A Medication Adherence Enhancement Program for Persons with Pulmonary Tuberculosis: A Randomized Controlled Trial Study

Wongduan Suwannakeeree, Wilawan Picheansathian, Wanchai Lertwatthanawilat, Akeau Unahalekhaka

Abstract: Successful tuberculosis treatment is strongly dependent on medication adherence throughout the full course of treatment. This randomized controlled trial examined the effects of the Medication Adherence Enhancement Program for persons with pulmonary tuberculosis on treatment success and medication adherence in a hospital in northern Thailand. Fifty participants meeting the inclusion criteria were randomly assigned to either an intervention (n=25) or control (n=25) group. The intervention group received the Program based on the social cognitive theory in addition to usual care, while the control group received only usual care. The Program duration was 8 weeks, and included 7 sessions: 5 for providing knowledge and raising self-efficacy for self-regulation to adhere to medication, and 2 for reminding and counselling. Medication adherence was assessed using the Anti-Tuberculosis Medication Adherence Scale, while treatment success was evaluated by using the Criteria to Identify Tuberculosis Treatment Outcomes of the World Health Organization. Fisher's exact test and Mann-Whitney U test were used analysed data.

Results revealed that the mean score of medication adherence inthe intervention group at 3 months after implementing the program was significantly higher than the control group. However, at 6 months after implementation, the mean score of medication adherence and treatment success of the participants in the intervention group was higher than the control group but not significantly different. Nurses may implement this Program to increase medication adherence in the short-term and improve treatment success in targeted persons.

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Introduction

Tuberculosis (TB) remains a major global health problem because of resource constraints, political conflicts and instability, and generalized Human Immunodeficiency Virus (HIV) epidemics.[1] Thailand is one of 11 countries not on track to meet Millenium Goal Development targets targets for reduction of TB incidence, prevalence, and mortality.[1] Successful TB treatment is heavily dependent on

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patients' medication adherence (MA) throughout the full course of treatment.[2-3] Approximately half of people with TB do not adhere to medication during the full course of treatment under routine practice conditions.[4-5] Non-adherence to a TB medication regime may result in prolonged infection, increased transmission rates of tubercle bacilli, require longer treatment regimens, increased treatment failure and relapse, and result in the development of anti-TB drugs resistance.[2-3] Emerging multi-drug resistance causes high costs for controlling, un-treatability, and fatality in 50% of the cases.[6-7]

Short-course chemotherapy (SCC) is recognized as one of the most cost-effective standard treatments and is recommended for persons with TB. The treatment is divided into two phases: an initial and continuation phase.[3] The treatment period recommended by the National Tuberculosis Program (NTP) in Thailand requires six months of pulmonary TB (PTB) treatment for new cases. The initial phase requires two months with four drugs. The continuation phase takes four months with two drugs and the drugs are taken daily.[8]

The target of the global TB control program launched by World Health Organization (WHO) was to successfully treat at least 85% of new sputum smear-positive cases of PTB under the Directly Observed Treatment, Short-course (DOTS) strategy.[9] This strategy has been mandated in Thailand since 1996. The treatment success of new Thai cases of PTB that were sputum smear-positive for TB (75-82%) did not meet the target rate set by WHO until 2009 (86%); however, this rate decreased to 85% in 2011.[1] The barriers to implementing the DOTS strategy in Thailand included insufficient budget and staff limitations;[10] the value of Directly Observed Treatment (DOT) being questioned because of the ideal method for watching patients swallow every dose of their tablets for at least 6 months; DOT was considered disrespectful of patients, since some refused DOT because of stigmatization.[11-13] Consequently, to solve the problem of medication non-adherence and increase treatment success, more effective strategies are needed for implementation among Thai persons newly diagnosed with PTB that are sputum smear-positive.

Several systematic reviews have indicated that there are many interventions that have been used significantly to improve TB MA and clinical outcomes.[13-16] However, multi-component intervention approaches are more effective in enhancing long-term MA among chronically-ill patients, including patients newly diagnosed with PTB.[16-18] Moreover, prior studies focusing on persons with PTB had limitations in that: the combined interventions were not developed based on a health behavior theory to justify the intervention approach or explain how the intervention did or did not improve MA and treatment outcomes[19-20]; used aquasi-experimental design;[19-22] did not follow-up the MA throughout the full course of treatment; nor compare treatment outcomes at the end of treatment.[21-22] Therefore, rigorous evidence supporting the effectiveness of a combined intervention based on health behavior theory with long-term MA and treatment outcomes among Thai persons newly diagnosed with PTB is needed to fill the gap.

Review of Literature

WHO estimated that in 2013 there were 9.0 million people had developed TB and 1.5 million died from the disease.[9] Approximately 50% of all new TB cases had sputum-smear positive PTB which was the major source of infection.[1] In 2012, WHO estimated that globally there were 2.5 million new PTB-sputum smear-positive cases (36 per 100,000 population) and 30,998 of these (46 per 100,000 population) were Thai cases.[1]

The aims of anti-TB drug treatment include curing for persons with TB, preventing death from active TB or its late effects, preventing TB relapse or recurrent disease, preventing the development of drug resistance, and decreasing TB transmission.[3]

Adherence to TB treatment is a complex and dynamic phenomenon with a wide range of factors, both patient-related and outside factors impacting medication-taking behavior.[23-25] The cognitive function is a patient-related factor, which can improve and predict accurate MA.[23,25] Therefore, incorporating the appropriate outside factors in enhancing or facilitating cognitive function and improving the cognitive process of persons with PTB is needed for enhancing TB MA behavior.

Social cognitive theory (SCT)[26] is a health behavior theory suggested for driving interventions for increasing long-term adherence to medication or prescribed practice.[27-28] Within SCT, behavior is depicted as dynamic, depending on aspects of both the environment and the person, which influence each other simultaneously. Although prior rigorous evidence has shown that combined interventions based on SCT[26] improved MA and clinical outcomes among chronically-ill patients,[29-30] the interventions for persons with PTB require more comprehensive strategy than others because PTB is a communicable disease, requires long-term treatment, and involves numerous factors.

The self-efficacy and self-regulation concepts of SCT[26] were used as the study framework. Self-regulation is the continuous process of self-generated thoughts, feelings, and actions. Self-efficacy operates during all phases of self-regulation: goal setting, self-monitoring, and self-reflecting. Therefore, self-efficacy promotes self-regulation capability for enhancing TB MA throughout the full course of treatment. The conjunction of self efficacy and self-regulation with the Medication Adherence Enhancement Program (MAEP), the intervention, was designed to increase self-efficacy for self-regulation to adhere medication. The strategies to promote a person's self-efficacy to perform specific actions include providing knowledge, promoting mastery, using a role model, verbal persuasion, and physiological and emotional arousal, as well as encouraging individuals to set goals, monitor themselves, reflect, and to have incentives. Along with this component, the participants were provided with appropriate environmental components to facilitate behavioral changes. We assumed that the continuous processes of raising self-efficacy in adhering to medication would directly improve the persons' cognitive function and encourage them to tailor the problem-solving strategies appropriately to their needs. In addition, participants would obtain confidence in engaging in self-regulation along the course of the TB treatment and then sustain their MA behavior and receive the full course of treatment.

The researchers expected that the MAEP would enhance a person's belief in his or her ability to perform specific tasks to adhere to TB medication throughout the full course of treatment, and consequently, improve treatment success. Therefore, the following research hypothesis was posed: persons newly diagnosed with PTB receiving the MAEP added in the usual care would have higher MA and treatment success than those receiving only usual care.

Method

Design: A randomized controlled trial (RCT), two-group post-test only design with the double-blind technique was used.

Ethical Considerations: Study approval was obtained from the Research Ethics Committee of the Faculty of Nursing, Chiang Mai University, and the ethics committee of the hospital used as a study site. All potential participants received written and verbal explanations about: the nature of the study; voluntary participation; what study involvement would entail; anonymity and confidentiality issues; and, the right to withdraw from the study at any time without consequences. Individuals agreeing to participate were asked to sign a consent form.

Study population and sample: The target population consisted of adults newly diagnosed with PTB who were registered and had visited for follow-up care at a TB hospital clinic in northern Thailand.

Inclusion criteria included: being 20-59 years of age; having been shown to have sputum smear-positive for PTB; never having taken anti-tuberculosis drugs previously; willing to start a SCC of a PTB drug regimen; being alert, oriented, and cooperative in the Program; able to communicate in Thai; being willing to participate and give permission to the researcher to visit their homes and contact them by telephone; have a family member that will support them during the Program session; and living within 50 kilometers of the hospital. The inclusion criteria for the participants' supporter in the MAEP included: being a family member and chosen by the participants; being responsible for supporting participants to take medication and tackle problems involving MA; being willing to participate in the study; and able to communicate in Thai.

The sample size was determined by the difference of two means[31] with a significance level of 0.05, a power of 0.80, and an effect size of .80.[32] The number of participants, including an extra number to compensate for the attrition rate of 12%,[33] was 58. Participants meeting the inclusion criteria were recruited by randomization, allocating the 29 participants to the intervention and control groups. Twenty five in the intervention and control groups completed all aspects of the study (86%). The dropout rate was7% in each group due to changes in the drug regimen because of severe TB drug side-effects (n=3) and the severe condition of the participant's co-morbidity (n=1); because participants did not complete the intervention sessions (n=2); or died (n=2) (see **Figure 1**).

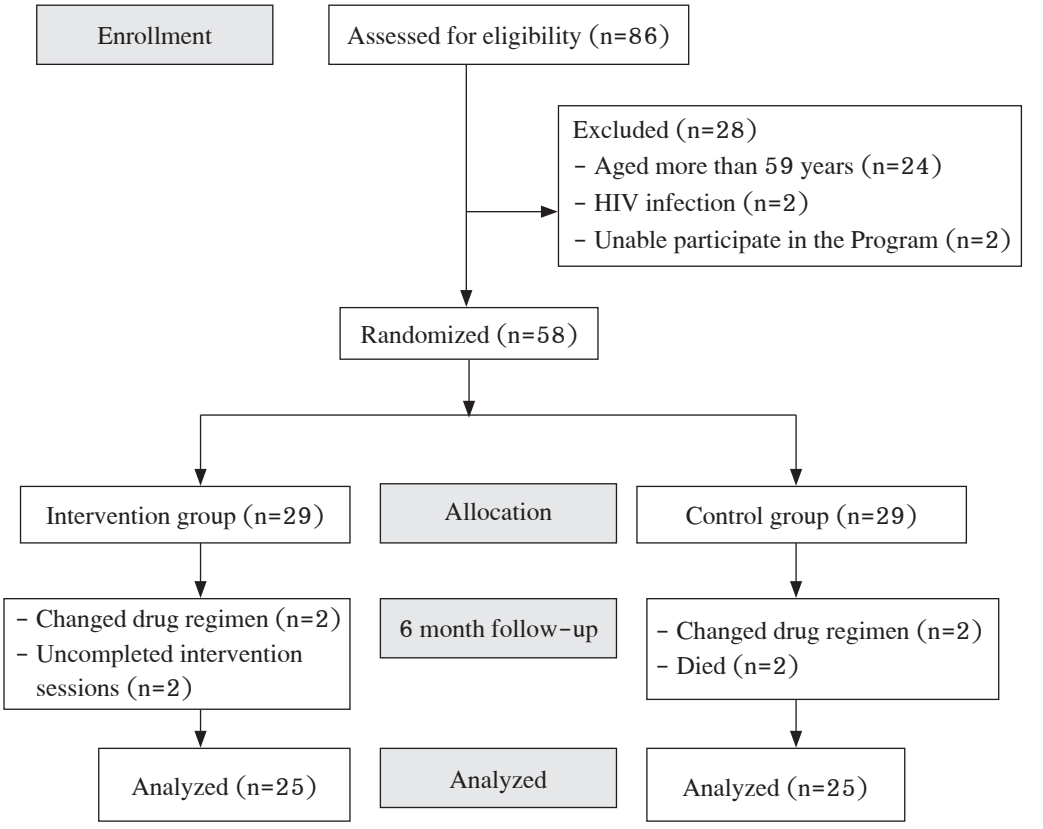

Figure 1 The participant recruitment procedures

Blinding: The double-blind technique was used to conceal the assignment results from the research assistant, who was trained for collecting MA data, and participants were not informed about assignation to either the intervention or control group.

Instruments: There were four instruments:

The Demographic and Clinical Data Collection Form, and the PTB-related Data Collection Form, developed by the principal investigator (PI), were adapted from an existing instrument,[8] collecting information on participant age, gender, occupation, monthly income, marital status, education level, co-morbidity, history of smoking, alcohol consumption, drug allergy, symptoms and signs of PTB, the results of the sputum examination, medicines being taken, TB drug side-effects, home visits by other health care workers, family supporter, and treatment outcomes.

The Anti-TB MA Scale (ATBMAS) also developed by the PI and was used for measuring the extent to which the participants' behaviors coincided with their prescribed TB medication regimen in the past month. The Scale was divided into 2 levels with the scores of 0 and 1 (1 = yes, and 0 = no). Examples of items are: "You take the right amount of anti-TB medicine every time" and "You take anti-TB medicine once a day." The ATBMAS had 5 items and possible scores ranged from 0-5. A total score was used to measure the level of MA of the participants. A higher score meant higher adherence, whereas a lower score meant lower adherence. Prior to using this instrument, five experts (one nursing instructor, one behavioral instructor, one nurse that works at the TB clinic, one TB control supervision nurse, and one physician who was an expert in PTB and behavioral change) assessed and approved the instrument's content validity (content validity index = 1). The pre-test reliability for the instrument was tested with 15 persons with PTB who met the eligibility criteria and calculated using Kuder-Richardson 20 method (KR-20), was .76 whereas the reliability of the instrument in the main study was .85. It took an average of 3 minutes for each participant to complete the instrument. Prior to using the ATBMAS, the research assistant was trained by the researcher, and the inter-rater reliability was found to be 1.

The Criteria to Identify TB Treatment Outcomes of WHO[3] was used for evaluating treatment success by a physician at the end of the treatment. Treatment success was considered to be the sum percentage of "cure" and "treatment completed." "Cure" was defined as follows: if a patient whose sputum smear or culture was positive at the beginning of the treatment but became negative in the last month of treatment and on at least one previous occasion. "Treatment completed" was defined as when a patient had completed treatment but did not have a negative sputum smear or culture result in the last month of treatment or on at least one previous occasion.

Intervention: The MAEP was developed by the PI based on self-efficacy and self-regulation concepts of SCT.[26] The Program included two components: the first component provided activities for enhancing self-efficacy for self-regulation to adhere to TB medication, and the second components provided environmental supports consisted of a choice of family supporter and telephone reminder and counselling. The Program was an individualized intervention and implemented in the first two months of TB treatment. The Program duration was 8 weeks, and included 7 sessions: 5 for providing knowledge and raising self-efficacy for self-regulation to adhere to TB medication, and 2 for telephone reminding and counselling. Program was content validated by the five experts who assessed and approved the ATBMAS's content validity. The details of the MAEP are presented in **Table 1**.

Table 1. The Schedule of MAEP

Session/Session lasted/Place	Persons involved in the session	Objectives	Activities	Instruments involved in the session
Session 1 (Week 0: after participant registration)/ 45 minutes/ TB clinic	Participant and family supporter	1. To establish relationship and provide overview information on the MAEP 2. To increase participant's and family supporter's knowledge and change negative attitude, perceptions or beliefs 3. To raise self-efficacy of the participant for setting goals and recording medication taking	1. Introduce self, obtain name of participant and family supporter 2. Provide knowledge about PTB and its treatment, the importance of family supporter, the practice guidelines along the course of TB treatment, TB drug adverse effects and how to manage them 3. Provide specific manuals to participant and family supporter 4. Explain and discuss, with demonstration and return-demonstration on how to manage medication for each dose, and how to set goals and record medication taking 5. Give the Training and Recording Forms for Self-Regulation to Adhere to Medication to the participant 6. Assign participant homework to record medication taking for one week 7. Suggest the participant contact the researcher by telephone if he/she faces some problems that cannot be solved by him or herself	1. A 30 minute video, "PTB and MA": first session focused on PTB and its treatment (8 minutes) and second session focused on guideline for patients to practice along course of TB treatment (14 minutes) 2. Patient's manual 3. Supporter's manual 4. The Training and Recording Forms for Self-Regulation to Adhere to Medication (TRF for SRAM)
Session 1/ 20 minutes/ TB clinic or participant's home	Family supporter	1. To increase family supporter's knowledge in supporter role 2. To raise family supporter's ability to assist and encourage the participant	1. Explain and discuss how to assist the participant for self-regulation to adhere to TB medication 2. Demonstration and return-demonstration on how to use verbal persuasion, and physiological and emotion arousal for encouraging the participant to self-regulate and adhere to TB medication 3. Demonstration and return-demonstration on how to assist the participant to use the TRF for SRAM	1. Supporter's manual 2. The TRF for SRAM
Session 2 (Week 1)/ 45 minutes/ participant's home	Participant and family supporter	1. To review and provide knowledge component 2. To review homework and progress made on recording medication taking	1. Review knowledge in the past session and provide knowledge about medication adherence and self-efficacy for self-regulation to adhere to TB medication	1. A 30 minute video, "PTB and MA": third session focused on MA and the causes of non-

Table 1. The Schedule of MAEP (continued)

Session/Session lasted/Place	Persons involved in the session	Objectives	Activities	Instruments involved in the session
		3. To raise self-efficacy of the participant for self- regulation to adhere to TB medication	2. Review homework assignment and reinforce progress made 3. Conduct scenario discussion, and discussion of the participant's experiences and provide feedback based on tailored problem-solving, and use verbal persuasion and physiological and emotional arousal to encourage the participant to be active in solving the problems and using self-regulation processes to adhere to TB medication 4. Demonstration and return-demonstration of goal-setting, self-monitoring and self-reflecting techniques 5. Set mutual goals and assign participant homework to observe and record medication taking, signs and symptoms, and feelings for three weeks 6. Assign participant homework to compare his or her behaviors during three weeks with target goals and give him/herself incentive if the behavior meets the target goals 7. Encourage the family supporter to continue supporting and encouraging the participant to use self-regulation processes to adhere to TB medication	adherence to TB medication and how to manage (8 minutes) 2. Two scenarios 3. The TRF for SRAM
Session 3 (Week 3: a few days prior to the participant's appointment) / 5-15 minutes/ Available	Participant	1. To remind the participant of the upcoming appointment or provide telephone counselling 2. To raise self- efficacy for self-regulation to adhere to TB medication	1. Provide a telephone call for reminding the participant of the pending appointment or counselling 2. Conduct counseling session consisting of tailored education messages based upon initial interview and subsequent assessment, discussion of the participant's experiences and provide feedback, and use verbal persuasion, and physiological and emotional arousal to encourage the participant to actively solve problems and use self-regulation processes to adhere to TB medication	-

Table 1. The Schedule of MAEP (continued)

Session/Session lasted/Place	Persons involved in the session	Objectives	Activities	Instruments involved in the session
Session 4 (Week 4)/30 minutes/ TB clinic	Participant and/or family supporter	1. To review and provide knowledge component 2. To review homework and progress made on recording medication taking, signs and symptoms, and feelings as well as self-evaluation and self-incentive 3. To raise self-efficacy of the participant for self-regulation to adhere to TB medication 4. To evaluate the self-efficacy of the participant for self-regulation to adhere to TB medication	1. Review knowledge in the past session and provide knowledge about how to raise self-efficacy for self-regulation to adhere to TB medication 2. Review homework assignment and reinforce progress made 3. Conduct a discussion of the participant's experiences and provide feedback based on tailored problem-solving, and use verbal persuasion, and physiological and emotional arousal to encourage the participant to actively solve problems and use self-regulation processes to adhere to TB medication 4. Ask the participant to demonstrate goal-setting and assign him/her homework to observe and record medication taking, signs and symptoms, and feelings for two weeks 5. Assign participant homework to compare his or her behaviors during two weeks with target goals and give him/herself incentive if the behavior meets the target goals 6. Measure the participant's level of self-efficacy for self-regulation to adhere to TB medication and discuss how to improve or sustain the level	1. The TRF for SRAM 2. The Self-Efficacy for Self-Regulation of Medication Adherence Scale (SE for SRMAS)
Session 5 (Week 6)/30 minutes/ participant's home	Participant and family supporter	Same as the objective numbers 2-4 in session 4	Same as the activity numbers 2-6 in session 4	1. The TRF for SRAM 2. The SE for SRMAS
Session 6 (Week 7: a few days prior to the participant's appointment)/ 5-15 minutes/ Available	Participant	Same as all objectives in session 3	Same as all activities in session 3	-

Table 1. The Schedule of MAEP (continued)

Session/Session lasted/Place	Persons involved in the session	Objectives	Activities	Instruments involved in the session
Session 7 (Week 8) / 45 minutes / TB clinic	Participant, modeling, and/or family supporter	1. To review homework and progress made on recording medication taking, signs and symptoms, and feelings as well as self-evaluation and self-incentive 2. To raise self-efficacy of the participant for self-regulation to adhere to TB medication. 3. To evaluate the progress of self-efficacy of the participant for self-regulation to adhere to TB medication 4. To provide the knowledge component and close the program	1. Review homework assignment and reinforce progress made 2. Discuss modeling and participant's experiences and provide feedback and use verbal persuasion and physiological and emotional arousal to encourage the participant to actively solve problems and use self-regulation processes to adhere to TB medication 3. Encourage modeling and the participant and/or family supporter to participate in the discussion and share their experiences 4. Ask the participant to use or adapt self-regulation processes to adhere to TB medication throughout the full course of treatment 5. Measure the participant's level of self-efficacy for self-regulation to adhere to TB medication and discuss how to improve or sustain the level 6. Provide knowledge for maintaining healthy status and close the program	1. The TRF for SRAM 2. The SE for SRMAS

Usual care: The control and intervention groups received routine care, which included health education about PTB, TB medication, and the side effects and prevention of TB transmission. When the participants follow-up visited the TB clinic, they were asked about any problems they had taking the medication and were given advice to solve their problems. They were also provided with home visits, late patient tracers, and fixed-dose combinations drugs or medication packaging. The added usual care from the Global Fund Project[34] during the study time period was money incentive; a participant received 1,200 baht (33.75 USD) in cash at the end four, five, or six months of treatment.

Data collection: The demographic, clinical, and PTB-related data of the participants were collected by the PI at baseline. At 3 and 6 months after entering the Program, MA was measured by the research assistant. Additionally, at the end of treatment (6 months after entering the Program), a doctor at the TB clinic evaluated the treatment outcomes for each participant.

Data analysis: Descriptive statistics were used to analyze the demographic, clinical, and PTB-related data. Chi-square and Fisher's exact test were used to examine the difference in the characteristics of the participants between groups at baseline. The Mann-Whitney U test was performed to examine the differences in the MA score

of the participants between groups, because the MA score of the participants did not distribute normally. Finally, Fisher's exact test was used to examine the differences in the treatment success rate of the participants between the intervention and control groups.

Results

No statistical differences were found between the intervention and control groups, regarding the demographic, clinical, and PTB-related data of the participants (see Table 2).

Table 2 Demographic, Clinical, and PTB-related Data of the Participants in the Control and Intervention Groups

Characteristics	Control group (n = 25)		Intervention group (n = 25)		χ^2	p-value/ Fisher's exact
	n	%	n	%		
Age (year)						
20-40	13	52.0	12	48.0	.080	.777
41-59	12	48.0	13	52.0		
Median (Range)	40(21-58)		42(23-54)			
Gender						
Male	17	68.0	17	68.0	.000	1.000
Female	8	32.0	8	32.0		
Marital status						
Married	12	48.0	19	76.0		.131
Single	8	32.0	3	12.0		
Divorced/separated	5	20.0	3	12.0		
Educational level						
Primary school	13	52.0	14	56.0	5.310	.070
Secondary school	3	12.0	8	32.0		
College/university	9	36.0	3	12.0		
Occupation						
Employee	17	68.0	17	68.0		.491
Merchant	5	20.0	3	12.0		
Farmer	1	4.0	1	4.0		
Student	2	8.0	1	4.0		
Ownbusiness	0	0.0	3	12.0		
Monthly income (baht)						
≤5,000	5	20.0	5	20.0	2.210	.530
5,001-7,500	4	16.0	8	32.0		
7,501-10,000	9	36.0	8	32.0		
>10,000	7	28.0	4	16.0		
Median (Range)	9,000 (1,000-50,000)		7,500 (2,000-30,000)			

Table 2 Demographic, Clinical, and PTB-related Data of the Participants in the Control and Intervention Groups (Continued)

Characteristics	Control group (n = 25)		Intervention group (n = 25)		χ^2	p-value/ Fisher's exact
	n	%	n	%		
Alcohol-consumption						
Never consumed	6	24.0	6	24.0	2.171	.338
Consumed in the past	3	12.0	7	28.0		
Currently consumed	16	64.0	12	48.0		
Smoking						
Never smoked	6	24.0	9	36.0		.305
Smoked in the past	6	24.0	2	8.0		
Currently smoked	13	52.0	14	56.0		
Co-morbidity						
Yes	9	36.0	5	20.0	1.587	.208
Hypertension	3	12.0	1	4.0		
Diabetes mellitus	3	12.0	1	4.0		
Cirrhosis	0	0.0	1	4.0		
Allergy	1	4.0	1	4.0		
Hyperthyroid	1	4.0	0	0.0		
CHF*	0	0.0	1	4.0		
COPD**	1	4.0	0	0.0		
No	16	64.0	20	80.0		
Symptoms and signs of PTB***						
Cough	25	100.0	25	100.0		-
Weight loss	20	80.0	23	92.0		.417
Fever	13	52.0	17	68.0	1.333	.248
Retrosternal pain	15	60.0	12	48.0	.725	.395
Tired	18	72.0	13	52.0	2.122	.145
Hemoptysis	4	8.0	6	24.0	.500	.480
Sputum examination**** result at baseline						
1+	8	32.0	7	28.0	1.540	.463
2+	6	24.0	10	40.0		
3+	11	44.0	8	32.0		

Note. *= Congestive heart failure
**= Chronic obstructive pulmonary disease
***= Some patients had more than one item of symptoms and signs of PTB
****= The result of one specimen contained the highest number of AFB bacilli

Table 2 Demographic, Clinical, and PTB-related Data of the Participants in the Control and Intervention Groups (Continued)

Characteristics	Control group (n = 25)		Intervention group (n = 25)		χ^2	p-value/ Fisher's exact
	n	%	n	%		
Number of medicine tablets in intensive phase						
3-4	18	72.0	18	72.0	.000	1.000
8-11	7	28.0	7	28.0		
Number of medicine tablets in continuous phase						
2-3	12	48.0	8	32.0	1.333	.248
4-5	13	52.0	17	68.0		
TB drug side-effects*						
Yes	16	64.0	21	84.0	2.599	.107
Skin itching without rash	4	16.0	8	32.0	1.754	.185
Muscle/joint pain	6	24.0	5	20.0	.117	.733
Skin itching with rash	4	16.0	5	20.0		1.000
Nausea/vomiting	2	8.0	6	24.0		.247
Peripheral neuropathy	2	8.0	2	8.0		1.000
Abdominal pain	1	4.0	1	4.0		1.000
Others**	3	12.0	6	24.0		.463
No	9	36.0	4	16.0		
Family supporter						
Spouse	12	48.0	13	52.0		.171
Son/daughter	3	12.0	1	4.0		
Sister/brother	3	12.0	0	0.0		
Cousin	2	8.0	1	4.0		
Mather/father	3	12.0	9	36.0		
Girlfriend/boyfriend	1	4.0	0	0.0		
Nephew/niece	1	4.0	1	4.0		

Note. *= Some patients had more than one item of TB drug side-effects
**=Such as headache, anorexia, influenza- like syndrome, insomnia

As noted in Table 3, at 3 months after entering the Program, the MA of the participants in the intervention groups was significantly higher than that in the control group, whereas at 6 months after entering the program, the MA of the participants in the intervention group was higher than that in the control group but not significantly different.

Table 3 Comparison of Medication Adherence of the Participants between the Intervention and Control Groups

Medication adherence	Control group (n=25)	Intervention group (n=25)	Z	p-value
	Median (Mean±SD)	Median (Mean±SD)		
At 3rd month after entering the program	4(3.92±1.11)	5(4.84±.47)	-3.552	.000
At 6th month after entering the program	5(4.12±1.58)	5(4.80±.50)	-1.518	.129

As shown in Table 4, there was no significant difference in treatment success between the control and intervention groups at the end of treatment. However, the treatment success in the intervention group (100%) was greater than the control group (96%).

Table 4 Comparison of Treatment Success of the Participants at the End of Treatment between the Intervention and Control Groups

Treatment success	Control group (n = 25)		Intervention group (n = 25)		Fisher's exact
	n	%	n	%	
Treatment success	24	96.0	25	100.0	1.000
Cure	20	80.0	23	92.0	.417
Treatment completed	4	16.0	2	8.0	.667
Treatment failure	1	4.0	0	0.0	

Discussion:

The results from this study revealed that the MAEP was effective in increasing MA at 3 months after entering the Program, but was unsuccessful in increasing MA and treatment success at 6 months after entering the Program. The increase of the MA score in the intervention group might have stemmed from the activities to enhance self-efficacy for self-regulation of TB MA and the environmental support provided by a family supporter and the telephone reminder and counseling in the MAEP.

The mechanisms underlying the improvement of MA in this study could have been due to the increased self-efficacy for self-regulation of MA in the Program. Effective self-regulation depends on feeling self-efficacious in using one's skills to achieve mastery.[26, 35] Self-efficacy operates during all three phases of self-regulation; the forethought, performance, and self-reflection phases.[36] Skillful self-regulators enter learning situations with specific goals and a strong sense of self-efficacy for attaining them. As they work on tasks, they monitor their performance and compare their attainment with their goals to determine progress. Self-perceptions of improvement enhance self-efficacy, motivation, and continued use of effective strategies.[37] During periods of self-reflection, their improvement was evaluated by themselves and they decided to adapt self-regulatory processes if necessary. Modifying goals or setting new ones was considered for the next step.[36-37] High self-efficacy in engaging in activities during the forethought phase becomes realized as self-efficacy for continued progress during the performance phase and self-efficacy for achievement in the self-reflection phase. These continuous processes, especially the self-monitoring activities, can improve cognitive function,[38] which is the most important factor predicting TB MA,[23,25] and encourage the participants themselves to actively solve problems in order to manage the numerous factors influencing TB MA.

The sources for raising self-efficacy in this study included mastery experience, modeling, verbal persuasion, and physiological and emotional arousal.[26, 35] The appropriate multi-session and effective educational strategies in the Program might have helped the participants to actually perform their goal behaviors and promoted their mastery experience so that they were able to attain high confidence in self-regulating for TB MA. The results of this study confirms the facts mentioned, that in order to perform a particular behavior, the person must know both what the behavior is and how to perform it, and such skill must be nurtured.[26]

The scenarios of the Program mentioned the problem-solving experiences of role models combined with the sessions for sharing the participant's perception of barriers with successful patient and discussed how to eliminate the barriers, were conducted in order to tailor the problem-solving strategies to the participants' needs. These activities might promote vicarious experiences for the participants to attain high confidence in regulating themselves for TB MA. The early individual approach with good relationships might assist a participant and his or her family supporter in feeling more comfortable responding to the PI's concerns, admitting the problems they were having, and even asking for help. The continuous processes of discussion and provide feedback based on good relationships and participant centeredness and problem-solving might promote the participant's adherence behavior through strongly positive verbal persuasion and physiological and emotional arousal.

The choice of family supporter, the telephone reminder and counselling, and having an available telephone contact with the PI during the Program were used to facilitate the participants' behavior changes for adhering to TB medication. These supports acted as environmental components that affected the participant's behavior.[26] It is easier for the participants to change their behaviors if they perceive the availability of environmental support during the behavior change processes and maintenance, then help to increase long-term success.[39] Choosing family supporter is a convenient and accessible strategy for participants and helps to decrease the problems of disrespect and stigmatization of TB.[7, 16] These methods might have helped the participants in the Program realize that they could get assistance when needed and feel more confidence in self-regulating for TB MA.

The results also showed that at 6 months after entering the Program, the MA of the participants in the intervention group was higher than that in the control group, but they were not significantly different (see Table 3). The added usual care interventions, which included money incentive and late patient tracers provided to the participants in both groups after entering the program for three months, might have affected the findings. According to the Global Fund Project,[34] during the study time period, the participants received 1,200 baht in cash at the end of four, five, or six months of treatment. In addition, the participants who did not return to the clinic for their appointments would be contacted by a nurse at the TB clinic on the appointment day by telephone and encouraged to visit the TB clinic on that day or another day. If this strategy failed, on the first day or as early as possible after missing the appointment, the community health care workers and/or volunteer community members would visit the participants' home to find out why they did not attended the clinic for treatment. Other methods were implemented if the participants subsequently failed to attend, including providing the participants with frequent home visits and taking the TB drugs to the participants' home. Most of the home visits in this study occurred after the participants had been in the Program for three months and that might be why they had missed the appointment; that is, because of the disappearance of the PTB symptoms.

These activities might confound the effect of the planned interventions at that time and motivated

or helped the participants in the both groups to get higher MA scores, even though the participants in the control group missed more clinical appointments (36%) than those in the intervention group (8%). Moreover, there was no significant difference in MA at 3 months compared to 6 months after entering the program in both groups. The findings from this study was not consistent with the evidence from the previous studies, which showed that adherence to most medical regimens was inversely proportional to the length of therapy with the symptoms disappearance.[17] The sustainable high score of MA in the intervention group (see Table 3) might have been affected by the MAEP or these confounding factors. However, money incentive and late patient tracers interventions require constantly budget and staff for implementation whereas the MAEP tried to enhance the participants to self-directed control and sustain their behaviors by themselves in the long-term.

The final results of this study indicated that the treatment success in the intervention group was not significantly higher than that in the control group (see Table 4). However, the treatment success rates in the intervention and control groups were higher than the target rate (85%) set by WHO.[9] The treatment success rates might have been affected by the high level of MA at 6 months after entering the Program in both groups.

In addition, the attrition of two participants from the control group might have potentially biased the results. These participants died before being evaluated for MA at 3 months after entering the Program, and were excluded from the study. This situation was a negative outcome of the TB treatment and had an effect on the proportion of treatment success and all treatment outcomes. Considering the details of the medication interruption in the both groups, there was a few cases experienced treatment interruption for a short time period, except for one participant in the control group, who had treatment failure outcome. This situation might have been the reason for the high rate of treatment success in both groups. The findings are congruent with a study of Podewils et al.[40] which indicated that the patients that had longer interruptions with sporadic variability had a significantly increased risk of poor outcomes compared to the patients that had short and regular interruptions. In addition, three or more non-consecutive days of interruption, or two or more consecutive days of interruption during the intensive phase, might have caused a negative outcome[41] and drug omission of upwards of four days caused a significant reduction in the cure rate.[42]

Limitations

In terms of the study's limitations, first, the participants were all taken from one selected hospital located in northern Thailand, and applying the finding to persons newly diagnosed with PTB in other settings needed to be taken into consideration. Second, it is likely that MA and treatment success were influenced by the confounding factors of the added usual care interventions, which included the money incentive and late patient tracers implemented during the study period. These may have attenuated the effects of the MEAP on the research findings. Third, the death of two participants in the control group, who were then excluded from analysis, may have affected the proportion of treatment success and all treatment outcomes. The death of the participants may have been influenced by their low MA behavior. Finally, the instrument used to measure MA in this study was new tool developed by the PI and did not really test the psychometric properties. The items may not be highly sensitive to capture the outcomes.

Conclusions and Recommendations

The MAEP developed for this study was effective in increasing MA in the short-term and helped to improve treatment success. The Program

can be integrated into the regular services of TB clinics for persons newly diagnosed with PTB. The three continuous processes of self-regulation and four sources for raising self-efficacy for self-regulation should be implemented to help the persons change their behavior so that they adhere to medication and improve their clinical outcomes. Nurses or other health care workers working in primary care units should be encouraged to monitor and support the family supporter. The video presentation, scenarios, and the patient's manual utilized in this study should be used to educate persons with PTB in clinical practice.

The findings provide evidence for nursing science regarding behavioral change approaches and clinical outcome improvement. They should be added to the knowledge of enhancing MA strategies for persons newly diagnosed with PTB. Further studies are needed to control for the confounded factors and repeated to compare the long-term outcomes or other outcomes such as death rate or the cost-effectiveness of the MEAP. Finally, the instrument for measuring MA should be considered for testing psychometric properties.

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โปรแกรมการเพิ่มความร่วมมือในการรักษาด้วยยาสำหรับผู้ที่เป็นวัณโรคปอด:การวิจัยเชิงทดลอง

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บทคัดย่อ:ผลสำเร็จของการรักษาวัณโรค ขึ้นอยู่กับความร่วมมือในการรักษาด้วยยาตลอดการรักษา การศึกษาครั้งนี้มีวัตถุประสงค์เพื่อทดสอบผลของโปรแกรมการเพิ่มความร่วมมือในการรักษาด้วยยาต่อผลสำเร็จของการรักษา และความร่วมมือในการรักษาด้วยยาของผู้ที่เป็นวัณโรคปอด ที่เข้ารับการรักษา ณ โรงพยาบาลแห่งหนึ่งในเขตภาคเหนือของประเทศไทย ทำการสุ่มกลุ่มตัวอย่างที่มีคุณสมบัติตามที่กำหนด เข้ากลุ่มทดลอง 25 ราย และกลุ่มควบคุม 25 ราย กลุ่มทดลองได้รับการดูแลตามโปรแกรมการเพิ่มความร่วมมือในการรักษาด้วยยาที่สร้างขึ้นตามแนวคิดทฤษฎีการเรียนรู้ทางปัญญาสังคมร่วมกับการดูแลตามปกติ ส่วนกลุ่มควบคุมได้รับการดูแลตามปกติเท่านั้น โปรแกรมใช้เวลาดำเนินการ 8 สัปดาห์ ประกอบด้วยกิจกรรม 7 ครั้ง เพื่อให้ความรู้ และจัดกิจกรรมเพิ่มสมรรถนะแห่งตนเพื่อกำกับตนเองในการให้ความร่วมมือในการรักษาด้วยยา 5 ครั้ง และเพื่อเตือนและให้คำปรึกษาทางโทรศัพท์ 2 ครั้ง เก็บรวบรวมข้อมูลโดยใช้แบบวัดการให้ความร่วมมือในการรักษาด้วยยา ประเมินความร่วมมือในการรักษาด้วยยา และใช้เกณฑ์การจำแนกผลการรักษาวัณโรคขององค์การอนามัยโลก ประเมินผลสำเร็จของการรักษา วิเคราะห์ข้อมูลโดยใช้สถิติทดสอบฟิชเชอร์และแมนวิทนีย์ ยู

ผลการวิจัยพบว่า กลุ่มทดลองมีค่าเฉลี่ยการให้ความร่วมมือในการรักษาด้วยยา หลังเข้าร่วมโปรแกรม 3 เดือนสูงกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ อย่างไรก็ตามหลังเข้าร่วมโปรแกรม 6 เดือน ค่าเฉลี่ยการให้ความร่วมมือในการรักษาด้วยยาและผลสำเร็จของการรักษาของกลุ่มทดลองสูงกว่ากลุ่มควบคุม แต่ไม่มีนัยสำคัญทางสถิติ ดังนั้นพยาบาลสามารถนำโปรแกรมนี้ไปใช้กับผู้ที่เป็นวัณโรคปอด เพื่อเพิ่มความร่วมมือในการรักษาด้วยยาในระยะสั้นเพื่อเพิ่มผลสำเร็จของการรักษา

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คำสำคัญ: ความร่วมมือในการรักษาด้วยยา วัณโรคปอด สมรรถนะแห่งตน การกำกับตนเอง ผลสำเร็จของการรักษา

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