CHAPTER 1

Introduction

1.1 Background and significance of the research problem

Tuberculosis (TB) remains a major global health problem. In 2012, the World Health Organization (WHO) estimated 8.6 million people developed TB and 1.3 million died from the disease. The number of TB deaths is unacceptably large given that most are preventable (WHO, 2013). The 22 high-burden countries (HBCs) for TB accounted for 81% of all estimated cases worldwide (WHO, 2010a). Among the 22 HBCs, seven have met all of the 2015 targets for reduction in TB incidence, prevalence, and mortality. Four more HBCs are on track to do so by 2015 but 11 countries are not on track to reduce those in line with the targets. Thailand is one of these 11 countries. The reasons given for this situation are resource constraints, political conflict and instability, and the generalized Human Immunodeficiency Virus (HIV) epidemics (WHO, 2013). Approximately 50% of all new TB cases were sputum smear-positive pulmonary tuberculosis (PTB) patients who were the major sources of infection (WHO, 2006). In 2012, WHO estimated that globally there were 2.5 million new cases of PTB-sputum smear-positive (36 per 100,000 population) and 30,998 of these (46 per 100,000 population) were Thai cases (WHO, 2013).

The impact of TB on individuals is often all-encompassing, affecting not only physical health, but also social, economic, and psychological well-being (Hansel, Wu Chang, & Diette, 2004; Rajeswari et al., 1999; Rajeswari, Muniyandi, Balasubramanian,& Narayanan, 2005). The initial reaction of patients to the disclosure of the diagnosis of TB varied from worry, suicidal thoughts, denial, and depression (Rajeswari et al., 2005). Tuberculosis patients had difficulty in their relationships with their spouses and family members because of the disease's airborne transmission (Ahsan et al., 2004). Approximately 20-30% of people who have had contact with TB patients may be infected with *Mycobacterium tuberculosis* (*M. tuberculosis*), and 1%

may develop TB (Jereb, Etkind, Joglar, Moore, & Taylor, 2003). Social stigmatization and isolation caused by an airborne transmission illness can result in anxiety, depression and reduction in quality of life (Hansel et al., 2004; Kelly, 1999; Lawn, 2000). Lung dysfunction and presence of respiratory failure among PTB patients is strongly associated with mortality (Chierakul & Chungsamarn, 2001). Without TB treatment, 50% of PTB patients will die and 25% will remain ill with chronic infectious TB by the end of five years following diagnosis (WHO, 2004). WHO estimated $7-8 billion per year is required for a full response to the TB epidemic in low- and middle-income countries in 2014 and 2015 (WHO, 2013).

Short-course chemotherapy (SCC) is recognized as one of the most cost-effective standard treatments and is recommended for TB patients. Properly applied SCC fulfils the aims of anti-TB drugs, which include curing the patient of TB, preventing death from active TB or its late effects, preventing TB relapse, preventing the development of drug resistance, and decreasing TB transmission (WHO, 2004). TB treatment is divided into two phases: an initial and continuation phases. The treatment period recommended by the National Tuberculosis Program (NTP) in Thailand requires six months for newly diagnosed PTB-sputum smear-positive patients. The initial phase requires two months with four drugs. The continuation phase takes four months with two drugs, and drugs are taken daily (Ministry of Public Health, 2008). Effective medication adherence induces the patients' sputum to become smear-negative within two months in the initial phase. However, poor adherence to medication during the course of treatment is a common cause of treatment failure (WHO, 2004).

Successful TB treatment is heavily dependent on the effective treatment of patients requiring medication adherence throughout the full course of treatment (Bashour & Mamaree, 2003; Blanc & Martinez, 2007; Phuangngernmak, 2001; Tipaht, 2008). Approximately half of TB patients did not adhere to medication during the full course of treatment under routine practice conditions (Kruk, Schwalbe, & Aguiar, 2008; Menzies et al., 2008). Non-medication adherence rates were 11-60% among newly diagnosed PTB patients with sputum smear-positive in Thailand (Chatwiriyacharoen, 2003; Lertmaharit, Kamol-Ratanakul, Sawert, Jittimanee, & Wangmanee, 2005). Improper TB medication taking behavior may result in prolonged infectiousness and

increased transmission rates of tubercle bacilli, requiring a longer treatment regimen, resulting in increased treatment failure and relapse, and developing anti-TB drugs resistance (Borgdorff, Floyd, & Broekmans, 2002; Mitchison, 1998; Pablos-Mendez, Knirsch, Barr, Lerner, & Frieden, 1997; Thomas et al., 2005). Emerging multi-drug resistance (MDR) causes high costs for controlling, un-treatability, and fatality in 50% of cases (Breathnach et al., 1998; Espinal, Kim, & Suarez, 2000; Grzemska, 2009). Therefore, in TB treatment success is the consequence of effective medication adherence including taking the right medicine, the right amount of medicine, the right dose, at the correct time, and continuously.

Factors that are barriers to adhering to TB medication include patient-related and outside factors. Focusing on patients with sputum smear-positive PTB, the most important factor is a patient-related factor. Cognitive function is a patient-related factor, which can be improved and can accurately predict medication adherence (Bam et al, 2006; Tipaht, 2008; Lertmaharit et al., 2005). The reasons quoted for non-adherence to medication included not being informed to take medication regularly (Bam et al., 2006), feeling better and misunderstanding that the disease was cured (Bam et al., 2006; Wattanatorn, 2002), forgetting to take medicine (Tipaht, 2008), and the condition not improving (Wattanatorn, 2002). The outside factors included the high number of medicine tablets (9-12 tablets) to be taken each time (Kowatanakul, Siangsung, & Nokyoongthong, 2001) and adverse drug reaction (Bam et al., 2006; Burakorn, 2004; Tipaht, 2008; Wattanatorn, 2002). Some patients are unable to afford transportation costs, are dissatisfied with the care (Bam et al., 2006; Shargie & Lindtjorn, 2007), and are not able to obtain the medicine during office hours (Arkaravichien, Usawamethapun, & Soonthornpas, 2003). Therefore, incorporating the appropriate outside factors to facilitate behavior change and improving the inner cognitive function among patients with sputum smear-positive PTB is needed for enhancing medication adherence throughout the full course of treatment.

The target of the global TB control program launched by WHO in 1991 was that by 2005 to successfully treat at least 85% of new sputum smear-positive cases of PTB under the Directly Observed Treatment, Short-course (DOTS) strategy (WHO, 2009). The DOTS strategy has five components, consisting of political commitment; case

detection through quality-assured bacteriology; standardized treatment with supervision and patient support, in which patients are directly observed daily to ensure that every dose of the treatment regimen is taken. This strategy is called Directly Observed Treatment (DOT); effective drug supply and management system; and monitoring and evaluation system and impact (Ministry of Public Health, 2008; WHO, 2004; WHO, 2009). The DOTS strategy has been mandated in Thailand since 1996. Although the results of the implementation have shown the treatment success rate of the PTB patients in 2001 was 75% and increased to 82% in 2008, it did not meet the target rate set by WHO. The treatment success rate did meet the target in 2009 with 86%, however, it decreased to 85% in 2010 and 2011 (WHO, 2013). The barriers to implementing the DOTS strategy in Thailand include a limitation of budget and staff (The Global Fund, 2008); the value of DOT being questioned, specifically whether or not watching patients swallow every dose of their tablets for at least six months is the ideal method of treatment; and DOT is considered disrespectful of patients. Some Thai TB patients refused DOT because of stigmatization (Ministry of Public Health, 2009; Phokaew, Arunkanjana, & Chaiwong, 2001; Volmink & Garner, 2007). Consequently, to solve the problem of medication adherence and preventing treatment success from decreasing, they need more effective strategies for implementation among Thai newly diagnosed PTB patients with sputum smear-positive.

Several systematic review studies indicated that there were many interventions that have been used that significantly improve TB medication adherence and clinical outcomes. These interventions consisted of DOT strategy (Parent, 1999; Suwannakeeree & Picheansathian, 2014; Volmink & Garner, 1997), simplification of dosage and packaging (Bangalore, Kamalakkannan, Parkar, & Messerli, 2007; Connor, Nafter, & Rodgers, 2004; Mathew, 2009), incentives (Parent, 1999; Volmink & Garner, 1997), reminders (Liu et al., 2008; Volmink & Garner, 1997), education (Volmink & Garner, 1997), and combined interventions (Hirsch-Moverman, Daftary, Franks, & Colson, 2008; Phanchaiya, 2010; Suwannakeeree & Picheansathian , 2014; Volmink & Garner, 1997). Additionally, accurate medication adherence has a number of cognitive components, availability of daily health education has a large independent effect on improving adherence among new smear-positive PTB patients (OR=6.27) (Bam et al., 2006). Although education is an important factor, educational strategies alone are not

sufficient for promoting sustained medication adherence behavior (Haynes, Wang, & Goales, 1987; Haynes et al., 2002). Social support may enhance adherence both because the presence of another individual helps to shape an illness representation more consonant with a desire to adhere and because it offers a reminder function. Thus social support may be a form of cognitive collaboration that provides event-based prospective cues to take medication. Tipaht's (2008) study showed that DOT by supporters increased the success rate of TB treatment (OR=5.00). Moreover, there is a growing consensus that multi-component intervention approaches are more effective in enhancing long-term medication adherence among chronically ill patients, including newly diagnosed PTB patients (Haynes, Achloo, Sahota, McDonald, & Yao, 2008; Roter et al., 1998; Suwannakeeree & Pichensathian, 2014, Wright, 2000). Therefore, educational and other interventions that improve and sustain cognitive function combined with external supporters are needed for enhancing medication adherence among PTB patients.

A systematic review by Volmink and Garner (1997) found that a combination of patient education and incentives was an effective strategy to promote adherence to curative or preventive TB treatments. In addition, a recent systematic review by Suwannakeeree and Picheansathian (2014) found that there were three effective combined interventions for enhancing medication adherence and improving treatment outcomes among newly diagnosed PTB patients including case management with DOT; the intensive triad-model program; and intervention package. Case management with DOT is effective when combined with education and DOT during the first two months and one home visit per week. The intensive triad-model program emphasised on roles and interaction of the healthcare provider, the TB patient, and treatment supporter, is combined with comprehensive health education and a home visit once a month. The intervention package is based on improved patient counselling and communication, along with decentralization of treatment, patient choice of their DOT supporter, and reinforcement of TB clinic staffs. However, all of these studies have limitations in that the interventions were not developed based on a health behavior theory to justify the intervention approach and explain how the intervention did or did not improve medication adherence and treatment outcomes. Two of these three studies used quasi-

experimental design, which did not divide the sample randomly into control and experimental groups, and/or test their baseline equality.

Most of studies in Thailand focused on medication adherence among these patients established interventions based on the health behavior theory and combined education with various interventions such as reminders (Boonpendecha, 2001; Chuldeja, 1997; Khortwong, 2001; Suksawat, 2002; Suntharasri, 1991; Suvateerapun, 1994; Wintachai, 1995), home visits (Nithakorn, 1999; Ungcharoensup, 2000), self-recording and food incentive (Prasansueb, 2009) or self-recording and unit-of-use packaging (Suntharasri, 1991). The results of these studies indicated a significantly improved knowledge or compliance behaviors or medical appointments (Boonpendecha, 2001; Chuldeja, 1997; Khortwong, 2001; Nithakorn, 1999; Prasansueb, 2009; Suksawat, 2002; Suntharasri, 1991; Suvateerapun, 1994; Ungcharoensup, 2000; Wintachai, 1995); increased perceived self-efficacy and outcome expectations (Boonpendecha, 2001; Chuldeja, 1997; Suksawat, 2002; Ungcharoensup, 2000); and improved perception of susceptibility, severity, and benefit and cost of PTB (Nithakorn, 1999; Suntharasri, 1991; Suvateerapun, 1994; Wintachai, 1995). However, the interventions in several studies did not increase sputum conversion rates in the 2^{nd} or 3^{rd} or 6^{th} month of treatment (Boonpendecha, 2001; Suksawat, 2002; Suntharasri, 1991; Suvateerapun, 1994; Wintachai, 1995; Khortwong, 2001). Although these studies were developed based on health behavior theory, they had limitations in that using quasi-experimental design, which neither did not divide the sample randomly into control and experimental groups, nor test their baseline equality. Most of these studies did not follow-up the medication adherence throughout the full course of treatment or compare treatment outcomes at the end of treatment. Therefore, the rigorous evidence supporting the effectiveness of combined intervention based on health behavior theory on long-term medication adherence and treatment outcomes among Thai newly diagnosed with PTB is needed.

Social cognitive theory (SCT) is a health behavior theory suggested for driving interventions for increasing long-term adherence to medication or prescribed practice (Munro, Lewin, Swart, & Volmink, 2007; Ruppar, 2010; Sirus, Richarson, Wishart, & Hanna, 2009). In this theory, human functioning is explained in terms of a model of

triadic reciprocality in which behavior, cognitive and other personal factors, and environmental events all operate as interacting determinants of each other (Bandura, 1986). The theory can explain the phenomenon of TB medication adherence, which is caused and predicted by a number of cognitive components, other personal and outside factors. The process to raise self-efficacy for self-regulation will improve patients' cognitive function, the most important factor predicting TB medication adherence. The continuous process of self-regulation will promote patients themselves for active solving problems; these strategies are fit for managing multi-factor influencing TB medication adherence.

Self-regulation is an effective strategy used to improve a person's ability to manage his or her disease including adherence behavior (Leventhal & Gameron, 1987; Reynolds, 2003; Van Dulmen et al., 2007). Self-regulation is the continuous process of self-generated thoughts, feelings, and actions that are planned and cyclically adapted to the attainment of personal goals (Bandura, 1991; 1993; Zimmerman, 2000) and emphasizes that patients themselves are active problem solvers and try to close the gap between their current health status and the goal (Leventhal & Gameron, 1987). Research findings revealed that combined interventions including goal setting, self-management plans, self-monitoring, reinforcement, and occasional rewards or incentives could improve medication adherence and clinical outcomes (Dick & Lombard, 1997; Haynes et al., 2008; Kripalani, Yao, & Hynes, 2007; Phanchaiya, 2010). Additional, WHO (2003) mentioned that for enhancing patient medication adherence, patients need to be informed, motivated, and skilled in the use of cognitive and behavioural self-regulation strategies.

Self-efficacy is the confidence a person feels about performing a particular activity, including confidence in overcoming the barriers to performing that behavior (Armitage & Conner, 2000; Bandura, 1986; Munro et al., 2007). Self-efficacy could explain between 4-26% of variance in adherence behaviors (Keller, Fleury, Gregor-Holt, & Thompson, 1999). In multivariate analysis, two variables were significantly related to adherence to highly active anti-retroviral therapy for one year, including poor effort in taking medication (OR=5.38) and high self-perceived capacity in following the regimen (OR=13.76) (Tuldra et al., 2000). In addition, self-efficacy was a central factor

of an effective model for medication adherence (McCann, Clark, & Lu, 2008). Effective self-regulation depends on feeling self-efficacious for using skills to achieve mastery (Bandura, 1986, 1993). Self-efficacy operates during all phases of self-regulation (Zimmerman, 2000). The stronger the perceived self-efficacy, the higher the goals and challenges people set for themselves, and the firmer their commitment to them (Bandura, 1991). Therefore, self-efficacy promotes self-regulation capability that is needed for enhancing TB medication adherence throughout the full course of treatment.

There have been some studies of effective interventions based on self-efficacy or the self-regulation concept among Thai newly diagnosed PTB patients. The interventions improved patients' knowledge, self-efficacy, outcome expectations, and compliance behaviors or appointments (Boonpendecha, 2001; Chuldeja, 1997; Katmanee, 2004; Suksawat, 2002; Tansakul, Luksamijarulkol, Kerdmongkol, & Sukwongtanon, 2003; Ungcharoensup, 2000), as well as attitudes towards TB treatment, and sputum conversion in the 2nd month of treatment (Tansakul et al., 2003). The limitations of all these studies are using quasi-experimental design, which did not divide the samples randomly into control and experimental groups, nor test their baseline equality. Most of these studies did not follow-up on the medication adherence throughout the full course of treatment or compare treatment outcomes at the end of treatment. Additionally, there has been some rigorous evidence supporting the effectiveness of the interventions based on self-regulation and/or self-efficacy concepts among chronic illness patients in increasing medication adherence (Barnason, Zimmerman, Hertzog, & Schulz, 2010; Chen, Sheu, Chang, Wang, & Huang, 2010; Smith, Rublein, Marcus, Brock, & Chesney, 2003) and clinical outcomes (Barnason et al., 2010). However, all of these studies are limited in that they followed-up patients in the short-term (≤ 3 months) and one study did not follow-up clinical outcomes (Chen et al., 2010). Some rigorous evidences from followed-up patients who received highly active anti-retroviral therapy for one year indicated that the interventions based on self-efficacy concept significantly increased medication adherence (Tuldra et al., 2000; Weber et al., 2004) and clinical outcomes (Tuldra et al., 2000).

However, there is no rigorous evidence supporting the effectiveness of combined intervention based on self-efficacy and self-regulation concepts of social cognitive

theory (Bandura, 1986), on long-term medication adherence and treatment success in Thai patients newly diagnosed with PTB. Considering the need for enhancing medication adherence throughout the full course of treatment and improving treatment success among these patients, a Medication Adherence Enhancement Program based on these concepts and needed long-term rigorous testing will be established to fill the gaps. This program is planned to raise self-efficacy for self-regulation to adhere to TB medication and provide environmental support to facilitate behavior change. The program is expected to increase medication adherence and improve treatment success. The finding will be beneficial for planning the best nursing practice for enhancing medication adherence throughout the full course of treatment, thereby increasing treatment success among Thai newly diagnosed PTB patients.

The TB clinic of Buddhachinaraj Hospital, Phitsanulok province provides health care service for TB cases in 20 Districts and cooperates with 29 primary care units. A registered nurse, two other health care providers, and a physician work in this clinic. The treatment used for PTB patients follows the NTP in Thailand and is free of charge. The usual care in the TB clinic consists of providing education, home visits, and late patent tracers as well as giving fixed-dose combinations drugs or medication packages, and setting appointment follow-up visits. Additionally, in 2011-2014, the TB clinic has joined with the Global Fund Project for giving the money incentive to the newly diagnosed PTB patients who have sputum smear-positive (The Office of Disease Prevention and Control 9 & Phitsanulok Provicial Health Office, 2013). However, the results of evaluating standard of TB care of the clinic did not meet the standard criteria for both the processes and outcomes of care, especially the cover rate of DOT strategy for newly diagnosed PTB patients who had sputum smear-positive and over rate of defaulted (The Office of Disease Prevention and Control 9, 2012; 2013). In addition, the treatment success rates of all newly diagnosed PTB patients who had sputum smear-positive ranged from 56.38-79.10% in 2011-2013 (The TB clinic of Buddhachinaraj Hospital, 2014). These treatment success rates did not meet the target rate (85%) set by WHO (2009). In order to promote the newly diagnosed PTB patients to enhance medication adherence behavior and increase treatment success, the Medication Adherence Enhancement Program focuses on self-efficacy for self-regulation and environmental supports should be implemented.

1.2 Research objectives

The purposes of this study were to examine the effects of the Medication Adherence Enhancement Program on medication adherence and treatment success among newly diagnosed PTB patients. The research objectives were as follows:

1.2.1 To compare medication adherence between newly diagnosed PTB patients receiving the Medication Adherence Enhancement Program and those receiving usual care.

1.2.2 To compare treatment success between newly diagnosed PTB patients receiving the Medication Adherence Enhancement Program and those receiving usual care.

1.3 Research hypotheses

1.3.1 Newly diagnosed PTB patients receiving the Medication Adherence Enhancement Program will have higher medication adherence than those receiving usual care.

1.3.2 Newly diagnosed PTB patients receiving the Medication Adherence Enhancement Program will have higher treatment success than those receiving usual care.

1.4 Definition of terms

Medication Adherence Enhancement Program is an individualized intervention which lasts eight weeks with seven sessions, based on the self-efficacy and self-regulation concepts of social cognitive theory (Bandura, 1986) for newly diagnosed PTB patients. The program consists of two components. The first component is activities for raising self-efficacy for self-regulation to adhere to TB medication. The activities in this component include providing knowledge, mastery experience, modeling, verbal persuasion, and physiological and emotional arousal. The second component is environmental support for facilitating behavior change, consisting of a choice of family supporters, and telephone reminders and counseling. The program is developed by the researcher in order to enhance each person's belief in his or her own

ability to perform specific tasks for self-regulation to adhere TB medication achieving a full course of treatment.

Newly diagnosed PTB patient is defined as a person aged 20-59 years old, who has been diagnosed with a new PTB-sputum smear-positive and has never taken anti-tuberculosis drugs.

Medication adherence is defined as the behavior of taking anti-tuberculosis drugs as regimens that are mutually set goals between patients and nurses or physicians. These behaviors include continuously taking medication for six months, along with taking the right medicine, the right amount of medicine, the right dose, and at the correct time. Medication adherence will be assessed using a self-reporting Anti-Tuberculosis Medication Adherence Scale developed by the researcher.

Treatment success is the sum percentage of "cure" and "treatment completed". "Cure" is defined as a patient whose sputum smear or culture is negative in the last month of treatment and on at least one previous occasion. "Treatment completed" is defined as a patient who has completed treatment but does not have a negative sputum smear or culture result in the last month of treatment and on at least one previous occasion (WHO, 2010b). Therefore, the results of normal chest radiography, and signs and symptoms improvement of a patient are used to support the result of treatment completed. "Cure" or "treatment completed" of individual patient is determined by a physician.

Usual care refers to the routine care activities which are provided to newly diagnosed PTB patients conducted by a nursing team in the TB clinic and other health care providers in primary care units.