COST-EFFECTIVENESS OF DIRECTLY OBSERVED TREATMENT, SHORT COURSE VERSUS SELF-ADMINISTERED TREATMENT OF PULMONARY TUBERCULOSIS

DOUNGNATE TONIMIT

A THESIS SUBMITTED IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR
THE DEGREE OF MASTER OF SCIENCE (PUBLIC HEALTH)
MAJOR IN INFECTIOUS DISEASE
FACULTY OF GRADUATE STUDIES
MAHIDOL UNIVERSITY
2000

ISBN 974-663-652-8

Thesis
entitled

COST-EFFECTIVENESS OF DIRECTLY OBSERVED TREATMENT, SHORT COURSE VERSUS SELF-ADMINISTERED TREATMENT OF PULMONARY TUBERCULOSIS

....
Miss Doungnate Tonimit
Candidate

....
Dr. Yaowaluk Ngoenwiwatkul,
D. D.S., M.P.HM., Dr. P.H.
Major-Advisor

....
Dr. Samrit Srithamrongsawat,
M.D., M. Sc.(Health Service Management)
Co-Advisor

....
Dr. Somsak Akksilp
M. D., M. Sc.
Co-Advisor

....
Lect. Pratana Satitvipawee,
B. Sc., M. P.H. (Bios.)
Co-Advisor

....
Prof. Liangchai Limlomwongse,
Ph. D.
Dean
Faculty of Graduate Studies

....
Assoc. Prof. Amornrath Podhipak,
B. Sc., M. S. (Biostat.), Ph. D. (Epid.)
Chairman
Master of Science (Public Health)
Major in Infectious Diseases
Faculty of Public Health

Thesis
entitled

COST-EFFECTIVENESS OF DIRECTLY OBSERVED TREATMENT, SHORT COURSE VERSUS SELF-ADMINISTERED TREATMENT OF PULMONARY TUBERCULOSIS

was submitted to the Faculty of Graduate Studies, Mahidol University
for the degree of Master of Science (Public Health)
on
May 10, 2000

Doungnate Tonimit
....
Miss Doungnate Tonimit
Candidate

....
Dr. Yaowaluk Ngoenwiwatkul,
D. D.S., M.P.HM., Dr. P.H.
Chairman

....
Dr. Viroj Tangcharoensathien,
Ph. D.
Member

....
Dr. Samrit Srithamrongsawat,
M.D., M. Sc.(Health Service Management)
Member

Pratana Satitvipawee
....
Lect. Pratana Satitvipawee,
B. Sc., M. P.H. (Bios.)
Member

....
Dr. Somsak Akksilp
M. D., M. Sc.
Member

....
Prof. Liangchai Limlomwongse,
Ph. D.
Dean
Faculty of Graduate Studies
Mahidol University

Kanda Vathanophas.
....
Assoc. Prof. Kanda Vathanophas,
M. D., M. Sc. In Hygiene (P. H. Microbiology)
Dean
Faculty of Public Health
Mahidol University

ACKNOWLEDGEMENT

Firstly, I would like to express my deep and hearty gratitude to Dr. Yaowaluk Ngoenwiwatkul, Department of Epidemology, Faculty of Public Health, Mahidol University, for her invaluable teaching, guidance and encouragement throughout the course of this work, including her constructive criticism and reviewing of the thesis.

For the detailed comments on proposed revisions and on the final manuscript, I am most grateful to Dr. Samrit Srithamrongsawat, deputy director of Office of Health Insurance, Dr. Somsak Akksilp, Director of 7th Zonal TB Center, Ubon Ratchathani and Dr. Viroj Tangcharoensathien, Health Systems Research Institute. I am indebted to Lect. Pratana Satitvipawee, Department of Biostatistic, Faculty of Public Health, Mahidol University for his useful guidance on the thesis.

I also wish to extend my deep appreciation to the staff of the health centers, hospitals, District Health Office and Provincial Health Office at Petchaburi, Ratchaburi and Prachuap Khiri Khan, for their kind help in field work.

Finally, I wish to express my deep thankfulness to my friends and my family for their valuable ideas, love and happiness.

Doungnate Tonimit

4136340 PHPH/M : MAJOR: INFECTIOUS DISEASES; M.Sc. (PUBLIC HEALTH)
KEY WORDS : DIRECTLY OBSERVED TREATMENT, SHORT COURSE / SELF-ADMINISTERED TREATMENT / COST-EFFECTIVENESS / TUBERCULOSIS

DOUNGNATE TONIMIT: COST-EFFECTIVENESS OF DIRECTLY OBSERVED TREATMENT, SHORT COURSE VERSUS SELF-ADMINISTERED TREATMENT OF PULMONARY TUBERCULOSIS, THESIS ADVISORS: YAOWALUK NGOENWIWATKUL, D. D. S., Dr. P H., SAMRIT SRITHAMRONGSAWAT, M. D., M. Sc. (Health Service Management), SOMSAK AKKSILP, M. D., M. Sc., PRATANA SATITVIPAWEE, M. P. H. (Bios)134 p. ISBN 974-663-952-8

Global resurgence of tuberculosis (TB) including multidrug resistant tuberculosis (MDR-TB) poses a challenge for TB control programmes. Currently, the Thai health service system offer Directly Observed Treatment, Short course (DOTS) and the conventional Self-Administered Treatment (SAT) as TB controlling strategies. DOTS has been used since 1996 and the number is expected to rise. However, little research has been undertaken on their cost-effectiveness particularly in Thailand. In this study, we investigated cost-effectiveness between DOTS and SAT by using a retrospective cohort design conducted on a cohort of 204 new pulmonary TB patients with sputum smear positive, regardless of HIV status. All registered patients between October 1, 1998 and March 31, 1999 were followed up until the occurrence of events or the day of study termination (November 30, 1999) and a cost per case cure was calculated for each strategy. In general, the TB patients were mostly unskilled male workers with the mean age of 45 years, graduated from primary school level. There was a high death rate particularly among smoking males aged 15-34 years. Results revealed that the proportion of defaulters at the second month of treatment was 2.6% for DOTS compared with 11.5% for SAT. The median time-to-cure among the DOTS group (184 days) was shorter than those among the SAT group (210 days). Our findings evidence that the cure rate of patients under DOTS (67.5%) was significantly higher than that under SAT (34.5%) with the net gain of 96%. The unadjusted analysis showed that patients under DOTS were more likely to be cured at 1.96 times higher than that of SAT ($p<0.01$). Using Cox's proportional hazard model, the patients treated under DOTS had the estimated relative hazard at 2.91 (95% CI 1.70-4.70) compared with those under SAT after adjusting for occupation and residence. Although an average cost per patient treated under DOTS (7,363 Baht) was higher than those under SAT (5,422 Baht), the difference was not statistically significant ($p=0.77$). In fact, a cost per case cured under DOTS (10,905 Baht) was lower than those under SAT (15,724 Baht). Sensitivity analysis indicated that the advantage of cost-effectiveness of DOTS and SAT was sensitive to cure rate but not for travel cost and labour cost. Moreover, sensitivity results indicated that the net gain between the two programmes should be at least 36% in order to maintain an economic advantage of DOTS over SAT. In conclusion, DOTS offer a higher cure rate than SAT resulting in increased cost savings for public health, thus DOTS is superior to SAT for TB control programmes. Further investigation on high death rates and implementing a modified DOTS (M-DOTS) strategy in SAT setting are recommended.

4136340 PHPH/M : สาขาวิชาเอก: โรคติดเชื้อ; วท.ม. (สาธารณสุขศาสตร์)

ดวงเนตร ไถนิมิตร์ : ต้นทุน-ประสิทธิผลของการรักษาวัณโรคปอดด้วยระบบยาระยะสั้นแบบมีพี่เลี้ยงเปรียบเทียบกับแบบดูแลตนเอง (COST-EFFECTIVENESS OF DIRECTLY OBSERVED TREATMENT, SHORT COURSE VERSUS SELF-ADMINISTERED TREATMENT OF PULMONARY TUBERCULOSIS), คณะกรรมการควบคุมวิทยานิพนธ์: เยาวลักษณ์ เงินวิวัฒน์กุล, D. D. S., Dr. P H., สัมฤทธิ์ ศรีธำรงสวัสดิ์, M. D., M. Sc. (Health Service Management), สมศักดิ์ อรรฆศิลป์, M. D., M. Sc., ปรารถนา สถิตย์วิภาวี, M. P. H. (Bios) 134 หน้า. ISBN 974-663-952-8

วัณโรคยังคงเป็นปัญหาสำคัญระดับโลก ปัจจุบันประเทศไทยใช้ระบบยาระยะสั้นแบบมีพี่เลี้ยงและแบบดูแลตนเองในงานควบคุมวัณโรค การรักษาวัณโรคแบบมีพี่เลี้ยงเริ่มมีการใช้มาตั้งแต่ พ.ศ.2539 จนถึงปัจจุบันและคาดว่าจะใช้การรักษาแบบมีพี่เลี้ยงเพิ่มมากขึ้น อย่างไรก็ตาม การวิจัยเกี่ยวกับต้นทุน-ประสิทธิผลของการรักษาแบบมีพี่เลี้ยงในประเทศไทยยังมีจำนวนน้อย ในการศึกษาครั้งนี้จึงได้เปรียบเทียบต้นทุน-ประสิทธิผลระหว่างการรักษาวัณโรคแบบมีพี่เลี้ยงและแบบดูแลตนเอง โดยทำการศึกษาแบบ Retrospective cohort ในกลุ่มตัวอย่างของผู้ป่วยวัณโรคปอดรายใหม่ที่มีผลการตรวจเสมหะพบเชื้อวัณโรคจำนวน 204 ราย ซึ่งขึ้นทะเบียนรักษาวัณโรคตั้งแต่ 1 ตุลาคม 2541 ถึง 31 มีนาคม 2542 ได้มีการติดตามผู้ป่วยจนกระทั่งเกิดเหตุการณ์ที่สนใจหรือสิ้นสุดการศึกษา (30 พฤศจิกายน 2542) และได้มีการคำนวณต้นทุนต่อการรักษาผู้ป่วยให้หายต่อคน ด้วยระบบยาระยะสั้นแบบมีพี่เลี้ยงและแบบดูแลตนเอง ลักษณะทั่วไปของผู้ป่วยวัณโรคส่วนใหญ่ทำงานรับจ้างทั่วไปและใช้แรงงานเป็นเพศชายมีอายุเฉลี่ย 45 ปี จบการศึกษาระดับประถม ผลการศึกษาพบว่ามีอัตราตายค่อนข้างสูงในกลุ่มของผู้ป่วยชายสูบบุหรี่และมีอายุระหว่าง 15-34 ปี สำหรับการเปรียบเทียบผลการรักษาของทั้งสองโปรแกรม พบว่าเดือนที่ 2 ของการรักษาแบบมีพี่เลี้ยงมีผู้ป่วยขาดการรักษาร้อยละ 2.6 ส่วนผู้ป่วยที่รักษาแบบดูแลตนเองขาดการรักษาร้อยละ 11.5 มัธยฐานของเวลาที่ใช้ในการรักษาแบบมีพี่เลี้ยง (184 วัน) สั้นกว่าการรักษาแบบดูแลตนเอง (210 วัน) อัตราการรักษาหายขาดแบบมีพี่เลี้ยง (ร้อยละ 67.5) สูงกว่าการรักษาแบบดูแลตนเอง (ร้อยละ 34.5) อย่างมีนัยสำคัญทางสถิติ และคิดเป็นอัตราการรักษาหายขาดสุทธิร้อยละ 96 การวิเคราะห์แบบตัวแปรเดี่ยวพบว่าผู้ป่วยที่รักษาแบบมีพี่เลี้ยงมีโอกาสรักษาหายเป็น 1.96 เท่า ของผู้ป่วยที่รักษาแบบดูแลตนเอง การวิเคราะห์โดย Cox ' s proportional hazard model พบว่าผู้ป่วยที่รักษาแบบมีพี่เลี้ยงมีโอกาสรักษาหายเป็น 2.96 เท่า ของผู้ป่วยที่รักษาแบบดูแลตนเองโดยมีการควบคุมอิทธิพลของที่อยู่อาศัยและอาชีพ ถึงแม้ว่าต้นทุนต่อการรักษาผู้ป่วย 1 ราย แบบมีพี่เลี้ยง (7,363 บาท) สูงกว่าการรักษาแบบดูแลตนเอง (5,422 บาท) แต่ไม่มีนัยสำคัญทางสถิติ ต้นทุน-ประสิทธิผลของการรักษาผู้ป่วยให้หายต่อคน แบบมีพี่เลี้ยง (10,905 บาท) น้อยกว่าแบบดูแลตนเอง (15,724 บาท) ในการวิเคราะห์ Sensitivity analysis พบว่าต้นทุน-ประสิทธิผลของการรักษาแบบมีพี่เลี้ยงและแบบดูแลตนเองมีความไวต่ออัตราการรักษาหายขาด โดยเฉพาะอย่างยิ่งเมื่ออัตราการรักษาหายขาดสุทธิสูงกว่าร้อยละ 36 ผลการวิเคราะห์แสดงให้เห็นว่าโปรแกรมการรักษาด้วยระบบยาระยะสั้นแบบมีพี่เลี้ยงจะให้ต้นทุน-ประสิทธิผลมากกว่าแบบดูแลตนเองเสมอ จากการศึกษาสรุปได้ว่าการรักษาวัณโรคด้วยระบบยาระยะสั้นแบบมีพี่เลี้ยงดีกว่าแบบดูแลตนเองเนื่องจากการรักษาแบบมีพี่เลี้ยงมีอัตราการรักษาหายขาดสูงกว่าการรักษาแบบดูแลตนเองซึ่งลดการแพร่เชื้อไปสู่ผู้อื่นและประหยัดต้นทุนได้มากขึ้น โดยมีข้อเสนอแนะให้มีการศึกษาค้นคว้าต่อไปในกรณีที่อัตราตายสูงและเสนอให้มีการดำเนินการรักษาด้วยระบบยาระยะสั้นแบบกึ่งมีพี่เลี้ยง (M-DOTS) ในพื้นที่ที่ยังมิได้ดำเนินการแบบมีพี่เลี้ยงเต็มรูปแบบ

CONTENTS

CONTENTS (Continued)

LIST OF TABLES

LIST OF TABLES (Continued)

LIST OF FIGURES

CHAPTER I

INTRODUCTION

1.1 Rationale and justification

Tuberculosis remains an enormous problem in the world. In 1993, World Health Organization (WHO) declared tuberculosis (TB) as a "global emergency" (1). In 1996, eight million new cases, three million deaths, and their projections indicated that one of every three of the world's population will be infected with TB (2). Worldwide, 30 million people may die due to TB between 1990 and 2000 (3). The South-East Asia region is the most case notifications of tuberculosis (4). The global tuberculosis epidemic is fuelled by dual infection with human immunodeficiency virus (HIV). TB is now the leading cause of death among HIV-positive people and up to 40 percents of AIDS deaths in Asia and Africa. It is estimated that by the end of nineteen century, HIV infected-person will annually cause nearly 1.5 million cases of TB that otherwise would not have occurred (4).

Tuberculosis incidence rate and number of cases in Thailand declined steadily during the decades, following the introduction of effective short–course chemotherapy (SCC) regimens in 1985. These trends have continued until 1991 and the lowest incidence rate is 76 per 100,000 population (Figure 1) (5). During 1992-1993, the upward trends were attributed by influencing of HIV epidemic. In the high HIV prevalent area such as Chiang Mai, the mortality proportion of the TB patients with HIV positive under 45 years old increased from 34% in 1989 to 51% in 1992 (6).

WHO estimated that in the year 2000 the estimated number of total new TB patients in Thailand would be 120,000 (7).

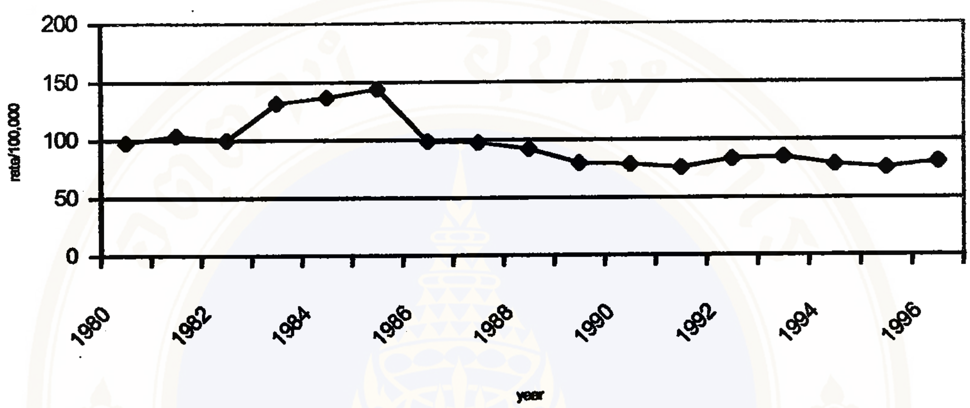


Figure 1 Trend of new TB case notification (1980-1996)

Source: Public health statistics, 1996

A short course chemotherapy (SCC) had been used as TB controlling programme (8-11). The Thailand National Tuberculosis Programme (NTP) has been used SCC since 1985 with treatment completion rate about 80 % but the cure rate, which was calculated by WHO in 1995, was as low as 50% (7). The weakness of NTP was caused mainly by routine operational difficulties in diagnosis, treatment, recording and reporting. The low cure rate of infectious cases is the major problem for TB endemic worldwide (1). Consequently, erratic or incomplete treatments of TB introduce the growth of drug-resistant bacilli and multiple drug-resistant tuberculosis (MDR-TB). An additional factor which led to the recent propagation of these drug-resistant strains is the concurrence of TB infection with HIV-infected person (12). MDR-TB patients are difficult to treat because the organisms resist to several antibiotics (11,13-16) which resulting in a prolonged hospitalization with more complication or surgical resection for cure (13,14). Thus, this leads to economic burden of public health (12,14,17).

The greatest challenges in controlled TB are political rather than medication. The major challenges are inadequate political commitment and funding, organisation of services, inadequate case management or a lower rate of treatment completion and over-reliance on BCG (8). Since 1993, the Directly Observed Treatment, Short course (DOTS) has been adopted by WHO as a strategy to combat tuberculosis worldwide (18). DOTS has been reported as an efficient strategy for controlling TB. Treatment outcomes were collected from 181 out of 212 countries showed that treatment success rate for DOTS was 78 percents (4). The success of DOTS has been shown in diverse areas of the world, such as China, Peru, Vietnam and Bangladesh where their cure rates rise to 95 percents (4,18). DOTS also provides the reduction of the prevalence of MDR-TB (19) and reduces the cost per case of TB treatment (20) by improvement the rate of treatment completion (19,21-27). In New York, introduction of DOTS has been associated with a sustained reduction in the number of new cases and a group of multidrug resistant diseases (3). Therefore, DOTS is considered as one of the cost-effective health intervention (20,28,29). In Thailand, the DOTS strategy was first implemented in 1996. Results in the first eight months were encouraging with 82 % cure rate (30). In Yasothorn province, the study by Akksilp (1996) found that DOTS had statistically significant higher cure rate than self-administered treatment (SAT) (27). Further more, the study by Kamolrattanakul, et al. (1997) agreed with Yasothorn study. In 1997, the TB mortality rate in Thailand began to decline that might be contributed by implementing DOTS (7). To our knowledge, there are few studies on cost-effectiveness of DOTS in Thailand. Thus, this present study aims to comparing of costs, effectiveness and cost-effectiveness between DOTS and SAT in Thailand.

1.2 Research Objective

General objective

Comparison cost-effectiveness between new pulmonary TB patients with sputum smear positive who treated under DOTS and those who treated under SAT in Thailand.

Specific objectives

1. To calculate the direct provider cost, consumer cost, full cost and average cost per patient treated under DOTS and SAT strategies.
2. To compare the effectiveness of patients treated under DOTS and SAT strategies.
3. To compare cost-effectiveness between DOTS and SAT strategies.

1.3 Research Hypotheses

1. The direct provider cost, consumer cost, full cost and average cost per patient treated under DOTS are not statistically significant different from those under SAT.
2. The effectiveness as defined by cure rate of DOTS is not statistically significant different from which of SAT.

1.4 Operational Definitions

1. A new pulmonary tuberculosis (PTB) refers to a new PTB who has these following characteristics:

1.1 A patient who has at least 2 sputum smears positive for acid fast bacilli (AFB), or

1.2 A patient who has one sputum smear positive for AFB and chest X-ray (CXR) abnormalities consistent with active TB, and

1.3 A patient who has never taken anti-TB drugs for more than one month.

2. Directly Observed Treatment, Short course (DOTS): A short treatment course for TB patient with the specific procedure in order to increase patient's compliance. The patients must take medicine under direct observation by health workers, health volunteers or patient relatives. The following procedures are recommended. After initial diagnosis, patients identify an observer either health workers, health volunteers or their relatives. Patients will be received anti-TB drugs for daily taken. If a health worker is an observer, a patient will visit a health center for taking the medicines daily or a health worker will visit a patient and observe patient taking medicines daily. If a relative is selected as an observer, the health worker will provide packages of anti-TB drugs for a week or more and supervise the observer and patient weekly at the initial phase and monthly during the continuation phase (Figure 2).

3. Self-administered treatment (SAT): a patient will be received an one month supply of anti-TB drugs (a short treatment course) and self-administered to taking their anti-TB drugs. Then, patients visit to district hospitals for their drugs refill monthly during 6 months course (Figure 2).

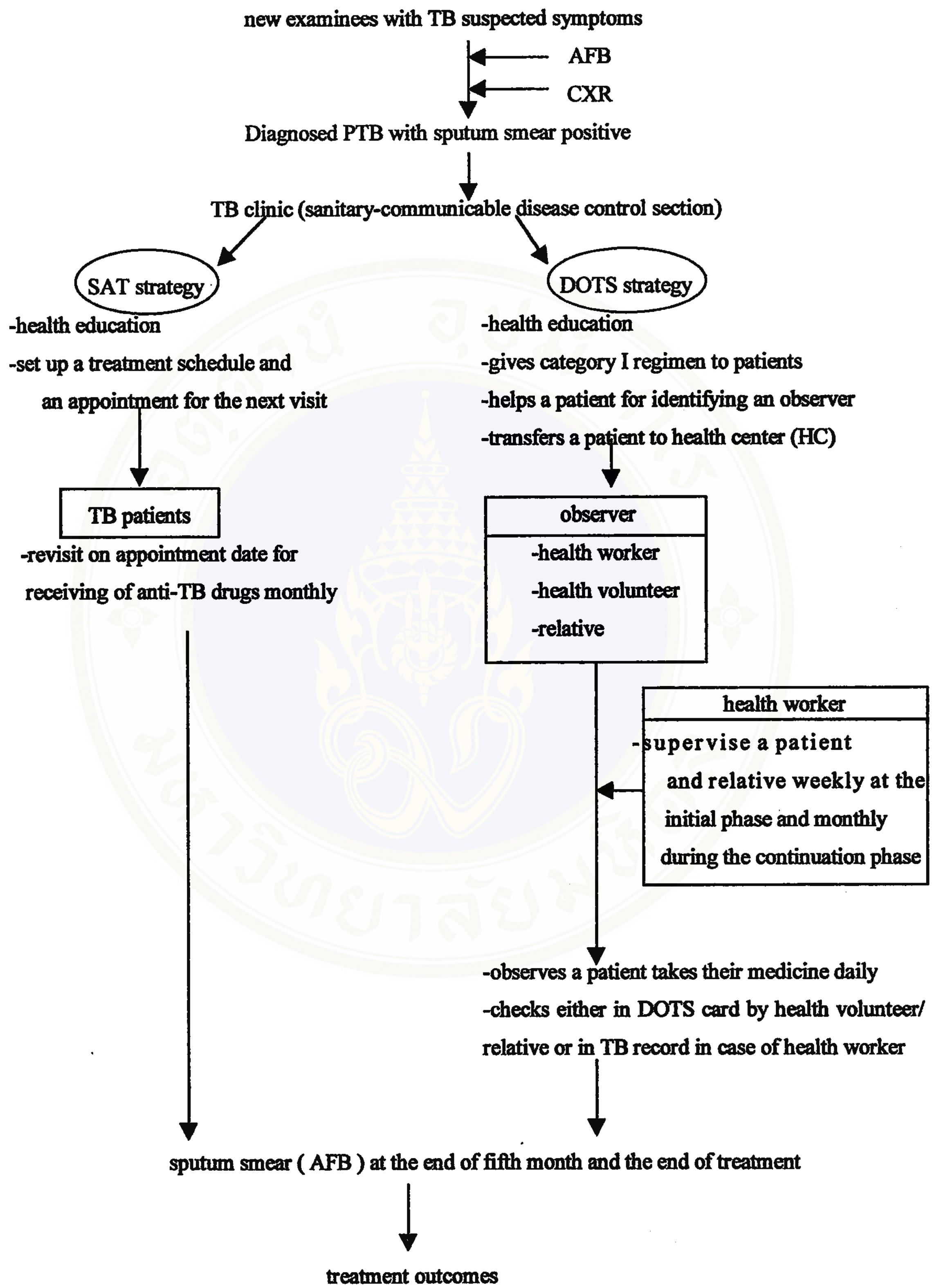


Figure 2 The steps of SAT and DOTS strategies

4. A short course refers to the standardised regimen category I which consists of four anti-TB drugs in an initial phase [Isoniacid (H), Rifampicin (R), Pyrazinamide (Z) and Ethambutol (E) or Streptomicin (S)] and two anti-TB drugs (HR) in a continuation phase.

4.1 An initial phase is usually 2 month duration for treatment, if the sputum smear is still positive at the end of second month, the initial phase treatment will be extended for another month with the same 4 drugs. If the sputum smear at the third month is still positive, the initial phase will be extended again. This extension will be ceased either the sputum smear is negative after monthly checking or the extension period is reached without negative result from sputum smear at the end of the fifth month.

4.2 The continuation phase is a 4 months duration which consists of two anti-TB drugs (HR). A treatment duration of a short course for TB will be 6,7 or 8 months for a treatment completion.

5. Treatment outcomes will be evaluated by sputum smear under microscopy at the end of the fifth month and the end of the treatment. Treatment outcomes could be classified in 6 categories (31):

5.1 Cured: initial sputum smear positive patient who completed treatment and had negative sputum smear results on at least two occasions during the continuation phase, including one at completion of treatment.

5.2 Completed: initial sputum smear positive patient who has completed treatment with only one negative sputum smear result at the end of the fifth month in the continuation phase and no sputum smear result at the end of treatment.

5.3 Defaulted: a patient who is loss to follow up for two consecutive months after registration.

5.4 Failed: initial sputum smear positive patient who remains sputum smear positive at the end of the fifth month after the start of treatment or at the end of the treatment.

5.5 Died: patient who died during treatment, irrespective of cause.

5.6 Transferred out: patient who has been transferred to another reporting unit and for whom his or her treatment outcome is not known.

6. Effectiveness is the cured rate which is calculated as a number of patients cured divide by a number of the patients registered and multiply by 100.

7. The full cost is the summation of direct provider cost and consumer cost. (Figure 3)

7.1 The direct provider cost is the summation of direct routine service cost and medical care cost.

7.1.1 The direct routine service cost is the summation of capital cost, material cost and labour cost of outpatient department (OPD), sanitary-communicable disease control section (SDC) and health center (HC).

A. Capital costs are defined as the rental cost for estimation of cost of the building utilization.

B. Material costs are cost of electric and water and travel cost. The travel cost assumed to be equal to the price of public transportation charge.

C. Labour costs refer to personnel expenses; salaries, wages, sick payment, overtime and allowances for housing. The time of health volunteer workers is translated into monetary cost using a standard minimum wage.

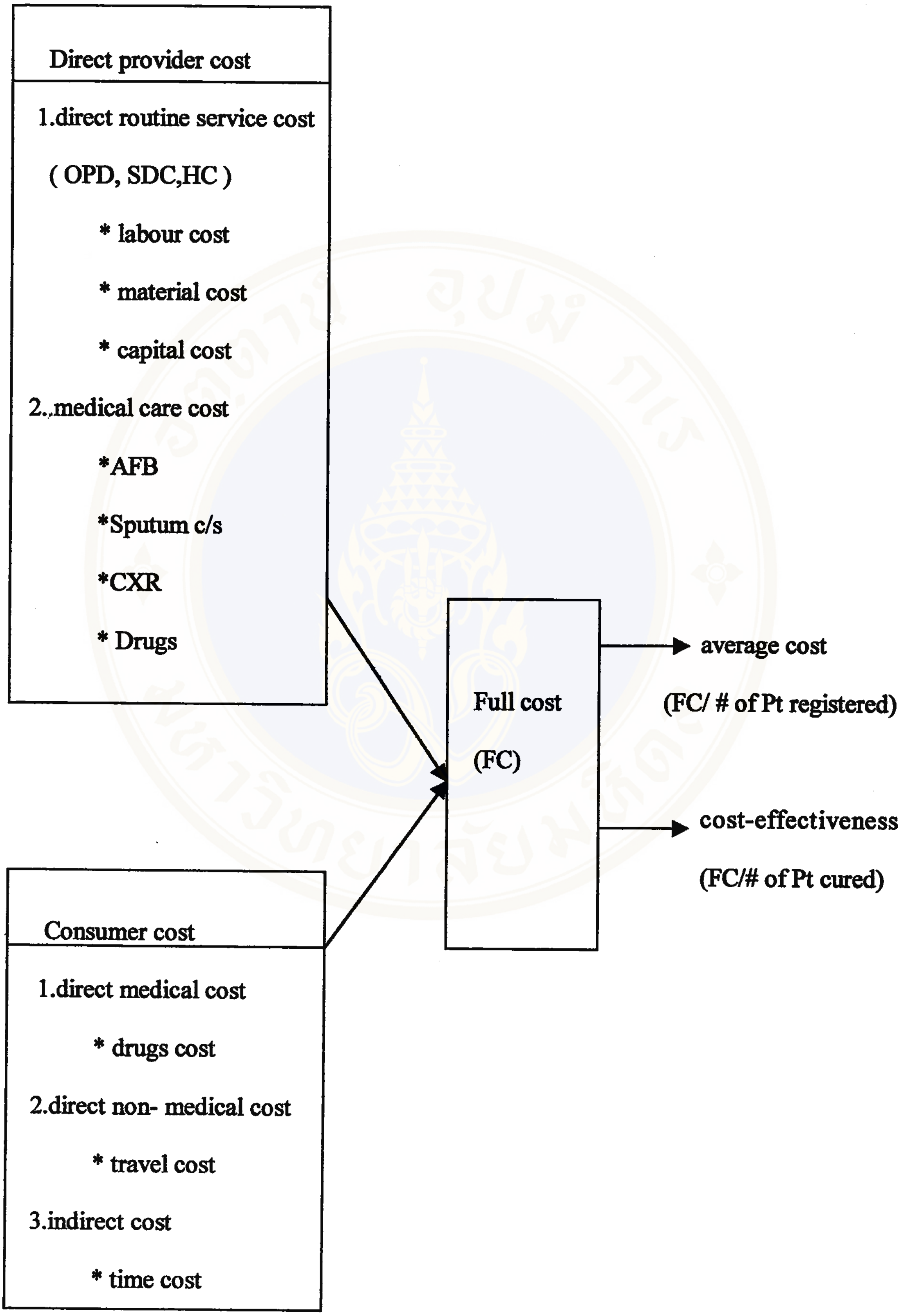


Figure 3 Costs component.

7.1.2 The medical care cost is the summation of cost of sputum examination (AFB), sputum culture and sensitivity (c/s), chest X- ray (CXR), TB drugs and other drugs related to TB. The unit cost of AFB, sputum c/s and CXR of previous study (32) is used for calculation after adjusted for difference timing. The unit cost of TB drugs quoted from Tuberculosis Division in 1999. Other drugs related to TB which were only paid by provider and estimated from price charge of each hospital in 1999.

7.2 The consumer costs consist of direct medical cost, direct non- medical cost and indirect cost.

7.2.1 Direct medical cost is the monetary expense for other drugs related to TB which was paid by patient (out of pocket).

7.2.2 Direct non-medical cost is the summation of travel cost of patients and their relatives.

7.2.3 Indirect cost refers to the time of patients and their relatives spending for travelling, waiting and receiving treatment which is translated into monetary cost using a standard minimum wage.

8. The average cost is calculated as the full cost divided by a number of patients engaged at the beginning.

9. Cost-effectiveness refers to average cost per case cured that is calculated as the full cost divided by a number of patients cured. The method provides the lowest average cost per patient cured is considered as the most cost-effectiveness.

1.5 Assumption

1. The health workers worked 20 days per month and 8 hours per day.

2. Time cost of health volunteers was translated into monetary cost using a standard minimum wage and they work 8 hours per day.

3. Travel cost of health workers, patients and relatives used the price of public transportation charge.

4. The average of travel cost and time of travelling, waiting and receiving treatment of each hospital were used in a case of missing information among respective TB patients.

1.6 Limitation

1. Cost calculation in this study is based on the direct provider cost and consumer cost, which the calculation method in this study may be underestimated of total full cost around 25 %. However, Burman, et al. (20) and Moore, at al. (29) studied cost analysis by using direct cost and concluded that direct cost would be appropriate to serve the health care planners and administrators in their planing and administration of health care delivery procedures.

2. Univariate sensitivity analysis, the traditional approach to sensitivity analysis, is conducted in this study only. It is examined one variable at a time. The analyst must choose which variables to vary, the amount of variation around the base value of the parameter. Thus the results of the sensitivity analysis depend on many subjective choices by the analyst. Although univariate analysis is incomplete, it is a logical and practical for cost-effectiveness analysis.

3. Recall error may occur according to retrospective cohort study.

4. Misclassification bias may occur as misclassification of alcohol and cigarette consumption.

5. Unit cost of AFB, CXR, sputum c / s of Sing-Dong study was used. The study may be overestimated of medical care cost.

6. Cost of other drugs related to TB may be underestimated because of incomplete information in medical records.

7. Accuracy data depend on the completeness of medical record. It could be improved if we can investigate laboratory result at laboratory registration.

1.7 Significance of the study

This may be the first study that is conducted on cost-effectiveness analysis between DOTS and conventional method in health care settings and community hospitals in Petchaburi, Ratchaburi and Prachuap Khiri Khan. The study findings will provide useful information for comparison of resource requirements for delivery of the TB service and guide public health policy.

CHAPTER II

LITERATURE REVIEW

2.1 Natural history of tuberculosis (TB)

2.1.1 Definition

A TB patient refers to patient who had the following symptoms such as weakness, fever, lost weight, cough more than 3 weeks, cough with blood and chest pain. In addition, TB diagnosis confirms with sputum smear positive for AFB or positive culture for AFB (33).

Tuberculosis is an infection disease caused by bacteria namely " *Mycobacterium tuberculosis* ". In identifying the tubercle bacillus, Koch' s work is recognized as the greatest single feat of bacteriologic science and one of the most important in the history of medicine. The disease usually affects the lungs, although in up to one-third of cases other organs are involved. If properly treated, tuberculosis caused by drug-susceptible strains is curable in virtually all cases. If untreated, the disease may be fatal within 5 years in more than half of case (34). Transmission usually takes place through the airborne spread of droplet nuclei produced by patients with infectious pulmonary tuberculosis.

2.1.2 Etiologic agent

Mycobacteria belong to the family Mycobacteriaceae and the order Actenomycetales. Of the pathogenic species belonging to the *Mycobacterium tuberculosis* complex (35) which is classified into many species as follow:

Mycobacterium tuberculosis is the causative agent of nearly all of the tuberculosis in humans; *Mycobacterium bovis* destroys cattle and requirement of pasteurization of milk; *Mycobacterium africanum* is a cause of disease in equatorial Africa ; and *Mycobacterium microti* is not pathogenic for humans but a primary pathogen of voles, in which it produces a disease similar to tuberculosis.

2.1.3 Transmission

Mycobacterium tuberculosis is most commonly transmitted from a patient with infectious pulmonary tuberculosis to other persons by droplet nuclei, which are aerosolized by coughing, sneezing, or speaking. The tiny droplets dry rapidly; the smallest (< 5 to 10 μm in diameter) may remain suspended in the air for several hours and may gain direct access to the terminal air passages (34). There may be as many as 3000 infectious nuclei per cough. In the past, a frequent source of infection was row milk containing *mycobacterium bovis* from tuberculous cows. Other routes of transmission of tubercle bacilli, such as through the skin or the placenta, are uncommon.

The important determinants of transmission are the intimacy and duration of that contact, the degree of infectiousness of the case, and the environment of the contact. Among infected persons, the incidence of tuberculosis is highest during late adolescence and early adulthood. The incidence among women peaked at 25 to 34 years of age higher than those among men. The risk of developing tuberculosis is several times higher among HIV-infected than among HIV-uninfected hosts. Other conditions known to increase the risk of active tuberculosis among persons infected with tubercle bacilli include silicosis, lymphoma, leukemia, and other malignant neoplasms, hemophilia, chronic renal failure and hemodialysis, insulin-dependent diabetes mellitus, immunosuppressive treatment, and conditions associated with malnutrition (34). Baskin, et al. (35) found that men were 1.9 times higher risk of TB than women. Patient who had heavy drunk was 2 times more likely to be TB than those never drink after adjusting for age and smoking. After adjustment for age and alcohol consumption, the relative risk associated with current smoking was 1.3 higher than those never smoke. Likewise, Alcaide, et al. (36) showed that patient who had active smoking was significantly associated with PTB when compared to those never smoke.

2.1.4 Natural history of untreated TB and its classification

The untreated tuberculosis was often fatal before the advent of chemotherapy. About one–third of patients died within 1 year after diagnosis, one-half within 5 year (34), 25% will be recovered (self-cured by strong immune defense) and 25% will remain ill with chronic of tuberculosis (26).

Tuberculosis is generally classified as 1) pulmonary and 2) extrapulmonary. Before the recognition of HIV infection, more than 80 % of all cases of tuberculosis were limited in the lungs (34). However, up to two-thirds of HIV-infected patients with tuberculosis may have both pulmonary and extrapulmonary disease or extrapulmonary disease alone.

A. Pulmonary tuberculosis can be categorized as primary or postprimary TB.

A.1. Primary disease (37) occurs on the first exposure to tubercle bacilli. Inhaled droplet nuclei which are small, thus the droplet nuclei could avoid the muco-ciliary defenses of the bronchi and lodge in the terminal alveoli of the lungs. Infection begins with multiplication of tubercle bacilli in the lungs. This is the Ghon focus. Lymphatics drain the bacilli to the hilar lymph nodes. The Ghon focus and related hilar lymphadinopathy form the primary complex. Bacilli may spread into blood system from the primary complex throughout the body. The immune response develops about 4-6 weeks after the primary infection. The size of the infecting dose of bacilli and the strength of the immune response determine the rate of progression. In most cases, the immune response can terminate the multiplication of bacilli. However, a few dormant bacilli may persist in some individual whose immune response could not prevent multiplication of bacilli. Therefore, TB would develop within a few months.

A.2. Postprimary TB (38) occurs after the latent period of months or years after primary infection. The process could be reactivation or reinfection. Reactivation means that dormant bacilli persisting in tissues for months or years after primary infection start to multiply. This may be in response to a trigger, such as suppression of the immune system by HIV infection. Reinfection means a repeat infection in a person who previous had primary infection. Post-primary TB usually affects the lungs but can involve any part of the body. The characteristic features of post-primary pulmonary TB are the followings: extensive lung destruction with cavitation; positive sputum smear; upper lobe involvement; usually no intrathoracic lymphadinopathy.

B. Extrapulmonary tuberculosis (39) may develop early in the course of pulmonary tuberculosis, or it may appear years after the primary pulmonary infection. Intraluminal spread, or lymphohaematogenous dissemination may occur as a result of direct extension. Extrapulmonary disease may be an indolent process or a rapidly progressive acute illness. Virtually any organ or system in the body may be involved as a solitary focus or in a disseminated disease. In general, haematogenous will spread from the primary pulmonary focus within the first 6 weeks of infection when bacterial multiplication is not impeded by host defense. The germ distributes following a circulation system, but well-oxygenated areas, such as apical-posterior areas of the lungs, kidneys, lymph nodes, vertebral bodies, subependymal meninges, epiphyses of long bones, bone marrow, and the reticuloendothelial system, favor the growth of *Mycobacterium tuberculosis* .

2.1.5 Diagnostics

Most cases of PTB are diagnosed according to the symptoms as following (40);

1.A patient had a cough for more than 3 weeks.

2.Blood in the sputum may vary from a few spots to a sudden coughing of a large amount of blood.

3.Breathlessness in tuberculosis is due to extensive disease in the lungs or to pleural effusion complicating the lung tuberculosis. The breathless patient frequently appears ill and has lost weight and will often have fever.

4.Pain in the chest is not uncommon in tuberculosis. Sometimes it is just a dull ache. Sometimes it is worse on breathing in. Sometimes it is due to muscle strain from coughing.

5.Occationally, the patient may seem to develop an acute pneumonia but could not recover after treatment with routine antibiotics.

Physical signs

1.General condition: The patient may be obviously ill. He may be very thin, with obvious loss of weight. He may be pale or has a flush due to fever.

2.Fever: There may be only slight rise of temperature in the evening. The temperature may be high or irregular. Often there is no fever.

3.Chest: Often there are no abnormal signs. The commonest is the crepitations in the upper part of one on both lungs.

The acid fast stained sputum smear is the time–tested method for detection of *Mycobacterium tuberculosis* . It is a simple and inexpensive method used worldwide (41) with high specificity almost 100% and sensitivity between 30% and 50% (37).

2.1.6 Short course treatment of tuberculosis

Standardised treatment regimens (short course) have four categories for the different TB cases. There are three main properties of anti-TB drugs: bactericidal ability, sterilizing ability, and the ability to prevent resistance. The anti-TB drugs possess these properties to different extents. Isoniazid (H) and Rifampicin (R) are the most powerful bactericidal drugs, active against all populations of TB bacilli. Pyrazinamide (Z) and Streptomycin (S) are also bactericidal against certain populations of TB bacilli. Pyrazinamide is active in an acid environment against TB bacilli inside macrophages. Streptomycin is active against rapidly multiplying extracellular TB bacilli. Ethambutol (E) and Thioacetazone (T) are bacteriostatic drugs used in association with more powerful bactericidal drugs to prevent the emergence of resistant bacilli (31).

Each of the standardised chemotherapeutic regimens is consisted of two phases: initial and continuation phases. Initial (intensive) phase is the duration that a patient spends two to four months and uses four anti-TB drugs daily under direct observation in order to reduce the number of tuberculosis organism. The continuation phase is the duration that a patient spends four to six months and uses two to three medications daily under direct observation (42).

A review of the literature showed that gender (43,44), income (46,47) and occupational (43) are significant associated with treatment regularity or compliance. Hudelson, et al. (44) suggested that defaulter was significantly higher among men than women. Francis, et al. (47) found that compliance was reduced for the lower socioeconomic group. Burman, et al. (48,49) and Oscherwitz, et al. (50) suggested that patients with alcohol abuse was noncompliance 3 times higher than those without alcohol abuse. However, Reichman (51), Vateesatokkit, et al. (52) and Maneeroungdet (53) found that there was no significant relation between the sociodemographic and treatment regularity or compliance.

2.1.7 HIV infection and tuberculosis

Human immunodeficiency virus (HIV) destroys the immune system that is critical to mounting a cell-mediated immune response. Therefore, predictably a high rate of progression from latent infection to active tuberculosis (39). A person who has HIV-positive is 30 times more likely to infect with TB than a person who has HIV-negative (4). Compared to an individual who is not infected with HIV, an individual infected with HIV has a 10 times increased risk of developing TB (38).

It is estimated that nearly two billion peoples worldwide are infected with *Mycobacterium tuberculosis.* Out of those, 16 millions are HIV infected. Five to six millions are dually infected with *Mycobacterium tuberculosis* and HIV. Seventy percents of TB/ HIV dually infected peoples living in sub-Saharan Africa and 20% in Asia (31). Generally, anti-TB chemotherapy is the same for HIV-infected as for HIV-uninfected TB patients, with the exception of the use of thioacetazone (4,31,42). Thioacetazone is associated with a high risk of severe, and sometimes fetal or skin reaction in HIV-infected individual (34). Therefore, Ethambutol should be used instead of thioacetazone in patient with known or suspected of HIV-infection.

The mortality of TB/ HIV patients living larger than 1 year after starting TB treatment is about 20 % (31). This mortality is greater than HIV negative TB patients. The excess deaths in TB/ HIV patients during and after treatment are partly due to TB itself or other HIV-related problems.

Tuberculosis with HIV infection were associated with widely disseminated disease (54,55). Richter, et al. (54) found that coexisting TB/HIV infection affected in clinics and laboratories , There was no apparently affected on radiograph. Fischi, et al. (55) concluded that tuberculosis causes multidrug resistant bacilli in HIV positive patients who have poor treatment response with an inability to eradication the organism caused substantial mortality. As HIV infection progress, CD4+ lymphocytes decline in numbers and functions. The immune system is less able to prevent the growth and local spread of organism. Then, disseminated disease is more common and poor response of treatment (38).

2.1.8 Epidemiology

A. Global situation

Mycobacterium tuberculosis infection caused about 9 million deaths in 1995 worldwide. These deaths comprise 25% of all avoidable deaths in developing countries. Ninety-five percents of TB cases and 98% of TB deaths are in developing countries. Seventy-five percents of TB cases in developing countries are in the economically productive age group (15-50 years) (38).

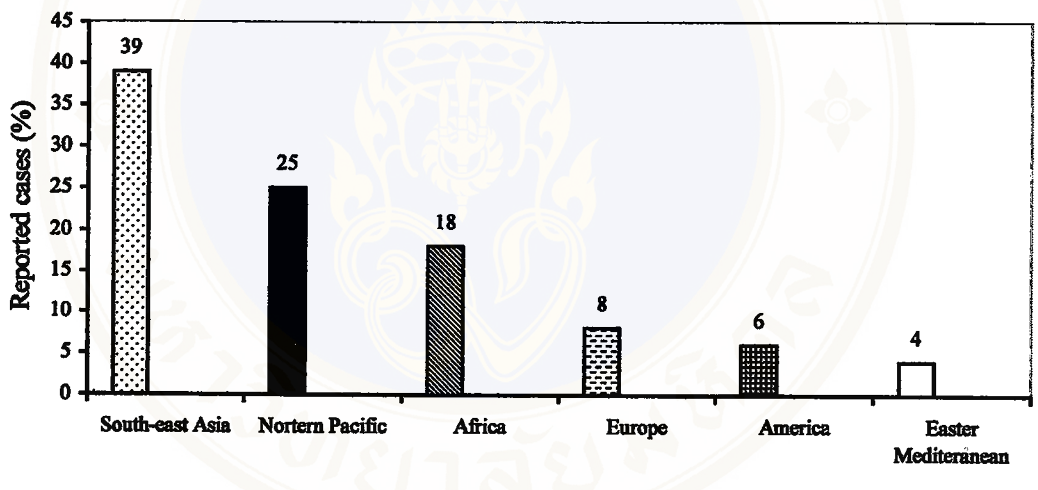


Figure 4 Reported tuberculosis cases by WHO Region, 1996. (total number of notified cases = 3,805,063)

Source: Adopted from WHO Geneva, TB controlling progeamme, 1997.

Of the 3.8 million cases reported to WHO in 1996, 39% were reported from the South-East Asia region (Figure 4). One million death occurred in the SEA region. Of the 4.5 million people who were HIV-positive in 1997, about one-third were also infected with TB. Between 56% and 80% of AIDS cases diagnosed in Thailand, India, Nepal and Myanmar were also infected with TB.

B. Situation in Thailand

Estimates of the total TB burden can be calculated from a series of surveys of the prevalence of infection and disease from 1962 through 1991. The estimated ARI was 2.3% in 1983 and 2.0% in 1987. Continuation of the downward trend of 3.5% annually would lead to an estimate of the ARI of approximately 1.4 % in 1998. This would be equivalent to an incidence rate of 70 TB cases with smear positive per 100,000 population. The policy of the government is only passive case-detection that carried out particularly symptomatic persons who want to detect TB at health facilities due to active case-detection is difficult and expensive. Practically when respiratory / TB suspected symptomatic persons visit the health facilities they have to be diagnosed at Zonal TB center 42.5%, 23.7% at provincial hospital, 33.5% at community hospital and 0.2% at health center (7).

Tuberculosis notification rate and case numbers declined steadily during the decades. Until 1992-1993, the upward trends were observed in the areas most afflicted by the emerging HIV epidemic, particularly in the upper Northern provinces, where the annual increasing rates of the case number is 10% (7). Case notification rate does not reflect the overall burden of tuberculosis in the community. The actual case numbers could be double, due to underdetection and underreporting. WHO estimated that in the year 2000 the numbers would be around 120,000 which 20% is attributed to the impact of HIV epidemic (7).

TB mortality rate increased from 5.9 per 100,000 in 1994 to 7.0 and 7.7 respectively, in 1995 and 1996. In 1997, that rate began to decline which was resulted from implementation DOTS in Thailand (7) (Figure 5). At national level, the reported cases of TB were highest among those age over 65 and lowest among those 10-14 years old (Figure 6). However, it should be noted that the number of reported cases among 25-34 years old were increasing during 1992 to 1996. At provincial level, the reported cases of TB particularly in central region of Thailand show increasing trend during 1996-1998 (Figure 7). Ratchaburi, Petchaburi and Prachuap Khiri Khan were reported a higher number of TB cases each year and Ratchaburi was the province with the highest reported TB cases among the three provinces.

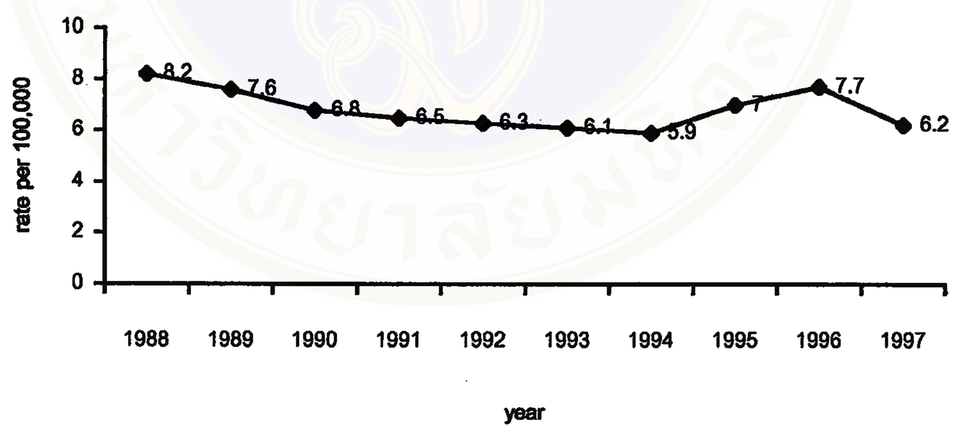


Figure 5 Trend of TB mortality rate per 100,000 population (1988-1997).

Source: Public Health Statistic 1997

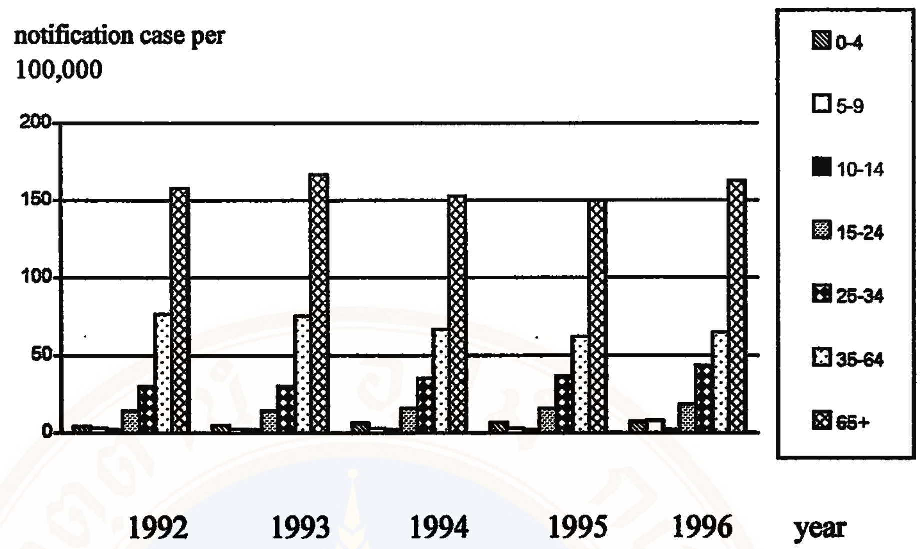


Figure 6 Notification case of tuberculosis per 100,000 population by age-group, Thailand, 1992-1996.

Source: Public Health Statistic, 1996.

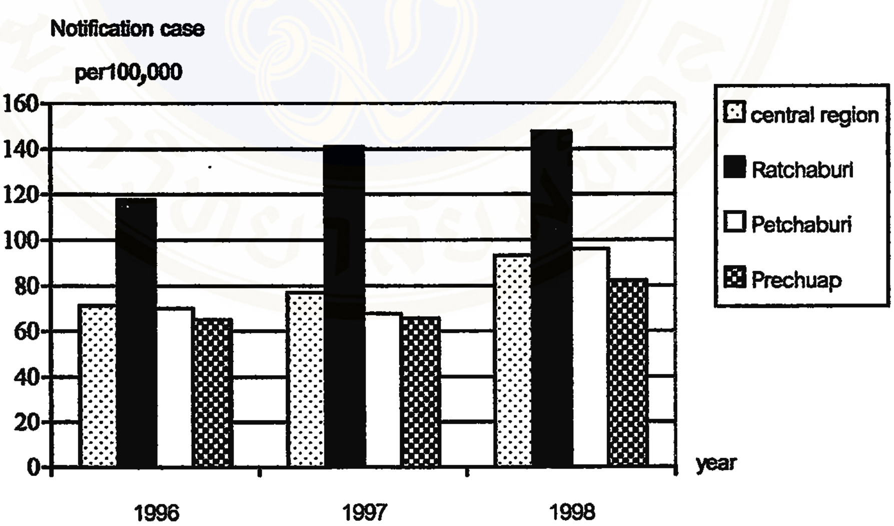


Figure 7 Notification case of tuberculosis per 100,000 population by selected three provinces 1996-1998.

Source: Public Health Statistic 1998

2.2 Tuberculosis controlling programme in Thailand

2.2.1 Self-administered treatment (SAT)

Tuberculosis control in Thailand has been launched by the Department of Health, Ministry of Public Health (MOPH) in late 1949 during which the disease remained one of the leading causes of death. National Tuberculosis Programme (NTP) has been conducted as the special project until 1966 and has been implemented through the existing health facilities since 1967.

In 1982, TB clinic, a technical and managerial system of standard case-finding and ambulatory chemotherapeutic services have been established. A nation wide introduction of 6-8 month short-course chemotherapy (SCC) has been initiated since 1985. The Social Medicine Section (SMS) and the Sanitary-Communicable Disease Control Section (SDC) of province and district hospitals respectively are responsible TB clinics and TB activities of the hospitals. Practically, when respiratory/ TB suspected symptomatic persons visit the hospital they have to be initially screened and investigated by the Outpatient Department (O.P.D) before being diagnosed by the doctors and being transferred to TB clinic. New examinees will be received the results of chest-x-ray and first spot sputum examination on their first day of visiting unless they need to collect two more sputum specimens on the second visit. The steps of rendering services to TB patients in hospital shown in Figure 8.

In SAT strategy, a patient will be received an one month supply of anti-TB drugs and self-administered to taking their anti-TB drugs. The patients visit to district hospital for their drugs refill monthly during 6 months course.

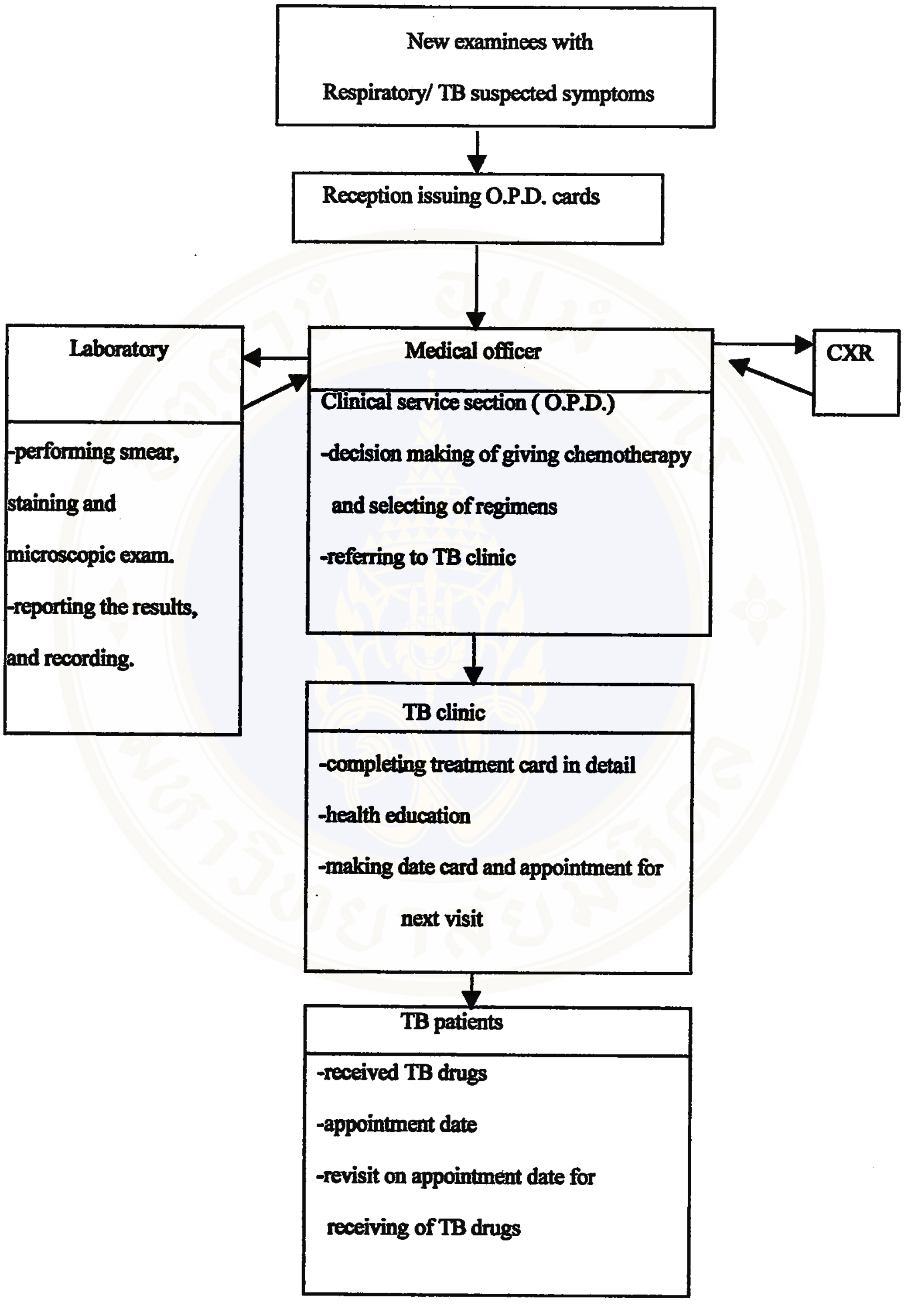


Figure 8 Flow chart showing process of rendering services to TB patients in hospital.

2.2.2 Directly Observed Treatment, Short course (DOTS)

With the notable success of NTP, tuberculosis cases and death declined year after year. Until 1992 because of high HIV burden, the new TB cases began to increase. Essential efforts have been made in order to cope with this situation. The Tuberculosis Programme Review was jointly conducted by MOPH and WHO in 1995 to strengthening the NTP. Weakness of NTP was identified in terms of diagnosis, treatment, recording and reporting system, and needs to be strengthened in line with WHO recommendations. Then, the newly revised control strategy, Directly Observed Treatment, Short-course (DOTS) was originated by NTP in 1996 in Thailand (7). The 5 main components of this strategy are the following (31):

1. Political commitment to give high priority to TB control.
2. Passive case-finding with sputum smear examination by microscopy.
3. Well-organized logistics for TB drugs.
4. Direct Observe Treatment by standardised short-course regimen of chemotherapy.
5. Good programme management based on accountability and supervision of health care workers including the evaluation of full cohort analysis of treatment outcomes.

The success of the DOTS strategy depends on the implementation of government commitment to the NTP. An early case is detected by sputum smear microscopy examination of TB suspects in general health services and a standardised treatment short-course anti-TB treatment regimen between six to eight months, with direct observation for at least the initial two months should be adhered. A regular, uninterrupted supply of all essential anti-TB drugs and monitoring system for programme supervision and evaluation are prudent.

Overall objectives of this strategy are reduction of mortality, morbidity and disease transmission and prevention of the development of drug resistance. By setting objectives at 85% cure rate among detected new cases of sputum smear-positive TB and 70% detection rate among existing cases of sputum smear-positive TB, the impact would reduce half of TB burden within 7 to 15 years.

Directly Observed Treatment (DOT) refers to the TB treatment programme which is assigned for increasing patient compliance rate (31). In DOTS strategy when respiratory/ TB suspected symptomatic persons visit the hospital they have to be initial screened, investigated and treated similar to those in SAT strategy. The difference of both DOTS and SAT are shown in Table1.

2.2.3 Effectiveness of DOTS

Directly Observed Treatment, Short-course is recommended by WHO for controlling TB worldwide. According to WHO reported, cure rate under DOTS was 72.0% global, 70.2% in SEAR region and 78% in Thailand (Table 2). The literature reviews presented that cure rate among new PTB patients under DOTS strategy was 60.0% to 89.7% whereas the cure rate among those under SAT strategy was 52.3% to 75.4%. Moreover, review of the literature shows that DOTS demonstrated effective strategy in all designs either descriptive (22), prospective (27,58,60,61) or retrospective (24,25). Diversity of observers of DOTS strategy such as nurse (22), health worker and health volunteer (23,27) and family member (61,27) indicated similar in the effectiveness of DOTS. The findings of direct observation with incentive

Table 1 The difference of both DOTS and SAT.

Items	SAT	DOTS
1.The patients take medicines	The patients take their medicines without observer.	The observer watches the patient swallowing the medicines. (The observer may be a health worker, health volunteer or family member)
2.DOTS card	No	The observer checks on DOTS card after the patient swallowing the medicines.
3.The patients facilitate	No (the patients are received treatment at the hospital for all course of treatment.)	Yes. The aim is to maximize drug compliance. Treatment will be offered as close to the patient's home (e.g. health center, district hospital) as possible.
4.Home visit of health worker	No	Weekly in the initial phase and monthly in the continuation phase.
5.Evaluation by sputum examination	monthly	At the end of initial phase, at the end of fifth month and at the end of the treatment.

Table 2 Comparison of DOTS treatment outcomes.

	WHO (56) 1996	WHO (56) 1996	WHO (56) 1996	Kamolrat -tanakul, Et al.(57) 1996-1997	Akksilp (27) 1996-1997	Siriwat, et al.(58) 1996-1997	Kungsa-worn, Et al.(59) 1995-1996
Study area	Global	South-East Asia Region	Thailand	Thailand	Yaso-thon Province	Pitsa-nuloke Province	Khon Kaen Province
Design	NA (report)	NA (report)	NA (report)	Random-ised control trial	Prospec-tive	Prospec-tive	Retro-spective cohort
Outcome of DOTS							
*cure	72.0	70.2	78.0	76.1	88.2	66.3	82.4
*complete	6.8	7.0	0.0	7.8	0.0	22.1	0.0
*died	3.7	8.4	4.3	6.3	7.4	3.5	0.0
*fail	5.8	1.8	1.7	1.4	0.0	0.0	0.0
*default	1.3	3.7	2.6	6.5	1.5	7.0	17.6
*transfer	2.7	2.4	1.7	1.9	2.9	1.2	0.0
Compa-rison group	NA (none)	NA (none)	NA (none)	SAT	SAT	SAT	Non-DOTS

NA: Not applicable
DOTS: Directly Observed Treatment, Short course
SAT: Self-administered treatment

(21,25) suggested that DOTS strategy provided a higher effectiveness compared to other strategy. Either daily dose (21) or intermittent therapy (19,22,60) also showed the success of DOTS. We described the studies of effectiveness of DOTS in following section.

Zeng ZF, et al (21) assessed the cure rate of 112,842 Chinese patients with smear positive tuberculosis after implement DOTS countrywide between 1991 and 1994. The findings showed that the cure rate was 89.7% among new patients and 81.1% among relapse cases.

Wilkinson, et al. (23) evaluated a community-based tuberculosis treatment programme involving DOTS in South Africa between 1981 and 1994. Of 2,186 TB patients were registered, 1,903 (87%) received DOTS. Treatment completion was defined as documented proof of taking every dose of six months course under DOTS. The study reported that the completion rate occurred 69%. However, the completion rate could be increased to 85% when transferred out patients were excluded

Neher, et al. (60) evaluated the effectiveness of a three times weekly, DOTS. From January 1990 to December 1993, 771 pulmonary TB and 115 extrapulmonary TB were studied at Katmandu, Nepal. The cure rate was measured as effectiveness of the programmes. They defined a cured sputum positive patient as one who has completed treatment and had two consecutive negative smears and culture at least at the end of treatment. The result showed cure rate of 411 new sputum smear positive patients was 69%.

Even though the results were ranged from 69% to 89.7%, the above studies did not compared effectiveness of DOTS with other programme. Thus results may not be appropriated information for the decision maker to select the alternative programmes.

Weis, et al. (19) compared the outcome of standard therapy with directly observed therapy (DOTS). They reviewed the charts of 988 patients with positive cultures for *Mycobacterium tuberculosis* in Tarrant county from January 1, 1980 through December 31, 1992. Patients who were registered from January 1980, through October 1986 were treated with unsupervised. From November 1986 to December 31, 1992, treatment was directly observed therapy. Relapse rate was measured as the effectiveness of the two strategies. A relapse was defined as a positive culture for *Mycobacterium tuberculosis* in a patient who had previously completed an adequate course of therapy. The results showed that the relapse rate decreased from 20.9% to 5.5% after institution of DOTS. The authors suggested that DOTS led to significant reductions of relapse. However, the data from this study were collected at different period. Its results of comparison may not reflect the actual effectiveness of the two strategies.

Chaulk, et al. (22) evaluated community-based DOTS for tuberculosis control by comparison completion rate in Baltimore with the five major US cities (Atlanta, Miami, Newark, San Francisco and Washington) which had the highest TB incidence in 1981 but which did not have comprehensive DOTS programme. All TB patients who were registered between 1986 and 1991 were analyzed by controlling confounding factors such as AIDS, immigration, unemployment and poverty. From 1986 through 1992, Baltimore' s DOTS had the highest completion rates (90.1%) when compared with the five cities which did not implement DOTS programme (75.4%, 74.0%, 53.6%, 84.6% and 70.8%, respectively). The authors concluded that DOTS could be increased the completion rate. The strength of the study was that the outcomes were compared in the same period with controlling confounders.

Davidson (25) compared treatment completion rates at 8 and 12 months after treatment initiation for new patients with active TB treated with either DOTS or self-administered therapy (SAT). All new TB patients (319 cases) were reported to the Philadelphia Department of Public Health between July 1, 1994 and June 30, 1995. Patients exclusion were those who died during initial hospitalization, patients lost to follow up and never started neither DOTS nor SAT, and patients who crossed over from SAT to DOTS with less than 2 months of missed therapy. The findings noted that at 8 months, 52% of DOTS patients completed treatment compared with 35% of SAT patients. At 12 months, completion rates were 70% for DOTS patients and 53% for SAT patients. Even though the study showed the higher effectiveness of DOTS over SAT but the results were suffered from loss to follow-up.

Alwood, et al. (26) compared the effectiveness of intermittent DOTS with daily SAT. They reviewed 107 charts with TB and HIV infection at Baltimore City between January 1984 and June 1992. Patients who died prior to receiving any anti-TB drugs were excluded. Patients who completed the initial four daily drugs regimen were included. Completion 6 months of therapy was defined as effectiveness of both therapies. The findings indicated that patients who received DOTS were 96% completion rate compared with 76% for SAT. Controlling confounders did not performed. The external factors may be affected the effectiveness of both DOTS and SAT strategies. The results of comparison may not reflect the actual effectiveness of the two strategies.

Previous studies were compared cure rate between DOTS and SAT. In general, DOTS showed the higher cure rate than SAT. However the unblinded randomised controlled trial (62) showed that self-supervised (60%) had more successful outcome than directly observation (54%) in new patients smear positive. That study provided DOTS at a clinic that the patients attend the clinic during working hours (five days a week) in order to take their medication under supervision by clinic nurses. The self-supervised method required patients or their family member to visit the clinic once a week in order to receive TB drugs. The difference in TB case management may lead to difference in compliance between two groups and resulting in this difference in the study findings.

Siriwat, et al. (58) compared treatment outcome between short course chemotherapy (SCC) and DOTS. The samples were 172 new smear sputum positive pulmonary TB patients who were registered at Tuberculosis Center Region 9, Phisanulok, Thailand, during September 1996 to October 1997. The authors randomized patients into 2 groups. Eighty-six cases were treated under DOTS while remaining received SCC. They defined cure rate as effectiveness of the strategy. The DOTS group showed the cure rate 66.3% compared with 52.3% for SCC. However, there were a switch over between DOTS and SAT group during the study period and it may be affected the results.

Kasetjaroen, et al. (61) compared treatment outcome between two strategies, directly observed by family members (DOTS) and another without any observers (non- DOTS). During October 1992 to May 1993, 232 new pulmonary TB with sputum smear positive, negative or culture positive for AFB were registered at Tuberculosis Center Region 12, Yala, Thailand. DOTS group enrolled 120 cases and non-DOTS group were 112 cases. They defined a percentage of patients completed treatment regardless sputum smear result at any time as the effectiveness of both strategies. The authors suggested that DOTS by family members revealed higher completion rate than non-DOTS (90.8% and 80.4%, respectively). Controlling confounder was not conducted. The finding may not reflect the actual effectiveness of the two strategies.

Kungsaworn, et al. (59) compared treatment outcome between regular short course chemotherapy (SCC) and DOTS. New and retreatment pulmonary TB with sputum smear positive (61 and 8 cases, respectively) were registered at Tuberculosis Center Region 6, Khon Kaen, Thailand, during July 1, 1995 to September 30, 1995, designed to SCC group. Those (51 and 15 cases, respectively) who were registered during July 1, 1996 to September 30, 1996, were in DOTS group. The results demonstrated cure rates were 82.4% and 75.4% among the new pulmonary TB in DOTS group and SCC group, respectively. In the retreatment patients, DOTS group showed cured rate 73.3% compared with 87.5% of SCC group. Results of the study should be interpret with caution because the authors compared two strategies in difference period.

Akksilp (27) assessed the ratio of types of observer feasibility of integration DOTS into routine public health and compared treatment outcome between DOTS and SAT. Two hundred and ninety six new pulmonary TB with sputum smear positive, 315 new pulmonary TB with sputum smear negative and 46 new extrapulmonary TB were registered at community and provincial hospital at Yasothon, Thailand, during October 1, 1996 to July 31, 1997. Thirty cases were excluded since they transferred out of Yasothon, 292 cases (44.64%) were treated under DOTS by family members 88%, Those 335 cases receiving SAT. The cure rate was measured as effectiveness among new pulmonary TB with sputum smear positive and completion rate were used among new pulmonary TB with sputum smear negative and extrapulmonary TB. The findings indicated that the cure rate 88.2% for DOTS compared with 56.8% for SAT among new pulmonary TB with sputum smear positive and DOTS achieved more completion rate than SAT among new pulmonary TB with sputum smear negative (73.7% and 69.9%, respectively).

In summary, the reviews of literature showed that DOTS strategy was more likely to provide a higher cure rate than SAT strategy but the magnitude of the difference in both strategies ranging from 7% to 31%.

2.3 Economic evaluation of TB control programme

If resources were not limited, then programme could focus exclusively on determining strategies which achieve the most units of effectiveness, regardless of cost. In tuberculosis control, a primary measure of effectiveness is patient cure. WHO has set a goal of 85% cure rate among detected new smear positive TB cases by the year 2000 (31). As stated previously, resource constraint has directed toward economic evaluation in public health field. Tuberculosis control programme may be needed to conserve resources which could be used in alternative programmes in public health. Besides, budget constraints during economic recession could reduce amount of funding for tuberculosis control thus how we can achieve the same or greater cure rate given limited resources.

Thus far, the evidence in favour of DOTS strategy reflects as increasing cure rates. However, additional cure rates may expensive for achieving. Given the growing pressure on scarce health care resources, there is an increasing interest in the application of economic evaluation. The management of Tuberculosis control programme may need to evaluate using cost-effectiveness analysis.

Cost-effectiveness analysis (CEA) is a form of full economic evaluation, where both the costs and consequences of health programmes or treatments are examined (63). A cost-effectiveness study involves assessing the gains (effectiveness) and resource input requirements (costs) of alternative ways of achieving a specified objective. The results are usually expressed in terms of cost per unit of effectiveness for each alternative. The alternative with the lowest cost per unit of effectiveness is the most cost-effective and is generally to be preferred on grounds of economic efficiency (64). CEA is recognized as a necessary and useful tool to determine optimal resource allocation within the health field. Not only does cost-effectiveness require less computation but it requires fewer assumption concerning intangibles which tend to be concentrated on the benefit side (65).

A wide variety of issues can be examined in cost-effectiveness studies, for instance, choices of technology, choices of delivery strategy, and choices of target. Although the issues addressed and the programme involved can be quite diverse, there are five steps that are required for every cost-effectiveness analysis such as 1.defining the programme's objectives, 2.identifying the possible ways of achieving those objectives, 3.identifying and measuring the costs of each option, 4.identifying and measuring the effectiveness of each option, 5.calculating the cost-effectiveness of each option and interpreting the results. All of five steps are described in the following sections.

2.3.1 Identify, measurement and valuation of resources

<u>A. Definition of cost</u>

There are two different approaches in performing cost analysis. The first is accounting (financial) cost and another method is economic cost.

According to Horngren and Sundem (66), accounting costs are measured by the monetary units that must be paid for goods and services and it was suggested by Coltman that accounting costs could be recorded on income statements (67).

On the other hand, Reynolds (68) stated economic cost includes the market price of purchased factors and the imputable cost of producer-owned factors and it was noted by Amacher and Ulbrich (69) that economic cost is the summation of the explicit (accounting) costs and the implicit or opportunity costs.

Likewise, Creese and Parker (64) declared financial cost is the cost in term of money paid for resources used, while economic cost is cost of using resources that could have been productively used elsewhere.

Cost in term of accounting cost is measured by money paid for resources used while economic cost is summation either accounting or opportunity cost.

B. Cost classification

Coltman , Reynolds and Drummond, et al. (67,68,63) classified cost into two types, "Fixed costs" are costs which do not vary with the quantity of output about one year whereas "Variable costs" are costs which vary with the level of output.

Horngern and Sundem (66) suggested to group cost into direct and indirect cost. Direct costs can be identified specifically and exclusively with a given cost objective in an economically feasible way. On the other hand, indirect costs cannot be identified specifically and inclusively with a given cost objective in an economically feasible way.

Creese and parker (64) group cost into two categories. Recurrent costs refer to resources that are used up in the course of a year such as personnel, supplied and maintenance. While capital costs refer to resources that are used longer than one year such as buildings, vehicles and equipment.

Drummond, et al. (63) distinguished costs into three categories. 1.Cost of organizing and operating the programme. 2.Costs are borne by patients and their families. These are included any out-of-pocket expenses incurred by patients and/ or family members as well as the value of any resource that they contribute to the treatment process. Patients and/ or family members may be absent from work while seeking treatment or participating in a health care programme. The anxiety and pain associated with treatment itself are also constitute a form of psychic cost. 3.Costs are borne externally to the health sector, patients and their families.

Kamol-Rattanakul and Kaewsonthi (70) classified cost into different groups depending on the basis of classification.

1. Costs could be classified by the way in which costs are incurred. Internal costs are the costs that are incurred by the organization or the institute providing the health care service whereas external costs are those costs incurred outside of the health care provider, such as time and travel costs for the patients, their relatives, and the community as a whole.

Classification of cost in this fashion is very important in health care planning and its policy because it is necessary to take both internal and external costs into consideration for resource allocation with reference to efficiency and equity concerns.

2. Costs can be categorized into two classifications with reference to "activities" which are happened internal and external to the organization. Direct costs

are the costs that are spent directly on the activities while indirect costs are those costs that are not spent directly on activities. The concept of indirect costs can be reflected by the economic value of any consequence that can not be counted as a direct cost.

3.Costs can be classified by "expenditure" on activities can be divided into two classifications further. Explicit costs (tangible costs) are the actual costs forgone in an activity and are measured in terms of money. On the other hand, implicit costs (intangible costs) are normally not measured in terms of money due to lack of market transactions. Implicit costs are determined in terms of utility, which is the basic of measure of economic well-being. For example, rational people may prefer to avoid grief, anxiety, frustration and pain. Therefore, these items are known as intangible costs. In the context of health care, "intangible costs" are particularly relevant as they enter into the assessment of many health care alternatives. The importance of intangible costs may vary according to the type of illness or treatment and to the importance attached to the viewpoint of the patient and his or her family. For example, delay and anxiety may affect the patient or his/ her employer, but do not affect the costs of the hospital.

4.Classification cost in term of medical and non-medical costs. Medical costs are those costs which are involved medical treatment and medical care, such as hospitalization, drug, physician fees, laboratory tests, x-ray procedures, etc. On the other hand, non-medical costs are the costs that are not incurred directly by the medical treatment, such as administration, food, transportation, clothing, etc.

There are some specific points when estimating costs for the purpose of cost-effectiveness analysis. For one thing, the cost and effectiveness measure must be linked for each alternative studied. The resources should be responsible for producing the effects. The costs and the effectiveness should be measuring over approximately the same period of time.

In this study, cost was categorised into provider cost and consumer cost particularly direct cost. The provider cost was distinguished into routine service cost and medical care cost.

Direct cost of patients service unit is summation of labour cost, material cost and capital cost.

Total direct cost = labour cost + material cost + capital cost.

C. Measuring and Valuating Capital Costs (64)

There are two methods for measuring and valuating capital cost.

1. To annualize the initial capital outlay over the useful life of the asset, the method must incorporate both depreciation aspects and the opportunity cost. The annual economic value is based on a) the replacement cost of the capital item (its price in the year for which costs are measured), b) its expected useful life year, c) opportunity cost for investing money in capital assets (reflected by the interest or discount rate).

2. Where market rates exist, they may be used to estimate capital cost, for example in the rental of buildings or leasing of equipment. This method also incorporates both the depreciation and the opportunity components of cost.

Our reviews indicated that, Floyd, et al. (28) calculated capital cost concerning expected useful life (5 years for a vehicle, 10 years for equipment and 30 years for building) and discount rate of 8%. Moore, et al. (29) used secondary source to estimate capital cost and its were based on 1994 annual rate. Likewise, Burman, et al (20) estimated hospitalization charge from secondary source but did not present capital cost calculation. Snyder (71) used straight-line depreciation with 3% discount rate to estimate building cost. In this study, estimating rental cost was used in order to value capital cost that this method incorporates both the depreciation and the opportunity components of cost.

D. Measuring and Valuating Labour Costs (64)

Salaries, wages and other expenses associated with personnel are frequently the single largest cost item in health programs. In most cases, it will be both the staff directly involved in the activities (e.g. nurses, health aids, trainers, supervisors) and other support staff (e.g. managers, cleaners, guards, drivers). The assessment will deal only with costs of the persons whose time, in whole or in part, are assigned to the program.

The full cost of employing someone is represented by an individual's gross earnings that is, the take-home pay plus any additional benefits, such as contributions to health insurance, social security and pension plans, overtime, hardship bonuses, holiday and sick pay, and allowance for uniform, housing and travel. If the worker receives any additional commodities such as housing or other non-monetary benefit, the value of these should also be estimated by using the prevailing prices of similar items. Fees or honoraria for short-term services of experts, advisors and others involved in the activity, who are not employees, should also be included.

From review of the literatures for TB studies, Floyd, et al. (28) used Gross salaries to calculate staff cost but labour cost of non-health worker was negligible.

Moore, et al. (29) valuated labour cost as salary and fringe benefits of registered nurse, licensed practical nurse, radiology technician and physician allocated to each patient by using 2,080-hours work year and the amount of time spent with each patient. Burman, et al (20) estimated personnel costs by using the current costs at the Denver Metro Tuberculosis Clinic and monitored staff visits at the clinic to estimate the nursing time. The cost of physician time was estimated using the salary and fringe benefits for a physician in the Denver Health and Hospital System. Snyder (71) did not present the details of labour cost. In this study, labour cost included salary and fringe benefits of physician, nurse, TB staff and health worker. Additionally, labour cost of health volunteer was accounted using standard minimum wage.

E. Measuring and Valuating Material Costs (64)

Supplies are materials used in the course of the year, as direct inputs to the principle activities performed by the program and other small items purchased during the year such as drugs, reagents for tests, needles, slides and stationery, etc. Supplies comprise a fairly large cost category for the program equipment is categorized separately. The difference between supplies and equipment lies largely in cost. For example, if the unit price of an item is less than 1,000 baht (or some other value) in spite of its utility is lasts for longer than one year, it would be simpler to allocate it in the recurrent input category for supplies. If the price of item is 1,000 baht or higher, then the capital cost category-equipment would be more appropriate to use.

The full costs of supplies should include the cost of transport to the point of use (i.e. any freight charges for import of materials and any internal distribution costs). The cost should include all the material consumed, including any item that is lost or wasted as well as the actual used for its intended purpose. Supply invoices, order forms, price lists and catalogues are sources of information about purchase or replacement prices.

In TB studies, Floyd, et al. (28) classified material cost in term of drugs, AFB, CXR and travel cost. Moore, et al. (29) and Burman, et al. (20) used many secondary source to estimate cost of drugs, AFB and sputum culture, complete blood counts, blood chemistry, CXR and travel cost. Snyder (71) did not present the details of material cost. In this study, cost of anti-TB drugs, other drugs related to TB, CXR, AFB, sputum c / s and travel cost were define as material cost, however, the cost of other laboratory investigation did not included.

F. Method for assessing present value (70)

Costs were adjusted for differential timing because more resource outlays occur earlier as capital expenditures. This is done by converting the initial purchase price into annual cost equivalent using the discount rate. This approach is the most convenient for a number of programme comparisons. In practice it is usually admissible to select a central best estimated discount rate:

1.consistent with economic theory (2% to 10%),

2.include any government recommended rates (5%, 7%, 10%),

3.include rates that have been used in other published studies to which you might wish to compare results (3% to 10%),

4.be consistent with current price.

Assessing value in the review of TB studies, Floyd. Et al. (28) and Snyder (71) used 8% and 3% of discount rate, respectively. Moore, et al. (29) and Bueman, et al. (20) adjusted charges to equivalent value by using Consumer Price Index. In this study, using 3% interest rate adjusted a cost of AFB CXR and sputum c / s to equivalent value in 1999.

2.3.2 Identify and measurement the effectiveness

Effectiveness or effects are outcomes that are not express in financial terms, such as the number of lives saved. Effectiveness is a measure of the extent to which objectives are achieved. There are a number of indicators or measures of effectiveness that reflect " intermediate " changes rather than " final " outcomes such as cure rate and death averted. Major advantage is the relative case with which they can be measured and interpreted. Even when the final health status data are not available, these intermediate measures can give some indication of the results. Measuring changes in health status is a difficult and expensive task.

Floyd, et al, (28) and Burman, et al. (20) chose cure rate of TB patients as the measure of effectiveness. Moore, et al (29) defined effectiveness outcomes such as completion therapy, cure, relapse and death from TB. Snyder (71) defined sick leave as the measure of effectiveness. In this study, the cure rate was defined as the measure of effectiveness of both DOTS and SAT strategies.

2.3.3 Uncertainty in cost-effectiveness analysis

Sensitivity analysis is the process of testing how changes in assumptions affect changes in results (63). Univariate sensitivity analysis is the traditional approach to sensitivity analysis. It is examined one variable at a time. The analyst must choose which variables to vary, the amount of variation around the base value of the parameter. Thus the results of the sensitivity analysis depend on many subjective choices by the analyst.

The following procedure was suggested for conducting sensitivity analysis.

1.Consider which of the estimates made in the analysis are available and informed guesses (e.g. the effectiveness of new and unproven, medical procedures), imprecision in the estimation procedure (e.g. hospitalization costs based on average) and methodological controversy or the potential for different value judgments (e.g. the choice of discount rate).

2.Set upper and lower bounds on the possible range of estimates. Depending upon the source of uncertainty or debate surrounding the estimation. This might be done by considering empirical evidence from other research studies, current practice in the literature or soliciting judgments from those who will determine based on the cost-effectiveness study.

3.Calculate study results based on combinations of the "best guess", "most conservative" and "least conservative" estimates of the variables concerned.

Burman, et al. (20) examined one-way sensitivity analyses and consider which of cost and failure rate to vary in sensitivity analyses. Moore, et al. (29) varied completion rate, cure rate and cost to analyse sensitivity analyses. Snyder (69) determined two scenarios for implementing DOTS either 1. A staff travel to the patient' s home to observe drugs intake, or 2. The patient travel to TB clinic three times weekly. In this study, sensitivity analyses were performed by varying labour cost, travel cost and cure rate.

2.3.4 Cost-effectiveness of DOTS studies

Table 3 and 4 provide methodological aspects and results of cost-effectiveness of DOTS from reviews of the literature.

For cost elements item, The difference in cost components among the studies may lead to difference in the study findings. Floyd, et al. (28) divided costs into 3 sectors: provider cost, patient cost and community cost. The provider cost consisted of direct and indirect of inpatient, outpatient and health clinic. The travel cost comprised travel cost and time cost. The community cost (cost income by health volunteer) were considered by the author to be nil. The study may be underestimated provider cost in which neglect the loss of income among health volunteers. Estimated costs were used in decision analysis (20,29). Burman, et al. (20) calculated only direct provider cost and patient time cost that mean earnings per day worked. Moore, et al. (29) conducted only direct cost of treatment of TB. Estimated costs of both strategies may not reflected the real cost of DOTS. Finally Snyder (69) used cost that differ between DOTS and SAT strategy which included direct and indirect provider cost and patient travel cost that reflected the different cost.

For outcome measure item, the difference in outcome measure among the studies may lead to difference in the study findings. Floyd, et al. (28) calculated cost effectiveness in three steps. First, the proportion of patients who completed treatment was multiplied by the cost of a patient completing treatment. Second, the cost of a patient not completing treatment was multiplied by the proportion of patients who did not completed treatment. Third, the resulting two cost were summed and divided by a number of patient cured. The cost per patient cure in that study may be underestimated

Table 3 The cost-effectiveness of tuberculosis treatment: methodological aspects.

	Floyd, et al. (28) 1996,South Africa	Moore, et al. (29) 1995,USA	Burman, et al. (20) 1996, USA	Snyder (71) 1997, Poland
Outcome measure	Cost per case cured, bed requirements in comparison with bed availability	Cost per relapse averted, cost per life save	Cost per patient cured including cost of treating failures of initial treatment	Saving cost
Patient population	Adult patients with new case of TB on smear testing	NA	Active TB cases	Pulmonary TB with culture positive and negative, and extrapulmonary
Effectiveness data source	Annual reports from Malawi 1989-1993,audits of Hlabisa 1991-1994	Literature review	Literature review	Poland Tuberculosis Treatment Programme
Cost elements	Health system, patients, community	Diagnosis, hospitalization, drugs, visits	Diagnosis, hospitalization, drugs, visits, patient	Diagnosis, hospitalization, drugs, visits, patient, sick leave
Cost data source	Interview, hospital pharmacy price list,1996 purchase price	Literature review, Baltimore City Health Department	Denver Metro Tuberculosis Clinic, monitoring staffs	Ministry of Health, Poland, estimating cost
Discount rate	Cost 8%	Cost 4%	Cost 5%, 8%	Cost 3%
Sensitivity analysis	NA	Completion rate, the drug-resistant TB rate, cure rate, cost	Cost, failure rate, proportion of treatment failure acquiring multidrug resistance	A number of the patient visit to local clinic, health worker hired to administer DOTS in patient home

NA: not available, DOTS: directly observed treatment, Short course, SAT: Self-Administered treatment,

FDCT: fixed-dose combination therapy

Table 4 The cost-effectiveness of DOTS : results and conclusions

	Floyd, et al. (28) 1996, South Africa	Moore, et al. (29) 1995, USA	Burman, et al. (20) 1996, USA	Snyder (71) 1997, Poland
Baseline results	Cost per case cured • DOTS: $ 890.50 • Conventional - best case: $ 2095.60 - worst case: $ 3700.40 bed requirements • DOTS: 47 beds • Conventional: 160 beds The numbers of beds for tuberculosis treatment in Hlabisa is fixed at 56.	Cost per relapse averted • DOTS: $ 14,378 • FDCT: $ 15,446 • Conventional: $ 17,305 Cost per life saved • DOTS: $ 13,966 • FDCT: $ 14,068 • Conventional: $ 15,200	Cost per case cure - tuberculosis control programme DOTS: $ 1,487 • SAT: $ 2,929 - health-care system • DOTS: $ 2,947 • SAT: $ 13,328 -health care system including patient time cost • DOTS: $ 4,232 • SAT: $ 15,401	Decrease in number of bed-days of inpatient are savings 136,080 zlote per year.
Sensitivity analysis	NA	" the marginal cost-effectiveness of DOTS relative to FDCT was most sensitive to variability in the direct cost of DOTS and less sensitive to relapse rates for DOTS and FDCT. "	" DOTS was less expensive than SAT through a wide range of cost estimates and clinical event rates. "	When patient travel to local clinic, incremental cost of implementing fully DOTS for 90% of patients saved 3,626 zlote per year (included reduced sick leave) and 50,546 zlote per year(excluded reduced sick leave). When health worker hired to administer DOTS in patient' home saved 30,854 zlote and 16,066 zlote per year (included and excluded reduced sick leave, respectively).
Author (s) conclusion	" DOTS is cheaper, more cost-effectiveness and more feasible than conventional treatment in managing tuberculosis. "	" Both DOTS and FDCT were cost-effectiveness to conventional therapy, although DOTS is probably most cost-effectiveness. "	" Despite its greater initial cost, DOTS is more cost-effectiveness strategy than SAT because it achieves a higher cure rate after initial therapy"	" The implementation of new strategy DOTS could save the government a significant amount of resource. "

NA: not available, DOTS: directly observed treatment, Short course, SAT: Self-Administered treatment, FDCT: fixed-dose combination therapy as it did not included cost of patient who died or lost during treatment. Whereas Burman, et al. (20) used cost saving to consider advantage of DOTS. They calculated cost saving as cost of initial therapy plus cost of therapy of patient who failed therapy. Finally, total cost of DOTS minus cost of SAT. Since this method was practical due to the availability of rational level therefore information may be appropriate for politician decision. Moreover, Snydar (71) addressed cost saving of reducing sick leave and this may provide additional information for policy makers, Moore, et al. (29) suggested cost per relapse averted and cost per life saved. These are advance measure of cost effectiveness that avoiding relapses has important public health implication for reduction of new case of TB. However, using cost per relapse averted and cost per life save may need more time and resource to conduct this type of economic evaluation.

For cost data source item, all of four studies were used secondary source to estimating costs. Using secondary source may lead to overestimate or underestimate of costs.

In summary, a review of the literature revealed that there were a vast differences in the technic of cost effectiveness analysis. For instance, there were either a primary measure of effectiveness such as patient cure or advance measure such as cost per life save. Its cost was determined by estimation from previous studies or secondary data. Therefore, these methods could not reflect the actual cost incurred during treatment. In this present study, cost-effectiveness between DOTS strategy and SAT strategy were compared. The intermediate outcome, cured rate, was defined as the effectiveness of both DOTS and SAT strategies. The study findings would provide useful information for comparison of resource requirements for delivery of the TB service and guide public health policy.

CHAPTER III

MATERIALS AND METHODS

3.1 Research design

The present study is a retrospective cohort study.

3.2 Study area and population

This study had been conducted in Phetchaburi, Ratchaburi and Prachuap Khiri Khan where are similar in geographical and socioeconomical characteristics such as occupation, average household size, income and expenditure (72).

New pulmonary tuberculosis (PTB) patients with smear-positive tuberculosis who were registered in TB registers at the community hospitals in Petchaburi, Ratchaburi and Prachuap Khiri Khan from October 1, 1998 to March 31, 1999.

3.2.1 Exposed group

New PTB patients with sputum smear positive who were treated under Directly Observed Treatment, Short course (DOTS). The patients were registered in TB registers at the community hospitals in Petchaburi, Ratchaburi and Prachuap Khiri Khan where the exposed was allocated from October 1, 1998 to March 31, 1999.

3.2.2 Nonexposed group

New PTB patients with sputum smear positive who were treated under self-administered treatment (SAT). The patients were registered in TB registers at the community hospitals in Petchaburi, Ratchaburi and Prachuap Khiri Khan where the nonexposed was allocated from October 1, 1998 to March 31, 1999.

3.2.3 Inclusion criteria

1.Outpatients at age 15 years or more with regardless of HIV status.

2.Treatment regimen was category I.

3.Exposed cases were treated under DOTS and were supervised for checking DOTS cards and daily packages.

4.Nonexposed cases were treated under SAT and were not being observed TB medicine taking.

3.2.4 Exclusion criteria

1.Patient who was pregnant.

2.Patients who were diagnosed renal failure or liver disease.

3.Patients who are foreigner.

4.Patients who were diagnosed PTB with tuberculosis of other organs.

5.Patients who were treated under SAT in DOTS area.

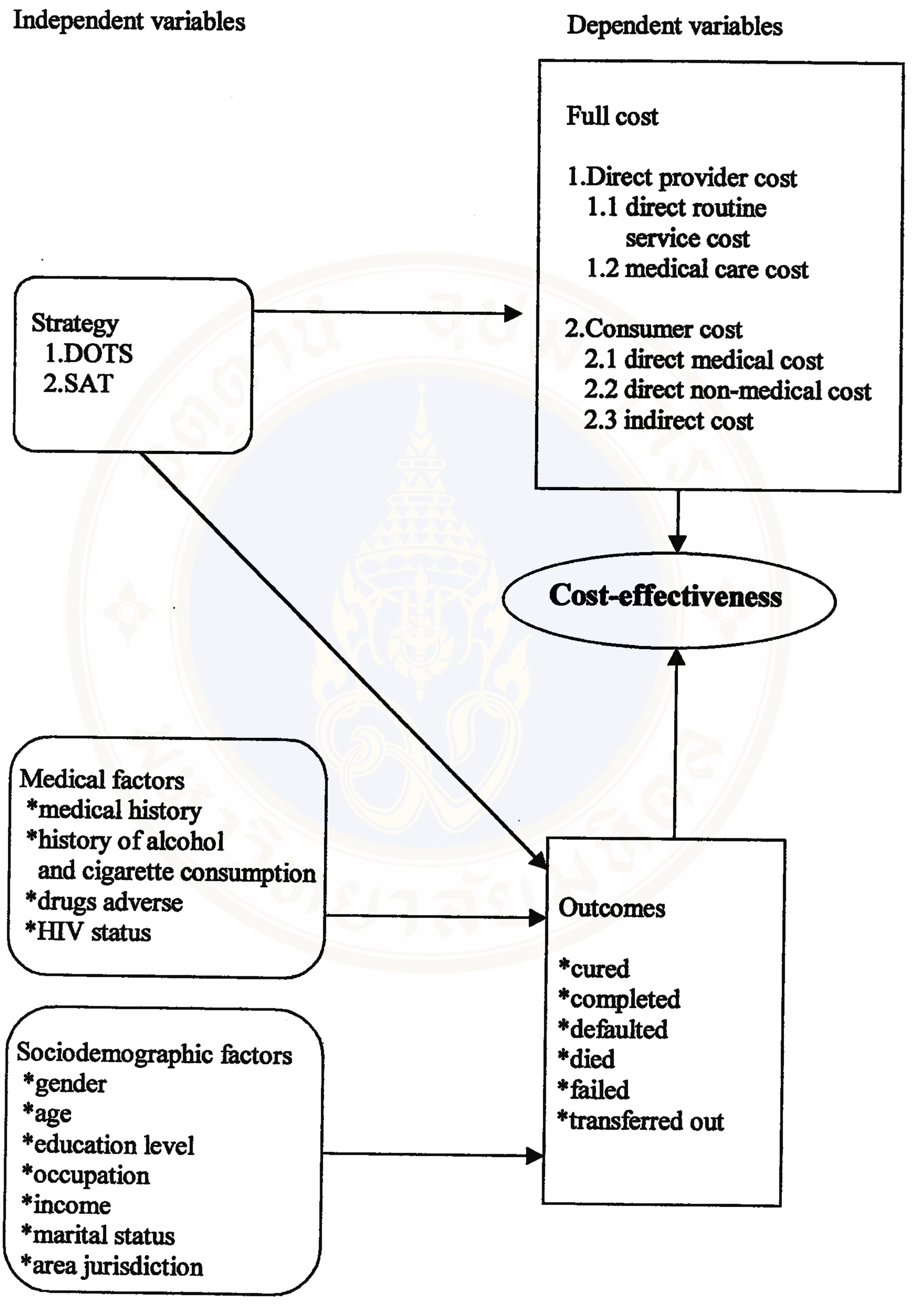


Figure 9 Conceptual framework

3.3 Instruments

The instruments were comprised of 3 main parts.

Part 1. The questionnaire and the records about the patient and their relative were included the following information (Appendix A):

- sociodemographic
- medical history
- history of alcohol and cigarette consumption
- expenditures of transportation, other drug, laboratory test and CXR
- time spent for travelling, waiting and receiving treatment.

Part 2.The records about treatment (Appendix C).

Part 3.The cost form was comprised of 3 different forms (Appendix D).

3.1 capital cost form

3.2 material cost form

3.3 labour cost form

3.4 Methodology

Costs data were collected retrospectively from financial records of fiscal year 1999. Treatment outcomes were collected from treatment card (TB 01) and medical record from October 1, 1998 to November 30, 1999. Characteristics and other data were collected prospectively through interviewed patients, their relatives, health volunteers and health staffs. These data were collected from June 15, 1999 to November 30, 1999.

In this present study, cost was included direct cost of provider and consumer cost. The patients were received diagnosis PTB at inpatient departments or outpatient departments and the procedures were similar in both DOTS or SAT strategies. Then the comparison of two strategies would start after initial diagnosis of PTB with regardless the cost of an initial investigation process.

Identification of costs was classified in direct provider cost and consumer cost. The direct provider cost consisted of direct routine service cost and medical care cost. The direct routine service cost meant that a cost of patient service unit [outpatient department (OPD), sanitary-communicable disease control section (SDC) and health center (HC)] that comprised of labour cost, material cost and capital cost. Table 5 demonstrates details of direct provider cost. The consumer cost was classified into 3 categories – direct medical cost, direct non-medical cost and indirect cost (Table 6).

Actual monetary costs were used in this study and the costs were presented in baht. Opportunity cost of time spending for travelling, waiting and receiving treatments was measured in the monetary unit.

The study used cost of sputum examination, sputum culture and sensitivity (c/s), and chest X- ray from Singdong (32), then its present value used Consumer Price Index for calculation.

Table 5 Direct provider cost.

Identification of cost	Cost measurement	Measurement unit
<u>Routine service cost</u> (OPD, SDC, HC) 1.capital cost -building	-estimated rental cost per month	-time used for TB patient
2.material cost -electricity and water -travel cost	-estimated cost per month -public transportation charge	-time used for TB activities -number of visits
3.labour cost -physician, nurse, TB staff and health worker -health volunteer worker	-actual salary and all fringe benefits -minimum standard wage	-time devoted to TB patient -time devoted to TB patient
<u>Medical care cost</u> 1.cost of sputum exam 2.cost of CXR 3.cost of sputum c/s	} cost per test from other study (32)	} number of test
4.cost of TB drugs	-cost per unit	-unit used
5.other drugs related to TB (included only paid by provider)	-estimated from prescription dose written in medical records and price charge of each hospital	-unit used

Table 6 Consumer cost

Identification of cost	Cost of measurement	Measurement unit
1.Direct medical cost		
-other drugs related to TB (included only paid by consumer)	- estimated from medical records and price charge of each hospital	-unit used
2.Direct non-medical cost (patient and relative)		
-travel cost	-public transportation charge	-number of visits
3.Indirect cost (patient and relative)		
-time cost (translated into monetary)	-standard minimum wage	-time spend for travelling, waiting and receiving treatment

3.5 Data collection

1.Assess information of new PTB from TB registers at community hospitals in Petchaburi, Ratchaburi and Prachaup Khiri Khan from October 1, 1998 to March 31, 1999.

2.Interviewed patients and their relatives at their residence about sociodemographic, medical history, risk behaviors, cost of travelling and treatment, time spent for travelling, waiting and receiving treatment. If the patient died or absence, information collected from the next of kin (Appendix A).

3.Interviewed health staff (doctor, nurse, TB staff, health worker and health volunteer) about time devoted to TB activities, travel cost of visiting and supervision, an estimated rental cost, electricity and water of their workplace (Appendix D).

4.Labour cost data were collected retrospectively through reviewing financial records of fiscal year 1999.

5.Cost data of other drugs related to TB were collected retrospectively from prescription doses written in medical records and using price charge of each hospital.

6.Assess information of outcomes from treatment card (TB 01) and medical records (Appendix C) from October 1, 1998 to November 30, 1999.

3.6 Outcomes measurement

Outcomes were determined by sputum smear under microscopy at the end of the fifth month and at the end of the treatment course. The laboratory staffs were blinded to the type of strategies that the patient had been received. The outcomes were classified into 6 categories:

1 Cured: initial sputum smear positive patient who completed treatment and had negative sputum smear results on at least two occasions during the continuation phase, including one at completion of treatment.

2 Completed: initial sputum smear positive patient who completed treatment with only one negative sputum smear result at the fifth month in the continuation phase and no sputum result at the end of treatment.

3 Defaulted: a patient who was loss to follow up for two consecutive months after registration.

4 Failure: initial sputum smear positive patient who remain smear positive at least 5 months after the start of treatment or at the end of the treatment.

5 Died: patient who died during treatment, irrespective of cause.

6 Transferred out: patient who had been transferred to another reporting unit and for whom the treatment outcome is not known.

The measurement outcomes of this study would be classified into 2 categories: cure and not-cure such as completed, defaulted, failure, died and transferred out.

In addition, sensitivity analyses were classified outcomes into 2 groups

1.success refers to patients cured and completed

2.unsuccess refers to patients defaulted, died, failure and transferred out.

3.7 Sample size and sampling method

Sampling frame

A list of new PTB outpatient with sputum smear positive at age 15 years old or more regardless of HIV status and were registered in TB register at community hospitals in Petchaburi, Rachaburi and Prachuap Khiri Khan between October 1, 1998 and March 31, 1999.

All patients who were registered in TB registers at community hospitals in Petchaburi, Ratchaburi and Prachuap Khiri Khan between October 1, 1998 and March 31, 1999 were included in the study. The sample size was calculated based on equation (73) below:

$$n_1 = \frac{(Z_{\alpha/2} + Z_\beta)^2 \times \bar{P}\,\bar{Q} \times (r+1)}{(p_1 - p_0)^2 \times r}$$

n_1= number of exposed group = 1

n_0= number of comparison group = 1

$Z_{\alpha/2}$= value of 1-α (α=5%, $Z_{\alpha/2}$=1.96)

Z_β =value of 1-β (β=20%, Z_β=0.84)

p_1 =proportion of cured rate in exposed group=0.48 ,0.66 (unpublished data based on Petchaburi and Prachuap Khiri Khan's treatment outcome 1998 ,respectively)

p_0= proportion of cured rate in comparison group=0.30 ,0.46 (unpublished data based on Petchaburi and Prachuap Khiri Khan's treatment outcome 1998 ,respectively)

$r = n_0 / n_1 = 1$

$\bar{P} = \frac{p_1 + r\, p_0}{1 + r}$ = 0.39 (Petchaburi), 0.56 (Prachaup Khiri Khan)

$\bar{Q} = 1 - \bar{P}$ = 0.61 (Petchaburi), 0.44 (Prachuap Khiri Khan)

N_1=77.07 (Petchaburi), 96.50 (Prachuap Khiri Khan)

Then, this study were based on data of Prachuap Khiri Khan and the sample size is 97 subjects in each group.

3.8 Data analysis

3.8.1 Costing analysis (70)

In this study, costs were calculated as follow;

1.Total capital cost = capital cost of OPD + SDC + HC

capital cost = (A x B/ C) x D

A = rental cost per month

B = proportion of time devoted to TB activities

C = numbers of visiting of TB patient per month

D = number of visiting OPD/ SDC/ HC of each patient

2.Total material cost = cost of electricity and water of OPD, SDC, HC + travel cost of staff

cost of electricity and water = (A x B / C) x D

A = cost of electricity and water per month

B = proportion of time devoted to TB activities

C = numbers of visiting of TB patient in TB clinic per month

D = number of visiting OPD/ SDC of each patient

travel cost of staff = A x B

A = travel cost of each patient per visit (using public transportation charge)

B = number of visits

3.Total labour cost = labour cost of doctor + nurse + TB staff + health worker + health volunteer

labour cost of doctor / nurse = (A x B / C) x D

A = average salary of doctor/ nurse per month

B = proportion of time devoted to TB activities

C = numbers of visiting of TB patient per month

D = number of visiting OPD/ SDC/ HC of each patient

This calculation assumed that health worker had 20 workdays per month and 8 hours per day.

labour cost of health volunteer = (A x 130/8) x B

A = time devoted for each TB patient per visit

B = numbers of visit to each TB patient

This calculation assumed that health volunteer worked 8 hours per day and minimum standard wage at Petchaburi, Ratchaburi and Prachuap Khiri Khan was 130 baht per day at 1999.

4. Total direct routine service cost = total capital cost + total material cost + total labour cost

5.Total medical care cost = cost of sputum examination (AFB) + cost of CXR + cost of sputum c/s + cost of TB drugs + cost of other drugs related to TB

total cost of AFB/ CXR/ sputum c/s = A x B

A = number of test

B = unit cost of AFB/ CXR/ sputum c/s used the cost of previous study (157.35,153.74,557.90 baht respectively) its present value used Consumer Price Index (CPI) at 1999 for calculation and following formula was used :

$$C_n = \frac{C_o \times CPI_n}{CPI_0}$$

C_n = the value in year n

C_o = the value in year 0

CPI_n = Consumer Price Index in year n (122.1)*

CPI_n = Consumer Price Index in year 0 (105.8)*

* source: http:// www. moc. go. th (as of April 2000)

Then, this study cost of AFB/ CXR/ sputum c/s = 180.95, 176.80, 641.59 baht respectively.

cost of TB drugs = A x B

A = number of consumer

B = unit cost

The unit cost of TB drugs quoted from Tuberculosis Control Division at 1999 as follow:

Isoniazid (H) = 0.065 baht/ tab

Pyrazinamide (Z) = 2.53 baht/ tab

Rifampicin (R) 300 mg = 4.95 baht/ tab

Rifampicin (R) 450 mg = 8.25 baht/ tab

Etyhambutal (E) = 1.692 baht/ tab

Streptomycin (S) 1 gm = 9.90 baht/ gm

cost of other drugs related to TB = A x B

A = number of consumer was collected from medical records.

B = price charge of each hospital

In this case, if the patient did not pay for other drugs related to TB were included in medical care cost of provider.

6. Total direct provider cost = total direct routine service cost + medical care cost

7. Total consumer cost = direct medical cost + direct non-medical cost + indirect cost

direct medical cost = A x B

A = number of consumer was collected from medical records.

B = price charge of each hospital

direct non-medical cost = A x B

A = number of visits

B = travel cost per visit which used public transportation charge

Direct non-medical cost was summation of travel cost of patients and their relatives.

indirect cost = A x B

A = number of visits

B = time cost were translated time spent for travelling, waiting and receiving treatment into monetary by using the minimum standard wage (130 baht per day) and the calculation assumed that the patients and their relatives worked 8 hours a day.

Indirect cost was summation of time cost of patients and their relatives.

8. Full cost = total direct provider cost + total consumer cost

9. Average cost = Full cost / number of patients registered

10. $$\text{Effectiveness (cured rate)} = \frac{\text{number of patients cured x 100}}{\text{number of patients registered}}$$

11. Cost-effectiveness = Full cost / number of patients cured

3.8.2 Analysis of the baseline characteristics of the two groups

1.Univariate analysis was done to describe the characteristics of each group, as follows:

1.1 For continuous variables, such as age and income, etc. The means and standard deviations were obtained.

1.2 Description of the discrete variables, such as marital status, gender, occupation, level of education, medical history, etc. were accomplished by showing their respective frequency distributions and percentages.

2.Characteristic and medical history of TB were grouped into 2 groups as following criteria:

- gender

  1.male 2.female

- age (reference 5)

  1. 35+ years 2.15-34 years

- patient income (average income of each province quoted from reference 68)

  1.average or lower 2.higher than average

- resided under jurisdiction

  1.no 2.yes

- marital status

  1.single, widow, separated 2.couple

- education level

  1.primary school or lower 2.secondarty school or higher

- occupation

  1.unskilled group (labour, agriculture, fisherman, housework)

  2.other (government official, commerce, student, monk, unemployed)

- additional drugs payment

  1.yes 2.no

- medical history of DM, CA, lung disease and steroid drugs used (reference 34)

  1. yes 2. no

- alcohol consumption (reference 43)

  1.drink, occasion, discontinued 2. Non-drink

- cigarette consumption (reference 43)

  1.smoke, occasion, discontinued 2. Non-smoke

- AFB examination at initial treatment

  1.mostly (+++) positive 2.low (+) and moderate(++) positive

- drug adverse

  1.yes 2.no

- chest X ray

1.cavity 2.non-cavity

3.Bivariate analysis was performed to compare the characteristics of the two groups using the following tests:

3.1 Chi-square test for two independent proportions (for the discrete variables) with the significance level at 0.05 or two-tail Fisher' s exact test, whichever was appropriate.

3.2 Student' s t-test for difference in mean for the continuous variables with the significance level at 0.05.

3.8.3 Comparative analysis of cured rate of both DOTS and SAT strategy

1.Kaplan -Meier of survival analysis was conducted on the difference of median time to cure between DOTS or SAT strategies and the comparison of survival curve between DOTS and SAT were performed using log rank test.

2.Cox' s proportional hazard model was performed to compare the difference of outcomes after controlling for confounders such as sociodemographic factors, and medical history.

3.8.4 Sensitivity analysis

Sensitivity analyses were conduced by varying labour cost, travel cost of consumer and effectiveness, as follow:

1. A labour cost increase 10%, 30% and 50% of both strategies,
2. A travel cost of consumer increase 10%, 30% and 50% of both strategies,
3. The effectiveness was varied by increasing 20% and decreasing 20%,

4. A number of completed cases whom were classified as unsuccess case at the previous analysis was assigned into success group.

5. Furthermore, we performed "Modified DOTS or M-DOTS (Improved SAT)" scenario which patients treated under DOTS in the first two months and in the continuation phase the patient received refill anti-TB drugs at health center. Assuming that default rate at the first two months under M-DOTS would equal to those under DOTS. In addition, number of cure patients under M-DOTS would be calculated from the number of cure patient under SAT at the end of treatment plus number of patient who would have been cured if not dropping out during the first two months. The details of calculation were described as follow.

1. A cost of the first two month was calculated as DOTS strategy by using a proportion of a number of patient visits among DOTS group multiply average cost of DOTS.

A | Cost of the first two month = proportion (DOTS) X average cost (DOTS)

2. A provider cost of continuation phase was calculated as a proportion of a number of patient visits among SAT group multiply average provider cost of SAT.

B | Provider cost (continuation phase) = proportion (SAT) X average provider cost (SAT)

3. A consumer cost of continuation phase was calculated as a proportion of a number of patient visits among SAT group multiply average provider cost of DOTS.

C

Consumer cost (continuation phase)	= proportion (SAT) X average consumer cost (DOTS)

4.

Average cost of " M-DOTS (Improved SAT)" = A + B + C

5.

Cost-effectiveness of " M-DOTS (Improved SAT)" = $\frac{\text{average cost}}{\text{cure rate}}$

CHAPTER IV

RESULTS

A total of 224 new tuberculosis patients were registered at TB registers of community hospital in Petchaburi, Rachaburi and Prachaup Khiri-Khan between October 1,1998 and March 1,1999. Twenty patients were excluded according to the exclusion criteria. For instance, one was diagnosed TB lymph node with PTB, one was diagnosed TB fallopian tube, one was continued treatment after defaulted, two were foreigner, 8 patients were transferred in and 7 patients were treated under SAT in DOTS area. Thus, there were 204 (91%) new PTB patients were enrolled in our study. Out of 204 enrolled patients, 117 (57%) received DOTS strategy and 87 (43%) were treated under SAT strategy.

4.1 General characteristics

All of 204 patients were followed up until the event had occurred or the day of the study termination (November 30, 1999). In general, the average time of follow up was 162 days (SD=58.2, ranging from 3 to 269 days). Table 7 provided sociodemographic information among TB patients who were treated under DOTS or SAT strategies. The sex ratio of male to female of DOTS patient was 3.3:1 which was similar to those 3.1:1 of SAT patient. DOTS patients were mostly married with 35 years old or more and graduated at primary school level or lower which were also similar to SAT patients. About employment, both DOTS and SAT patients were unskilled worker. However, there were differed in the rank order of the worker field.

Table 7 Comparison of sociodemographic characteristics among TB patients who were treated under DOTS or SAT strategies.

	DOTS(%) (N=117)	SAT(%) (N=87)	*p*-value
Gender (male)	90 (76.9)	66 (75.9)	0.86
Marital status (single/ widow/ separated)[b]	44 (37.9)[f]	24 (29.6)[g]	0.23
Age (35 or more)[a]	70 (59.8)	61 (70.1)	0.13
(mean ± SD)	(43.4±16.9)	(48.1±17.7)	
Income (< average)[c]	63 (54.3)[f]	61 (75.3)[g]	<0.01
(mean ± SD)	(3252.4±3619.8)	(1969.3±3013.1)	
Resided under jurisdiction (no)	6 (5.1)	25 (29.6)	<0.01
Education (primary school or lower)[d]	98 (84.5)[f]	70 (86.4)[g]	0.71
Occupation (unskilled)[e]	98 (84.5)[f]	64 (79.0)[g]	0.32
Drugs payment (no)	79 (68.1)[f]	57 (70.4)[g]	0.74

a: reference group was 15-34 years.

b: reference group was couple.

c: average refer to average income of each province

d: reference group was secondary school or higher.

e: unskilled group refer to labourer, agriculturist, fisherman and houseworker

f: N=116, g: N=81

DOTS patients were mostly work as labour or work in agriculture field whereas the top two categories for SAT patients were labour and housework. The difference characteristics between DOTS and SAT patients were average income and residential area. In fact, the average income among DOTS patients were slightly over 3,000 baht whereas among SAT patients were under 2,000 baht. In addition, patients who had lower average income of each province of DOTS group (54%) was significantly less than SAT group (75%) (p<0.01). About residential area, patients who were treated under DOTS (5%) resided out of jurisdiction of their community hospital significantly less than those under SAT (29%) (p<0.01).

The medical history and risk behaviors of TB patients who were treated under DOTS or SAT strategies are summarized in Table 8. All of variables between DOTS and SAT patients did not significantly differ. For instance, eighty-three percents of DOTS patients were no history of DM, CA, lung disease and steroid drugs abuse. Almost half of DOTS patients (48%) were drugs adverse with highly positive sputum smear (44%). Almost of all DOTS patients (81%) were non-cavity CXR. Risk behaviors of alcohol and cigarette consumption of DOTS patients were 68% and 74%, respectively. SAT patients were no history of DM, CA, lung disease and use of steroid drugs (82%) and 55% of them were no drugs adverse. Forty-two percents of SAT patients were highly positive sputum smear with non-cavity CXR (76%). Three-fourth of SAT patients was cigarette smokers and 70% were alcohol drinkers.

Table 8 Medical history and risk behaviors of TB patients who were treated under DOTS or SAT strategies.

	DOTS(%) (N=117)	SAT(%) (N=87)	*p*-value
Medical history (yes)[a]	20 (17.1)	16 (18.4)	0.81
Drugs adverse (yes)	56 (47.9)	39 (44.8)	0.67
AFB (+++) [b]	52 (44.4)	42 (48.3)	0.59
CXR (cavity)[c]	16 (19.0)[f]	17 (23.9)[g]	0.46
Alcohol consumption (ever)[d]	79 (68.1)[h]	57 (70.4)[i]	0.74
Cigarette consumption (ever)[e]	86 (74.1)[h]	61 (75.3)[i]	0.85

a: history of DM/ CA/ lung disease/ steroid drugs abuse

b: reference group refer to low (+) and moderate (+ +) positive sputum smear

c: reference group refer to non-cavity

d: ever group included drink, occasion, discontinue

e: ever group included smoke, occasion, discontinue

f: N=84, g: N=71, h: N=116, i: N=81

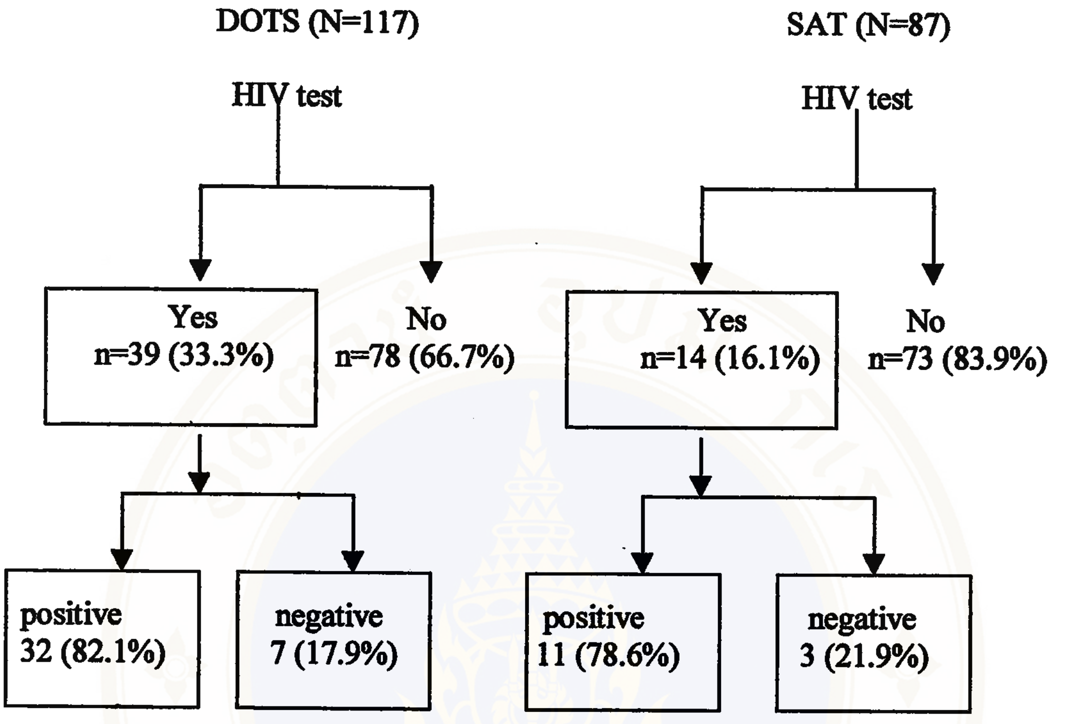


Figure 10. Comparison of HIV results between patients treated under DOTS and SAT.

Figure 10 showed the flow chart of HIV investigation among patients treated under DOTS and SAT. As can be seen, nearly two-third of patients under DOTS strategy investigated HIV serology and approximately one-sixth of SAT strategy. However, it should be noted that DOTS and SAT patients were reported of HIV positive similarly.

Table 9 Number (percents) of observers who administered direct observation of DOTS strategy.

Observer	Number , n(%)
Wife	42 (36.2)
Husband	4 (3.5)
Daughter	20 (17.2)
Son	4 (3.4)
Father	3 (2.6)
Mother	19 (16.4)
Other kin	15 (12.9)
Health volunteer	5 (4.3)
Friend	4 (3.5)

Table 9 described the types of direct observers who administered directly observation of DOTS strategy. The main group of direct observers was the next of kin (92.3%) particularly wife (36.2%). While the lowest proportion of observer were friends (3.5%). Only 4.3% of the patients were directly observed by health volunteers.

Table 10 Comparison of treatment outcomes among TB patients who were treated under DOTS or SAT strategies using WHO definition.

	DOTS (%) (N=117)	SAT (%) (N=87)	Total (%)
Cured	79 (67.5)	30 (34.5)	109 (53.4)
Completed	3 (2.6)	18 (20.7)	21 (10.3)
Defaulted	7 (6.0)	26 (29.9)	33 (16.2)
Died	21 (17.9)	8 (9.2)	29 (14.2)
Transferred out	3 (2.6)	2 (2.3)	5 (2.5)
Failure	4 (3.4)	3 (3.4)	7 (3.4)
Total	117	87	204

4.2 Effectiveness of TB Control Programme

Treatment outcomes between DOTS patients and SAT patients under WHO definition are summarized in Table 10. In general, DOTS show a higher cure rate (67.5%) and lower defaulted rate (6%) than SAT (34.5% and 29.9%, respectively). However, it should be noted that there was a higher proportion of completion rate, patients whom completing treatment course without sputum results, in SAT than DOTS. There were similar in transfer out and failure rate between the two strategies but patients under DOTS were died (17.9%) at a higher rate than SAT (9.2%).

Table 11 Comparison of death cases among DOTS and SAT patient.

	DOTS		SAT	
	Total (N=117)	HIV positive (n=32)	Total (N=87)	HIV positive (n=11)
First month	7	3	2	1
Second month	4	3	1	1
Third month	2	2	2	0
Fourth month	4	3	3	1
Fifth month	1	1	0	0
Sixth month	2	1	0	0
Seventh month	1	1	0	0
Total death	21	13	8	3

There were a total of 29 death cases in our study, 21 case in DOTS and 8 in SAT. In Appendix E, patients, who died, were mostly smoking males with primary education level and aged between 15-34 years. It should be noted that there was a higher death rate among patients under DOTS than SAT particularly at the first two months. In fact, TB patients with HIV positive had died at 55.2% of total death cases and higher proportion of death cases among TB patients with HIV positive were in DOTS and SAT were 61.9% and 37.5% respectively.

Table 12 Comparison of drop out at the end of each month among TB patients who were treated under DOTS or SAT strategies.

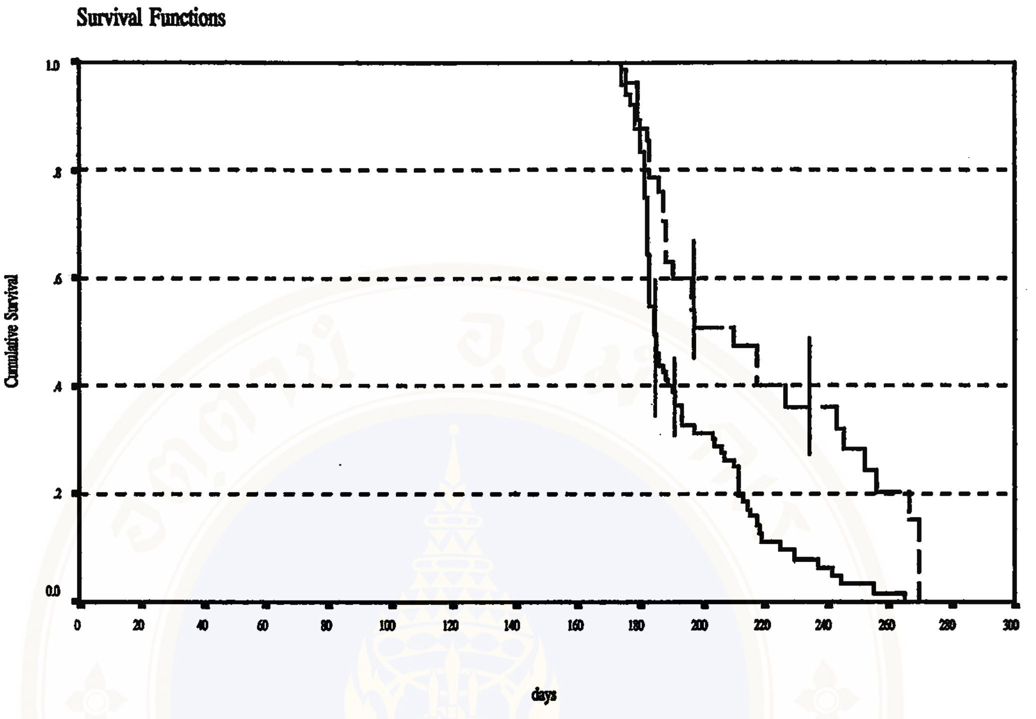
	DOTS (%)	SAT (%)
First month	1(7.7)	11(37.9)
Second month	6(46.1)	9(31.0)
Third month	1(7.7)	3(10.4)
Fourth month	1(7.7)	3(10.4)
Fifth month	2(15.4)	1(3.4)
Sixth month	2(15.4)	2(6.9)
Total	13	29

A total of 42 patients who were experienced lost to follow-up during the treatment course and detailed of each month were described in Table 12. Generally, patients who were treated under SAT dropped more than those under DOTS. In particularly, at the first two months patient treated under SAT strategy dropped higher than those under DOTS strategy. In addition, this first two months period is crucial because it is recognized as the infectious period of TB thus defaulter could transmit the disease to their community on contacted persons. Moreover, in continuing phase, findings show that SAT patients were lost to follow up at a higher rate than DOTS patients.

Table 13 Comparison of defaulter among TB patients who were treated under DOTS or SAT strategies.

	DOTS (%) (N=117)	SAT (%) (N=87)	Total (%)
At the first two months of treatment course	3 (2.56)	10 (11.49)	13 (6.37)
Third month	1 (0.85)	10 (11.49)	11 (5.39)
Fourth month	2 (1.71)	3 (3.45)	5 (2.45)
Fifth month	0	2 (2.30)	2 (0.98)
Sixth month	1 (0.85)	1 (1.15)	2 (0.98)
Total	7	26	33

As WHO classification, defaulters were a patient who lost to follow-up for two consecutive months after registration. There were a total of 33 defaulters at the end of treatment course under DOTS or SAT strategies and detailed of monthly defaulters are described in Table 13. Our findings revealed that, at the first two months of treatment course, a proportion of defaulters under SAT strategy was higher than those under DOTS strategy (11.5% and 2.6%, respectively). These findings in Table 12 and 13 suggested that DOTS patients were returning to treatment course after being loss to follow-up at a higher rate than SAT patients.



—— DOTS - - -SAT
Log rank test $p<0.01$

Figure 11 Difference in Kaplan-Meier survival curves between DOTS and SAT strategies.

Figure 11 showed a difference in survival between patients who treated under DOTS strategy (median 184 days, 95%CI= 181.92-186.08) and those under SAT strategy (median 210 days, 95%CI= 189.80-232.20). During 180 days all of TB patients were expected receiving completed treatment course for TB. After 180 days of treatment course, the proportion of patients who were treated under DOTS strategy (mark line) remaining in treatment was less than those under SAT strategy (dot line) and the difference was statistically significant using log rank test. In other words, the proportion of those who were cured was higher in DOTS as compared to those in SAT.

Table 14 Factors associated with outcomes of TB patients.

Variables	Cure	Not-cure	Risk Ratio	95% CI
Strategies				
DOTS	79(67.5)	38(32.5)	1.96	1.43-2.68
SAT	30(34.5)	57(65.5)		
Occupation				
Unskilled	89(54.9)	73(45.1)	0.96	0.70-1.32
Other	20(57.1)	15(42.9)		
Income (mean ± SD)[a]	(2838.35± 3544.11)	(2584.20± 3307.82)		
Age (mean ± SD)[b]	(46.9±16.6)	(43.5±18.1)		
35-86	79(60.3)	52(39.7)	1.47	1.08-1.99
15-34	30(41.1)	43(58.9)		
resided under jurisdiction				
No	15(48.4)	16(51.6)	0.89	0.60-1.31
Yes	94(54.3)	79(45.7)		
Additional drugs payment				
Yes	26(42.6)	35(57.4)	0.70	0.51-0.96
No	83(61.0)	53(39.0)		
Alcohol consumption				
Ever	74(54.4)	62(45.6)	0.95	0.73-1.24
Non-drink	35(57.4)	26(42.6)		

a:p=0.61 b: p=0.16

Table 14 described factors associated with treatment outcomes of TB patients. The results of unadjusted analysis showed that patients who were treated under DOTS strategy had been cured 1.96 times higher than those under SAT strategy (95% CI=1.43-2.68).

In order to test hypothesis regarding the effect of strategy on time to cure for TB, we have conducted Cox ' s proportional hazard model. First, we construct the full model by selecting potential variables in the full model, and then construct the final model. The steps of selecting the potential variables in the model were as follow.

First, we conducted univariate Cox regression, according to the results of the analysis, we chose strategy, age, additional drugs payment, occupation, residence, alcohol consumption and HIV status as the important predictors into full model. Appendix G illustrated the results of univariate analysis. The literature reviews presented that alcohol consumption associated with outcome of TB treatment. Then alcohol consumption was selected for further analysis. Age, additional drugs payment, occupation, residence and HIV status were also selected for further analysis. Results of Cox regression analysis are presented in Table 15. For the full model, two predictors were significantly related to survival (time-to-cure): strategy (Hazard ratio 3.08, 95%CI 1.89-5.01) and occupation (Hazard ratio 0.38, 95%CI 0.22-0.65).

In addition, there were two variables, additional drug payment and residential area, which may have affected on the outcomes. Since additional drug payment were one of a small part of expenditure by patient while the travel cost from home to health center/ hospital was a major part of expenditure, thus we select residential area to be included in the final model.

Table 15 Cox regression analysis of TB treatment outcomes.

Model	Factors	Hazard ratio (95%CI)	Wald Statistic	*p*-value
Full	Strategy	3.08 (1.89-5.01)	20.20	<0.01
	Age	1.00 (0.99-1.02)	0.63	0.43
	Additional drugs payment	1.50 (0.90-2.50)	2.42	0.12
	Occupation	0.38 (0.22-0.65)	12.29	<0.01
	Residence	1.54 (0.85-2.80)	2.03	0.15
	Alcohol consumption	0.88 (0.56-1.39)	0.30	0.59
	HIV status (positive)	0.62(0.23-1.64)	0.93	0.34
	HIV status (unknown)	0.78(0.32-1.90)	0.30	0.59
Overall	X^2=34.75 df=8	*p*-value<0.01		
Final	Occupation	0.41 (0.24-0.68)	11.51	<0.01
	Strategy	2.91 (1.70-4.70)	18.96	<0.01
	Residence	1.69(0.93-3.05)	3.05	0.08
Overall	X^2=28.66 df=3	*p*-value<0.01		

In the next step, residence, strategy and occupation were chose as the three most important predictors at presentation in final model. The patients who were treated under DOTS strategy had been cured 2.91 times higher than those under SAT strategies after adjusting for occupation and residence. The patients who were government official, commerce, student, monk or unemployed had been cured 2.44 times higher than those were labourer, agriculturist, fisherman or houseworker after adjusting for strategies and residence.

4.3 Cost assessment for TB Control Programme

As demonstrated in Table 16, total direct provider cost for DOTS patient was comprised direct routine service cost for more than 50% whereas majority in direct provider cost in SAT patient was medical care. The labour cost was demonstrated as the highest proportion of direct routine service cost for both strategies.

Table 16 Comparison of direct provider cost components between DOTS patients and SAT patients.

	DOTS (%)(baht)	SAT (%)(baht)
1.Direct routine service cost		
1.1 Labour cost	319,401.55 (40.76)	133,115.45 (32.31)
1.2 Material cost	37,054.42 (4.73)	8,390.63 (2.04)
1.3 Capital cost	99,078.26 (12.65)	46,413.12 (11.27)
Subtotal direct routine service cost	**455,534.23 (58.14)**	**187,919.20 (45.62)**
2.Medical care cost		
2.1 cost of AFB	54,465.95 (6.95)	39,809.00 (9.66)
2.2 cost of CXR	11,138.40 (1.42)	6,541.60 (1.59)
2.3 cost of sputum c/s	0 (0.00)	1,924.77 (0.47)
2.4 cost of drugs	262,409.60 (33.49)	175,732.10 (42.66)
Subtotal medical care cost	**328,013.95 (41.86)**	**224,007.47 (54.38)**
Total direct provider cost	**783,548.18**	**411,926.67**

Table 17 Comparison of total consumer cost between DOTS patients and SAT patients.

	DOTS(%)	SAT(%)
1.Direct medical cost (baht)	956.00 (1.23)	3,221.00 (5.39)
2.Direct non-medical cost(baht)	55,310.00 (70.96)	44,208.00 (73.95)
3.Indirect cost(baht)	21,677.01 (27.81)	12,352.28 (20.66)
Total consumer Cost (baht)	**77,943.01**	**59,781.28**

Data regarding consumer cost components were summarized in Table 17. For consumer cost, direct non-medical cost (travel cost of patients and their relatives) was most costly item of both DOTS and SAT strategies (approximately 71% and 74%, respectively). While direct medical cost which was additional drug payment were less than 5% of total consumer cost in both strategies.

Table 18 Comparison of cost components, average cost and cost-effectiveness between DOTS and SAT strategies.

	DOTS (%) (n=117)	SAT (%) (n=87)
1.Direct routine service cost (baht)	455,534.23 (52.88)	187,919.20 (39.84)
2.Medical care cost(baht)	328,013.95 (38.07)	224,007.47 (47.49)
3.Consumer cost (baht)	77,943.01 (9.05)	59,781.28 (12.67)
Full cost (baht)	861,491.19	471,707.95
Average cost (baht/pt treat)	7,363.17	5,421.93
Number of case cured	79	30
Cured rate (%)	67.52	34.48
Cost-effectiveness	**10,904.95**	**15,723.60**

Table 18 demonstrated cost components and cost-effectiveness between DOTS and SAT strategies. For directly observed treatment, it accounted for approximately 53% of direct routine service cost, 38% of medical care cost and almost 9% of consumer cost. On the other hand, for SAT it accounted for approximately 40%, 47% and 13%, respectively.

The average cost of DOTS was approximately 2,000 baht expensive than SAT strategy. However the cost per patient cured showed that DOTS strategy was lower than SAT strategy (approximately 10,905 baht vs 15,724 baht).

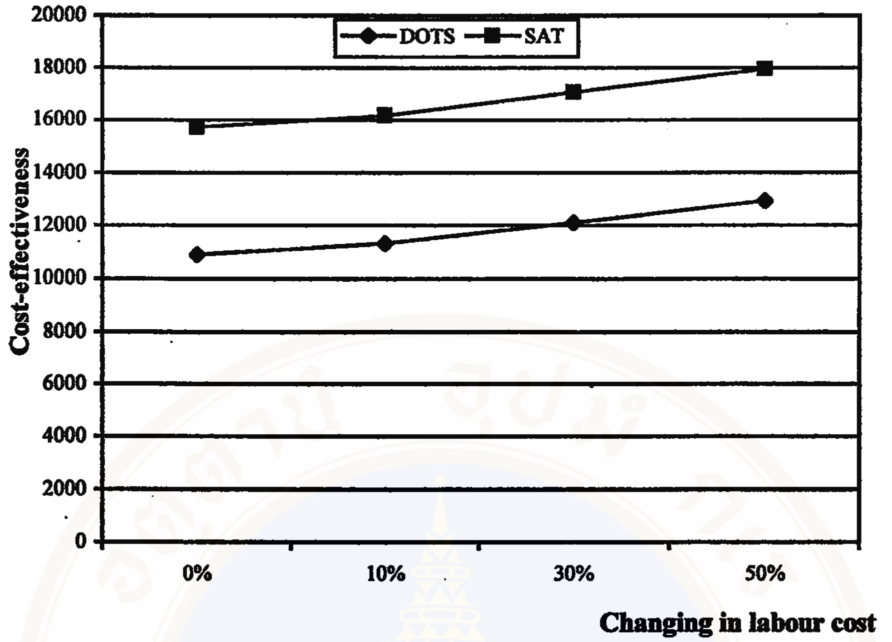


Figure 12 Sensitivity analysis by increasing labour cost.

We have tested the sensitivity of cost-effectiveness of both DOTS and SAT to the variations of these following assumptions, namely a variation of labour cost, travel cost and effectiveness. The results were described below.

Sensitivity analysis by increasing labour cost were presented graphically in Figure 12. The results showed that cost-effectiveness for DOTS is more likely to sensitive to the increase of labour cost than cost-effectiveness for SAT. However, as revealed by the graph, DOTS provide lower cost per case cured when compared to SAT.

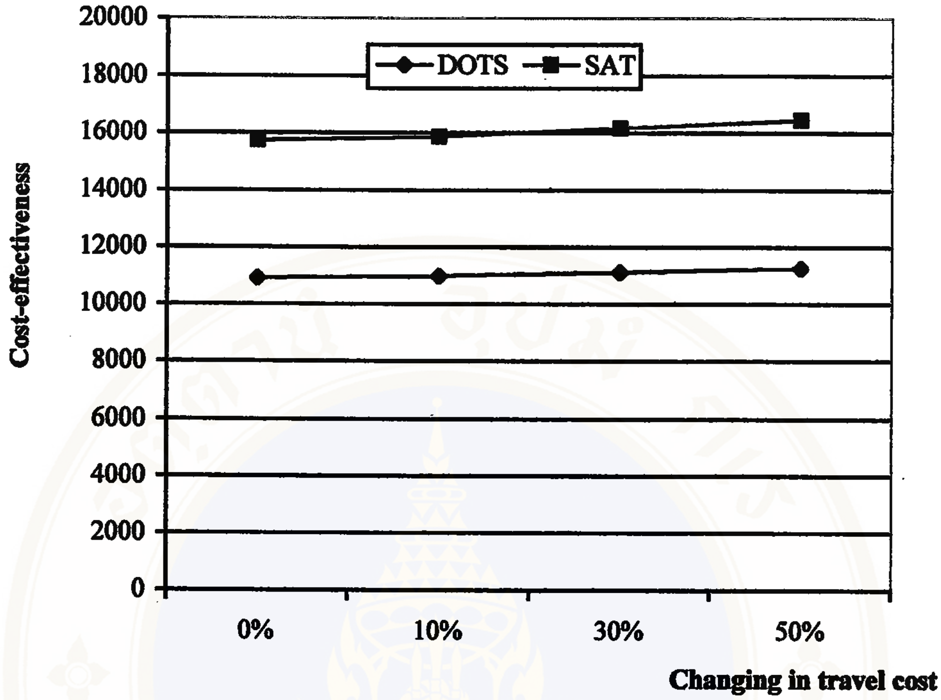


Figure 13 Sensitivity analysis by increasing travel cost.

In Figure 13, we conduct sensitivity analysis by increasing travel cost up to 50% of its original cost of both DOTS and SAT. As can be seen, DOTS offers a lower cost per case cured when compared to SAT. The results showed that SAT strategies is sensitive to the increasing of travel cost.

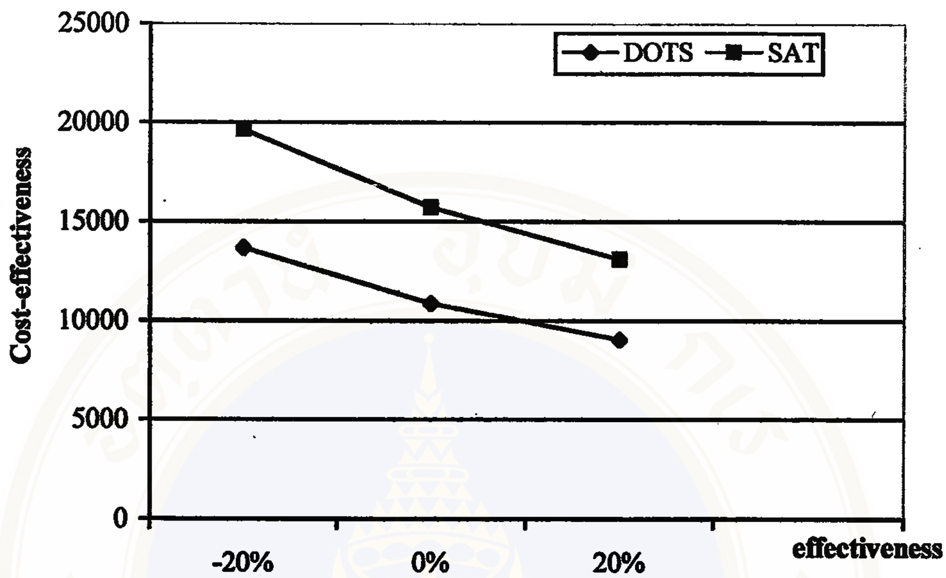


Figure 14 Sensitivity analysis by increasing 20% and decreasing 20% of effectiveness.

From review of the literature, effectiveness was indicated as the important factor affecting cost per case cured. In this study, we varied the effectiveness (cure rate) by increasing 20% and decreasing 20% of its original proportion. The results of sensitivity analyses were presented graphically in Figure 14. Increasing 20% of effectiveness of both strategies, cost-effectiveness of both strategies become close together reflecting that cost per case cured of these two strategies seem to sensitive to the increasing of effectiveness particularly for SAT. Decreasing 20% of effectiveness, graphs indicated consistency of a cost per case cured between DOTS and SAT strategies.

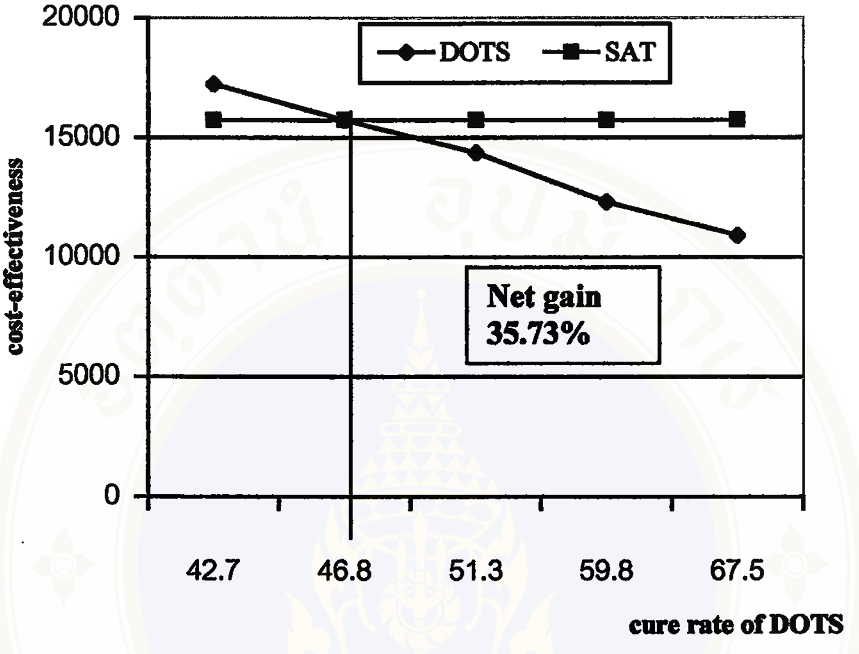


Figure 15 Sensitivity analyses by increasing of effectiveness of DOTS

However, by holding SAT cure rate constant and varying DOTS cure rate, we found that at 46.8% of DOTS cure rate, cost per case cured between the two strategies were equal. Furthermore, we calculated net gain as follow.

$$\text{Net gain} = \frac{\text{cure rate of DOTS} - \text{cure rate of SAT}}{\text{cure rate of SAT}} \times 100$$

At this point, net gain was 35.73%.

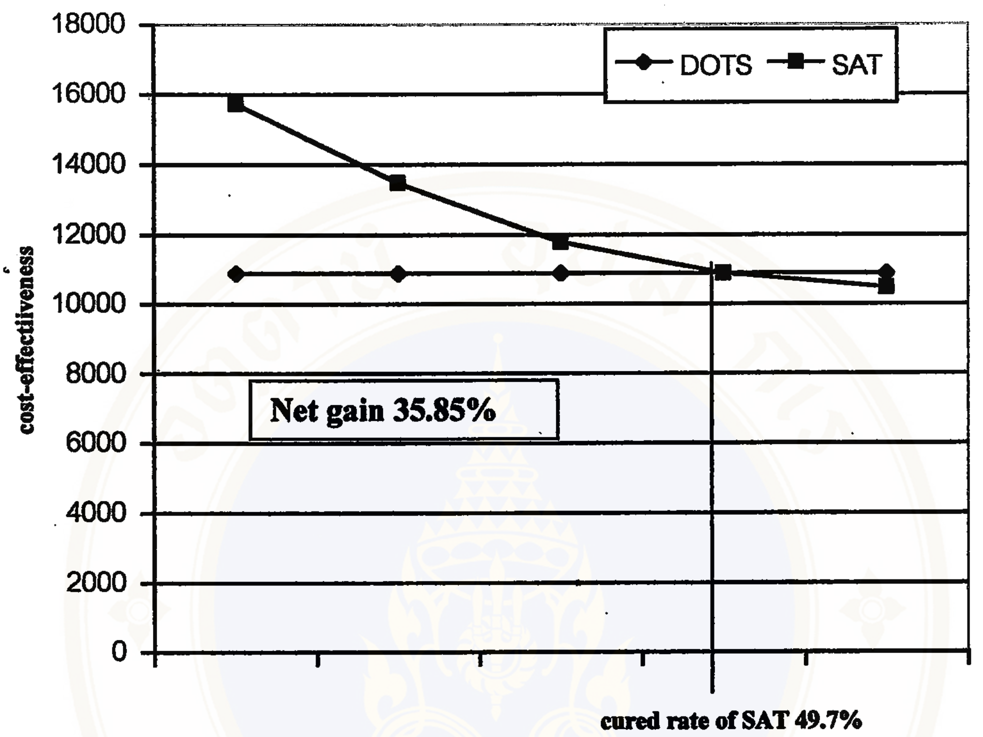


Figure 16 Sensitivity analyses by increasing of effectiveness of SAT.

Additionally, we extend the sensitivity analysis of effectiveness of SAT. By holding effectiveness of DOTS constant at 67.5% and increasing SAT's effectiveness. For any value of cured rate of SAT increased, a trend of a cost per case cured decreased, cost per case cured between two strategies become close together. At 49.7% of cure rate under SAT programme, both strategies were at equal point. In this case, net gain was 35.85%. At 50% cured rate of SAT which was reported by Thailand NTP in 1995, the figure showed that SAT strategy become slightly higher cost-effectiveness than DOTS strategy.

Table 19 Sensitivity analysis by including completion rate into cure rate.

	DOTS (full cost =	(N=117) 861,491)	SAT (full cost =	(N=87) 471,708)	Net gain* (%)
	%	C-E.	%	C-E	
Cure rate	67.52	10,904.95	34.48	15,723.60	95.82
Success rate (cure rate + complete rate)	70.08	10,505.99	55.17	9,827.25	27.02

C-E : cost-effectiveness

$$\text{* Net gain} = \frac{(\text{cure rate of DOTS - cure rate of SAT}) \times 100}{\text{cure rate of SAT}}$$

In further analysis, completed rates of both strategies were calculated instead of cure rate thus the effectiveness of DOTS become 70.08% and 55.17% in SAT (Table 19). It was shown that SAT indicate a higher cost-effectiveness than DOTS.

Table 20 Comparison of cost-effectiveness of DOTS, Modified DOTS and SAT.

	DOTS	Modified DOTS	SAT
Average cost (Baht / pt treated)	7,363.17	5,893.02	5,421.93
Cured rate (%)	67.52	43.68	34.48
Cost-effectiveness	10,904.95	13,491.35	15,723.60

Furthermore, we performed "Modified DOTS or M-DOTS (Improved SAT)" scenario that patients treated under DOTS in the first two months and in the continuation phase the patient received refill anti-TB drugs at health center. Since the first two months under DOTS would improve default rate from 11.49% to 2.56% (Table 13) therefore the number of cure patients under Modified DOTS scenario would increase from 30 to 38. The cure rate of this scenario was 43.68%. Table 20 presented results of the Modified DOTS scenario. It should be noted that cost per patient cured under Modified DOTS was around 2,500 Baht higher than those under DOTS. In other word, cost per patient cured under Modified DOTS was around 2,200 Baht lower than those under SAT. The findings suggested that Modified DOTS could be an alternative strategy for controlling TB in a non DOTS setting in order to improve cure rate.

CHAPTER V

DISCUSSION

Tuberculosis (TB) in Thailand is an alarming situation in a recent year. At present, Thai CDC offers DOTS and SAT as TB controlling programme. However, there were few studies about its cost-effectiveness. In this study, we conducted a retrospective study to examine cost-effectiveness between DOTS and SAT among new PTB patients with sputum smear positive.

A cohort of 204 new PTB patients were registered at TB registers in Petchaburi, Ratchaburi and Prachuap Khiri Khan between October 1, 1998 and March 31, 1999. Fifty-seven percents of the patients received DOTS and 43% of the patients were treated under SAT. All of patients were followed up until the occurrence of events or the day of the study termination (November 30, 1999).

The results of this study indicated that cured rate of DOTS was 67.5% higher than those under SAT (34.5%). In other words, the net gain of cure rate was 95.6%. The defaulters at the second month of treatment under DOTS (2.6%) were smaller than those under SAT (11.5%). The median time-to-cure among DOTS group was 184 days when compared to 210 days among SAT group. The joint impact of seven determinants (residence, occupation, additional drugs payment, alcohol consumption, HIV status, strategy and age) on survival time was analysed using Cox regression. Strategies, residence and occupation were considered a possible moderator and predictors. Patients who were treated under DOTS were more likely to be cured at 2.91 (95% CI=1.70-4.70, p<0.01) time higher than those under SAT after adjusting for residence and occupation. An average cost per patient treated under either DOTS or SAT programme did not show significant difference (7,363 baht vs 5,422 baht, p=0.77). However, a cost per case cured under DOTS (10,905 baht) was lower when compared to those under SAT (15,724 baht).

Our findings showed that the cured rate of DOTS (67.5%) was similar to the study of Siriwat, et al (66.3%). However, it was lower than the figure of Thailand NTP (78.0%) and the global (72.0%) in 1996. And other previous studies (57,27,60) showed a higher cure rate of 76.1%, 82.4% and 88.2%, respectively. This may be due to a high proportion of death rate (17.9%) in this study, that was higher than a figure of Thailand NTP (4.3%) and the global (3.7%) in 1996. Likewise, the studies of Akksilp (27) and Siriwat, et al. (58) reported a low death rate (7.5% and 3.5%, respectively). Because 37.2% of TB-HIV positive had died, thus, HIV infection may accelerate disease progression. Additionally, smoking tobacco may also contribute to high death rate. In fact, those who died were more likely to be smoking male at aged of 25-34 years.

Although cured rate is the intermediate outcome, the cure rate is appropriate for this study. Because, first, the cured rate is the potential differences between DOTS and SAT strategies with respect to reduce TB cases of both strategies. Second, the cured rate is the outcome of interest to decision makers. In addition, defaulted rate also provide information for public health workers. Results revealed 6.0% of defaulted rate, in similar to Siriwat, et al. (58) and Kamolrattanakul (57). In contrast, the lost to follow up was higher than the figure of Thailand NTP (2.6%), the global (1.3%) and Akksilp (1.5%) in 1996. It should be noted that, DOTS strategy reduced the defaulters from 30% in SAT to 6% in DOTS. Since the first two months of TB treatment is the crucial infectious period of TB (39), if a TB patient with positive sputum smear interrupted treatment in this period, an estimated of two or three contacts will be infected by each positive sputum smear (34). DOTS strategy was confirmed to be superior to SAT strategy due to the fact that defaulter in the first two months of DOTS was almost 5 times lower than SAT. Additionally, DOTS patients who lost to follow-up during the first two months were returning to treatment course at a higher rate than SAT patients, thus DOTS offer a superior reduction in infection rate.

The median time-to-cure of patients under DOTS was 184 days that was shorter than 210 days of those under SAT. The treatment duration was reduced that was as the results of administers of DOTS strategy. These findings indicate the increasing productivity gain for patient under DOTS. In other words, the lost of opportunity cost is increased among SAT patient due to a longer duration of treatment.

Within DOTS programme majority of observers were family members. Previous studies also supported our findings that directly observed by family members were feasible (27,57). Even though we can not test association between types of observers and treatment outcome, Wilkinson, et al. (23) and Kamolrattanakul, et al. (57) demonstrated that the results of directly observed by health workers and non-health workers were similar.

Our findings revealed that the average cost of DOTS was a little higher than SAT (7,363 baht and 5,422 baht, respectively). In similar, Moore,et al. (29) suggested that cost per patient treated under DOTS was expensive than cost under conventional treatment. These difference may be due to the fact that DOTS programme included cost of observers and outreach visit but SAT was carried no cost of these activities. In contrast, Floyed, et al (28) concluded that DOTS was 2.8 times lower cost than those under SAT. This difference may be due to including the cost of hospital stay in the study but not in our study.

Since the present study performed direct provider cost perspective but not included indirect provider cost. In fact, SAT strategy consumed more indirect provider cost than DOTS due to the SAT programme based in hospital. Thus, cost saving in DOTS may be even larger than the estimated cost in the present study.

From direct routine service cost component, DOTS invested almost twice more in material cost than SAT because DOTS strategy comprised of treatment, directly observation and supervision of observers. On the other hand, SAT strategy has performed only on treatment. The other cost components, labour cost and capital cost, were similar.

From consumer point of view, direct non-medical cost (travel cost) was highest cost for both strategies. In this study, we used public transportation in term of travel cost to reduce a wide range of travel cost but this may result in underestimation of travel cost in both strategies. DOTS showed lower travel cost than SAT (70.96% and 73.95%, respectively) due to the fact that DOTS treatment was based in the community. DOTS strategy is expected that patients invested lower time cost than those for SAT. However, the results show that DOTS patients invested slightly higher indirect cost (time cost) than SAT patients because some of patients went to either hospital or health center to receive refill anti-TB drugs and AFB test, while all those who were treated under SAT strategy went to hospital once a month.

Despite of the differences in the costing methodology and the scope of studies, a number of reports indicated that DOTS was a more cost-effectiveness strategy than

SAT strategy (20,28,29). Also our findings evidenced that DOTS was more cost-effectiveness than SAT strategy.

Since DOTS is a dominant strategy in comparison with SAT, sensitivity analysis would be necessary to assess the cost advantage of DOTS. The cost advantage of DOTS is also stable through the wide range of changes in value of labour cost and travel cost. The sensitivity analysis demonstrates that changes in cure rate could hampered the cost advantage of DOTS. Decreasing cure rate in both DOTS and SAT strategies were unlikely to affect the cost effectiveness. In contrast, increasing cure rate for both strategies seems to improve cost-effectiveness among the two strategies. Additionally, including complete cases into success group, a success rate of DOTS raised to 70.08%, while SAT success rate increased to 55.17%. At this point, SAT was superior cost-effectiveness to DOTS strategy. By holding a cure rate of SAT at 34.5% and the cure rate under DOTS programme decreased, at 46.8% of cure rate of DOTS or at net gain of approximately 36%, the cost-effectiveness of DOTS equaled to SAT. If the cure rate under SAT programme increased while holding a cure rate of DOTS at 67.5%, in this case, at 49.7% of cure rate of SAT or at net gain of approximately 36%, the cost-effectiveness of DOTS equaled to SAT. Even though, improved cure rate in SAT would offer a similar cost per case cured between DOTS and SAT, it should be noted that SAT offer a lower cure rate though with the same cost per case cured. Therefore, the effects of the lower cure rate may introduce a public health burden due to recurrent diseases among unsuccessful treated cases. The results of Modified DOTS scenario demonstrated that cost per case cured under Modified DOTS was cheaper than SAT but more expensive than those under DOTS. In addition, the cure rate of

Modified DOTS was in between those of DOTS and SAT (43.68% , 67.52%, 34.5% respectively).

In summary, our findings evidenced that DOTS strategy is an effectiveness health intervention to control TB. Because, first, DOTS strategy achieved higher cured rate than SAT strategy or approximately 95% net gain in cure rate. Second, the patients treated under DOTS had been cured with shorter duration than those under SAT. Third, DOTS defaulters occurred at lower rate than SAT defaulters particularly in the first two months.

The results of this study would be generalized to the new PTB with sputum smear positive with aged 15 years or more whom registered at community hospital. With the limitation of this study, it may have recall error and misclassification bias occured. Recall error may due to retrospective nature in data collection. Misclassification may occur in some risk behavior such as alcohol and cigarette consumption which were collected by interviewing patients. In addition, it may be overestimated of cost since we used the unit cost of AFB, CXR, sputum c/s from the Zonal Tuberculosis Center study, however, the difference would be small. The advantage of the present study were that we collected the data of effectiveness and cost from the primary information, thus the cost-effectiveness would represent the actual magnitude than the study from secondary data.

Retrospective cohort design yields the causal relationship and incidence case when compared with cross-sectional design which cannot yield the causal relationship and just present prevalence case. Retrospective cohort design uses longer follow-up period than case-control design. But it yields relative risk directly and studies many outcomes from one risk factor while case-control design yields relative risk indirectly and studies only one disease from one factor. However, randomize control trial is the strongest design to study relationship of exposure to the factors before the disease develop but it is more expensive and use long follow-up period than retrospective cohort design.

CHAPTER VI

CONCLUSION AND RECOMMENDATIONS

Even though tuberculosis (TB) incidence rate and number of cases declined during the past decades, since 1992, TB cases were increasing dramatically. These upward trends were attributed by influencing of HIV epidemic and poor TB management due to public health apathy, lower case detection rate and lower cure rate.

For some years now, DOTS has been a recommendation strategy by WHO for controlling TB worldwide. Currently, Thai CDC has adopted DOTS as a strategy to combat TB in Thailand since 1996. However, there were little research about cost-effectiveness of DOTS implemented in Thailand. It is necessary that not only DOTS programme should be evaluated on its effectiveness but also the differences of the cost-effectiveness among the different TB controlling programme should be compared. Thus, study of this kind would evidence the highest cost-effectiveness TB controlling programme for policymakers. The purpose of this study was to examine cost-effectiveness between two TB controlling strategies DOTS and SAT.

A retrospective cohort design was conducted among the new PTB patients with sputum smear positive who were registered at community hospital in Petchaburi, Ratchaburi and Prachuap Khiri Khan. Outpatients aged 15 years or more with regardless of HIV status and receiving category I regimen were included. The exclusion criteria were: pregnancy, foreigner, renal failure, liver disease and TB of other organs. A patient who was treated under SAT in DOTS area were excluded. Data collections were performed by interviewing patients and relatives at their residence, health staffs and health volunteers and reviewing accounting records and medical records.

A cohort of 204 new PTB patients were registered at TB registers of the three selected provinces between October 1, 1998 and March 31, 1999; 57% of the patients received DOTS and 43% of the patients were treated under SAT. All of 204 patients were followed up and data collections were performed between October 1, 1998 and November 30, 1999. In general, our subjects were mostly unskilled male workers, graduated at primary school level with the mean age 45 years. Approximately three-fourth of them had ever used of tobacco or drink alcohol. The average income of patients treated under DOTS was 3,289 baht per month compared to those 1,966 baht under SAT. The results showed that the proportion of patients treated under DOTS (5%) who resided out of jurisdiction of their community hospital was lower than that of SAT (29%) ($p<0.01$). None of the other variables approaches statistical significant, however. In addition, defaulters at the second month of treatment course revealed 2.6% for DOTS strategy compared with 11.5% for SAT strategy. As expected, the median time-to-cured among DOTS group was 184 days compared with 210 days among SAT group. The cure rate of patients treated under DOTS (67.5%) was higher than under SAT (34.5%). The unadjusted analysis showed that patients under DOTS were more likely to be cured at 1.96 (95%CI=1.43-2.68) times higher than those under SAT ($p<0.01$). The results of Cox' s proportional hazard model showed that patients who were treated under DOTS strategy had 2.91 times more likely to be cured when compared to those under SAT strategy after adjusting for occupation and residential area. There were evidence of lower cure rates for those who were unskilled workers or marginalized people (controlling for strategy and residence).

Cost components of both strategies were direct routine service cost, medical care cost and consumer cost. Among these three categories, the direct routine service cost and the medical care cost were most costly items. For instance, results show that the direct routine service cost was accounted approximately half of the total cost for all patients under DOTS. While the medical care cost was a major component of the total cost for SAT. Consumer cost of DOTS accounted for approximately 9% of total cost compared to 12% of total cost in SAT strategy. Even though, average cost of DOTS was a little higher than SAT strategy (7,363 baht vs 5,422 baht) but the difference was not statistically significant (*p*-value=0.77). However, cost per case cured under DOTS (10,905 baht) was lower than cost under SAT (15,724 baht).

Our sensitivity analysis demonstrated that DOTS strategy was considered as cost-effectiveness programme over SAT strategy. By varying labour cost and travel cost at 10%, 30% and 50% from the actual value, the results reflected a small and insignificant effect of labour cost and travel cost on cost-effectiveness in TB treatment by both strategies. In addition, DOTS strategy showed consistency more cost-effectiveness than SAT strategy when the cured rates of both strategies were 20% increasing and 20% decreasing together. By holding SAT cure rate constant and varying DOTS cure rate, it should be noted that at 46.8% of DOTS cure rate, cost per case cured under DOTS and SAT were equal. On the other hand, by holding DOTS cure rate constant and varying SAT cure rate, SAT would offer the similar cost per case cured at 49.7% cure rate. Even though, a cost per case cured is similar at the equilibrium point or at net gain approximately 36%, DOTS strategy offered advantage of achieving high cured rates.

From the finding the following conclusion were drawn:

The patients who were treated under DOTS strategy achieve higher cure rate, lesser defaulter and shorter median time-to-cure than those under SAT strategy. The patients under DOTS had 2.91 times more likely to be cured when compared to those under SAT after adjusting for residence and occupation.

Average cost is slightly higher in DOTS than in SAT but not statistically significant. Costs incurred for treatment a new PTB to be cured under DOTS strategy was nearly 5,000 baht lower than under SAT strategy. Finally, DOTS strategy offers more cost-effectiveness than SAT strategy.

Recommendations from the present study

For policy recommendations

1. Our sensitivity analyses suggested that cure rate of DOTS at 55% would have no comparative advantage over SAT of cure rate at 34.48%. Thus, the public workers should maintain net gain of at least 36%. In addition, WHO estimated 50% of SAT cure rate in Thailand therefore we should have cure rate of DOTS higher than 80% in order to achieve both economic-advantage and impact of treatment for TB.
2. SAT strategy could be improved by follow up those in complete categories at the end of treatment course in order to improve cure rate.
3. There is potential improvement of SAT delivery anti-TB drugs at health center.

4. According to results of "Modified DOTS or Improved SAT", TB patients should be treated under DOTS particularly in the first two months of treatment course and then treated under SAT (but receiving medicines at health center) in the continuation phase. The cost per case cured would be reduced due to the reducing travel cost, time cost for supervision. Thus, "Modified DOTS or Improved SAT" may be an alternative strategy for controlling TB since DOTS could effectively reduce defaulters during the infectious period of TB and may increase practicability of TB controlling programme.
5. According to our findings, unskilled worker or marginalized population should be treated under DOTS and an intensive follow up is need.

For future studies

With the limitation of this study, further studies should be replicated in the larger scale or among TB patients with sputum smear negative or among AIDS group. In particular, new studies should include indirect cost and also intangible cost. Additionally, research should be conducted in the area of cost-benefit or cost-utility. Further studies regarding high death rates among TB cases in these 3 provinces are warrant investigation. Finally, pilot study should be conducted in order to examine the feasibility and it effectiveness of "Modified DOTS or Improved SAT" as an alternative TB controlling strategy in non-DOTS area Thailand.

REFERENCES

1.Broekmans JF. Success in possible but it has to be fought for. World Health Forum 1997; 18: 243-7.

2.Weiss KB, Anderson WW. Tuberculosis poverty's penalty [Editorial]. AM J Respir Crit Med 1998; 157: 1011.

3.Squire SB, Wilkinson D. Strengthening DOTS though community care for tuberculosis [Editorial]. BMJ 1997; 315: 95-6.

4.World Health Organization. WHO report on the global tuberculosis epidemic 1998. Geneva: WHO; 1998.

5.กระทรวงสาธารณสุข. สถิติสาธารณสุข. ม. ป. ท; 2540.

6.Payanandana V, et al. Information in preparation for external review of the national tuberculosis programme, Thailand. Bangkok: department of Communicable Disease Control; 1995.

7.Ministry of public health. Battle against TB: National Tuberculosis Programme Thailand, 1999

8.Murray CJ, Dejonghe E, Chum HJ, Nyangulu DS, Salomao A, Styblo K. Cost effectiveness of chemotherapy for pulmonary tuberculosis in three sub-Saharan African countries. Lancet 1991; 338: 1305-8.

9.Joesoef MR, Remington PL, Jiptuherijanto PT. Epidemiological model and cost-effectiveness analysis of tuberculosis treatment programme in Indonesia. Int J Epidemiol 1989; 11(1): 134-9.

10.Cohn DL, Catlin BJ, Peterson KL, Judson FN, Sbarbaro JA. A 62-dose, 6-month therapy for pulmonary and extrapulmonary tuberculosis. Annals of Internal Medicine 1990; 112(6): 407-14.

11.Manalo F, Tan F, Ssbarbaro JA, Iseman MD. Community-based short-course treatment of pulmonary tuberculosis in a developing nation. Am Rev Respir Dis 1990; 142: 1302-5.

12.Kent JH. The epidemiology of multidrug-resistant tuberculosis in the United States. Medical Clinics of North America 1993; 77(6): 1391-409.

13.Edlin BR, Tokors JI, Grieco MH, Crawford JT, Williams J, Sordillo EM,et al. An outbreak of multidrug-resistant tuberculosis among hospitalized patients with the acquired immunodeficiency syndrome. N Engl J Med 1992; 326: 1514-21.

14.Mahmoudi A, Iseman MD. Pitfalls in the care of patients with tuberculosis : common errors and their association with the acquisition of drug resistance. JAMA 1993; 270: 65-8.

15.Wies S, Nwanyanwu OC, Gomez E. Outbreak of multidrug-resistant tuberculosis-Texas, California and Pennsylvania. MMWR 1990; 39(22): 369-72.

16.American Thoracic Society. Treatment of tuberculosis and tuberculosis infection in adults and children. Am J Respir Crit Care Med 1994; 149: 1359-74.

17.Iseman MD, Cohn DL, Sbarbaro JA. Directly observed treatment of tuberculosis. N Engl J Med 1993; 25: 576-8.

18.Kochi A. Tuberculosis control-is DOTS the health breakthrough of the 1990s? World Health Forum 1997; 18: 225-32.

19.Weis SE, Sloeum PC, Blais FX, King B, Nunn M, Burgis G,et al. The effect of directly observed therapy on the rates of drug resistance and relapse in tuberculosis. N Engl J Med 1994; 330: 1179-84.

20.Burman WJ, Dalton CB, Cohn DL, Butter JR, Reves RR. A cost-effectiveness analysis of directly observed therapy vs self-administered therapy for treatment of tuberculosis. CHEST 1997; 112: 63-70.

21.Zeng ZF, Zou JQ, Sheng DY, Hua CY, Xin D, Ping CS, et al. Results of directly observed short-course chemotherapy in 112842 Chinese patients with smear-positive tuberculosis. Lancet 1996; 347: 358-62.

22.Chaulk P, Moore KR, Rizzo R, Chaisson R. Eleven years of community-based directly observed therapy for tuberculosis. JAMA 1995; 274(12): 445-51.

23.Wilkinson D, Davies GR, Connolly C. Directly observed therapy for tuberculosis in rural South Africa, 1991 through 1994. Am J Public Health 1996; 86: 1094-7.

24.Davidow AL, Marmor M, Alcabes P. Geographic diversity in tuberculosis trends and directly observed therapy, New York City, 1991 to 1994. Am J Respir Crit Care Med 1997; 156: 1445-500.

25.Devidson BL. A controlled comparison of directly observed therapy vs self-administered therapy for active tuberculosis in the urban United States. CHEST 1998; 114: 1239-43.

26.Alwood K, Keruly J, Moore KR, Stanton DL, Chaulk CP, Chaisson RE. Effectiveness of supervised, intermittent therapy for tuberculosis in HIV-infected patients. AIDS 1994; 8: 1103-8.

27.สมศักดิ์ อรรฆศิลป์. ประเภทของผู้ควบคุมกำกับการรับประทานยาและ ผลในการรักษาวัณโรค แบบมีผู้สังเกตโดยตรงภาคสนาม : กรณีศึกษา จังหวัดยโสธร. วารสารโรคติดต่อ 2540; 23 (4): 534-40.

28.Floyd K, Wilkinson D, Gilks C. Comparison of cost effectiveness of directly observed treatment (DOT) and conventionally delivered treatment for tuberculosis : experience from rural South Africa. BMJ 1997; 29(315): 1407-11.

29.Moore RD, Chaulk CP, Griffiths R, Cavalcante S, Chaisson RE. Cost-effectiveness of directly observed versus self-administered therapy for tuberculosis. Am J Respir Crit Care Med 1996; 154: 1013-9.

30.World Health Organization. Tuberculosis in the South-East Asia Region. New Delhi: Regional Office for South-East Asia; 1998.

31.World Health Organization. Treatment of tuberculosis : guideline for national programmes. Second edition. Italy: WHO; 1997.

32.นฤมล สิงห์ดง. การวิเคราะห์ต้นทุนของการรักษาวัณโรคปอด ณ ศูนย์วัณโรคเขต. วิทยานิพนธ์ ปริญญาวิทยาศาสตรมหาบัณฑิต ภาควิชาเวชศาสตร์ป้องกันและสังคม. บัณฑิตวิทยาลัย จุฬาลงกรณ์มหาวิทยาลัย, 2539.

33.สำนักงานปลัดกระทรวงสาธารณสุข. กองระบาดวิทยา. นิยามผู้ป่วยโรคติดเชื้อเพื่อการเฝ้าระวังทางระบาดวิทยา. กรุงเทพ: โรงพิมพ์องค์การสงเคราะห์ทหารผ่านศึก; 2539.

34.Fauci A.S., et al. Harrison' s principles of internal medicine. 14th. New York U.S.A.: McGraw Hill; 1998.

35.Baskin SE, Gale JL, Noel SS, Nolan CM. Tuberculosis risk factors in adults in King county, Washington, 1988 through 1990. Amer J Pub Health 1994; 84 (1): 1750-6.

36.Alcaide J, Altet MN, Plans P, Parron L, Folguerw LI, Salto E, et al. Cigarette smoking as a risk factor for tuberculosis in young adults: a case-control study. Tubercle and Lung Disease 1996; 77: 112-6.

37.Brewis RAL, et al, editor. Respiratory medicine. Second edition. London: W.B. Sounders company; 1995.

38.World Health Organization. TB/ HIV: A clinical manual. Geneva: World Health Organization; 1996.

39.Hoeprich PD, Jordan MC, Ronald AR, editor. Infectious disease. Fifth edition. Philadelphia: J.B. Lippincott company; 1994.

40.Crofton J, Horne N and Miller F. Clinical tuberculosis. London: The Macmillan Press LTD; 1992.

41.กระทรวงสาธารณสุข. แนวทางการดำเนินงานด้านชันสูตรวัณโรคระดับชาติ. กรุงเทพ: ชุมนุม-สหกรณ์การเกษตรแห่งประเทศไทย; 2541.

42.กระทรวงสาธารณสุข. แนวทางการดำเนินงานควบคุมวัณโรคแห่งชาติ. กรุงเทพ: ชุมนุมสหกรณ์การเกษตรแห่งประเทศไทย;2541.

43. ชนะ นฤมาน. ความสัมพันธ์ระหว่างการสนับสนุนทางสังคมและปัจจัยอื่นต่อความสม่ำเสมอในการรักษาของผู้ป่วยวัณโรคปอด. วิทยานิพนธ์ปริญญาวิทยาศาสตรมหาบัณฑิต สาขาโรคติดเชื้อ. บัณฑิตวิทยาลัย มหาวิทยาลัยมหิดล, 2540.

44.Hudelson P. Gender differentials in tuberculosis: the role of socio-economic and cultural factor. Tubercle and Lung Disease 1996; 77: 391-409.

45.Johansson E, Diwan VK, Huong ND, Ahlberg BM. Staff and patient attitudes to tuberculosis and compliance with treatment: a exploratory study in a district in Vietnam. Tubercle and Lung Disease 1996; 77: 178-83.

46.พวงรัตน์ กมุทมาศ. การศึกษาปัญหาของผู้ป่วยวัณโรคที่รับการรักษาไม่สม่ำเสมอและแนวทางแก้ไข. วัณโรคและโรคทรวงอก 2530; 8(2): 77-80.

47.Francis V, Korsch BM, Morris MJ. Gaps in doctor-patient communication. N Engl J Med 1969; 280(10): 335-40.

48.Burman WJ, Cohn DL, Rietmeijer CA, Judson FN, Sberbaro JA , Reves RR. Noncompliance with directly observed therapy for tuberculosis. CHEST 1997; 111: 1168-73.

49. Burman WJ, Cohn DL, Rietmeijer CA, Judson FN, Sberbaro JA , Reves RR. Short-term incarceration for the management of noncompliance with tuberculosis treatment. CHEST 1997; 111: 57-62.

50.Oscherwitz T, Perterson JT, Roger S, Sciortino S, Alper A, Royee S, et al. Detention of persistently nonadherent patient with tuberculosi. JAMA 1997; 278 (10): 843-6.

51.Reichman LB. The single most important remainding problem in contemporary medicine. Thai Tuberc Chest Dis 1994; 15(1): 1-4.

52.ประกิต วาทิสาธกกิจ ประไพ สุเทวีบุรี พูนเกษม เจริญพันธ์ สุมาลี เกียรติบุญศรี และ ศรีสุวรรณ บูรณรัชดา. การจัดบริการการรักษาผู้ป่วยนอก. วัณโรคและโรคทรวงอก 2529; 7(2): 107-10.

53.ขนิษฐา มณีเรืองเดช. ปัจจัยที่มีผลกระทบต่อการมารับการรักษาไม่สม่ำเสมอของรายป่วยวัณโรคปอดของจังหวัดสระบุรี. วิทยานิพนธ์ปริญญาวิทยาศาสตรมหาบัณฑิต สาขาโรคติดเชื้อ. บัณฑิตวิทยาลัย มหาวิทยาลัยมหิดล, 2529

54.Richter C, Parenboom R, Mtoni I, Kitinya J, Chande H, Swai AB, et al. Clinical features of HIV-seropositive and HIV-seronegative patients with tuberculous pleural effusion in Dar es Salaam, Tanzania. CHEST 1994; 106: 1471-6.

55.Fischi MA, Daikos GL, Uttamchandani RB, Poblete RB, Moreno JN, Reyes RR, et al. Clinical presentation and outcome of patients with HIV infection and tuberculosis caused by multiple-drug-resistant bacilli. Annals of Internal Medicine 1992; 117: 184-90.

56. World Health Organization. Global tuberculosis control WHO report; 1999.

57. Kamolrattanakul P, Sawert H, Lertmaharit S, Kasetjaroen Y, Akksilp S, Tulaporn C, et al. Randomized controlled trial of directly observed treatment (DOT) for patients with pulmonary tuberculosis in Thailand. Trans R Soc Trop Med Hyg 1999; 93(5): 552-7.

58.นัยนา ศิริวัฒน์, ปิยะนันท์ เอี่ยมตาล และ มานพ แช่มสนิท. การศึกษาเปรียบเทียบผลการรักษาวัณโรคปอดรายใหม่ด้วยระบบการรักษาแบบมีพี่เลี้ยงกับแบบกินยาเองในศูนย์วัณโรคเขต9 พิษณุโลก. โรคติดต่อ 2541; 24(4): 552-557.

59.สมัย กังสวร, สุพจน์ ขันขาว, มะลิ เรืองทรัพย์ และ สุภาพ โปรยบำรุง. การศึกษาเปรียบเทียบผลการรักษาผู้ป่วยวัณโรคปอดด้วยระบบยาระยะสั้นตามปกติและแบบมีพี่เลี้ยงกำกับดูแล. วัณโรคและโรคทรวงอก 2540; 18(1): 7-16.

60.Neher A, Breyer G, Shrestha B and Feldmann K. Directly observed intermittent short-course chemotherapy in the Kathmandu valley. Tubercle and Lung Disease 1996; 77: 302-307.

61.ยุทธิชัย เกษตรเจริญ, เพชรวรรณ พึ่งรัศมี, ไพฑูรย์ มณีแสง, พรรณี หัสภาค, วีณา ตันไสว และแดง ทองเหม. การควบคุมกำกับการรับประทานยาในผู้ป่วยวัณโรคโดยสมาชิกครอบครัว. วัณโรคและโรคทรวงอก 2538 ;16(4): 237-249.

62.Zwarenstein M, Schoeman JH, Vundule C, Lombard CJ, Tatley M. Randomised controlled trial of self-supervised and directly observed treatment of tuberculosis. Lancet 1998: 352: 1340-3.

63.Drummond MF, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes. 8th edition. New York: Oxford University; 1995.

64.Creese A, Parker D. Cost analysis in primary health care: A training manual for programme manager. Geneva: WHO; 1994.

65. Gold MR, Seigel JE, Russell LB, Weinstein MC. Cost-effectiveness in health and medicine. New York: Oxford University Press; 1996.

66.Horngern CT, Sundem GL. Introduction to management accounting. 8th edition. New Delhi; Prentice-Hall: 1990.

67.Coltman MM. Cost control for the hospitality industry. 2nd edition. New York: Van Nostrand Reinwold; 1989.

68.Reynolds LG. Economics. Illinois: Homewood; 1966.

69.Amacher RC, Ulbrich HH. Principles of microeconomics. 3rd edition. California: South-Western Publishing; 1986.

70.สมคิด แก้วสนธิ และ ภิรมย์ กมลรัตนกุล. เศรษฐศาสตร์สาธารณสุข: การวิเคราะห์และประเมินผลบริการสาธารณสุข. พิมพ์ครั้งที่ 3. กรุงเทพ: จุฬาลงกรณ์มหาวิทยาลัย; 2536.

71.Snyder D. Cost savings from new strategies for tuberculosis control in Poland. WHO: Geneva; 1998.

72.National Statistical Office. Report of the 1996 household socio-economic survey. Bangkok: Office of the Prime Minister; 1996.

73.ชยันตร์ธร ปทุมานนท์. ระบาดวิทยาการแพทย์. กรุงเทพ: พีเอชอาร์ซีจีพับลิเชอร์; 2541.

APPENDICES

APPENDIX A

Interview Form: TB Patient

ID. No……..

1.Hospital…….

2.Name……..

3.Address……..

4.Strategy ( )1.DOTS ( )2.SAT

5.Medical history………

6.Age………..year

7.Reside under jurisdiction ( )1.yes ( )2.no

8.Gender ( )1.male ( )2.female

9.Marital status

( )1.single ( )2.couple ( )3.widdow/separated

10.Occupation

( )1.government official/ enterprise ( )2.labour ( )3.agriculture

( )4.fisherman ( )5.commerce ( )6.other…..

11.Education level

( )1.primary school ( )2.secondary school

( )3.diploma ( )4.university level ( )5.other……

12.Additional drugs payment ( )1.yes ( )2.no

13.Cigarette consumption

( )1.smoke ( )2.non-smoke

( )3.occasional ( )4.discontinued………month

14.Alcohol consumption

( )1.drink ( )2.non-drink

( )3.occasional ( )4.discontinued………month

15.Patient' s income per month………..Baht

16Travel cost

16.1 hospital to house……………..Baht/ visit

16.2 health center to house……….Baht/ visit

17.Number of visit

17.1 At hospital…………..visit

17.2 At health center………visit

18.Time spent for travelling

18.1 hospital to house……………..minutes

18.2 health center to house………..minute

19.Time spent for waiting and receiving treatment

19.1 At hospital…………..minute

19.2 At health center………minute

Interview Form: DOTS observer

1.Name........

2.Age..........year

3.Gender ( )1.male ( )2.female

4.Marital status
( )1.single ( )2.couple ( )3.widdow/separated

5.Occupation
( )1.government official/ enterprise ( )2.labour ( )3.agriculture
( )4.fisherman ( )5.commerce ( )6.other.....

6.Education level
( )1.primary school ( )2.secondary school
( )3.diploma ( )4.university level ( )5.other......

7.Relationship with patient.................

8Travel cost
16.1 hospital to house................Baht/ visit
16.2 health center to house.........Baht/ visit

9.Number of visit
9.1 hospital..............visit
9.2 health center.........visit

10.Time spent for travelling
10.1 hospital to house................minutes
10.2 health center to house..........minute

11.Time spent for waiting
11.1 At hospital...............minute
11.2 At health center..........minute

APPENDIX B

DOTS CARD

Month..........

Observer 1..
2..

Date	Taking anti-TB drugs (please ✓)	Date	Taking anti-TB drugs (please✓)

APPENDIX C
Medical records

ID.No……….. source…………

Name…………

H.N…………..

1.hospital………………………………

2.strategy ( )1.DOTS ( )2.SAT

3.starting date of treatment……………….

4.sputum smear at beginning of treatment………..

5.CXR ( )1.cavity ( )2.non-cavity

6.anti-TB drugs

Isoniazid……………...mg/ day
Rifampicin……………mg/ day
Pyrazinamide…………mg/ day
Ethambutal……………mg/ day
Streptomycin…………mg/ day

7.drugs adverse………………………

8.HIV status ( )1.positive ( )2.negative ( )3.unknown

9.laboratory result of sputum smear at the end of second month……………

10. laboratory result of sputum smear at the end of the fifth month……………

11. laboratory result of sputum smear at the end of treatment course……………

12.last date of treatment……………….

13.treatment outcome……………………..

Drugs and investigation records

Name…………..
HN…………….
Source…………

List / Date	Drugs cost/ charge (Baht)	AFB (Baht)	CXR (Baht)	Other (Baht)	Total (Baht)

APPENDIX D

Capital cost form

Date of collecting data..
Source..

Hospital/ health center	Estimated rental cost per month (Baht)	Rental cost allocated to TB clinic per month (Baht)	Total visits of TB patient per month		Capital cost	
			DOTS	SAT	DOTS	SAT
1. 2. 3.						
Total						

Material cost form 1 (electricity and water)

Date of collecting data...

Source...

Hospital/ health center	Estimated cost of electricity and water per month (Baht)	Cost of electricity and water allocated to TB clinic per month (Baht)	Total visits of TB patient per month		Cost of electricity and water cost	
			DOTS	SAT	DOTS	SAT
1. 2. 3.						
Total						

Material cost form 2 (travel cost of staff particularly DOTS strategy)

Hospital/ Health center..
Source ....

Number	Patient name	Travel cost per round trip (Baht)	Number of visits	Total cost	Remark
Total					

Labour cost form

Hospital/ Health center...

Date of collecting data...

Source...

Number	Name	Salaries / wages (Baht)	Overtime payment (Baht)	Sickpay (Baht)	Other (Baht)	Total (Baht)	Time devoted to TB activities
Total							

APPENDIX E

Table 21 Comparison of treatment outcomes between patients treated under DOTS and SAT strategies by sociodemographic characteristics.

Variables	Not-cure, n (%)	cure, n (%)	*p*-value
Gender			
Male	77(49.4)	79(50.6)	0.15
Female	18(37.5)	30(62.5)	
Age			
35-86	52(39.7)	79(60.3)	0.008
15-34	43(58.9)	30(41.1)	
Income			
< average	56(45.2)	68(54.8)	0.86
>average	32(43.8)	41(56.2)	
Reside under jurisdiction			
No	16(51.6)	15(48.4)	0.54
Yes	79(45.7)	94(54.3)	
Marital status			
Single/widow/separated	34(50.0)	34(50.0)	0.28
Couple	54(41.9)	75(58.1)	
Education level			
Primary or lower	75(44.6)	93(55.4)	0.96
Secondary or more	13(44.8)	16(55.2)	
Occupation			
Labour/agriculture/ fisherman/housework	73(45.1)	89(54.9)	0.81
Government official/student/ monk/commerce/ unemployed	15(42.9)	20(57.1)	
Additional drugs payment (out-of-pocket)			
Yes	35(57.4)	26(42.6)	0.016
No	53(39.0)	83(61.0)	

Table 22 Comparison of treatment outcomes between patients under DOTS and SAT strategies by medical history and risk behaviors.

Variables	Not-cure, n(%)	cure, n(%)	*p*-value
History of DM/CA/lung Disease/steroid abuse			
Yes	21(58.3)	15(41.7)	0.12
No	74(44.0)	94(56.0)	
AFB at initial treatment			
Highly positive	44(46.8)	50(53.2)	0.95
Low or moderate positive	51(46.4)	59(53.6)	
CXR			
Cavity	11(33.3)	22(66.7)	0.06
Non-cavity	63(51.6)	59(48.4)	
Drugs adverse			
Yes	39(41.1)	56(58.9)	0.14
No	56(51.4)	53(48.6)	
Alcohol consumption			
Drink/occasion/discontinue	62(45.6)	74(54.4)	0.70
Non-drink	26(42.6)	35(57.4)	
Cigarette consumption			
Smoke/occasion/discontinue	69(46.9)	78(53.1)	0.27
Non-smoke	19(38.0)	31(62.0)	
Strategy			
DOTS	38(32.5)	79(67.5)	<0.001
SAT	57(65.5)	30(34.5)	

APPENDIX F

Table 23 Comparison of death cases between patients treated under DOTS and SAT strategies by sociodemogrophic characteristics.

Variables	Death		*p*-value
	yes, n (%)	no, n (%)	
Gender			
Male	23(79.3)	133(76.0)	0.70
Female	6(20.7)	42(24.0)	
Age			
15-34	16(55.2)	57(32.6)	0.03
35-64	7(24.1)	88(50.3)	
65-86	6(20.7)	30(17.1)	
Income			
< average	15(51.7)	109(64.9)	0.18
>average	14(48.3)	59(35.1)	
Reside under jurisdiction			
No	3(10.3)	28(16.0)	0.43
Yes	26(89.7)	147(84.0)	
Marital status			
Single/widow/separated	13(44.8)	55(32.7)	0.21
Couple	16(55.2)	113(67.3)	
Education level			
Primary or lower	23(79.3)	145(86.3)	0.33
Secondary or more	6(20.7)	23(13.7)	
Occupation			
Labour/agriculture/ fisherman/housework	24(82.8)	138(82.1)	0.94
Government official/student/ monk/commerce/ unemployed	5(17.2)	30(17.9)	
Additional drugs payment (out-of-pocket)			
Yes	11(37.9)	50(29.8)	0.38
No	18(62.1)	118(70.2)	

Table 24 Comparison of death cases between patients under DOTS and SAT strategies by medical history and risk behaviors.

Variables	Death		*p*-value
	yes, n(%)	no, n(%)	
History of DM/CA/lung Disease/steroid abuse			
Yes	6(20.7)	30(17.1)	0.64
No	23(79.3)	145(82.9)	
AFB at initial treatment			
Highly positive	10(34.5)	84(48.0)	0.18
Low or moderate positive	19(65.5)	91(52.0)	
CXR			
Cavity	4(23.5)	29(21.0)	0.81
Non-cavity	13(76.5)	109(79.0)	
Drugs adverse			
Yes	10(34.5)	85(48.6)	0.16
No	19(65.5)	90(51.4)	
Alcohol consumption			
Currently drink	9(31.0)	25(14.9)	0.03
Occasion/discontinue/never	20(69.0)	143(85.1)	
Cigarette consumption			
Currently smoke	19(65.5)	78(46.4)	0.06
Occasion/discontinue/never	10(34.5)	90(53.6)	
HIV status			
Positive	16(100.0)	27(73.0)	0.02
Negative	0	10(27.0)	
Strategy			
DOTS	21(72.4)	96(54.9)	0.08
SAT	8(27.6)	79(45.1)	

APPENDIX G

Table 25 Univariate Cox' s regression analysis of strategies, medical history and Sociodemographic characteristics.

Variables	B	SE	Exp(B)	95%CI	χ^2	*p*-value
Strategy	0.49	0.23	2.33	1.49-3.64	14.64	<0.01
Age	-0.01	0.01	0.99	0.98-1.01	0.74	0.39
Gender	-0.01	0.22	0.99	0.64-1.51	0.003	0.95
Income	6.3E-05	2.6E-05	1.00	1.00-1.001	6.03	0.01
Occupation	-0.74	0.26	0.48	0.29-0.79	8.64	<0.01
Marital status	0.06	0.21	1.06	0.71-1.60	0.08	0.78
Additional drug payment	0.32	0.23	1.38	0.88-2.16	1.95	0.66
Education level	-0.33	0.27	0.72	0.42-1.23	1.46	0.23
Residence	0.10	0.28	1.11	0.64-1.92	0.14	0.71
Medical history	-0.49	0.28	0.61	0.36-1.06	3.10	0.08
CXR	0.58	0.26	1.79	1.08-2.96	5.21	0.02
AFB	-0.27	0.19	0.77	0.52-1.12	1.88	0.17
Drug adverse	-0.41	0.20	0.66	0.44-0.97	4.48	0.34
Alcohol consumption	-0.23	0.21	0.80	0.53-1.20	1.17	0.28
Cigarette consumption	-0.17	0.22	0.85	0.55-1.29	0.60	0.44
HIV positive	-0.28	0.49	0.75	0.29-1.97	0.35	0.84
HIV unknown	-0.23	0.42	0.80	0.35-1.83	0.35	0.84

APPENDIX H

Table 26 Data of Sensitivity analyses (C- E = cost-effectiveness)

A. Changing in labour cost of both strategies

DOTS			SAT		
Labour cost	Full cost	C - E	Labour cost	Full cost	C - E
10%=31,940.16	893,431.35	11,309.26	10%=13,311.56	485,019.51	16,167.32
20%=95,820.47	957,311.66	12,117.87	20%=39,934.64	511,642.59	17,054.75
30%=159,700.78	1,021,191.97	12,926.48	30%=66,557.73	538,265.68	17,942.19

B. Changing in travel cost of consumer of both strategies

DOTS			SAT		
Travel cost	Full cost	C - E	Travel cost	Full cost	C - E
10%=5,531.00	867,022.19	10,974.96	10%=4,420.80	476,128.75	15,870.96
20%=16,593.00	878,084.19	11,114.99	20%=13,262.40	484,970.35	16,165.68
30%=27,655.00	889,146.19	11,255.02	30%=22,104.00	493,811.95	16,460.40

C. Changing in effectiveness of both strategies

DOTS (Full cost = 861,491.19)			SAT (Full cost = 471,707.95)		
effectiveness	# of pt cure	C - E	effectiveness	# of pt cure	C - E
-20%=54.0%	63	13,674.46	-20%=27.6%	24	19,654.50
0%=67.5%	79	10,904.95	0%=34.5%	30	15,723.60
+20%=81.0%	95	9,068.33	+20%=41.4%	36	13,103.00

Table 26 Data of Sensitivity analyses (continue)

D Holding cure rate of SAT constant and varying DOTS cure rate

Effectiveness(%)	Number of pt cure	C- E of DOTS	C- E of SAT
67.5	79	10,904.99	15,723.60
59.8	70	12,307.02	15,723.60
51.3	60	14,358.19	15,723.60
46.8	54.79	15,723.60	15,723.60
42.7	50	17,229.82	15,723.60

C-E = cost-effectiveness

D. Holding cure rate of DOTS constant and varying SAT cure rate

Effectiveness(%)	Number of pt cure	C- E of SAT	C- E of DOTS
34.5	30	15,723.60	10,904.95
40.3	35	13,477.36	10,904.95
46.0	40	11,792.69	10,904.95
49.7	43.25	10,904.95	10,904.95
51.8	45	10,482.39	10,904.95

C-E = cost-effectiveness

BIOGRAPHY

NAME	Miss. Doungnate Tonimit
DATE OF BIRTH	20 January 1967
PLACE OF BIRTH	Samut Songkhram, Thailand
INSTITUTIONS ATTENDED	Bangkok Nursing College, 1985-1989
	Diploma in Nursing Science
	(Equivalent to Bachelor of Science in Nursing)
	Ramkhamhaeng University, 1989-1994
	Bachelor of Science (Psychology)
	Mahidol University, 1998-2000
	Master of Science (Public Health)
	Major Infectious Disease
POSITION & OFFICE	1989-Present,
	Somdet Phraphutthalertla Hospital
	Position: Professional Nurse