion (RR 1.02, 95% CI 0.88 to 1.18 and RR 1.04, 95% CI 0.91 to 1.17).

Table 3.2 Collective Table of Evidence (cont.)

No.	Authors/Year/ Title and Source of Publication	Type of Evidence and Level	Population/ Outcomes Measurement	Methodology	Outcomes/Results
2.	M'Imunya et al., 2012. Patient education and counselling for promoting adherence to treatment for tuberculosis (review). *Cochrane Database of Systematic Reviews,* 5.	Systematic Review. Level –I	Three RCTs with 1,437 participants; 558 were adults. Outcomes measured by negative sputum smears and treatment completion rates.	1) Search methods: Searched databases, mRCT; checked the reference lists of evidence; contacted related researchers and organizations. 2) Study selection: Published full text RCTs in all languages from 25 April 2007 to 24 November 2011. Assessed the outcomes of education or counselling, or both, on cure and treatment completion in people who received active or latent TB treatment. 3) Data extraction and QA: Done by reviewers with the use of a pre-designed form contacted authors regarding unclear and missing data to clarify; assessed quality by screens of eligibility, methodological quality, and extracted data; resolved differences by discussion. 4) Data analysis: Used Review Manager 5, RR and 95% CI.	This review concluded that **e**ducation or counselling may enhance treatment completion for latent TB. No studies assessed the outcomes of interventions on active TB treatment adherence. 1) For people with latent TB treatment, education significantly increased treatment completion (24% in the intervention group and 12% in the control group, RR 1.94, 95% CI 1.03 to 3.68). However, treatment completion rates of both groups were low and the three trials included in this review were low quality.

Table 3.2 Collective Table of Evidence (cont.)

No.	Authors/Year/ Title and Source of Publication	Type of Evidence and Level	Population/ Outcomes Measurement	Methodology	Outcomes/Results
3.	Liu et al., 2014. Reminder system to improve patient adherence to tuberculosis clinic Appointments for diagnosis and treatment (review). *Cochrane Database of Systematic Reviews,* 11.	Systematic Review. Level –I	Seven individual RCTs and two quasi-RCTs with 4,654 participants; 2,789 were adults. Outcomes measured by proportion of clinic appointments, treatment completion, and TB diagnosis.	1) Search Methods: Searched databases, mRCT, Indian Journal of Tuberculosis, checked reference lists, and contacted authors to identify relevant studies. 2) Study selection: Published full-text RCTs and quasi-RCTs in all languages until 29 August 2014. The interventions compared participants with and without routine appointments for TB diagnosis, prophylaxis or treatment. 3) Data extraction and QA: Done by two reviewers; used data extraction form; contacted authors to clarify about missing data; resolved differences by discussion with a third reviewer and assessed the quality of evidence by the GRADE approach. 4) Data analysis: Synthesized by Review Manager 5, RR and 95% CI.	The review indicated both pre-appointment reminder phone-calls and default reminders to be sensible strategies with small but potentially significant benefits. 1) For people with active TB, pre-appointment reminder phone-calls and default reminders by letters or home visits increased clinic attendance and treatment completion {(RR 1.32, 95% CI 1.10 to 1.59) & (RR 1.14, 95% CI 1.02 to 1.27) and (RR 5.04, 95% CI 1.61 to 15.78) & (RR 1.17, 95% CI 1.11 to 1.24)} 2) For people on prophylactic TB treatment, pre-appointment phone-calls increased clinic attendance and three monthly phone-calls or nurse visits increased final clinic visits {(RR 1.30, 95% CI 1.07 to 1.59) and 93% vs. 65%.}

Table 3.2 Collective Table of Evidence (cont.)

No.	Authors/Year/ Title and Source of Publication	Type of Evidence and Level	Population/ Outcomes Measurement	Methodology	Outcomes/Results
					3) For people undergoing TB screening, pre-appointment phone-calls and take home reminder cards did not increase rates of return to clinic for skin test result.
4.	Liu et al., 2010. Reminder systems and late patient tracers in the diagnosis and management to tuberculosis (review). *Evidence-Based Child Health: A Cochrane Review Journal, 5*, 1206-1245.	Systematic Review. Level –I	Seven RCTs and two quasi-RCTs, with 5,257 participants; 3,942 were adults. Outcomes measured by adherence to treatment and clinic appointments	1) Search Methods: Searched databases, mRCT, Indian Journal of Tuberculosis; checked reference lists and contacted authors and organizations to identify relevant studies. 2) Study selection: Published full text RCTs and quasi-RCT in all languages until June 2008. The interventions were late patient tracers with and without reminders; participants who required active or prophylactic treatment and TB diagnosis. 3) Data extraction: Performed by two reviewers; used data extraction form; contacted authors to supply missing data	This review found three studies to be late patient tracers and five out of six studies to be reminders helpful for increasing adherence to TB treatment and clinic appointments. 1) For late patient tracers: i) The posting of letter reminders increased rates of treatment completion and clinic appointment compared with no late patient tracers (RR 0.44, 95% CI 0.24 to 0.83 and RR 0.53, 95% CI 0.34 to 0.83). ii) Home visit plus health education significantly decreased the rates of failure to return for treatment on

Table 3.2 Collective Table of Evidence (cont.)

No.	Authors/Year/ Title and Source of Publication	Type of Evidence and Level	Population/ Outcomes Measurement	Methodology	Outcomes/Results
				to clarify issues and resolved discrepancies by discussion. 4) Data analysis: Synthesized by Review Manager 5; used RR and 95% CI to assess effects.	scheduled appointments compared with no late patient tracers at 3.8% vs. 17.5% (RR 0.21, 95% CI 0.11 to 0.43). 2) A automated telephone messages decreased the rates of failure to return for skin test reading and significantly increased the rates of scheduled appointment at prophylaxis and treatment clinics but with no significant difference between reminders and no reminder groups in diagnosis clinics {(7% vs. 12%, $p < 0.05$) and (RR 0.72, 95% CI 0.58 to 0.89 & RR 0.69, 95% CI 0.56 to 0.86 but RR 0.94, 95% CI 0.79 to 1.12)}.

Table 3.2 Collective Table of Evidence (cont.)

No.	Authors/Year/ Title and Source of Publication	Type of Evidence and Level	Population/ Outcomes Measurement	Methodology	Outcomes/Results
5.	Lutge et al., 2012. Material incentives and enablers in the management of tuberculosis (review). *Cochrane Database of Systematic Reviews*, 1.	Systematic Review. Level –I	Eleven RCTs Outcomes measured by treatment success and cure rates.	1) Search Methods: Searched databases, mRCT; checked reference lists and contacted authors and organizations to identify relevant studies. 2) Study selection: Published full text RCTs in all languages until 22 June 2011. Interventions with material incentives, people on diagnostic testing, receipt of active or prophylactic TB treatment. 3) Data extraction and QA: Performed by two reviewers; used data extraction form; resolved differences by discussion and agreement between two reviewers; assessed quality by the GRADE approach. 4) Data analysis: Synthesized by Review Manager 5; used RR and 95% CI to assess effects.	According to the review, incentives failed to increase treatment completion for latent or active TB. 1) For people with active TB, material incentives did not significantly improve long-term adherence and completion of active TB therapy (RR 0.98, 95% CI 0.86 to 1.12). 2) For people with prophylactic TB treatment, material incentives might improve initiation and completion rates for prophylaxis in some settings (RR 1.58, 95% CI 1.27 to 1.96 and RR 1.79, 95% CI 0.70 to 4.58). 3) For people undergoing diagnosis, incentives may increase return rates for skin test results (RR 2.16, 95% CI 1.41 to 3.29).

Table 3.2 Collective Table of Evidence (cont.)

No.	Authors/Year/ Title and Source of Publication	Type of Evidence and Level	Population/ Outcomes Measurement	Methodology	Outcomes/Results
6.	Nglazi et al., 2013. Mobile phone text messaging for promoting adherence to anti-tuberculosis treatment: A systematic review. *Bio-Medical Central Infectious Diseases, 13* (566).	Systematic Review. Level –I	One RCT and three non-RCTs. Outcomes were measured by adherence to treatment through proportion of cure, treatment completion and drug resistance.	1) Search Methods: Searched databases; checked peer-reviewed journal articles and grey literature as well as reference lists of relevant studies, conference reports and selected websites; contacted authors and organizations to identify relevant studies. 2) Study selection: Two authors screened the eligibility of studies; selected published full-text RCTs and non-RCTs in all languages until 15 February 2013. Interventions were mobile phone SMS vs. no interventions among participants on TB treatment. 3) Data extraction and QA: Two reviewers extracted data; used quality data forms. One reviewer entered data into the software; checked by a second reviewer. Discrepancies were resolved by discussion and agreement; quality was assessed by GRADE.	This review found the quality of the four studies to be low with high risk for bias. 1) The results of only one RCT showed that SMS interventions did not significantly improve adherence to TB treatment compared to SAT (RR 1.49, 95% CI 0.90 to 2.42). 2) One of the non-RCTs showed that SMS interventions did not significantly improve cure and success rates compared to DOTS (62.35% vs. 66.4% and 72.94% vs. 69.4%). 3) A non-RCT found DOTS plus SIMpill reminders to significantly increase cure and smear conversion rates vs. DOTS (RR 2.32, 95% CI 1.60 to 3.36 and RR 1.62, 95% CI 1.09 to 2.42). .

Table 3.2 Collective Table of Evidence (cont.)

No.	Authors/Year/ Title and Source of Publication	Type of Evidence and Level	Population/ Outcomes Measurement	Methodology	Outcomes/Results
				4) Data analysis: Analyzed by Review Manager 5.2, used RR and 95% CI to assess the effects.	4) The other non-RCT indicated that SMS reminders increased rates of clinic attendance on scheduled days compared to standard care (RR 1.56, 95% CI 1.06 to 2.29)
7.	Suwankeere et al., 2014. Strategies to promote adherence to treatment by pulmonary tuberculosis patients: A systematic review. *International Journal of Evidence-Based*	Systematic Review. Level –I	Ten RCTs; eight quasi-RCTs; 7,972 patients. Outcomes were measured by treatment completion, cure and success rates.	1) Search Methods: Searched databases, published and unpublished studies. Used key words as search terminology, checked reference lists and bibliographies, contacted organizations to identify relevant studies. 2) Study selection: Two authors screened all studies, selected published full text RCTs and quasi-RCTs in English and Thai languages, from 1990 to 2010. Interventions were DOT, DOTS and case management and compared with different types of DOT; participants were new TB patients.	According to the review, DOT combined with other interventions improved adherence to TB treatment. The interventions included DOT with patients' choice of DOT supporters, DOTS, case management with DOTS, intensive triad-model program and intervention package. Healthcare providers should perform the interventions and modify for local conditions and situations wherever suitable. 1) For new TB patients on treatment, DOT increased cure and success rates but did not increase completion rates in

Table 3.2 Collective Table of Evidence (cont.)

No.	Authors/Year/ Title and Source of Publication	Type of Evidence and Level	Population/ Outcomes Measurement	Methodology	Outcomes/Results
	Healthcare, 12(1), 3-16.			3) Data extraction and QA: Two reviewers extracted data; used data extraction tools and entered data into software to analyze. Any differences in opinion were resolved through discussion; quality was assessed by standardized critical appraisal tools. 4) Data analysis: Analyzed by Review Manager 5.2, used RR and 95% CI to assess effects.	comparison to SAT (76% vs. 67%; 84% vs. 67%; 7.7% vs. 7.8%). 2) For new TB patients on treatment, no significant differences were found between DOT by healthcare workers and self-supervision in cure, completion and success rates (RR 1.06, 95% CI 0.93 to 1.22, p = 0.33, RR 0.95 95% CI 0.38 to 2.36, p = 0.92; RR 1.07, 95% CI 0.96 to 1.20, p = 0.21). 3) For new TB patients on treatment, no significant differences were found between DOT by family members and self-supervision in cure and completion rates; statistically significant higher results were found from DOT by family members in success rates (RR 1.02, 95% CI 0.08 to 1.31, p = 0.85; RR 1.07 95% CI 0.70 to 1.63, p = 0.76; RR 1.07, 95% CI 1.00 to 1.15, p = 0.04)

Table 3.2 Collective Table of Evidence (cont.)

No.	Authors/Year/ Title and Source of Publication	Type of Evidence and Level	Population/ Outcomes Measurement	Methodology	Outcomes/Results
					4) For new TB patients on treatment, DOT by family members increased success rates but did not increase cure and completion rates vs. DOT by case managers (RR 1.05, 95% CI 1.00 to 1.11, p = 0.04; 76% vs. 73%; 7% vs. 5%) 5) For new TB patients on treatment, DOTS case management increased treatment completion rates with significantly improved success rates vs. patients receiving routine care and those who did not (96.9 vs. 68.6 vs. 68.6, p = 0.007; 93.7 vs. 68.6 vs. 68.6, p = 0.023) 6) For new TB patients on treatment, intensive triad-model program increased success rates and with significantly improved cure rates vs. the control group (96.0 vs. 84.9%, p = 0.057; 95.3 vs. 78.9% p = 0.02).

Table 3.2 Collective Table of Evidence (cont.)

No.	Authors/Year/ Title and Source of Publication	Type of Evidence and Level	Population/ Outcomes Measurement	Methodology	Outcomes/Results
					7) For new TB patients on treatment, intervention package improved treatment success rates more than those who received routine TB care (RR 1.18, 95% CI 1.03 to 1.34)
8.	Wright et al., 2015. Community-based directly observed therapy (DOT) versus clinic DOT for tuberculosis: A systematic review and meta-analysis of comparative	Systematic review of meta-analysis. Level –I	One RCT and seven non-RCTs. Primary and secondary outcomes were measured by treatment success and loss to follow-up.	1) Search methods: Searched databases; used key words as search terminology and checked reference lists of identified studies. 2) Study selection: Two reviewers completed selection criteria and selected published full text RCT & non-RCTs in all languages until 9 July 2014. The intervention was DOT; outcomes were compared community-based DOT to clinic DOT and participants were new TB patients.	This review focused that community-based DOT (CB DOT) achieved higher treatment success than clinic DOT. Although, only one RCT was included in this review, the results of the review should be cautioned. 1) For people on TB treatment, CB DOT significantly increased success rate vs. clinic DOT (OR 1.54, 95% CI 1.01 to 2.36, p = 0.046, I^2 heterogeneity 84%).

Table 3.2 Collective Table of Evidence (cont.)

No.	Authors/Year/ Title and Source of Publication	Type of Evidence and Level	Population/ Outcomes Measurement	Methodology	Outcomes/Results
8.	effectiveness. *Bio-Medical Central Infectious Diseases, 15*(210).		.	3) Data extraction and QA: Investigators autonomously extracted the data; differences in evidence selection and data extraction were resolved by discussion; quality was assessed by GRADE approach. 4) Data analysis: Used Review Manager Version 5.3; 95% CI, OR, I^2 to analyze the data.	2) No statistically significant variations were found between CB DOT and clinic DOT for loss to follow-up (OR 0.86, 95% CI 0.48 to 1.55, p = 0.62, I^2 83%).

3.2 Conclusion

The following conclusions can be drawn from the selected eight systematic reviews:

3.2.1 Brief summary of the evidence

Various TB populations were identified in these selected studies, including active or latent TB patients (Karumbi & Garner, 2015; M'Imunya et al., 2012), active or latent TB patients and patients undergoing TB diagnosis (Liu et al., 2014; Liu et al., 2010; Lutge, Wiysonge et al., 2012), patients on TB treatment (Nglazi et al., 2013), as well as new TB patients (Suwankeere, & Picheansathian, 2014; Wright et al., 2015).

According to the eight studies, the six evidence indicated significant effects of the interventions for promoting adherence to TB treatment (Karumbi & Garner, 2015; Liu et al., 2014; Liu et al., 2010; M'Imunya et al., 2012; Suwankeere & Picheansathian, 2014; Wright et al., 2015). Two studies indicated non-significant effects. Among these two studies, one was a material incentive and enabler intervention. The results of the study showed ineffective intervention in increasing treatment completion rates and the evidence was low quality (Lutge et al., 2012). The other study involved mobile phone text message intervention. This study was also low quality evidence with high risk for bias. The intervention in the study was also unsuccessful in improving adherence to TB treatment (Nglazi et al., 2013).

Of the six studies, three main interventions showed significant results in improving adherence to TB treatment. The evidence regarding effective interventions for promoting adherence to TB treatment can be summarized as follows:

1) Interventions combined with DOT

- DOT alone cannot provide solutions for improving adherence to TB treatment, even while DOT is performed by health care providers. Thus, other interventions need to be combined with DOT to improve adherence (Karumbi & Garner, 2015; Suwankeere & Picheansathian, 2014; Wright et al., 2015). According to DOT, there were no significant differences between DOT by family members or community health care workers at home and by health care workers at health facilities, DOT by health workers and self-supervision, DOT by family members and self-supervision, and DOT by family members and case managers (Karumbi & Garner,

2015; Suwankeere & Picheansathian, 2014). Therefore, patients can select a treatment supporter from health care workers, family members, community members or volunteers and case managers or former patients living near the patients depending on convenience.

- Other interventions combined with DOT can promote adherence to treatment as follows:

a) Case management with DOTS consists of patients' hospital education with two months of DOT and weekly home visits.

b) The triad-model program is composed of strengthening the activities of health care providers, TB patients and treatment supporters with patient education and monthly home visits.

c) Intervention package include strengthening counseling, decentralization of treatment, active supervision and patient selection of a DOT supporter (Suwankeere & Picheansathian, 2014).

2) Education: Both education and counselling interventions are effective strategies. These strategies can be applied to improve treatment completion (M'Imunya et al., 2012).

3) Reminder systems: Reminder systems are successful strategies for improving adherence to TB treatment and clinic appointments. These strategies are composed of two types of reminders. Telephone calls or letters can be used before a scheduled appointment as pre-appointment reminders. Posting letters or home visits can also be used after a missed appointment as default reminders. In addition, there is no strong evidence to support that other reminders such as automated telephone messages improve adherence to TB treatment (Liu et al., 2014; Liu et al., 2010).

Based on the outcome measurement, most of the studies included outcomes measured by cure rates, success rates and treatment completion rates with the proportion of attendance at scheduled appointments. All of the aforementioned are related to TB treatment adherence.

Finally, it can be concluded that DOT combined with other interventions, education and counselling and reminder systems is more effective in improving treatment adherence among adult patients with TB.

3.2.2 Recommendations

Based on the reviewed evidence on promoting adherence to treatment among adult patients with TB and all eight of the studied evidence in the form of systematic reviews, the following recommendations are proposed after analysis and synthesis all of the evidence:

1) DOT alone is unable to improve TB treatment adherence. DOT should be combined with other interventions to promote adherence (Karumbi & Garner, 2015/Level I; Suwankeere & Picheansathian, 2014/Level I; Wright et al., 2015/Level I).

2) TB patients should choose a treatment supporter or observer based on the patients' convenience. Treatment supporters can be health care workers, family members, community members or volunteers, case managers and former patients to ensure DOT. DOT should be performed by the selected supporter either at home or in a health facility as appropriate (Karumbi & Garner, 2015/Level I; Suwankeere & Picheansathian, 2014/Level I; Wright et al., 2015/Level I).

3) Other interventions or strategies combined with DOT should be employed to improve TB treatment adherence**.** Health care providers should perform these interventions with modification and application of the interventions based on local conditions and situations wherever suitable (Suwankeere & Picheansathian, 2014/Level I).The interventions combined with DOT include the following:

- Case management of DOTS is an effective strategy that should be implemented to improve treatment completion and success rates in TB patients. The activities of case management DOTS strategy should consist of providing patients' education in hospital, performing DOT for the first two months, conducting one home visit per week by the case manager in order to motivate and improve the patients' and family members' knowledge and support in order to achieve better treatment outcomes (Suwankeere & Picheansathian, 2014/Level I).

- Intensive triage model program should be used with DOT to increase success and cure rates. The components of this intervention were composed of strengthening the activities of health care workers, TB patients and treatment supporters, patient education regarding TB and the importance of treatment, monthly

home visits to encourage medication adherence with assurance by health care providers and treatment supporters (Suwankeere & Picheansathian, 2014/Level I).

- Intervention package is a successful intervention that should be applied with DOT to increase treatment success rates for new TB patients. Intervention package should include strengthening counseling aimed at improving relationships with patients and providers with decentralization of treatment, active supervision of activities and patient selection of a DOT supporter in order to improve adherence and completion of TB treatment (Suwankeere & Picheansathian, 2014/ Level I).

4) Education or counselling interventions can enhance adherence to TB treatment for latent TB patients. Therefore, these interventions should be employed to improve successful treatment completion of latent TB patients (M'Imunya et al., 2012/Level I).

- Patient education procedures should be delivered through various methods including mass media to cover a broad range with information from the provision of written, audiovisual, and computer based patient education materials by health care providers or organizations and individualized counseling to promote adherence and completion of treatment (M'Imunya et al., 2012/Level I).

- In education and counselling sessions, health care providers should provide patients with current and complete information about their health. Health care providers should also emphasize tuberculosis infection as well as the importance of therapy and therapy adherence, potential adverse effects and dietary habits in order to change knowledge, attitude and practice with the building of a trusted environment, enhancement of the health care provider-patient relationship and assistance for patients in handling their own health care (M'Imunya et al., 2012/Level I).

- Education and counselling should be performed in individual or group sessions with the study participants by a trained counselor to provide proper guidance and help patients manage health problems better with improved adherence (M'Imunya et al., 2012/Level I).

5) Reminder systems are effective strategies for improving adherence to treatment and clinic appointments are as follows:

- Telephone calls should be implemented as a pre-appointment reminder before scheduled appointments to contact patients before subsequent appointments to increase clinic attendance for TB diagnosis or treatment, remind patients to take medication and increase attendance at appointments to ensure adherence (Liu et al., 2010/Level I; Liu et al., 2014/Level I).

- Letters or home visits should be applied as default reminders after patients have missed appointment in order to increase clinic attendance and treatment completion for active TB patients. Late patient tracers could be used to overcome barriers to attendance for treatment by making contact with the patient, helping patients understand the need to attend treatment, determining the reasons for failure to attend when patients fail to attend an appointment (Liu et al., 2014/Level I; Liu et al., 2010/Level I).

CHAPTER IV
CONCLUSION AND SUGGESTIONS

4.1 Conclusion

Tuberculosis (TB) is a serious public health problem of global proportions and a major cause of mortalities due to a single infectious agent. TB generally causes harm to the lungs and other body parts. Close proximity to infectious person, weakened immune systems and low socioeconomic status are the main risk factors for this disease. TB patients suffer from several physiological, psychological and financial problems. However, non-adherence to treatment is the main problem encountered in TB treatment. Different types of interventions or strategies can be employed to improve TB treatment adherence.

Bangladesh is a low socioeconomic country. Based on the context of Bangladesh, most patients have limited knowledge about TB and its treatment or complications. The knowledge of health care providers in the management of TB patients is also low. In Bangladesh, the DOT strategy was launched many years ago for TB prevention and control based on the WHO recommendations. However, DOT alone cannot be effectively implemented in Bangladesh. Therefore, effective strategies need to be identified. The objective of the present study is to summarize current evidence-based interventions to promote adherence to treatment among adult TB patients.

According to the PICO framework, the author searched for systematic reviews from several electronic databases/sources in the Mahidol University library system. The author also conducted a manual search from reference lists of evidence. Appropriate key words also used for searching to help obtain the best evidence included “tuberculosis”, “interventions” and “adherence to treatment”. After searching, the author selected eight evidence acquired from full-text studies published in English from 2010 to 2016. The evidence was appraised by the method and criteria of Melnyk and Fine-Overholt (2015) by answering the following three questions: i)

Are the results of the study valid? ii) What are the results? iii) Will the results help in caring for patients?

Of the eight studies, six evidence indicated significant effects and two evidence were found to be ineffective in promoting TB treatment adherence. Of six studies, three main interventions showed significant results to promote TB treatment adherence. These interventions are composed of DOT combined with other interventions, education and counselling and reminder systems.

The author asserts that DOT alone is unable to improve TB treatment adherence, even when DOT is performed by healthcare providers. No significant differences were found among treatment supporters and places for implementing DOT, which can be performed either at home or in health facilities. Therefore, patients can select a treatment supporter to improve treatment adherence. Moreover, other interventions combined with DOT include: 1) case management with DOTS; 2) intensive triad-model program with DOT; 3) intervention package with DOT.

In addition, education and counselling interventions are both effective strategies. Reminder systems are also successful strategies for improving TB treatment and clinic appointment adherence. Telephone calls or letters should be used before a scheduled appointment as pre-appointment reminders. Furthermore, letters or home visits should be used after a missed appointment as default reminders. In addition, no strong evidence was found to support other reminders such as automated telephone messages in improving TB treatment adherence. All of the study outcomes were measured by cure rates, success rates and treatment completion rates with the proportion of attendance at scheduled appointments. All of the aforementioned have been found to be related to TB treatment adherence.

Finally, it can be concluded that adherence is essential to TB treatment completion. TB treatment completion can also reduce transmission, incidence, morbidity and mortality rates in addition to lowering the overall costs of TB control programs. The aforementioned evidence can also be helpful for health care providers and organizations in improving the quality of care for TB patients. These effective adherence promoting interventions are feasible in the context of the author’s clinical setting in Bangladesh.

4.2 Suggestions

According to the findings of the present study, the author would like to offer the following suggestions for nursing practice and research on interventions for promoting adherence to treatment among adult patients with TB:

4.2.1 Nursing practice

1) Clinical practice guidelines should be developed on interventions for promoting adherence to treatment among patients with TB by using the recommendations acquired from the effective evidence. The guidelines should be made in simple language with modifications and applications based on the health system and context of the clinical setting in Bangladesh whenever possible. Prior to implementation, the merits and feasibility of the guidelines should be discussed with hospital administrators, at which time permission and support should be sought for implementation of the guidelines. Next, a pilot study should be conducted to evaluate the feasibility and effectiveness of the guidelines.

2) Training programs should be arranged for nurses, health care providers and treatment supporters to equip them with necessary knowledge and skills on interventions for promoting TB treatment adherence in addition to building awareness about effective management of TB patients. Then the aforementioned health service providers should implement the guidelines into clinical practice settings at the hospital and community levels.

3) After implementation, the guidelines should be evaluated for effectiveness.

4) The guidelines should be reviewed and updated regularly to achieve the goals.

5) The guidelines should be disseminated in all rural to referral level hospitals to improve the quality of care, reduce financial burdens and promote TB treatment adherence.

4.2.2 Nursing research

1) More clinical trials with strong designs and systematic reviews including high quality of evidence are required to confirm effective interventions for improving TB treatment adherence.

2) All of the studies were conducted in other countries. Therefore, clinical trials are recommended in order to evaluate the interventions for promoting TB treatment adherence in Bangladesh.

3) Research should be conducted to evaluate and improve the knowledge of nurses on interventions for improving TB treatment adherence in Bangladesh.

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