

Preliminary Evaluation of Taiwan's Tuberculosis DOTS Strategy

Chien-Bang Hsu¹; Hsiu-Yun Lo², Cheng-Yi Lee², Shiang-Lin Yang²,
Kwei-Feng Wang¹, Shih-Yan Yang³

1. Third division, Centers for Disease Control, Department of Health

2. Fifth division, Centers for Disease Control, Department of Health

3. Second branch, Centers for Disease Control, Department of Health

From Chinese version, pp,184-203

Abstract

Since April 2006, under the mobilization plan to reduce tuberculosis by half in a decade, Taiwan has implemented DOTS (Directly Observed Treatment, Short-course) in full scale. According to data collected from December 2007, the DOTS implementation rate among smear-positive patients reached 92.6%. Apart from the increase in quantity of DOTS, the quality of DOTS was also enhanced through careful supervision. Preliminary cohort data indicates that the treatment success rate of the smear-positive cases under DOTS and not under DOTS, the sputum conversion rate in 3 months and the defaulted rate have improved in either 2005 (before DOTS) or 2006 (after DOTS); thus showing that significant results in Taiwan's DOTS implementation.

DOTS requires a complete strategy, especially the 5 elements recommended by WHO. These need continuous evaluation and research in order to discover and amend any flaws and thus elevating the quality.

Received: Feb 22, 2008 ; Accepted: Mar 5, 2008.

Correspondence author: Chien-Bang Hsu ; Address: 7F, No.9, Sec.1, Zhongxiao E. Rd., Taipei City, Taiwan, R.O.C Email: clark@cdc.gov.tw

Keywords: Tuberculosis, Halve tuberculosis in a decade, DOTS, smear-positive

Introduction

A. Literature review

In 1994, the World Health Organization (WHO) established DOTS (Directly Observed Treatment, Short-course) as an important strategy in fighting tuberculosis [1] and administering preventative measures. In 1997, WHO declared that “DOTS is the most important development in the century in the number of saved patients” [2]. They also established the global standard procedures in resisting tuberculosis [3]. The purpose of DOTS is to confirm that the patients take every dosage and on a regular basis under the direct supervision of health care personnel or care workers in order to cure and prevent the production of medicinal resistant bacteria. Along with the International Union Against Tuberculosis and Lung Disease (IUATLD), Rifampin should be protected and “only under supervision by a third party can Rifampin be administered in the prevention of medicinal resistance to the drug appears.” [4]. The successful administration of DOTS not only technically relies upon the direct observation of the patients and the taking of the medication, but also the case and concern for the patients themselves. The following five elements are needed: (1) Political commitment with increased and sustained financing, (2) Case detection through quality-assured bacteriology, (3) Standardized treatment, with supervision and patient support, (4) An effective drug supply and management system, (5) Monitoring and evaluation system, and impact measurement.,

The concept for DOTS originated in the 1950's when drugs for tuberculosis started to appear. At the time, many medical centers had medical personnel

supervise the administration of drugs and documented large-scale and systematic DOTS. In Hong Kong during the 50's, cases were treated in 25 medical centers with direct supervision 6 days a week for 6 months. After the treatment, the drug was self administered for 16.5 months [6]. Until the mid 70's, there were reports on DOTS that included the use of Rifampin. Starting in 1981, 6-month treatment regimen started to emerge [7]. This directly observed method and short course treatment has gradually merged in to what we know today as DOTS. Due to the large number of personnel involved in the project, many poor countries are unable to participate whereas developed countries believe that only educating individual cases is sufficient; thus there is no need to proceed with the project or that it is only operated on minority groups. In that time period, the global focus was only on the drugs prescription and the change in treatment regimens.

Only until the end of the 20th century, with the reemerging of tuberculosis, the medical field has started to reconsider the methods for controlling the tuberculosis. The uncooperative attitudes of the patients and the disintegrating public health system have lead to the drug to be unable to fulfill its potential. Many researches between 1966 and 1996 have proved that DOTS can elevate the cure rate of the patients respectively in comparison with self administration. Self administration has only a median cure rate of 61.4% whereas Enhanced DOTS can reach 91.0% [8]. In addition, the effect is quite significant in both developed countries and poorer countries [9-14]. The research in Denver by Burman et al. has proved that although the costs for the preliminary administration for DOTS are higher, the clinical and epidemiological results toward the later period are quite significant. Therefore, the results in terms of cost-effectiveness show that DOTS is better than self administration [15]. Research in other areas has also proved the effects of DOTS [16]. DOTS has

now become WHO most recommended preventative measure. According to an annual survey of 2007, DOTS has been used by 187 WHO members by 2005. The areas that use DOTS take up 89.0% of the global population. The DOTS treatment success rate reached 84.0% in 2004.

However, other voices on whether WHO's promotion of DOTS can fight and eradicate tuberculosis has also risen [17-18]. The first question is aimed at the whether the operation is complete or not. If not, despite the high treatment success rate and high case detection rate [19-20], the root of the problem is still unsolved with the increasing number of patients. The increase of AIDS has also changed the infliction rate of those infected carriers [21-22]. In addition, the appearance of multi-drug resistant tuberculosis has lead to the use of DOTS-Plus. The arise of these questions will influence and change the methods of administration and results of DOTS.

B. Current status and trend of tuberculosis in Taiwan

In 2006, there were a total of 832 deaths with death rate was 3.6 per hundred thousand. The standardized death rate was 2.9 as the 13th in the cause of death and the first in the notifiable communicable diseases. Compared with the past, the death rate of tuberculosis has declined to 3.6 persons in 2006 from 294.44 persons in 1947 per hundred thousand. Despite the fact that the death rate has decreased, the speed of the decrease has slowed. In 2005 and 2006, the incidence rate was 72.47 and 67.38 persons per hundred thousand. Incident tuberculosis numbers were 16,472 and 15,378 persons [24].

In 1999, new DOTS patients in Taiwan's mountainous regions were followed until June 30, 2001 with a result of 88.3% treatment success rate; thus showing higher results in comparison with the 76.6% in rest of the nation. The defaulted rate of 5.3% in the tuberculosis patients was also lower than the nation's defaulted

rate of 6.6% [25]. Data showed that the use of DOTS in Taiwan can elevate the cure rate of tuberculosis cases and effectively reduce the defaulted rate. In July of 2002, DOTS was used on all smear-positive cases. Despite the fact that the implementation rate reached 91.1% in 2005, 64.2% of the care workers were family members. This is completely different from what WHO had in mind in promoting DOTS. Therefore, much advice from local experts is still needed.

Effective administration of DOTS in Taiwan

Since April 1, 2006, the Department of Health has started to use DOTS under the mobilization plan to reduce tuberculosis by half in ten years. In regards to the fact that each area is different, it is difficult to establish one project that will fit the needs of different regions. Therefore, the center facility plans, acquires resources, and offers the structures and principles while the local facilities are in charge of conducting the project.

The principles established for DOTS are as following: (1) The patients are the main priority. The time and place for the patients to take their medication are set with the patient's convenience and comfort as the top priority. (2) Patients participating in DOTS are required to accept health education beforehand in order to understand their rights and obligations. They may choose to participate in the program or not. Those that agree to participate in DOTS need to fill out an agreement form. (3) Care workers need to visit and supervise the taking of the medication for at least 5 days a week and the patient need to self administer the medication for a time period of at least 6 months. (4) DOTS stations need to be established. Each county needs to establish DOTS stations according to the rationality, number of patients, and medical resources. (5) Drugs need to be recalled back to DOTS stations for safekeeping. After being

separated by public health nurses, the drugs are taken by care workers to administer to the patients. (6) Care workers participating in DOTS must receive training for a certain amount of time before hand and once every year in order to increase their expertise and experience. (7) Counselors (public health nurses) need to be able to manage the work status of the care workers on a daily basis. The visit routes, visit logs, and visit situations need to be filed into the database. (8) Any special condition of individual cases found by the care workers need to be reported to the counselor and dealt with immediately. (9) DOTS stations need to hold meeting regularly. (10) Individual cases that have been diagnosed and hospitalized for the first time can allow public health nurses and care workers to visit under the right circumstances in order to enhance the will in participating in DOTS. (11) Supervision and screening is applied to reward the good and eliminate the poor.

The budget for DOTS in Taiwan was 59.9 million NTD in 2006 and 200.7 million in 2007. The budget for 2008 is 250.5 million NTD. The resources invested in DOTS by the government have grown respectively and most of the resources (70.0%) are used to pay the care worker salaries. The number of care workers in 2006 and 2007 were 377 and 543 with a ratio of 3:1 (female: male). Secondly, the resources were used to provide nutrient coupons for individual cases. The budget mentioned above are not counted into the time and resources used by government personnel. The DOTS subjects for 2006 and 2007 are cases in which the acid fast stain resulted positive or the negative acid fast stains with positive cultivated results. With the stable structure and mature experience, the project will cover those uncooperative cases which do not have acid fast stain evidence or negative results (such as the homeless) and those potential infected persons who participate in the project of preventative distribution of the drug.

The management standards for the administration of DOTS includes the administration rate (see Figure 1), the ratio of the care workers' visits (actual visit days / required visit days), the number of patients a care worker visits, and the DOTS logs. The result standards include the successful treatment rate, the negative transference rate in 3 months, and the defaulted rate. In order to be sure DOTS is administered, DOTS also includes a supervision system. Apart from management and follow up through the data base, counselors should also be responsible for management and supervision of the care workers. In addition, government facilities' (center and local alike) personnel will also conduct phone inquiries with the cases along with visitation and irregular visits. These irregular visits found flaws such as drugs that were not recalled back to DOTS station and the administration of the drug without supervision.

Epidemiology data Analysis

A. Study subjects

From the Centers of Disease Control national tuberculosis database, confirmed smear-positive cases reported in 2005 and 2006 are the main analysis subjects. In 2005, the new smear-positive cases numbered 5,756 persons and 5,564 in 2006. Results of the treatment in a 12 month cohort, and eliminating those which data is insufficient or abnormal, the number of cases that are excluded from the database total up to 219 in 2005 and 86 in 2006; thus the final count for those in the database total up to 5,537 in 2005 and 5,478 in 2006.

B. Definitions of treatment result

Treatment success: The patient was cured and completed the treatment.

Cured: The patient who has shown smear-positive results shows negative in the last month of treatment. There must be at least one negative acid fast

stain result before the late month of treatment.

Completed treatment: The patient has completed his/her treatment yet does not reach the standard for cured or failed.

Failed: Smear-positive patients which after 5 months or more treatment still show positive results.

Defaulted: The patient's treatment was stopped for 2 months or more.

Died: The patient died during the treatment due to any number of causes.

Transferred out: The patient transferred to other locations and the result of the treatment is unknown (e.g. moving abroad).

Not evaluated: After 12 months of treatment, the patient is still receiving treatment or shows no results under the records.

C. Definition for the negative transference rate of smear-positive tuberculosis cases in 3 months:

negative transference of confirmed smear-positive cases reported in 2006 in 3 months / confirmed smear-positive tuberculosis cases *100 [26].

D. Data analysis

According to the described calculations by the software SPSS version 14.0, along with the χ^2 test for comparing treatment results between DOTS and non-DOTS groups, and between year of 2005 and 2006.

E. Results

A total of 15,378 persons were reported as confirmed tuberculosis cases. Among these, 5,564 (36.2%) persons were smear-positive cases. The median for age is 65 years (Q1=47 years, Q3=77 years). Male cases numbered up to 3,999 (71.9%) persons with a median of age of 65 years (Q1=49 years, Q3=77 years). Female cases totaled to 1,565 (28.1%) persons with a median of age of

63 years (Q1=42 years, Q3=77 years). In the 5,564 smear-positive cases, 3,616 (65.0%) joined DOTS with non-DOTS 1,948 (35.0%) persons. The male case numbers of DOTS and non-DOTS are relatively 2 times greater than those of female cases. This is similar to the fact that male cases were usually greater than female cases by 2 times in Taiwan's tuberculosis history. Looking at the age span, the median age for DOTS cases is 64 years (Q1=47 years, Q3=76 years) and the median age for non-DOTS cases is 67 years (Q1=48 years, Q3=78 years), 3 years higher than DOTS cases. There is significant difference in median age between the two groups. Still examining the age span, both DOTS and non-DOTS cases' age are starting to increase and those over the age of 65 take up 50.0% of the cases. This is related to the fact that over half of the tuberculosis cases in Taiwan belong to the elderly above 65 years of age. These two groups do not show much difference in calculations, showing that the age span is not much different in the two groups.

Examining the bacteria evidence, the DOTS cases with smear-positive and cultivated bacteria amounted to 2,966 persons (82.0%), which is much higher than those non-DOTS cases of 1,441 persons (74.0%). In comparing this batch of smear-positive cases' negative transference in 3 months, DOTS transference rate is 47.0%, higher than non-DOTS cases of 33.0%. This shows that DOTS cases have a much higher negative transference rate than non-DOTS cases (Table 1) As seen in the figure, the transference rate in DOTS cases and non-DOTS cases are also different in each county (see Figure 2).

In comparing the results of the 12 month treatment period of DOTS cases and non-DOTS cases, the results show that the successful treatment rate for DOTS cases is 75.1%, which is much higher than those non-DOTS cases 51.6% ($P < 0.001$) (see Figure 3). The cure rate for DOTS cases is 50.0% and completed

treatment rate is 25.1%. Both of these figures are higher than non-DOTS cases' cure rate of 29.7% and completed treatment rate of 21.8%. In other words, the treatment results are much better for the DOTS cases in comparison with non-DOTS cases. Looking at the death rate, non-DOTS case death rate is 1.5 time higher than DOTS case death rate. Non-DOTS death rates 37.7%, whereas DOTS death rate is 13.6% ($P<0.001$). In the defaulted rate, non-DOTS case defaulted rate is 5.0%, which is much higher than DOTS case 3.5% ($P<0.001$). In other words, participating in DOTS reduces the chance of death or defaulted. Although the defaulted rate of DOTS cases was higher than non-DOTS cases, there were no statistically significant differences.

Due to the fact that the DOTS project started administering in 2006, the follow up results of the smear-positive cases are compared with those of 2005 in order to understand the effect of DOTS on the treatment. The cure rate of 2006 is 42.8%, which is higher than the 26.8% of 2005. Although the completed treatment rate for 2006 is 24.0% and 37.2% for 2005, the overall successful treatment rate in 2006 reached 66.8%, whereas 2005 was 63.9%, showing a 3% difference. This has also displayed a significant difference in the statistics ($P<0.001$). There is also respective difference in the death rate of the two years. The death rate of 2006 is lower than 2005's 2.3%; thus showing a difference in statistics ($P<0.001$) (Table 3).

Discussion

DOTS has already started to show the effects in Taiwan. Almost all of the smear-positive cases enroll in the program. This is a great aid in managing the individual cases, lowering the defaulted rate, and increasing the treatment success rate and even the cure rate. There are still many aspects that need improvement

in Taiwan's DOTS program. We will examine these through the 5 elements proposed by WHO.

A. Political commitment with increased and sustained financing

This is the first element that is needed to insure the success of DOTS and also the most important one in insuring the administration of the program. Whether the government wants to proceed with DOTS or not will influence the distribution of personnel and resources, the vertical and horizontal contact net of the center and local government facilities, and the ability to fulfill its functions. In addition, it also influences the willingness to cooperate on the behalf of medical personnel, public and private medical facilities, and even non-government organizations. Although the Department of Health promised to offer resources to local facilities with the administration of DOTS in 2006, the actual operation was conducted conservatively due to the inexperience and unconfident status of the local facilities. However, by the second year, local facilities started to increase the number of care workers involved due to the increased confidence and budget. This can be seen in the increase in numbers of case workers and administration rate. From the start of DOTS administration, the minister of the Department of Health strongly promoted the program and the pros and cons of the administration which pushed the local facilities to proceed with the program. At the same time, the aggressive promotion of the program by the local administrators will lead to the good results shown by the workers in many aspects. However, there is still much to improve in this aspect. First, the horizontal contact network is still weak. Tuberculosis cases are not only medical issues but also economic and social issues. Apart from health related facilities, other facilities rarely participate in the DOTS program. Secondly, the cooperation from non-government facilities is not enough. Apart from the

resources regularly provided by the National Tuberculosis Association, no other non-government organizations have participated in the program. If other public and private medical facilities could participate in the program, the effects would be much significant. An example would be the PPM (Public-Private and Public-Public Mix) in Taichung where the middle and large sized local hospitals establish DOTS stations in which the participation rate of the patients is higher. Other areas can also use the same method. In addition, the base level workers and the budget system regulations have also cause problems in the administration of the program.

B. Case detection through quality-assured bacteriology

There are two main elements in this aspect. The first is to make the preliminary diagnosis through acid fast stain and not only thorax X rays. Acid fast stain is not only cost friendly, but also able to determine whether the patient is contagious or not and whether the condition is acute or not [27]. With only an X ray, there may be misjudgment, even by experts [28]. In the past, the diagnosis for tuberculosis in Taiwan was mainly established on the thorax X-rays of the patient. However, in 2001 with the establishment of the tuberculosis prevention system, the Department of Health has adjusted the policy to encourage the use of acid fast stains to aid in the diagnosis. The Department of Health has also established a testing laboratory for tuberculosis which provides testing services. Currently, the rate of diagnosis in the preliminary testing has reached at least 90.0%. The standard is 3 sets of acid fast stain with an average of 2.5 sets. However, the positive initial diagnosis rate is 43.8% [29] which is still lower than the WHO standard of 65-80% [30]. This means that there is still much to be improved in the methods of collecting and preserving the samples and laboratory technologies. This may be due to the fact that many of the facilities that have

hospitals do the testing are not under management. In the WHO tuberculosis project supervision and evaluation manual, it is mentioned that most smear-positive patient transfer to negative after 2-3 months of treatment. However, at the same time, there are still as many as 25.0% of patients which still have positive results even after good supervision and quality medication in the initial phase [26]. According to Table 2, Taiwan's negative transference rate in both DOTS and non-DOTS cases in 3 months is still quite low. This may be due to many factors such as the habits of doctors who prescribe the tests, or that worker fail to press for results, or that individual cases fail to cooperate in taking the tests. The management of acid fast stains and the evaluation of negative transference still need improvement in order to reflect the actual situation.

Theatrically, the administration of DOTS will lower the defaulted rate. However the defaulted rate of 2006 is slightly higher than that of 2005 as seen in Table 3. The cause may be that the definition of defaulted (whether the treatment was stopped for 2 or more months) before DOTS (2005) was not yet complete. Therefore, some of the cases were categorized as unable to evaluate or fall cases may be influenced by other factors. Many need further examination in order to confirm the situation.

The second part that needs to be considered is the discovery of the patients. Most patients as discovered after the patient seeks medical assistance yet there are no cases that are actively discovered. This is due to the fact that most actively found cases usually have lower levels of cooperation and completed treatment rate [31]. Another reason is due to the fact that it cost more to find patients which do not comply with cost effectiveness. Only in locations such as China in which medical resources are lacking and the discovery rate is too low [20] do they actively search for patients. Currently, with the accessible medical assistance

here in Taiwan, the problem mentioned above will not occur. Therefore, most cases still are discovered after the patients seek medical assistance. Thorax X rays are administered in high-dangerous groups such as the mountainous regions and prisons. Infectious preventive law requires that doctors must report and tuberculosis (or suspected tuberculosis cases) with 7 days. Most doctors can follow the regulation, yet the lateness of diagnosis is still a serious problem. According to the analysis of cases in 2006, the patients received tuberculosis medication on the average 12.8th time of treatment. More than half of the patients went through 6 medical centers before being discovered as a smear-positive tuberculosis patient. The median for lateness in diagnosis is 43 days (inter-quartile range, 7-138 days) [32]. The awareness and education should be elevated in doctors and the quantity and quality of the test should be enhanced in order to increase doctors' confidence in the tests and use these as the evidence for future diagnosis.

C. Standardized treatment, with supervision and patient support

All initial treated patient, whether infected with HIV or not, must receive international standardized prescribed treatment. In the initial phase (the first 2 months of treatment), they must receive medication that includes isoniazid, ethambutol, rifampin, and pyrazinamide. In the next 4 months continuation phase (the third to sixth week of treatment) pyrazinamide is stopped and isoniazid, ethambutol, and rifampin are continued. In order to avoid medicinal acquired resistance, the patient should take the medication under direct supervision. After visiting in the field and inspection, there are still patient who are taking the wrong medication or dosage. In addition, there are cases in which the patient is taking dosage that fits their weight range yet shows either too large or too small dosages with no particular reason. In order to solve this problem, there should be

manuals that become doctors' references, relative organizations should collaborate in educating doctors, experts should provide evaluation, and public health systems should discover problems in drug administration. It is planned to integrate the evaluation system into the Health Insurance program in order to prevent mistreatment problems.

D. An effective drug supply and management system

With Taiwan's current conditions and resources, the provision of anti-tuberculosis medication should not be a problem. Currently, experts recommend fixed-dose combinations which are easy to take and reduce the chance of the patients only using one kind of medication. It can also reduce the chances of mistakes in prescribed medication and aid in the administration of DOTS. Currently the Rifater dose on the market is not ideal. If a 50 kg patient takes five doses, Isoniazid may reach 400mg which may be too much. However, with patients 70 kg or more, the Pyrazinamide dosage will only reach 1,250 mg, which is not enough. This should be improvised [33].

E. Monitoring and evaluation system, and impact measurement

Looking that the results of tuberculosis treatment patients (the negative transference rate after treatment) and the results of the preventive strategies, evaluation data and generation analysis is needed. After reporting the tuberculosis patient cases in Taiwan to the completion of management in the database, local health centers should visit the individual cases, document the medication administrating situation, especially those DOTS cases which also need to have a daily DOTS log. However, due to the change in personnel, the lack of personnel, the lack of experience, large workloads may all lead to incomplete data or time dates. Many prescription problems may also lack the correction by doctors. In order to improve these situations, computer evaluation, irregular

inspections, and continuous education will elevate the expertise and experience of public health personnel and care workers. Rewards can also elevate the spirits of the workers. In addition, enhancing the test process can also provide scientific evidence for doctors. In the future, national tuberculosis follow-ups, management, and treatment research can result in a more complete database.

Conclusion

DOTS does not simple refer to the visual supervision of drug administration where care workers merely supervise the taking of the drug, it is a complete preventive system that combines medical assistance and public health. All aspects such as the discovery of patient, diagnosis methods, management systems, and regular criticism, must be combined in order to proceed with DOTS.

Afterword

Taiwan's preliminary effects in the administration of DOTS include a special trait - the passionate and skilled in communication care workers. After visiting San Francisco, USA and attending the care worker meetings in Taiwan, the author has discovered that the care and concern shown by care workers in the USA seems to be a bit unnatural and too formal. Perhaps this is due to the cultural habit differences. On the other hand, the 500 or so care workers in Taiwan become involved in the patient's lives, from their homes to the planting of vegetables and many other experiences. Some can even prepare meals for the elderly that live alone and many establish a trusting relationship. Some aboriginal cases even call the care workers "mother". Many of the care workers treat these kinds of relationships as a challenge and achievement for themselves. They are an important element in achieving the success of Taiwan's DOTS project.

References

1. World Health Organization. WHO tuberculosis programme: framework for effective tuberculosis control, 1994. Available at: http://whqlibdoc.who.int/hq/1994/WHO_TB_94.179.pdf (Accessed Feb 2008).
2. World Health Organization. WHO calls for immediate use of new tuberculosis breakthrough (press release). 1997.
3. World Health Organization. TB: a crossroads. WHO report on the global tuberculosis epidemic, 1998. Available at: http://whqlibdoc.who.int/hq/1998/WHO_TB_98.247.pdf (Accessed Feb 2008).
4. Enarson DA, Rieder HL, Arnadottir T. Tuberculosis guide for low income countries. In IUATLD, ed. Tuberculosis guide for low income countries, 3rd ed. Frankfurt am Main: pmi Verl-Gruppe, 1994: 74.
5. World Health Organization. An expanded DOTS framework for effective tuberculosis control. Available at: http://www.who.int/entity/tb/publications/expanded_dots_framework/en/index.html (Accessed Feb 2008).
6. Moodie AS. Mass ambulatory chemotherapy in the treatment of tuberculosis in a predominantly urban community. *The American Review Of Respiratory Disease*. 1967; 95: 384-97.
7. Iseman MD, Albert R, Locks M, et al. American Thoracic Society. Medical Section of the American Lung Association. Guidelines for short-course tuberculosis chemotherapy. *The American Review Of Respiratory Disease*. 1980; 121: 611-4.
8. Chaulk CP, Kazandjian VA. Directly observed therapy for treatment completion of pulmonary tuberculosis: Consensus Statement of the Public

- Health Tuberculosis Guidelines Panel. JAMA: The Journal Of The American Medical Association. 1998; 279: 943-8.
9. Weis SE, Slocum PC, Blais FX, et al. The effect of directly observed therapy on the rates of drug resistance and relapse in tuberculosis. The New England Journal Of Medicine. 1994; 330: 1179-84.
 10. Frieden TR, Fujiwara PI, Washko RM, et al. Tuberculosis in New York City - turning the tide. The New England Journal Of Medicine. 1995; 333: 229-33.
 11. Results of directly observed short-course chemotherapy in 112,842 Chinese patients with smear-positive tuberculosis. China Tuberculosis Control Collaboration. Lancet. 1996; 347: 358-62.
 12. Chowdhury AM, Chowdhury S, Islam MN, et al. Control of tuberculosis by community health workers in Bangladesh. Lancet. 1997; 350: 169-72.
 13. Crows S. DOTS is effective even in nomadic populations. Lancet 1997; 350:343.
 14. World Health Organization. Global tuberculosis control - WHO report 1998. Available at:http://whqlibdoc.who.int/hq/1998/WHO_TB_98.237.pdf (Accessed Feb 2008).
 15. Burman WJ, Dalton CB, Cohn DL, et al. A cost-effectiveness analysis of directly observed therapy vs self-administered therapy for treatment of tuberculosis. Chest. 1997; 112: 63-70.
 16. Murray CJ, DeJonghe E, Chum HJ, et al. Cost effectiveness of chemotherapy for pulmonary tuberculosis in three sub-Saharan African countries. Lancet. 1991; 338: 1305-8.
 17. Brewer TF, Heymann SJ. To control and beyond: moving towards eliminating the global tuberculosis threat. Journal of Epidemiology and

Community Health 2004; 58: 822-5.

18. Dye C. Tuberculosis 2000-2010: control, but not elimination The Comstock Lecture. The International Journal of Tuberculosis and Lung Disease. 2000; 4: S146-S52.
19. The effect of tuberculosis control in China. Lancet. 2004; 364: 417-22.
20. MOH, China, Report on nationwide random survey for the epidemiology of Tuberculosis in 2000, Journal of Chinese Anti-Tuberculosis Association. 2002; 24: 65-107.
21. Whalen CC, Johnson JL, Okwera A, et al. A trial of three regimens to prevent tuberculosis in Ugandan adults infected with the human immunodeficiency virus. Uganda-Case Western Reserve University Research Collaboration. The New England Journal Of Medicine. 1997; 337: 801-8.
22. Selwyn PA, Sckell BM, Alcabes P, et al. High risk of active tuberculosis in HIV-infected drug users with cutaneous anergy. JAMA: The Journal Of The American Medical Association. 1992; 268: 504-9.
23. Department of Health, ROC (Taiwan). Available at http://www.doh.gov.tw/EN2006/DM/DM2.aspx?now_fod_list_no=9377&class_no=390&level_no=2 (Accessed Feb 2008).
24. National Surveillance Network of Communicable Diseases, Taiwan Centers for Disease Control. Available at <http://www.cdc.gov.tw> (Accessed Feb 2008).
25. Taiwan Centers for Disease Control, Taiwan Tuberculosis Control Year Book 2000, 2001: 29 (in Chinese).
26. World Health Organization. Compendium of Indicators for Monitoring and Evaluating National Tuberculosis Programs. Available at:

- http://www.who.int/tb/publications/tb_compendium_of_indicators/en/index.html (Accessed Feb 2008).
27. Rouillon A, Perdrizet S, Parrot R. Transmission of tubercle bacilli: The effects of chemotherapy. *Tubercle*. 1976; 57: 275-99.
 28. Koppaka R, Bock N. How reliable is chest radiography? In Frieden T, editor. *Toman's tuberculosis: case detection, treatment, and monitoring—questions and answers*. 2nd edition. Geneva (Switzerland):World Health Organization;2004.51-60.
 29. Taiwan Centers for Disease Control, Taiwan Tuberculosis Quality Management Index Monthly Report, 2007. Available at <http://www.cdc.gov.tw> (Accessed Feb 2008) (in Chinese).
 30. World Health Organization. WHO Report 2007. Global tuberculosis control -surveillance, planning, financing. Available at: http://www.who.int/tb/publications/global_report/2007/en/index.html (Accessed Feb 2008)
 31. Rieder H. What is the role of case detection by periodic mass radiographic examination in tuberculosis control ? In: Frieden T, Toman's tuberculosis:case detection, treatment, and monitoring—questions and answers. 2nd edition. Geneva (Switzerland): World Health Organization;2004. p72-9.
 32. Wen-lin Lai, Epidemiological study of diagnostic and treatment delay among tuberculosis patients in Taiwan: a population-based study using National Health Insurance claims data, Master Thesis in National Cheng-Kung University, 2006 (in Chinese).
 33. Taiwan Centers for Disease Control, Taiwan Tuberculosis Clinical Guideline (Edition II), 2006 (in Chinese).

Figure 1. DOTS Administration Rate of Taiwan's Smear-Positive Cases (July 2006 ~ December 2007)

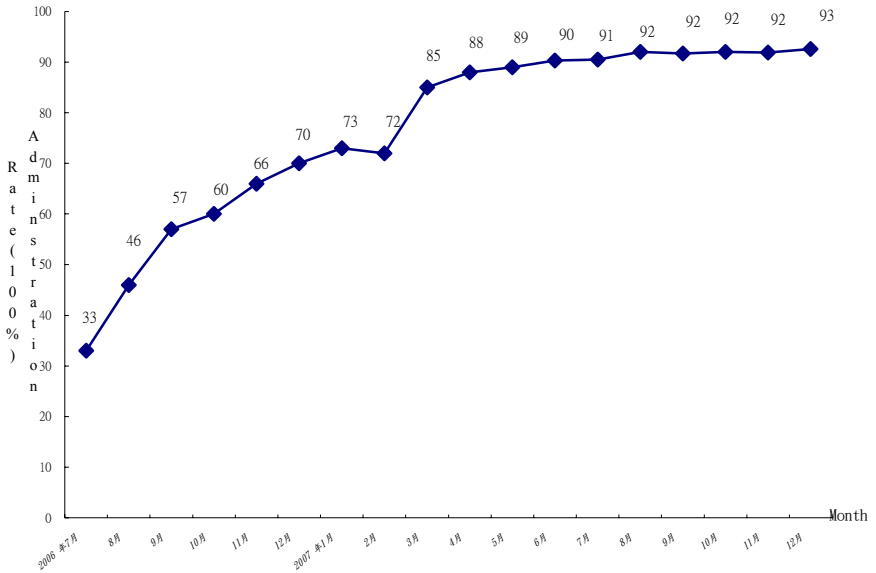


Table 1. Demographic Characteristics of Smear-Positive Cases in 2006

	DOTS		non-DOTS		p-value
	Number	%	Number	%	
New cases	3,616	65.0	1,948	35.0	
Gender					
Male	2,612	72.2	1,387	71.2	0.41
Female	1,004	28.8	561	28.8	
Age (years)					
mean \pm s.d.	60 \pm 19		63 \pm 19		< 0.001
median(Q1, Q3)	64 (47, 76)		67 (48, 78)		< 0.001
Age group (years)					
0-14	21	0.6	5	0.3	
15-24	172	4.8	74	3.8	
25-34	232	6.4	117	6.0	
35-44	367	10.1	190	9.8	
45-54	546	15.1	279	14.3	
55-64	498	13.8	245	12.6	
> 65	1,780	49.2	1,038	53.3	
Bacteriology (smear-positive)					
Positive transference	2,966	82	1,441	74	< 0.001
Negative transference	1,702	47	642	33	< 0.001

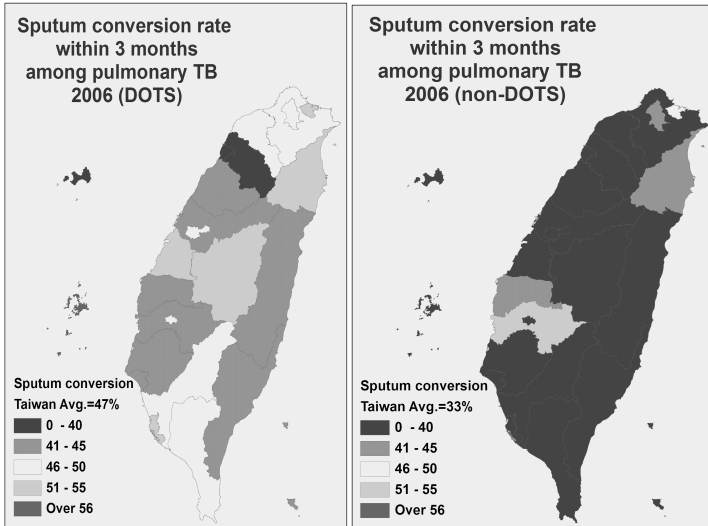


Figure 2. Negative Transference Rate in 3 Month of Taiwan's Tuberculosis Cases (DOTS and non-DOTS)

Table 2. Comparison of Cohort Treatment Results between DOTS and non-DOTS

	DOTS		non-DOTS		$(P_{\text{DOTS}} - P_{\text{non-DOTS}})$ 95% CI
	N=3,541	%	N=1,937	%	
Treatment success	2,659	75.1	999	51.6	20.9 ~ 26.2 ***
Cured	1,770	50.0	576	29.7	
Completed treatment	889	25.1	423	21.8	
Died	483	13.6	730	37.7	-26.5 ~ -21.6 ***
Defaulted	125	3.5	97	5.0	-2.6 ~ -0.3 *
Failed	46	1.3	16	0.8	-0.1 ~ 1.0
Transferred out	2	0.1	0	0.0	
Not evaluated	226	6.4	95	5.0	-2.1 ~ 1.0

Note: "Cohort treatment" indicates each smear-case receives treatment and follow-up for 12 months. CI: Confidence Interval.

*, *** indicates a statistical significance observed at $\alpha = 0.01$ and 0.001 respectively.

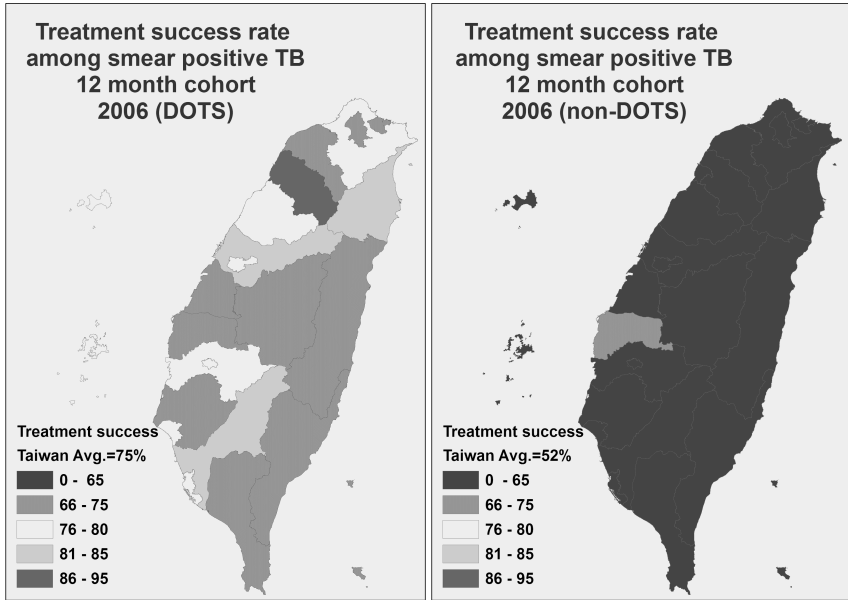


Figure 3. Successful Treatment in 12 Months of Taiwan’s Smear-Positive Cases (DOTS and non-DOTS)

Table 3. Comparison of Cohort Treatment Results between Year 2005 and Year

	2006 Smear-Positive Patients.				$(P_{DOTS}-P_{non-DOTS})$ 95% CI
	2005		2006		
	N=5,537	%	N=5,478	%	
Treatment success	3,537	63.9	3,658	66.8	1.1 ~ 4.8 ***
Cured		1,482	26.8	2,346	42.8
Completed treatment	2,055	37.1	1,312	24.0	
Died	1,350	24.4	1,213	22.1	-3.8 ~ -0.7 *
Defaulted	119	2.1	222	4.1	1.3 ~ 2.6 ***
Failed	100	1.8	62	1.1	-0.2 ~ -0.1 *
Transferred out	7	0.1	2	0.0	
Not evaluated	424	7.7	321	5.9	-2.7 ~ -0.9 ***

Note: “Cohort treatment” indicates each smear-case receives treatment and follow-up for 12 months. CI: Confidence Interval.

*, *** indicates a statistical significance observed at $\alpha = 0.01$ and 0.001 respectively.