CHAPTER I

INTRODUCTION

1.1 Rationale and Justification

Tuberculosis (TB) is an infectious disease caused by a microorganism, Mycobacterium tuberculosis, discovered by Robert Kock in 1882. The microorganism usually enters the body by inhalation through the lungs. They spread from the initial location in the lungs to other parts of the body via the blood stream, the lymphatic system, via the airways or by direct extension to other organs. Tuberculosis, clinically, can be mainly divided into two types: 1) Pulmonary tuberculosis is the most common form of the disease, occurring in over 80% of cases, it is the only form of tuberculosis, which may be infectious and 2) Extra-pulmonary tuberculosis is the tuberculosis affecting organs other than the lungs, most commonly pleura, lymph nodes, spine, joints, genitourinary tract nervous system or abdomen. TB may affect any part of the body (TB-A Global Emergency, 1994).

1.1.1 Global tuberculosis situation

Tuberculosis is one of the major public health problems worldwide, especially in the developing countries. While about one-third of the global population is infected with tuberculosis, there are approximately 8 million new cases with 1-2 million deaths each year. Most importantly, however, 95% of TB cases and 98% of TB deaths are in developing countries. Nearly 75% of TB cases are in the economically most productive age group (15-59 years). Moreover, TB is showing an increasing trend due to poverty, rapid population growth, increasing migration, poor health infrastructure, increasing multi-drug resistance and TB/HIV dual infection. In 1993, WHO declared TB as a global emergency. To respond to this emergency,

WHO adopted and promoted a new strategy and framework for effective TB control. DOTS is the name of the WHO recommended TB control programme to be implemented within the framework of National tuberculosis control program. The World Bank considers DOTS as one of the most cost-effective of all health care interventions. It has also recommended that effective TB treatment should be a part of the essential clinical services package available in primary health care (WHO,1998).

The internationally recommended DOTS strategy is an inexpensive strategy that could prevent millions of TB cases and deaths over the coming decade. The DOTS strategy for TB control consists of five key elements: 1) Government commitment to sustained TB control, 2) Detection of TB cases through sputum smear microscopy among people with symptoms, 3) Regular and uninterrupted supply of high-quality anti-TB drugs; 4) 6-8 months of regularly supervised treatment (including direct observation of drug-taking for at least the first two months), 5) Reporting systems to monitor treatment progress and programme performance (WHO n.d.).

The global target for TB control is to cure at least 85% of new smear positive cases and detect at least 70% of such cases. DOTS is the only strategy which has achieved these results on a program basis (WHO n. d.).

The DOTS strategy emphasizes completion of treatment and thereby cure of the patient. By doing so, it stops TB at the source, and prevents the spread of the disease, the development of MDR-TB, and complications of TB, relapse and death.

Therefore, DOTS strategy can 1) Produce cure rates of up to 95% even in the poorest countries. 2) Prevent new infections by curing infectious patients. 3) Prevent the development of drug resistance by ensuring that the full course of

treatment is followed. 4) And a six-month supply of drugs for treatment under the DOTS strategy costs as little as US$ 10 per patient in some parts of the world.(WHO, 2004 and WHO n. d.). That's why DOTS strategy is believed to be the most cost –effective intervention for controlling the current TB epidemics as mentioned by the World Bank (WHO, n. d.).

Globally 180 countries have already begun implementation. All countries in the South-East Asia Region have introduced the DOTS strategy and have achieved high cure rates in areas where this strategy has implemented. Even in countries with severe resource constraints, DOTS has been successfully implemented. For example, in Thailand, the DOTS strategy was started in 1996,and implemented in 8 pilot districts of the North-East region. Based on these experiences, DOTS was gradually expanded into the whole country by the end of 2002(WHO, 2003).

1.1. 2 Tuberculosis and DOTS Program in Thailand

According to the WHO report in 2003, Thailand reported 137 all forms of TB patients among 100,000 population (86,000 all form of TB cases, 38,000 smear positive TB cases and13,000 death of TB). These statistics put Thailand as one of those 22 TB high burden countries in the world (WHO, 2003).

The situation in Bangkok is far worse than other areas of Thailand.

For instance, in 2002, the estimated number of all forms of TB patients per 100,000 population in Bangkok is 189. It can, therefore, be estimated that Bangkok has 15,000 all forms of TB cases and 7,000 sputum smear positive cases (WHO, 2003).

Even though DOTS has already covered 100 % of the Country, the quality of the program performance is not good. For instance, the mortality rates have increased because of the co-existing HIV/AIDS. Treatment success rate and default rate were reported 77 % and 8.9 %, respectively in 2002. With the comparison of global target (success rate more than 90% and default rate less than 4%), all these figures are quite worrisome (WHO, 2003).

1.1. 2.1 Achievements:

The DOTS program was implemented in 1996, and eventually covered the entire country by 2002. A high level of political commitment to DOTS implementation backed by a strong health infrastructure. This commitment also resulted in maintaining the TB control budget during the severe economic crisis in 1998. In view of the high rates of HIV infection in parts of the country, guidelines for counseling, treatment of latent infection with TB (TLIT), and intensive screening and monitoring of co-infected people in the high prevalence HIV/AIDS locations in northern Thailand have been established. These efforts are being pursued in harmony with HIV prevention program; although Multi-drug resistant-TB does not pose a significant threat at present, the National Tuberculosis Program has initiated steps to address potential MDR-TB in high HIV/AIDS settings (WHO, 1998).

1.1. 2. 2 Challenges

The overall success rate for the whole country in 2002 was 77%. The overall default rate was 8.9% in 2002 (WHO, 2003). A small number of provinces report high default rates; the transfer system in these areas needs to be strengthened; in other districts, high default rates indicate a weakness of the DOT System, several regions report extremely high death rates of up to more than 30%; continued high death rates currently seen in many provinces are attributed to the impact of HIV.

Urban TB control, especially in Bangkok is recognized as a key challenge, which has reported a low treatment success rate and a high default rate, 68.9 % and 21% in 2002, respectively, in comparison with overall success and default rates of 77% and 8.9% (WHO, 2003).

1.1.3 National tuberculosis control program, Thailand

TB is a major health problem in Thailand. There have been many efforts to control this disease from the government, but TB still remains as a major threat. The National TB Program (NTP) is functioning by extending its services to all 75 provinces of the country through the general health services. The goal of National TB control Program is to reduce the mortality, morbidity and transmission of TB to such a level that it is no longer a public health problem, in order to attain the goal, NTP has set objectives of achieving 85% cure rate and 90% success rate as recommended by WHO.

According to the country-specific estimation done by WHO (Corbett EL et al, Arch Int Med 2003; 163:1009), the estimated total incidence for Thailand was reported as 137 per 100,000 populations. Based on a population size of 63 million, the estimated annual numbers of cases and death are 38,000(sputum

smear-positive TB disease), 86,00 (total incidence of TB disease) and 13,000 (deaths from TB disease) (WHO, 2003).

The serious current tuberculosis situation in Thailand will be further aggravated by the HIV/Tuberculosis co-epidemic and the spread of drug resistance. The increase in the multi-drug resistant TB (MDR-TB), resulting from unsupervised drug regimens containing Rifampicin, has created the worsening of the TB situation in Thailand.

The HIV epidemic heightens the need to focus on the identification and successful treatment of infectious TB patients. Poor TB control programs often fail to cure even half of all detected infectious cases, but do succeed in keeping them alive longer and thus increasing TB transmission.

The emergence of drug resistant-TB is a serious concern for many developing countries like Thailand. According to the data provided by external review in 2002, the prevalence of multi-drug resistant TB is more than 4% among the TB patients in Thailand (WHO, 2003). The most important cause of multi drug resistance is due to patient's non-compliance to treatment. The DOTS strategy focuses on the cure of every TB case, good TB control which cure patients has proven successful in preventing drug resistant TB in many countries.

The present success of DOTS has been achieved in those provinces which have a high population density and easy access to health services. This is not typical of most of Thailand, and methods of supervising treatment in areas which recorded poor treatment outcome, have to be developed (WHO, 1995).

Various experiences in the different parts of the world have shown that it is not possible to achieve 85% cure rate of TB treatment without implementing DOTS (National Tuberculosis Center, 1997).

DOTS is a new strategy to treat the tuberculosis patient and get high compliance. Under DOTS a patient has to swallow the drugs in front of DOT observer in order to confirm that the drug has been taken properly. However there is no fixed criteria to implement DOTS and get high compliance of patient with treatment in different situations. DOTS is not easy. It requires a commitment from health worker, patients and the community. Direct observation of treatment is a way of providing the necessary support to the patient that will enable him to complete a full course of treatment, without such support cure rates will be low and TB control will not be achieved (Global Tuberculosis Control, 1999).

In order to ensure the directly observing treatment (DOTS), different types of DOT observers are involved in different countries and settings. For Thailand, the national guidelines outlined three alternative methods for DOTS as follows: 1) Health care workers (HCW) or TB clinic staff give the medicines to the patients at the health facility every day; 2) Village health volunteers (VHV) give the medicine to the patient daily and health centre staff supervise the VHVs on a weekly basis; and 3) Family members provide the medicines to the patients daily and health centre staff visit the patients at home once a week to verify the DOTS cards, check the balance of the drugs and also check for the color of urine (WHO, 2003).

However, there is a lot of discussions between researchers and people concerned on how those different DOT observers work and how much they

influence on program performance including treatment outcome and compliance.

In order to clarify all those issues, some studies have been conducted in different countries and regions. So far there has been no consolidated conclusion on different DOT observers, and the results differ from different researchers, regions and countries.

The main results of the past research are as follows.

The effect of different types of DOT observers on treatment outcome has differed from study to study.

A study done by Mathema showed that health personnel supervising DOTS resulted in higher treatment success rates than that of the community and family member supervising DOT, i.e. 91%, 57% and 57%, respectively (Mahema, 2001).

A study done in the Southern part of Thailand by Pungrassami showed that community supervised DOTS had a better result in treatment success rate than the health personnel and family member supervised DOTS, i.e. 89.7%, 87.1% and 85.3%, respectively. And cure rate was 77%, 86% and 75 % in health personnel, community volunteer and family member DOT observer, respectively, and default rate was higher(7%) in health personnel supervised group than other two groups(4% and 4%). But this difference was not statistically significant (Pungrassa. 2002).

A study done by Kamolratankul P. showed similar results in cure and success rates between health personnel, community volunteer and family member, i.e. cure rate-79%,74% and 77%, and success rate-88%, 79% and

84%, respectively. For default rate, community volunteer supervised group reported higher rate (15%) than health personnel-group (4%) and family member supervised group (6%) (Kamolratankul, 1999).

As for the impact of DOT on outcome of treatment, some studies showed that the practice of strict DOT during the first 2 months was not associated with sputum conversion and treatment success rates (Petchawn, 2002).

However, other studies proved that DOT definitely contributes to the improvement of the treatment outcome. A study conducted by Akkslip S. showed that the cure rate in DOT group was higher (85%) than that of non DOT group (71%) (Akkslip, 1999) and a study conducted in Thailand showed that cure , success and default rates in DOT group were better than that of non-DOT group, in overall, i.e. (76%:67%, 84%:76% and 7%:13%, respectively, each other), (Kamolratanakul, 1999). A study conducted by Pungrassami. P in Thailand also showed the similar result, i.e. cure, success and default rates in DOT group were 80%, 84% and 5%, respectively, compared with non-DOT group (71%, 82% and 9%, respectively) (Pungrassami, 2002).

After an extensive literature review, it can be assumed that there are a lot of other factors influencing treatment outcome. The factors include socioeconomic, demographic, patient oriented and health service oriented factors, particularly in those complex settings.

The purpose of this study is to determine the effect of different DOT observers on treatment outcome together with other confounding factors.

1.2. Hypothesis

The outcome of tuberculosis treatment differs with different types of DOT observers, and with DOT and non - DOT, after controlling/adjusting other potentially relevant factors such as socioeconomic, demographic and behavior factors, and disease condition of TB patients.

1.3. Research questions

■ What is the difference in outcome of treatment between different types of DOT observers among new smear positive pulmonary TB patients in Bangkok, Thailand, registered during the period of Oct. 2002 to September. 2004?.

■ How does the socioeconomic, demographic and behavioral factors, and disease condition of TB patients influence the treatment outcome among TB patients registered in Bangkok, Thailand during the period of Oct.2002 to Sept. 2004?.

1.4 Research Objectives

1. 4.1 General objective

To improve treatment outcome of Tuberculosis patients in Bangkok, Thailand.

1. 4. 2 Specific objectives

- To investigate the difference in treatment outcomes between different types of DOT observers among new smear pulmonary tuberculosis patients registered in Bangkok, Thailand during the period of Oct. 2002 to Sept. 2004.
- To determine the socioeconomic, demographic and behavioral factors, and disease condition of TB patients influencing on treatment outcomes among TB patients registered in Bangkok, Thailand during the period of Oct. 2002 to Sept. 2004.

1. 5 Conceptual Framework

Conceptual framework for relationship between different types of DOT observers and treatment outcome among new smear positive pulmonary Tuberculosis patients along with other confounding factors.

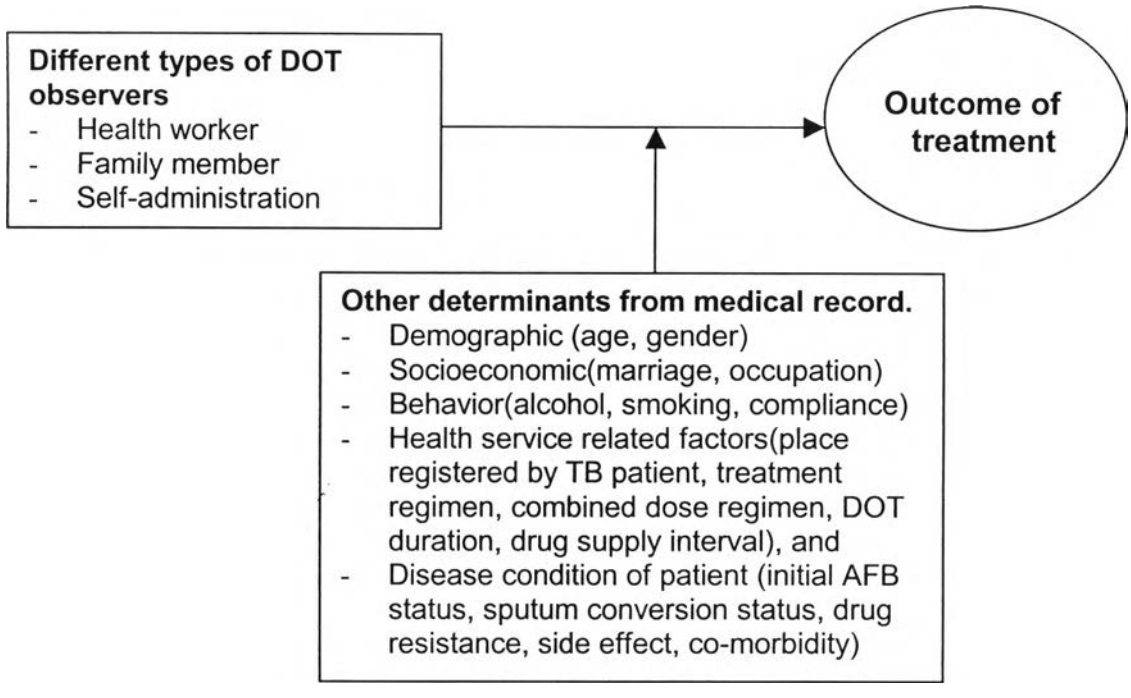

Figure 1: Conceptual framework

1. 6 Operational definitions

DOTS: DOTS is the internationally recommended strategy to ensure cure of tuberculosis. It is based on five key principles that are common to disease control strategies, relying on early diagnosis and cure of infectious cases to stop spread of tuberculosis. This specific strategy for TB control is developed by Dr. Karel Styblo of the International Union against Tuberculosis and Lung disease and adopted by WHO. DOTS is the abbreviation of the Directly Observed Treatment of Short course chemotherapy (WHO, 1999).

DOT: Refers to the directly observed Treatment during the intensive phase for all new smear positive cases, continuation phase of Rifampicin-containing regimens and the whole re-treatment regimen, which is one of the five components of DOTS strategy. DOT can be undertaken by health personnel, family member or community volunteer.

Sputum smear positive: It means patient having examined sputum for acid fast bacilli for three consecutive specimens and among the three investigated specimens, at least one specimen of sputum is examined as containing acid fast bacilli at the time of presentation. It is categorized into four groups such as scanty (+-), one plus (+). Two plus (++) and three plus (+++).

New smear positive pulmonary tuberculosis patient: it refers to the patient who has a sputum smear positive result, and has never received any TB treatment or has received treatment for less than 2 months in the past.

Family member DOT observer: The person who observes the daily dose of drug intake of a TB patient during the course of treatment, who lives in the same household.

Health personnel DOT observer: the person who observes the daily dose of drug intake of a TB patient during the course of treatment, who works in the hospital or health center.

Self-administrator (SA): Refers the TB patient who takes treatment without supervision of DOT observer.

Socio-economic and demographic characteristics: Refers to patient's social and demographic background including sex, age, marital status and occupation.

Age: It refers to the age (year) at the time that the patient registered in the health center. It is further categorized into 6 age groups based on the WHO standard, i.e. 1-14 age group, 15-24 age group, 25-34 age group, 35 – 44 age group, 45-54 age group and 55 and above age group.

Gender: It refers to the sex of TB patient i.e. male and female

Marital status: According to the marital status of TB patients, the TB patient is categorized into 3 groups: unmarried (single), married or widow/widower/separated.

Occupation: the occupation of TB patients are categorized into 6 groups: 1) government officer who is working in a government organization, 2) non government employee who is working in a private company or organization, 3) unemployed who is a jobless person, 4) housewife, 5) farmer/laborer who are working in field of agriculture or factory and 6) others who do not fit in any above categories such as a student or child.

Behavioral characteristics: Refer to patient's habit including alcohol consumption, smoking and compliance with treatment.

Alcohol consumption: It refers to the patient who has a habit of drinking alcohol occasionally or daily at the time when the patient registered in the health center. And it is categorized into two groups i.e. have a habit and no habit.

Smoking: It refers to the habit of patients whether they smoke cigarette or not at the time that they had registered in the health center. And it is categorized into two groups i.e. smoking and no smoking.

Compliance: Refers to patient's obedience to treatment schedule given by DOT observer. It is reflected by patient's regularity, continuity in taking daily drugs/collecting monthly drugs, This will be assessed through reviewing patient's treatment card to check whether patients never or ever missed treatment by counting the number of missing doses.

Health service related characteristics: Refers to the ***place*** of registration for TB patient whether it is TB chest clinic under ministry of public health or public health centers under Bangkok Metropolitan Administration (BMA), ***treatment regimen*** whether it is intermittent or daily regimen, ***formulation of drugs*** whether it is a combination form or separate form, ***directly observed treatment (DOT) duration*** whether it is the first two months of the treatment or the whole course of treatment, and ***Drug supply interval to the patients*** means that whether the drugs are delivered on a daily, weekly, or monthly basis.

Sputum conversion status at the end of the intensive phase treatment: It means that whether positive sputum result is converted into negative or not at the end of the 2^{nd} or 3^{rd} month of treatment which is the main indicator to anticipate the treatment outcome at the end of treatment.

Drug resistance status: It refers to any TB drug resistance status whether TB bacilli is resistant to any particular TB drugs or to both Rifampicine and Isoniazide (multi-drug resistance TB) and it will be categorized into 4 groups such as 1) no tested. 2) no resistance, 3) resistance to any TB drug, and 4) resistance to both Rifampicine and Isoniazide.

TB drug side effect: It means any reaction due to drug intake that leads to temporary or permanent discontinuation of treatment involving one or more drugs in the treatment regimen.

Other co-morbidities: it refers to whether TB patients have diseases other than TB or not, such as heart disease, diabetes and so on.

Treatment outcome

1) **Cured:** It refers to patients who completed 6 months of treatment and had 2 negative sputum examinations during treatment, of which one was at the end of treatment.

2) **Cure rate:** defined as the percentage of patients who completed 6 months of treatment and had 2 negative sputum examinations during treatment, of which 1 was at the end of treatment.

3) **Treatment completed**: It refers to patient who completed 6 months of treatment but did not have a sputum specimen examination at the end of treatment.

4) **Treatment completion rate**: defined as the percentage of patients who completed 6 months of treatment but did not receive 2 sputum examinations during treatment.

5) **Died:** It refers to TB patient who died for any reason during the treatment period.

6) **Death rate:** defined as a percentage of TB patients who died for any reason during the treatment

7) **Failed**: it refers to TB patients whose sputum result is positive at or after the fifth month of treatment.

8) **Failure rate**: defined as a percentage of TB patients whose sputum result is positive at or after the fifth month of treatment

9) **Defaulted:** it refers to TB patients who stopped treatment for at least 2 consecutive months of the treatment, then see when the patient defaulted whether in intensive phase or continuous phase

10)**Defaulter rate:** defined as the Proportion ofpatients who stopped treatment for at least 2 consecutive months of the treatment

11)**Transferred out:** it refers to patients who moved to another place and whose outcome of treatment was unknown.

12)**Transfer rate:** defined as the Proportion ofpatients who moved to another place and whose outcome of treatment was unknown.

13)**Treatment success rate**: defined as the combined percentage of Cure and completion rates.