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External review of "Halving TB in 10 years program in Taiwan, 2006 – 2015"

TAIWAN CDC

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Executive summary

Taiwan has a strong national program for the treatment, prevention, and control of tuberculosis (TB) which is still the number one infectious cause of death in Taiwan. Combined with economic and demographic changes in the population, the activities within the national TB program, including the “Halving TB in 10 Years Program, 2005–2016,” are resulting in a sustained decrease in TB incidence in all parts of the Taiwanese population. A continuation of the present trends will not achieve the target of halving the TB incidence rates from 2005 to 2016, but the trends are coming quite close to achieving that target.

Recommendations have been made, based on an external review by an independent international team, which will contribute to a further strengthening of the program and will also enable some increased efficiencies in the use of resources. The recommendations should be adapted to meet the needs of Taiwan: Taiwan’s excellent data collection systems, surveillance activities, mycobacteriology laboratories, and epidemiologic research should be used to guide the customization and implementation of the recommendations. Key recommendations include:

- Strengthen adherence to national guidance on the treatment of TB.
- Increase the use of testing for latent TB infection, which includes the use of interferon-γ release assays (IGRAs) for contacts of TB, with chest radiography reserved for those with positive results or symptoms in most circumstances.
- Reduce the use of routine chest radiographic screening, including in the follow up of patients who have completed treatment.
- Maintain the investment in laboratory systems to ensure a high level of service and contribution to the care of patients.
- Increase the age for the treatment of latent TB infection in conjunction with IGRA testing of contacts, to further reduce the incidence of TB.
- Screen students from high incidence countries for TB and include international migrant workers in the national TB statistics.
- Increase the use of intermittent treatment regimens in the treatment of TB disease and latent TB infection in order to reduce the work burden of direct observation.
- Strengthen systems for infection control for congregate settings which include residents who are at high risk of TB.
- Study the dynamics of TB transmission in the population and high-risk subgroups of the population by combining the results from genotyping and epidemiologic investigations.
- Increase the evaluation of the specific components of the “Halving TB” plan by using collated local and national data and operational research.

The approach to the treatment, prevention, and control of TB in Taiwan provides a model for other countries in the region. The combination of adequate resources, political will, and a strong national program, and an expert and enthusiastic workforce, are critical factors in the success of the national TB program. This combination must be sustained and strengthened to maintain progress in the control of TB.

Introduction

At the invitation of Taiwan Center for Disease Control (TCDC), an independent international panel reviewed the Taiwan national TB program and the plan to halve the incidence of TB in ten years ("Halving TB in 10 Years Program in Taiwan 2006–2015"). The outcome of the review is also intended to inform the development of a prospective scheme for the next ten year national TB control program to be implemented in 2016–2025.

The panel, which included experts in the field of TB from the United States, Singapore, Japan, and the United Kingdom, carried out the review over six days in February–March 2013. The panel heard presentations on the occurrence of TB and its prevention and control in Taiwan from national specialists from TCDC, hospital clinicians, and local community based TB workers. In addition, the panel visited hospitals, TB laboratories, branch offices of TCDC, and local health centers as well as accompanied program workers in the observation of patients receiving TB treatment. Additional information was made available to the panel on request.

Although TB remains the number one infectious cause of death, TB incidence rates have been declining in Taiwan in recent years in all age groups and in all parts of the country. Over the same period, the standard of living of the population in Taiwan has improved rapidly as measured by gross domestic product which has risen to US$20,000 per capita in 2011. The panel recognized that the decline in TB observed during this period was probably resulting from the demographic changes and the improvement of living standards generally in the Taiwanese population, as well as the impact of treatment of patients with TB and the wider TB control program. The panel was asked to recommend potential ways to accelerate the decline in rates of TB which, despite the current declining trend, will not reach half of the 2006 levels by 2015. While many of the recommendations of the panel will contribute to a further decline in TB rates, none are thought likely to lead to such a substantial acceleration of the decline that the target of half the 2006 rate will be achieved by 2015. Many of the recommendations, however, are intended to provide ways to improve resource allocation and increase the efficiency of the current program.

The panel was extremely impressed by the strength of the Taiwanese national TB program and its commitment to collecting and using evidence for selecting the best practices for Taiwan. The program appears to have strong national and local political support. The national program is guided by a strategy with guidelines for clinicians, laboratorians, and public health workers. The system of national health insurance and coverage from central funds for other co-payments for most patients with TB means that ability to pay is not a barrier to effective TB treatment. The national program provides social support, where this is needed, to patients on TB treatment. The system of "no reimbursement without notification" has ensured that almost all patients with TB enter the national system with case information being collated in an excellent national web-based surveillance system. The review panel met staff of the national program who were all well informed about TB and their role and who were enthusiastic and diligent in their work.

Such are the strengths of the national TB program in Taiwan that the panel considers that it could be a model for other programs in the region. An indication of the strength of the

program is the willingness of the Taiwanese authorities to open up the national program to external international review and scrutiny.

This report is divided into sections reflecting key issues in the prevention and control of TB in Taiwan. Each section includes recommendations for operational strengthening of the system and recommendations for related research. The recommendations are collected together into a summary at the end of the report.

Epidemiology

The epidemiology of TB in Taiwan today reflects historical and demographic changes in the population over the past century. These include— (1) rapid economic development since the early 1970s, (2) immigration from mainland China in 1949 and from Japan prior to 1945, (3) disparities between the immigrant groups and their offspring born and raised in Taiwan, (4) high rates of TB in the aboriginal population groups of the island, (5) universal access to medical care through National Health Insurance (NHI) with its system of guiding practice through reimbursement policies, and (6) adaptation of the WHO-recommended "DOTS" strategy.

NHI provides universal access to healthcare services, thus eliminating financial barriers to medical and public health services for TB. In 1997, NHI implemented a "No-notification→no-reimbursement" policy, resulting in near-universal reporting of TB cases. After officially adopting the DOTS strategy in 2006, with its highly standardized recording and reporting system, surveillance data became even more accurate.

The epidemiology of TB in Taiwan today exemplifies the age-period-cohort effect described by Wade Hampton Frost. Age-stratified TB morbidity and mortality over the past decades consistently reflect this birth cohort effect. For example, TB incidence in Taiwan among those born in 1952 fluctuates with a relatively narrow range of 60–70 cases/100,000 persons/year and rises to 650–770 among those born in 1922. At present, 52% of Taiwan's TB cases occur in the 10% of the population aged ≥65 years.

For each age range, TB incidence decreases with each calendar year. For example, among those aged 65–74 years, it decreased from 292/100,000 in 2002 to 147/100,000 in 2011. Among those aged 75–84 years, it decreased from 553/100,000 in 2002 to 340/100,000 in 2011. Among those aged 0–14 years, reflecting TB transmission in Taiwan after 1997, TB incidence decreased from 5/100,000 to 2/100,000 over the same 10 year period. Therefore, in the modern era of universal access to healthcare and reliable surveillance data, the main determinant of Taiwan's TB incidence and the decreasing trend in TB incidence is the age distribution and origin of different segments of the population, including the year-by-year aging and mortality of the elderly population. Taiwan's rapid economic development since the 1970s increased the GDP per capita from <$1000 in 1971 to >$20,000 in 2011. The low and diminishing TB burden in those born after 1970 reflects this rapidly increasing standard of living.

As a result of these historical, political, and socioeconomic determinants, the number of reported TB cases in Taiwan is decreasing at a steady rate of approximately 4% to 5% per year. This trajectory will probably continue for the foreseeable future, not quite reaching the goal of halving 2006's TB incidence by 2015, although it will be close. To reach its goal, Taiwan would need to double the rate of decrease from 5% per year to 10% per year or the annual decrease in case counts from about 650 cases to about 1200 cases per year. It may be possible, but it would require substantial changes in TB control policies and practices because 10% per year decreases in TB incidence are uncommon, and such a large acceleration of the decrease in the burden would be nearly unprecedented.

Realistically, primary prevention strategies (e.g., find infectious cases and promptly start effective therapy) will not sharply reduce TB incidence in the short term, although such measures are the foundation of TB control in the long term. Reaching the target of halving incidence would require preventing an additional 2000 TB cases by 2015. One possibility would be to provide preventive treatment for greater than 40,000 recently infected individuals. These persons have a roughly 5% chance of developing TB with 2 years and effective treatment might prevent 2000 cases of TB. However, the feasibility of doing this would have to be determined in the context of other TB control priorities.

A better understanding of the epidemiology and transmission of TB can help TB control programs focus their efforts onto effective strategies and to evaluate the impact of interventions. The panel recommends that TCDC study the dynamics of the TB transmission of TB infection in the population and high-risk subgroups of the population by combining the results from genotyping and epidemiologic investigations.

Case detection and diagnosis

Passive case detection relies on finding TB patients among symptomatic persons seeking healthcare. The DOTS strategy was based originally on passive case detection by sputum-smear microscopy for acid-fast bacilli (AFB) because it was inexpensive, feasible in low-income settings, and because it detects the most infectious cases. Because of NHI, the infrastructure, the human resources, and the technologically advanced medical care, passive case detection is highly developed and effective in Taiwan, although its efficiency and expense have room for improvement. In contrast, active case finding requires the healthcare system to take the initiative in determining which persons are at high risk of developing TB, seeking them out, and evaluating them to diagnose and treat any who have active TB disease.

In both strategies, the principal tools for case detection and diagnosis for the individual patient are the same: (1) medical history, (2) physical examination, (3) tests for immunological sensitization of *M. tuberculosis*, (4) radiography, (5) microbiology, and (6) histopathology.

A 2008 study in Taiwan demonstrated TB treatment was initiated based on radiography alone in more than 45% of cases. However, radiographic abnormalities are reported to have a sensitivity for TB of 80% to 94% and specificity for TB of 67% to 73%. Given the relatively low prevalence of TB in person suspected to have TB, this could lead to inappropriate treatment for TB in persons with an abnormal chest radiograph but who do not have TB. Furthermore, there is a risk of cancer from exposure to X-ray radiation; although small, it increases with the number of chest radiographs. The panel raised concerns that Taiwan's program might rely too much on chest radiography for screening and active case finding; for follow-up of patients receiving treatment and after treatment; and for those with ongoing risk of developing TB such as healthcare workers and TB contacts.

The results from the mycobacteriology laboratory are crucial for current TB control efforts. Isolation of *M. tuberculosis* from patient specimens confirms the TB diagnosis and enables testing for drug susceptibility and genotype. For pulmonary TB, the routine specimen is spontaneously expectorated sputum. Concerns were discussed that the quality of some expectorated sputum specimens were inadequate, particularly those from patients who did not have a productive cough. For confirming the diagnosis of pulmonary TB in such instances, sputum induction with aerosolized hypertonic saline, a relatively simple, safe, and low-cost procedure, may be used to overcome this problem.

In general, in an era of economic constraints, finding and treating more TB cases with less effort and lower cost become important considerations. To this end, the panel recommends increased used of economic analysis, cost-effectiveness analysis, risk-benefit analysis, and decision analysis for developing rational policies, and increased use of social and behavioral sciences to promoted the associated behavioral changes among healthcare professionals.

Laboratory systems

The standard laboratory services available for the laboratory confirmation of TB include AFB-smear microscopy (Ziehl-Neelsen and fluorescent stains), culture on solid (Lowenstein-Jensen, LJ) and liquid media (Mycobacterium Growth Indicator Tube, MGIT), species identification (immunochromatographic test or molecular test), and first-line drug susceptibility testing (agar proportion method). Second-line drug susceptibility testing is available for all isolates with rifampin resistance, including multidrug-resistant (MDR) TB isolates.

The testing is provided by a network, overseen by the National TB Laboratory, of eight contract laboratories (three of which are regional reference laboratories), 24 authorized laboratories, and primary laboratories. Primary laboratories collect specimens, do AFB smear microscopy, and ship specimens to authorized laboratories. Some primary laboratories also do culture. Authorized laboratories do AFB smear microscopy, culture on solid and liquid media, species identification, and first-line drug susceptibility testing. Any MDR TB isolate is transferred to the National TB Reference Laboratory for second-line drug susceptibility testing. In addition to the diagnostic testing, the three regional reference laboratories do molecular tests on sputum specimens to detect rifampicin resistance in known contacts of MDR TB cases and persons at high risk of MDR TB (relapse or treatment failures). The National TB Reference laboratory conducts first-line and second-line drug susceptibility testing, strain typing (spoligotyping, 15-locus MIRU typing, IS6110 RFLP) for outbreak investigations, and research. Spoligotyping is also used for the differential diagnosis of disease caused by *M. bovis*, *M. bovis* BCG, and *M. tuberculosis* strains.

The total estimated laboratory testing in 2011 included 834,000 AFB smears, 827,000 cultures, 88,000 species identification tests, and 30,000 drug susceptibility tests. In 2011, about 9,780 cases were bacteriology confirmed. The authorized TB laboratories do the majority of the TB diagnostic testing. Each authorized laboratory has three to five staff members assigned to daily work in the laboratory and conducts tests on 30,000 to 45,000 specimens per year. This is a very large workload, which may be excessive if the large workload detracts from the quality of testing. The effect of this large workload on laboratory performance and capacity should be reviewed regularly. It may be necessary to establish additional authorized laboratories. The program may also consider the feasibility of testing fewer specimens per patient. The current Taiwanese standard is three specimens for the initial diagnostic testing. The World Health Organization has recommended an algorithm that includes testing of only two specimens in programs with quality-assured laboratories. The National TB Reference Laboratory estimated that by testing only two instead of three specimens, about 4% of TB cases might be missed. On the other hand, reducing the workload in high volume laboratories in other countries has shown improvements in case detection rates. Any change is testing recommendations must be carefully considered by the program, clinicians, laboratorians, and policy makers.

Thirty-one of the thirty-two authorized TB laboratories are accredited by the Taiwan Accreditation Foundation or the College of American Pathologists and accreditation of the thirty-second laboratory is expected in 2013. This is an outstanding accomplishment and

should be of considerable pride to the Taiwanese laboratories and program. The laboratory facilities either meet the BSL-3 containment criteria or are BSL-2 facilities with negative pressure containment rooms. This is in compliance with the most recent recommendations of the World Health Organization for biosafety in the TB laboratory. The eight quality indicators monitored by the National TB Reference Laboratory on a per specimen basis include smear positive rate, culture positive rate, contamination rate for the first LJ culture, specimen transport times, and turnaround times for smear, growth detection on LJ medium, identification of *Mycobacterium tuberculosis*, and drug susceptibility testing.

- The smear positivity rate is 6.8% overall and the culture positivity rate is 12.3% overall. These rates depend not only on laboratory performance but also on the population being tested. The positivity rates are stable over time which indicates good quality laboratory performance. However, these rates are somewhat less than would be expected for testing of symptomatic persons (i.e., typical passive case finding). This raises the possibility that specimens are being tested from persons that have a low likelihood of having TB. On the other hand, active case finding and intensive contact investigations can lead to lower positivity rates. The program should determine the underlying reasons for the low positivity rates and evaluate the current recommendations for testing to ensure that there is a balance between the need to find TB cases and the laboratory capacity to do the testing.
- The contamination rate for the first LJ culture is about 3% which is very good. It is recommended that the program also measure and monitor the contamination rate of the MGIT cultures.
- More than 99% of specimens are received by the contract TB laboratories within the targeted 3 days from specimen collection. This is excellent. It is recommended that individual laboratories monitor specimen transport times from individual collection sites to discover any potential transportation problems.
- The targeted turnaround time of 24 hours for AFB smear microscopy is met for more than 99% of specimens. Laboratories should report turnaround time from receipt of specimens to recording of AFB smear results. To provide a realistic performance measure, it is often necessary to separate turnaround times for specimens received from Monday through Thursday from those that are received on Friday afternoon but not tested until the next work day (Monday).
- The targeted turnaround time of 21 days for the detection of growth was met for only about 60% of the specimens submitted to the contract laboratories. This turnaround time is for detection of growth on LJ. The program should confirm that the laboratories are reporting the time to detection of growth and not the time to detection of *M. tuberculosis* (growth plus species identification). If only the latter is easily reported, the program should consider changing the performance indicator to 28 days for growth detection and species identification. It is also recommended that the program monitor the turnaround time for growth detection or growth detection plus identification in liquid culture (MGIT).
- The targeted turnaround time (28 days) for drug susceptibility testing is being met for about 90% of isolates. This is acceptable performance for the agar proportion method. If drug susceptibility testing is done using MGIT, that turnaround time should be monitored separately.
- It was noted that the non-contract laboratories performed a little less well than the contract laboratories. It is recommended that the program continue efforts to bring the

performance of the non-contract laboratories to the same level as the contract laboratories.

Overall, the performance indicators provide a good assessment of laboratory performance. One additional performance indicator to monitor is the percentage of AFB-smear positive initial diagnostic specimens that yield positive cultures for any mycobacteria (target ≥95%). This indicator monitors the performance of the liquification and decontamination process and is useful for interpreting the culture-contamination rates. The program may also consider setting the performance targets the indicators for the growth based indicators as turnaround times for 90% of strains. This is because there are strains of *M. tuberculosis* that grow more slowly than the average *M. tuberculosis* strain. This is often the situation with MDR TB strains.

The high quality of the work in the laboratory results from a comprehensive training and quality assessment program. The regional reference laboratories provide training and external quality assessment for AFB-smear microscopy. The National TB Reference laboratory provides training and external quality assessments programs for culture, identification, and drug susceptibility testing. The quality assurance program is time-consuming and labor intensive. Sufficient resources must be allocated to the quality assurance program to maintain the excellent performance of the Taiwanese TB laboratories.

The current testing algorithm is to (1) process specimens (liquification, decontamination, and concentration), (2) perform AFB smear microscopy and inoculate cultures from the concentrated sample, (3) identify the species of any growth observed in the cultures, (4) conduct first-line drug susceptibility for all *M. tuberculosis* isolates, and (5) conduct second-line drug susceptibility testing for all rifampicin-resistant isolates. This is a good algorithm for susceptible isolates. To improve the testing algorithm, it is recommended that—

- Second-line drug susceptibility testing be conducted for all rifampicin-resistant isolates, not just MDR TB strains. This is because there appears to be an unusually large rate of rifampicin-resistant isolates that are not MDR TB isolates, and treatment of rifampicin-resistant TB is more difficult than treatment of susceptible TB.
- A role for molecular diagnostic tests in the detection of TB and the detection of rifampicin resistance should be explored. Molecular diagnostic testing has great potential to improve the prompt detection of TB and drug-resistant TB and initiation of effective therapy. The TB laboratories in Taiwan are well prepared to take advantage of recent advances in molecular diagnostic testing. The program and laboratory should evaluate the potential use of molecular diagnostics in Taiwan. Given the excellent specimen transport system, a centralized or regionalized high-throughput molecular testing approach may be more cost effective than a decentralized approach that relies on expensive tests such as the Cepheid GeneXpert MTB/RIF Assay. Operational research to evaluate the cost and performance of such testing algorithms is essential to provide the evidence for implementation.
- Second-line drug susceptibility testing must include testing to at least the injectable second-line agents available in Taiwan (capreomycin and kanamycin) and the fluoroquinolones used in Taiwan (levofloxacin and moxifloxacin). The national laboratory does this routinely, but some variability in this was observed in the regional reference laboratories.

The laboratory confirmation of tuberculosis is complicated by the high frequency of non-tuberculosis mycobacteria found in sputum specimens. It is thought that up to half of AFB-positive or mycobacterial culture-positive samples are positive because of the presence of non-tuberculosis mycobacteria. At the National Taiwan University Hospital, the non-tuberculosis mycobacteria accounted for about 70% of the mycobacteria-positive specimens. Thus, it is important that the laboratory should rapidly identify the species of *Mycobacterium* that is present in a sample to guide treatment decision. For AFB-smear positive samples, a molecular diagnostic test may be the most efficient way to detect the presence of *M. tuberculosis* and allow prompt initiation of therapy. The frequency of NTM warrants investigation. Studies should be done to determine the characteristics of patients with NTM, clinical significance of NTM-positive cultures, and potential impact of NTM detection on TB diagnosis (e.g., mixed infections).

The electronic laboratory information systems in the contract laboratories and National Reference Laboratory are outstanding and provide much useful information. The program is encouraged to expand this laboratory information and reporting system to as many of the authorized laboratories as possible. The use of the laboratory information system may provide an opportunity for the laboratory to facilitate reporting of the isolation of *M. tuberculosis* to the clinician and TB control program.

The National TB Laboratory plays a strong leadership role for the TB Laboratory Network through its testing activities, quality assurance activities, and research. Adequate resources must be provided to the National TB Reference Laboratory to maintain and strengthen its leadership. The program and laboratory should work together to develop a research program for the laboratory that builds the evidence needed for national recommendations and policy. This could include evaluation of the performance and costs of different testing algorithms and of new diagnostic tests, characterization of new molecular tests and testing approaches (e.g., centralized sequencing for drug resistant strains), and molecular epidemiology studies.

Understanding the molecular epidemiology of TB is essential to guide TB control efforts to prevent transmission. The National Laboratory currently has the capability to conduct typing of *M. tuberculosis* strains, although they do not have adequate resources to conduct large-scale molecular epidemiology projects. The current strain-typing capacity must be increased to accommodate TB outbreak investigations and molecular epidemiology. The program and laboratory should work together to develop studies to define the molecular epidemiology of TB in the general population and high risk populations. In particular, is there transmission from the elderly to children, from elderly persons to elderly persons, from foreign workers to Taiwan residents, and among aboriginal people?

Current strain typing methods include spoligotyping, 15-locus MIRU, and IS6110 RFLP. Given the large proportion of Beijing-family strains in Taiwan, the laboratory should consider using 24-locus or 27-locus MIRU typing for better discrimination of Beijing-family strains. The use of strain typing for the differential diagnosis of *M. bovis* BCG in about 30 extrapulmonary TB cases in children less than 5 years old per year is useful. On the other hand, given the low frequency of *M. bovis* TB (i.e., 0.4% of cases overall), spoligotyping to differentiate *M. bovis* and *M. tuberculosis* should be reserved for specific epidemiologic investigations.

Management of TB cases

The clinical care of patients with TB in Taiwan is directed by a physician, usually based in hospital, in tandem with local public health systems for delivering and monitoring outpatient care. National clinical treatment guidance is provided by TCDC and adheres to evidence-based internationally accepted recommendations on the treatment of TB. Successful outcome of treatment is reported in a very high proportion of patients treated, which suggests that clinical management is highly effective (see below).

Physicians are encouraged to follow the national guidance but are not obliged to do so. Variation from the standard guidance was observed frequently by the panel: examples included extension of the 2-month initial phase to 3 or more months, extension of the total length of treatment from 6 months to 9 or more months and frequent deviation from the standard combination of drugs recommended. A survey of in-hospital therapy was reported in which 28% of patients received “non-standardized regimen in combination,” 32% of patients received “inadequate/over dosage,” and 19% of patients received treatment with “inappropriate frequency.” At 12 months after commencement of treatment, the outcome of treatment could not be evaluated in 4% to 5% of cases, and, in most of these instances, the problem was reported to be that the patients were still receiving treatment.

The panel believed that the variation from standard recommended treatment occurred much more frequently than could be justified on clinical grounds. International experience indicates that consistently good results, including the avoidance of drug-resistant and multidrug-resistant TB, are achieved by adherence to standard regimens. In addition, standard regimens avoid excessive treatment of patients and related costs. The panel recommends that a survey be conducted of all treatment courses implemented, and the reasons for variation from national standard regimens, with a view to providing evidence about treatment practice. This evidence should be used, in combination with the international literature, to place strong pressure on all physicians to adhere to national guidance in treating all patients other than when clinical circumstances oblige variation.

At the time of diagnosis, the clinical condition of some patients is poor and they require inpatient care. During this period, infection control is considered so as to ensure that patients do not to present a threat to other patients, hospital staff, or visitors. The priority is to ensure that patients with infectious forms of TB are isolated and that staff, other patients, and visitors are protected. This is particularly important for those with pulmonary smear positive disease but also for those with pulmonary smear negative disease where potential contacts may be vulnerable. Patients with infectious drug-resistant disease are managed in negative pressure isolation where this is available. Patients who are not infectious, but need hospital care due to their clinical condition, are admitted to general hospital wards.

Patients who are well enough to be managed in their own home should be allowed to go home if at all possible. Patients with infectious disease are advised not to return to school or work or other equivalent setting until they have completed two weeks of treatment. For patients with infectious forms of TB, an assessment should be carried out by the community team to determine the appropriateness of care at home. In most instances, where the patient is well enough, it should be possible to manage care while the patient is at home

unless there are concerns about compliance with treatment or infection control, especially when there are vulnerable contacts in the home from whom the patient cannot be separated. The panel found evidence that some clinicians were requiring patients to stay in a hospital during the early weeks of their treatment in the belief that this was essential for preventing spread of infection in the community. The panel recommends that, where an assessment in the community indicates that the patient can be safely managed in the community, all patients should be managed at home unless there are overwhelming clinical or infection control reasons to do otherwise.

Modern TB therapy is highly effective. With patients for whom cure is documented or with patients for whom culture results were negative and treatment was completed, relapse after completion of treatment is uncommon. International guidance indicates that patients can be safely discharged at the end of treatment having been provided with information about their condition and the need to seek medical care early for further assessment if they develop symptoms that could be due to TB. The panel saw evidence, however, that patients who had successfully completed treatment were often being followed up with repeat chest radiography at 6-month and then annual intervals. This is unnecessary and wasteful of resources, and it subjects patients to potentially harmful radiation. The panel recommends that patients be discharged from follow up at the end of successful treatment and that further follow up be reserved for those patients who have had drug resistant disease or other complications of their treatment course.

Most patients are enrolled onto directly observed therapy, short course (DOTS), which is administered both in hospital and in the community. The quality of DOTS is assessed routinely using the proportion of doses actually directly observed. While 84% of DOTS was administered to the highest level of quality in 2011 (level A — 70% or more of doses witnessed in the intensive phase, 60% or more in the continuation phase), 16% of patients were administered directly observed therapy to a lower standard. The panel recommends that every effort be made to increase the proportion of patients treated with the highest standard of DOTS in the intensive phase and that similarly high levels of supervision be achieved in the continuation phase for patients with any kind of complication of treatment or in whom problems with compliance are anticipated or observed.

Treatment in the continuation phase currently employs daily dosing regimens. The panel recommends the investigation of the use of intermittent regimens in the continuation phase which could considerably reduce the burden of observation in DOTS for the health team. A similar issue applies to the application of directly observed preventive treatment which is currently administered daily. The panel recommends the exploration of intermittent treatment for latent infection such as nine months of isoniazid twice a week. However, the panel notes that international experience has shown that patients who have HIV infection and extensive pulmonary TB disease should receive daily regimens throughout the course of treatment — this re-enforces the need to know the HIV-infection status of all TB patients.

Direct observation of receipt of every dose of treatment is labor intensive. This remains essential for treatment of disease during the intensive phase and for patients with complications of treatment or problems with compliance. For many patients, however, during the continuation phase of treatment of active disease, and for many patients taking treatment for latent infection, observation of treatment may be achieved to an adequate level without direct observation on site and still achieve effective treatment. Taiwan has

recently been investigating the use of electronic forms of treatment observation which is reported to be particularly acceptable to a younger generation of IT-familiar patients. The panel recommends that further study be carried out to evaluate methods to achieve remote observation of treatment (of disease and latent infection) using electronic methods while ensuring that overall effectiveness of treatment is not allowed to decline. Caution should be exercised, however, to ensure that direct observation of treatment is continued for all patients in the intensive phase and for patients in the continuation phase where there have been treatment complications, problems with compliance, or any drug resistance.

The intensive phase of standard treatment with four drugs lasts for 2 months to be followed by 4 months of two drugs. Drug susceptibility results should be available by the 2-month point and any alteration to treatment initiated on the basis of the results.

Patients with mono-resistance to either isoniazid or rifampicin require a change to the standard treatment regimen, and treatment should be managed on the basis of advice from the TB laboratory and national and international guidelines.

Patients with multidrug-resistant TB (MDR TB) require both alteration and extension of their treatment which should be based on drug susceptibility information. A project to assess the application of the WHO DOTS Plus approach in Taiwan (Taiwan MDR TB Consortium, TMTC) has recently been carried out and was demonstrated to be highly effective in increasing the proportion of patients achieving a successful outcome. The panel recommends that this approach be rolled out to include all patients in Taiwan who have MDR TB. Information on the regimen used, combined with patient information, drug susceptibility pattern, and treatment outcome, should be collected for every case in order to monitor the effectiveness of the DOTS Plus program.

Outcome of TB treatment

Information on the outcome of TB treatment in Taiwan is available for the years 2005 to 2010. Treatment “success” was reported in approximately 70% of patients who started treatment during this period. This is lower than the WHO-recommended minimum level of 87% successful treatment and seems to suggest that the results in Taiwan are suboptimal, by international standards, in treating TB patients. The data, however, require further scrutiny before any conclusions can sensibly be drawn. For example, treatment failure is reported in approximately 3.0% of cases, which suggests that treatment “success” is better than reported.

Patients older than age 65 years account for approximately half of all TB patients in Taiwan but only one tenth of the population. This contrasts with the pattern of TB incidence in the majority of countries around the world where a greater proportion of TB cases occur in young adults. The rates in each population segment, age 65–74 years, age 75–84 years, and age older than 85 years, are progressively larger. The likelihood of dying having been diagnosed with TB increases very substantially in older patients: only 3.8% of those younger than 50 years in 2010 died whereas 25.9% of those older than 50 years died. About a quarter of those dying after the diagnosis of TB were reported to have died before treatment commenced. Many of those dying while still receiving treatment were reported to have died as a result of other conditions rather than from TB itself.

In approximately 5% of TB cases in Taiwan, the outcome of treatment cannot be evaluated at 12 months and this is usually because the patient is still receiving treatment. The panel was concerned that in some instances this was because the treatment has been altered from the standard recommended regimen without adequate reason. Less than 2% of patients are reported to default from treatment which is a low rate. A very small number of patients are transferred to other countries so that their outcome cannot be determined.

In the light of this more complete understanding of the facts behind the statistics of treatment outcome, the panel believes that Taiwan achieves a high level of successful treatment completion in those patients where treatment completion is feasible. Monitoring of treatment completion should be continued. The panel recommends that more detailed investigation be carried out into the causes of death in those dying while on TB treatment, and in those dying before TB treatment starts, to determine how many deaths are preventable.

Contact Investigations

Per current national policies, contact investigations are initiated for all TB cases, regardless of sputum-AFB-microscopy and culture status. Contact investigations are done around both pulmonary cases and extrapulmonary cases without evidence of pulmonary disease.

- Chest radiography is done for all contacts at the start of the investigation.
- Contact investigations are done around extrapulmonary TB index cases to find the source of infection and co-prevalent cases.
- For index cases of pulmonary TB, the types of tests for the contact investigations depend on the (1) the AFB results from sputum-smear microscopy and culture for the index case, (2) the presence of a pulmonary cavity in the index case, and (3) the age of the contacts.
    - For index cases with AFB seen on sputum-smear microscopy,
        - For contacts age 25 years and younger, chest radiography and a tuberculin skin test. The chest radiograph is done at the start of the investigation, but the skin test is delayed until at least 1 month after the end of the exposure period, in allowance for the latency of delayed-type hypersensitivity. This is true for all groups of contacts who are tested with tuberculin.
        - For contacts age 25 years and older, chest radiography but not a skin test.
    - For index cases with negative results from sputum-smear microscopy but a positive culture result or a pulmonary cavity (but not necessarily both),
        - For contacts age younger than 13 years, chest radiography and a skin test.
        - For contacts age 13 years and older, chest radiography but not a skin test.
    - Chest radiography is repeated at 12 months, for—
        - Contacts who are younger than 13 years, if the skin test result was positive but preventive therapy was not taken.
        - Contacts who are age 13 years and older, all contacts unless TB was diagnosed from first-round evaluation or in the interim.

The average number of contacts per index TB case was 8.1 in 2011. This means more than 102,000 contacts for the 12,634 cases that year.

The review panel did not see information about how many contacts younger than age 13 years are investigated annually. However, for the contacts who were diagnosed with positive skin test results (i.e., latent *M. tuberculosis infection*, LTBI), the results are very good. The number started on preventive therapy in this age group was 2,455 (80%) of the 3,068 who were eligible. Of those who started, approximately 90% were treated under direct observation (i.e., DOPT). Fully 90% of those who started treatment completed it, which is a much better rate than reported from most operational settings worldwide.

The review panel also did not see information about how much chest radiography is being done for contacts who were evaluated with radiography only (i.e., without a skin test) and

what the yields of these activities were. In 2011, active case finding with chest radiography overall found 808 cases (6.4% of the national total of 12,634), and this includes contact investigations. Assuming that all 808 cases were detected through contact investigations, the case yield would be 0.7% (808/102,335). This yield rate is slightly low: most studies of contact investigations have found a rate of 1%–2%.

The review panel also did not see information about how many contact investigations were done around extrapulmonary-only index cases or pulmonary cases with negative AFB sputum-smear and culture results. These two classes of TB cases are less likely to be contagious in comparison to bacteriologically-confirmed pulmonary TB cases, and the slightly low yield rate of contact investigations might be explained by the inclusion of contacts to non-contagious types of TB. The yields of all kinds of TB contact investigations in Taiwan should be compared, for selecting the strategies that are more productive and thus more purposeful.

Recommendations:
Extensive resources are being invested in the many activities that comprise contact investigations. Therefore, the yield and costs of contact investigations should be assessed. The first area for exploration would be the yield of universal chest radiography for contacts. The analysis should focus on these groups:

- For contacts who were tuberculin skin tested, a comparison of the radiography yield in tuberculin reactors and tuberculin non-reactors.
- Contacts who had only chest radiography (and not skin tests before radiography).
- Contacts of extrapulmonary-only TB.
- Contacts of pulmonary TB that was not confirmed by bacteriology.

In addition, for each group that is subjected to routine repeat chest radiography at 12 months, the yield should be determined.

If, as anticipated, the yield of chest radiography is low for some of the current activities, the panel expects that recommendations similar to the following will be supported by the findings:

- The order of priority for investigating pulmonary TB cases that are confirmed by *M. tuberculosis* cultures should be (1) those with AFB seen on sputum smear microscopy and (2) those without AFB on sputum smear microscopy. Culture-confirmed cases with negative AFB microscopy results but with a pulmonary cavity are uncommon: they can be grouped with those having positive microscopy results (i.e., higher priority).
- Laryngeal TB cases should be investigated as higher priority regardless of AFB bacteriological findings.
- Extrapulmonary TB cases should not be investigated except when the index patient is a child, and then with the intention only of finding a source of infection for the child.
- Pulmonary TB cases without bacteriologic confirmation generally should not be investigated except when the index patient is a child, and then with the intention only of finding a source of infection for the child.
- Pulmonary TB cases without bacteriologic confirmation can be investigated electively if the contacts are especially vulnerable to TB (e.g., childcare pupils, dialysis mates).
- Expand the testing for LTBI to progressively older age groups. Usage of IGRA instead of the skin test will obviate the concerns about segments of the population

with multiple BCG dosage, and it will avoid severe tuberculin reactions in persons who have had previous positive skin test results. Older age groups (i.e., older than the current cut-off age of 25 years) should be included incrementally, as the medical community gains experience with patients who could have a greater rate of isoniazid-associated hepatitis because of age. In anticipation of potential problems, TCDC should institute national sentinel surveillance and intense scrutiny for adverse effects.

The panel recommends the following modifications to the contact investigation procedures:

- Interview all contacts for TB symptoms and pertinent medical history (e.g., diabetes mellitus or HIV infection).
- Consider using IGRA instead of the TST for contact investigations, especially in situations where the more accurate identification of LTBI is important, e.g., in congregate settings such as prisons, mental institutions and nursing homes.
- Reserve chest radiography for contacts with TB symptoms or positive results from the skin test or IGRA. Cease doing routine repeat chest radiography at 12 months.
- In select circumstances, such as investigating confirmed outbreaks or evaluating contacts who are nonverbal, routine chest radiography can be applied.

Currently, information about symptoms is not captured in the database. It is recommended that this information be added to enable future analysis.

Latent TB Infection

As a rule, the tuberculin skin test can be used to screen for LTBI. The reduced specificity of the skin test for BCG-vaccinated populations may increase the number of persons with false positives who are then subjected to the unnecessary risk of INH-associated hepatitis. Setting the skin-test cutoff at 10mm increases the specificity of the test, but at the expense of losing sensitivity in comparison to setting a smaller skin-test cutoff. A loss of sensitivity will cause some LTBI to be missed, which will lead to otherwise preventable TB cases.

IGRAs may be more useful than the tuberculin skin test in contact investigations, especially where BCG vaccination coverage is almost universal and where older segments of the population received multiple (i.e., ≥2) BCG doses. (See also above recommendations about introducing IGRA testing into contact investigations.) When the result of either the skin test or IGRA is positive, the contact should be interviewed about TB symptoms again and a chest radiograph should be done to ascertain the absence of TB disease, which defines LTBI.

Hepatitis is the major safety concern with the 9-month INH regimen, and a patient-candidate for this regimen should be assessed for the risk of hepatotoxicity. A history of alcohol use, underlying liver conditions, hepatitis B or C viral carriage, and concomitant potentially hepatotoxic drugs should be obtained. In those born before 1986 (the year universal hepatitis B vaccination at birth began in Taiwan), hepatitis B serology should be done. In those who are at risk of hepatitis C (e.g., injection drug users), hepatitis C serology should be done.

The optimum methods for monitoring the safety of patients who are taking INH for LTBI is not known, and most guidance is based on observational studies and expert opinion. The following recommendations are based on common elements in guidelines or standards from the National Institute for Health and Clinical Excellence (i.e., NICE), the American Thoracic Society, and the Public Health Agency of Canada:

- Patients who are taking INH should be educated about the warning symptoms of hepatitis, and they should be seen monthly by a clinician (beyond the community treatment observer) and asked about these symptoms and warned to stop taking INH and seek healthcare in the event of these symptoms. The community treatment observers also should be trained in how to elicit these symptoms from their patients.
- Serum transaminase concentrations should be measured for patients who have hepatitis symptoms at any moment during treatment.
- Baseline serum transaminase concentrations should be measured for patients who
    - are older than 35 years
    - have a history of alcohol abuse or liver disease
    - have hepatitis B or C carriage
    - have any other risk so determined by the history (e.g., other medications)
- Serum transaminase concentrations should be measured at routine intervals only if a baseline value was greater than the upper limit of normal or the patient has one of the medical risks for liver injury.

Currently, INH preventive therapy is given daily for 9 months under direct observation (i.e., DOPT). Although the quality of DOT for TB cases is satisfactory as judged by the categories A, B and C performance indicators, there is room for improvement because the definition thresholds for the indicator categories are relatively lenient. Resources should be focused on improving performance for TB case DOT before focusing on DOPT.

Recommendations:

- The panel proposes using the twice-weekly INH regimen, while closely monitoring local experience and national data for this regimen's safety and efficacy. The twice weekly-regimen would reduce the workload for the treatment observers who can then devote more time to DOT for TB cases.
- If direct observation of LTBI treatment (DOPT) remains the standard practice, then the use of Rifapentine and INH once weekly for 12 weeks can be considered, but it must be emphasized that this regimen should only be given under direct observation and when active disease has been diligently excluded. This regimen should not be adopted for widespread use until pilot projects in Taiwan have demonstrated its safety and feasibility. Currently, the usage of the INH-Rifapentine regimen is widespread only in the United States, and the experience with this regimen there should be tracked for the early indications of safety and feasibility in public health programs.

BCG vaccination

BCG vaccination is routine for all newly born infants in Taiwan. Babies are vaccinated soon after birth using the intradermal method with a vaccine manufactured in Taiwan using the Tokyo172 strain. The vaccine coverage was as high as 98% during the past several years. In order to monitor for adverse reactions associated with BCG vaccination, the Taiwan program has established a good surveillance system for BCG vaccine injury. This system is supported by the molecular epidemiology investigations to show whether isolates from a patient with extrapulmonary tuberculosis are *M. bovis* BCG.

Recommendations:

- In view of the high incidence rate of TB in Taiwan overall, the benefit from the current BCG vaccination program to infants is clear, and therefore the program should be maintained with a high coverage and technical level and with safety consideration on adverse reactions.
- The quality of vaccine and vaccination technique should be regularly assessed with post-vaccination tuberculin skin test using a sampling strategy.
- Trends of TB incidence and vaccine adverse reactions should be monitored carefully, in order to allow discussions on the balance of benefit and cost/risk of BCG vaccination, for the future modification of the policy, such as discontinuation or targeted vaccination to selected groups or areas.

High Risk Populations

Certain subgroups of Taiwan's population have higher TB incidence rates or are more vulnerable to TB and merit specific consideration, including the aboriginal peoples, persons from specific geographic regions, the elderly, HIV-infected persons, persons living in nursing homes and psychiatric hospitals, and persons from high-incidence countries, for example, Indonesia.

Taiwan controls TB among guest worker immigrants from high-incidence countries by systematic chest radiography that is tied to remaining documented for legal status in the country. On the other hand, the panel was informed of several apparent outbreaks or pseudo-outbreaks of TB in universities involving students from other countries. The panel recommends that students who come from other countries to study in Taiwan's schools, colleges, and universities be screened for TB, but the epidemiology of TB in these students should be studied for designing efficient screening activities, and the frequency and the methods of screening should be evaluated with data showing the productivity and efficiency. (See other recommendations about curtailing the present, extensive usage of chest radiography.)

HIV infection is relatively uncommon in Taiwan. Less than1% of all TB patients are coinfected with HIV. However, the HIV situation should not be regarded as static, and among TB patients aged 15–54 years the prevalence of HIV infection already ranges from 2.0% to 5.2% for males and 1.1% to 3.0% for females. Because of a reluctance to broach the subject of HIV testing, physicians are hesitant to test all TB patients for HIV infection, which hinders their ability to care for TB patients co-infected with HIV. In contrast, screening HIV-infected persons for TB is standard practice. Effective antiretroviral treatment and other medical services are available to all HIV-infected persons through NHI. HIV testing all TB patients is recognized globally as a standard of practice. The panel recommends that Taiwan moves rapidly towards testing all TB patients for HIV, just as all HIV patients should be evaluated for TB. Effective behavioral interventions have been developed in many countries and cultures to assist physicians and other healthcare providers learn to speak with their patients about getting tested for HIV.

Taiwan's aboriginal population comprises 2.3% of the total population (approximately 528,000 persons), including 25%–35% (approx. 170,000 persons) of the population of two mountainous and relatively rural counties on Taiwan's east coast, Hualien and Taitung. This region is home to many of Taiwan's aboriginal peoples, and the TB burden is affecting them disproportionately more. The high incidence rate of TB in these groups has led to extensive use of radiographic screening to detect TB disease. From general experience globally, mass radiography for active case finding has been shown to have little effect on a population's TB incidence. As noted in several sections of this report, the panel is concerned about too much reliance on chest radiography, especially for screening and active case finding. The combination of IGRA testing to indicate infected persons followed by chest radiography may reduce the reliance on radiography and improve the accuracy and economy of case detection.

Although international evidence of the TB risk conferred by diabetes mellitus is now undeniable, the epidemiological studies of the TB-diabetes association in Taiwan show inconclusive results. Nonetheless, diabetes probably is contributing to TB incidence in Taiwan in some regions or population segments, such as the aboriginal tribes of the mountainous regions, and diabetes complicates the treatment of TB. Similarly, the roles of chronic renal failure and other diseases are unclear in Taiwan. The options would be to continue studying the epidemiology of these intersecting problems or to apply international guidance to decisions about Taiwan's strategies for TB prevention.

Outbreak investigations and infection control in congregate settings

Per Taiwan national policy, a suspected cluster is defined as at least two cases connected to the same institution within one year, with proximity or a relationship creating the likelihood of exposure. The cluster is designated as “possible” by an advisory committee if genotypes of the *M. tuberculosis* isolates are not available, and it is designated as “confirmed” if the cases are linked by genotypes. In the period 2011–2012, TCDC received reports of 150 suspected outbreaks. The detection of outbreaks has relied on the TCDC branch office or the local health bureau finding a matching institutional address or a similar patient type (e.g., long-term care). Recently, an outbreak also can be uncovered by an automatic sentinel-surveillance alarm called “contact becomes a case,” which is triggered when a patient who has been registered in the national data as a TB contact subsequently is reported as having a TB case.

The public health nurse (PHN) is dispatched to the setting to re-interview the patients about the exposure linkages, and this phase is to be completed within 10 days of detecting a suspected outbreak. The TCDC branch office instructs the health bureau to initiate genotyping of the *M. tuberculosis* isolates if the PHN believes that transmission was possible, but the genotyping is done in most instances anyway. The TCDC branch office reports suspected outbreaks to the Third Division of TCDC.

The PHN collects information in a standardized national format, which becomes part of the information put before a local advisory committee. A pulmonologist and an infectious diseases specialist are invited as advisory committee members to guide the interventions. The committee recommends a plan, such as the priorities for the investigation, the scope of the investigation, what additional information should be collected by the PHN, and how many persons will be included for skin tests or possibly IGRAs. All persons who are listed as contacts are evaluated with chest radiography, regardless of whether the situation is designated as an outbreak. The advisory committee monitors the findings from the ongoing investigation and continues to influence the process, including whether genotyping is done.

The subsequent actions depend on genotype results. For outbreak investigations, genotyping includes spoligotype, MIRU15, and RFLP. For non-matching patterns, contact tracing remains routine, as per standard national policy for contact investigations. Any infection control problems that were noted coincidentally are reported to the advisory committee, and further assessments will clarify the problems. Most responsibility for changes rests on the institution. TCDC will pay for skin testing if it is recommended. Any additional chest radiography will be funded by either NHI or the institution. The costs for environmental or administrative changes are borne by the institution.

If genotypes match, TCDC designates the cluster as a confirmed outbreak. For long-term care settings, the major approaches are to assess the indoor environment and to increase the frequency of symptom screening and chest radiography. By policy since late 2012, the contacts undergo chest radiography every 6 months for 2 years after finding the last case. Not necessarily everyone in the institution is included, depending on the findings of the contact investigation. The healthcare workers maintain an annual schedule for radiography, unless the TB exposure has exceeded the national threshold of 40 hours (without use of

personal respiratory protection), in which instance chest radiography is done every 6 months for 2 years, the same as it would be for other contacts.

After an outbreak is confirmed at a school, the major change is to increase of emphasis on tests and treatment for LTBI. For contacts younger than age 13 years, tuberculin testing will have been done regardless of the index patient, as per guidelines for routine contact investigation. For contacts ages 13 through 25 years, tuberculin testing will be done only after exposure to sputum-microscopy-positive index patients unless the event is a confirmed outbreak, in which instance, the contacts in the 13–25 age group will be tested and treatment will be offered to the infected subjects. However, the decisions about additional tests and treatment are guided by the advisory committees—some clinicians are reluctant to administer INH monotherapy because of anecdotes of treatment-associated adverse effects.

Three outbreak investigations were presented to the review panel: one in a 658-bed veterans' long-term care and psychiatric hospital in Tainan, one in a 4,000-bed long-term psychiatric hospital in Hualien, and one in a university in Taipei. In both of the healthcare-associated outbreaks, most of the residents and the TB patients were elderly. In the outbreak at Tainan, 48 cases (33 in long-term care patients, 14 in psychiatric patients, and 1 in a healthcare worker) were included, 2010–2012, with four genotype clusters, the largest cluster with 13 cases. In the outbreak at Hualien, 62 cases were included, with 51 culture confirmed, 2009–2012, and 20 of the *M. tuberculosis* isolates were grouped into five clusters, with 7 isolates/cases in the largest cluster. In the outbreak at Taipei, 24 cases among 892 students at a large urban university were included, with 11 of 20 isolates/cases falling into one genotype cluster. In each outbreak, the public health response was focused on either environmental controls or activities for case finding. The university outbreak also included some testing for latent *M. tuberculosis* infection with subsequent treatment. Some of the students who had TB were from overseas, but the contribution to this case cluster was not discussed during the review.

TCDC first published TB infection control guidance for healthcare settings in 2003, with subsequent updates. The contents include early case detection, environmental controls, administrative controls, and personal protection for healthcare workers. TCDC and the Ministry of Labor jointly published engineering guidance for infection control. The content of these two sets of guidance was not reviewed during this visit except for selected sections, and the infection control practices in healthcare settings were not systematically assessed. The review team visited the Chest Hospital in Tainan, Department of Health, Tainan, and toured the 51-bed airborne-infection isolation unit and noted that negative pressure was correctly maintained for the patient rooms, but half of the rooms lacked antechambers, which could be reducing the effectiveness of the environmental controls. The other infection control activities at this hospital were proficient. The team also visited the 11-bed airborne-infection isolation unit in Wanfang Hospital in Taipei City and observed it to be proficient, in terms of administrative and environmental controls. Practices for personal protection and visitors were not assessed.

Healthcare workers at inpatient care settings undergo chest radiography annually, as a requirement for institutional accreditation. The yield has not been determined. Surveillance for latent infection, for example, annual testing with IGRA, is not done.

Concluding observations:

- The events that were described as outbreaks seem to have been a mixture of cases from recent transmission, prevalent cases, and possibly unrecognized multi-event recent institutional transmission. Some clusters might have matching genotype patterns because of background prevalence of certain strains, and the current methods do not allow an assessment.
- Without question, *M. tuberculosis* is being transmitted in some large institutions in Taiwan, and the circumstances at these institutions are conducive to transmission:
    - A large underlying TB prevalence rate in several types of institutional populations.
    - The tendency toward late TB diagnosis in elderly patients who in addition have a large incidence rate.
    - The proximity and the extended contact with source cases in institutions.
    - At least in some institutions, insufficient ventilation.
- The relative contribution of institutional transmission to the national TB burden is unknown, and measuring this relative contribution is important for deciding resource allocation.
- TCDC monitors the compliance with the annual chest radiography of healthcare workers, but the yield and the effectiveness of annual chest radiography has not been determined nationally.
- The sentinel-surveillance alarm called “contact becomes a case” creates the opportunity for investigating outbreaks outside of institutional settings: this could be especially important in mountainous regions (i.e., Hualien County and Taitung County) where the epidemiological profile is suggestive of recent transmission to younger segments of the population.

Recommendations:

- The relative contribution of institutional transmission to the national burden should be measured by a combination of systematic genotype studies and epidemiological models.
- If the fractional contribution of transmission in healthcare is determined to be sufficiently large, TCDC should undertake a campaign for reducing the size and frequency of outbreaks:
    - Ongoing education of healthcare workers on approaches for earlier TB diagnosis.
    - Assessment of time-to-diagnosis in institutional settings, for usage in quality improvement.
    - Periodic (e.g., biannual) review of national guidelines for healthcare TB infection control.
    - Nationwide improvement of adherence to guidelines on administrative and environmental controls for preventing transmission, for example, the inclusion of a single antechamber in each airborne-infection isolation room.
    - Consideration of more intensive standard environmental control measures, such as portable ultraviolet air purifiers, in settings with patient populations having high TB incidence rates, for example, veterans’ hospitals, but especially in settings where TB outbreaks already have been confirmed.
- TCDC and collaborating agencies should determine the need for adopting more intensive administrative and environmental controls in settings besides healthcare institutions, on an institution-by-institution basis, depending on the demonstration of

transmission or the high risk that would be predicted by the nature of the institutional population, for example, psychiatric patients.
    - Students from overseas could be required to undergo TB screening on entry to Taiwan; the testing methods could include chest radiography or IGRA, and the productivity and efficiency of these screening activities should be assessed by collecting data on the results and analyzing the yields.
    - Other institutions, such as homeless shelters or dormitories for foreign workers, might need improvements in routine environmental controls.
- The Taiwan national TB program, led by TCDC, should move toward IGRAs instead of, or in addition to, tuberculin skin tests, and subsequently new emphasis on treating contacts with latent infection, beyond the current age limitations. TCDC should institute national sentinel surveillance and intense scrutiny for adverse effects, in order to immediately detect any serious problems associated with treatment of latent infection. (See also sections on contact investigations and LTBI.)
- The utility of annual chest radiography for occupational screening of healthcare workers should be determined, as one part of a larger strategy of reassessing the systematic routine radiology.
- Community (i.e., non-institutional) outbreaks should be studied, starting with the “contact becomes a case” alarm system, epidemiology, and focal studies of *M. tuberculosis* genotyping. These findings should be generalized to TB control practices for contact investigations.

Surveillance and Data Management

Overall, the data management system is well designed, it is linked with relevant health-related databases, and it facilitates high quality surveillance by the Taiwan national TB program.

The current web-based system introduced in 2001 is a comprehensive TB database that includes records of patients' history, clinical findings, and progress, and details of patient's contacts. The initial report of a new patient from a diagnosing doctor can be obtained either with a mailed or faxed report form or through the TCDC web-based Communicable Disease Reporting system. Reporting is mandatory, and at the same time, supported by the medical fee reimbursement in the NHI system to which the reporting is a prerequisite.

The basic key of this system is the personal identification number of the Taiwan nationals. This key enables linkage of this system with other related databases such as the Death Registry and the NHI database. Also, the system allows laboratorians and hospital staff to enter and access results of tests and other patient information.

In addition to the aggregate data outputs such as tables of number of new cases according to several background factors for surveillance purpose to be included in the annual report, the system automatically produces a series of tables and lists for administrative purposes, e.g., patients with drug resistance, patients not receiving DOTS observers visits, etc. Also, the system has alert functions to remind workers of the necessary actions.

This is a pioneering example of the comprehensive use of an electronic data system integrated into the general health related information system. Furthermore, this system has a profound potentiality toward the future, given the progress of electronic information system in terms of hardware as well as software, such as combined uses with smart phone.

Recommendations:

- The high level of security of the data in the system should be maintained.
- The accuracy and completeness of data, especially those inputted manually by workers in the periphery should be evaluated.
- The use of this information system for epidemiological, microbiological, clinical, and operational studies on TB and related factors should be encouraged.
- In order to avoid errors and to save labor, the use of remote electronic data entry, such as with a smart phone, should be explored.
- The data collection elements should be expanded to enable more efficient contact investigations; for example, symptoms of TB during a possible outbreak.

Summary of Recommendations

Epidemiology

- Study the dynamics of the TB transmission of TB infection in the population and high-risk subgroups of the population by combining the results from genotyping and epidemiologic investigations.

Case detection and diagnosis

- The review panel is concerned that Taiwan's program might rely too heavily on chest radiography, especially for screening and active case finding in high risk populations; not only for initial thoracic imaging, but also for follow-up of persons receiving treatment, after treatment or at with ongoing risk such as healthcare workers and TB contacts.
- For persons unable to produce an adequate expectorated sputum specimen, the use of sputum induction or bronchoscopy procedures may be considered.
- In general, in an era of economic constraints, finding and treating more TB cases with less effort and lower cost become important considerations. To this end, the panel recommends increased used of efficiency studies, economic analysis, cost-effectiveness analysis, risk-benefit analysis, and decision analysis for developing rational policies, and increased use of social and behavioral sciences to promoted the associated behavioral changes among healthcare professionals.

Laboratory systems

- The very large workload in the authorized TB laboratories should be carefully monitored. Adequate resources should be provided to maintain the high level of services. Additional laboratories may be need if the workload remains at the current level.
- Adequate resources should be provided to the external quality assessment system.
- Laboratories should be required to report the recovery of *M. tuberculosis* isolates to the clinician, local TB control officer, and TCDC. In the United States, we have found that such a system helps ensure that all TB cases are reported the TB Control Program.
- The use of molecular diagnostic tests to detect TB and rifampicin resistant TB should be explored. Operational research to evaluate the performance and implementation of molecular tests is needed.
- Second-line drug susceptibility testing
  - should be conducted for all rifampicin-resistant isolates, not just MDR TB strains.
  - should include testing to at least the injectable second-line agents available in Taiwan (i.e., capreomycin and kanamycin) and the fluoroquinolones used in Taiwan (i.e., levofloxacin and moxifloxacin).
- Performance indicators
  - Individual laboratories should monitor specimen transport times from individual collection sites to discover any potential transportation problem.
  - Turnaround times for growth detection and contamination rates should be monitored for both liquid solid cultures.

    - The percentage of AFB-smear positive specimens that yield positive cultures (target 95%) should be monitored.
- The program and laboratory should work together to develop studies to define the molecular epidemiology of TB in the general population and high risk populations.
- The laboratory should investigate the utility of 24-locus and 27-locus MIRU typing for molecular epidemiology and outbreak investigations.
- The frequency, clinical significance, and clinical and epidemiologic characteristics of patients that produce specimens containing NTM should be investigated.

Management of cases of TB

The panel recommends —

- A survey of all treatment courses implemented, and the reasons for variation from national standard regimens, with a view to providing evidence about treatment practice. This evidence should be used, in combination with the international literature, to place strong pressure on all physicians to adhere to national guidance in treating all patients other than when clinical circumstances oblige variation.
- Less reliance on in-hospital care and more case management with patients at home, unless there are overwhelming clinical or infection control reasons to do otherwise.
- The discharge of most patients from follow up at the end of successful treatment. Any further follow up after treatment should be reserved for those patients who have had drug resistant disease or other complications of their treatment course.
- A high priority on increasing the proportion of cases treated with the highest standard of DOTS in the intensive phase, and similarly high levels of supervision in the continuation phase in patients with any kind of complication of treatment or in whom problems with compliance are anticipated or observed.
- The adoption of intermittent regimens in the continuation phase, which could considerably reduce the burden of observation in DOTS for the health team.
- The exploration of intermittent treatment for latent infection such as nine months of isoniazid twice a week.
- Further studies of remote observation of treatment (of disease and latent infection) using electronic methods while ensuring that overall effectiveness of treatment is not allowed to decline. Caution should be exercised, however, to ensure that direct observation of treatment is continued for all patients in the intensive phase and for patients in the continuation phase where there have been treatment complications, problems with compliance, or drug resistance.
- The adoption of the Taiwan MDR TB Consortium, TMTC, approach to include all patients in Taiwan who have MDR TB. Information on the regimen used, combined with patient information, drug susceptibility pattern and treatment outcome, should be collected on all cases in order to monitor the effectiveness.

Outcome of TB treatment

- The panel recommends that more detailed investigation be carried out into the causes of death in those dying while on TB treatment, and in those dying before TB treatment starts, to determine if an appreciable burden of preventable deaths is occurring.

Contact Investigations

The yield and costs of contact investigations should be assessed. The first area for exploration would be the yield of universal chest radiography for contacts. The analysis should focus on these groups:

- For contacts who were tuberculin skin tested, a comparison of the radiography yield in tuberculin reactors and tuberculin non-reactors.
- Contacts who had only chest radiography (and not skin tests before radiography).
- Contacts of extrapulmonary-only TB.
- Contacts of pulmonary TB that was not confirmed by bacteriology.

In addition, for each group that is subjected to routine repeat chest radiography at 12 months, the yield should be determined.

The panel recommends the following on when to initiate contact investigations:

- The order of priority for investigating pulmonary TB cases that are confirmed by *M. tuberculosis* cultures should be (1) those with AFB seen on sputum smear microscopy and (2) those without AFB on sputum smear microscopy. Culture-confirmed cases with negative AFB microscopy results but with a pulmonary cavity are uncommon: they can be grouped with those having positive microscopy results (i.e., higher priority).
- Laryngeal TB cases should be investigated as higher priority regardless of AFB bacteriological findings.
- Extrapulmonary TB cases should not be investigated except when the index patient is a child, and then with the intention only of finding a source of infection for the child.
- Pulmonary TB cases without bacteriologic confirmation generally should not be investigated except when the index patient is a child, and then with the intention only of finding a source of infection for the child.
- Pulmonary TB cases without bacteriologic confirmation can be investigated electively if the contacts are especially vulnerable to TB (e.g., childcare pupils, dialysis mates).
- Expand the testing for LTBI to progressively older age groups. Usage of IGRA instead of the skin test will obviate the concerns about segments of the population with multiple BCG dosage, and it will avoid severe tuberculin reactions in persons who have had previous positive skin test results. Older age groups (i.e., older than the current cut-off age of 25 years) should be included incrementally, as the medical community gains experience with patients who could have a greater rate of isoniazid-associated hepatitis because of age. In anticipation of potential problems, TCDC should institute national sentinel surveillance and intense scrutiny for adverse effects.

The panel also recommends the following modifications to the contact investigation procedure:

- Interview all contacts for TB symptoms and pertinent medical history (e.g., diabetes mellitus or HIV infection)..
- The use of IGRA can be considered. IGRA testing would be especially useful in populations where BCG vaccination coverage is almost universal and especially in the age groups having multiple (i.e., ≥2) BCG doses.
- Reserve chest radiography for contacts with TB symptoms or positive results from the skin test or IGRA. Cease doing routine repeat chest radiography at 12 months.
- In select circumstances, such as investigating confirmed outbreaks or evaluating contacts who are nonverbal, routine chest radiography can be applied. .

Latent TB Infection

- If INH is used for treating LTBI, the panel proposes using the twice weekly regimen, while closely monitoring local experience and national data for the regimen's safety and efficacy. The once-weekly 12-dose INH-Rifapentine regimen should be considered, with a cautious, gradual introduction starting with pilot projects. This regimen should only be given under DOPT.
- Patients receiving INH should be seen at least monthly to monitor clinically for side effects especially hepatotoxicity and to encourage adherence.
- Serum transaminase concentrations should be measured if symptoms or signs suggest hepatotoxicity at any time during treatment.
- Serum transaminases need not be measured at regular intervals for most patients.
- Baseline serum transaminases should be measured for patients who are age 35 years and older.
- Baseline and sequential measurements of serum transaminases should be done when there are risk factors present (e.g., alcohol abuse, underlying liver disease, hepatitis B or C carriage, concomitant therapy with hepatotoxic drugs or if the baseline transaminases are elevated).

BCG vaccination

- The current BCG vaccination program should be maintained with a high coverage and technical level and with safety consideration on adverse reactions.
- The quality of vaccine and vaccination technique should be regularly assessed with post-vaccination tuberculin skin test using a sampling strategy.
- Trends of incidence of tuberculosis and adverse reactions should be monitored carefully, for the future modification of the policy, such as discontinuation or targeted vaccination to selected groups or areas.

High Risk Populations

- The panel recommends that students from other countries who attend Taiwan's schools, colleges, and universities be screened for TB, but the optimal methods and schedule of screening should be determined by studying the epidemiology of TB in these students and routinely assessing the efficiency and productivity of the screening activities.
- The panel recommends that Taiwan moves rapidly towards testing all TB patients for HIV infections, just as all HIV patients should be evaluated for TB.
- For diabetes and other chronic medical conditions that may increase TB incidence, the Taiwan national TB program can consider two courses of action: pursue further epidemiological studies for demonstrating the risk factors that are most important in Taiwan, or adopt international guidance for preventing TB in such groups.

Outbreak investigations and infection control in congregate settings

- The relative contribution of institutional transmission to the national burden should be measured by a combination of systematic genotype studies and epidemiological models.
- If the fractional contribution of transmission in healthcare is sufficiently large, TCDC should undertake a campaign for reducing these outbreaks:
    - Ongoing education of healthcare workers on approaches for earlier diagnosis.

    - Assessment of time-to-diagnosis in institutional settings, for usage in quality improvement.
    - Periodic review of national guidelines for healthcare TB infection control.
    - Nationwide improvement of adherence to guidelines on administrative and environmental controls for preventing transmission.
    - Consideration of more intensive standard environmental control measures, such as portable ultraviolet air purifiers, in all settings with patient populations having high TB incidence rates.
- TCDC and collaborating agencies should determine the need for adopting more intensive administrative and environmental controls in settings besides healthcare institutions, on an institution-by-institution basis.
    - Students from overseas could be required to undergo TB screening on entry to Taiwan: the testing methods could include chest radiography or IGRA, and the productivity and efficiency of these screening activities should be assessed by collecting data on the results and analyzing the yields.
    - Other institutions, such as homeless shelters or dormitories for foreign workers, could require improvements in environmental controls.
- The Taiwan national TB program, led by TCDC, should move toward IGRAs instead of, or in addition to, tuberculin skin tests, and subsequently new emphasis on treating contacts who have latent infection, beyond the current age limitations. TCDC should institute national sentinel surveillance and intense scrutiny for adverse effects during treatment of LTBI, in order to immediately detect any serious problems.
- The utility of annual radiography for occupational screening of healthcare workers should be determined, as one part of a larger strategy of reassessing systematic routine radiology.
- Community (i.e., non-institutional) outbreaks should be studied with the “contact becomes a case” alarm system, epidemiology, and focal studies of *M. tuberculosis* genotyping. The findings should be generalized to TB control practices for contact investigations.

Surveillance and Data Management

- The high level of security of the data in the system should be maintained.
- The accuracy and completeness of data, especially those inputted manually by workers in the periphery should be evaluated.
- The use of the information systems for epidemiological, microbiological, clinical, and operational studies on TB and related factors should continue and be encouraged.
- In order to avoid errors and to save labor, the use of remote electronic data entry, such as with a smart phone, should be explored.
- The data collection elements should be expanded to learn more from contact investigations, for example, symptoms of TB.

Annex 1 ：2014/1/16 Addendum 1 to the report, External review of "Halving TB in 10 years program in Taiwan, 2006 – 2015":

1. Usage of sputum induction or more aggressive methods for collecting respiratory specimens for mycobacteriological studies
2. Frequency of routine specimen collection for mycobacteriological studies during TB treatment

Statement of problems

After the international external review team visited Taiwan and whilst it still worked on its report, the team members discussed the schedule for collecting sputum specimens for mycobacteriology during the treatment for pulmonary TB and about the need for interventions for obtaining valid sputum specimens. These discussions were motivated by (1) the team's observation that the number of specimens processed in the mycobacteriology laboratories of Taiwan exceeded both the capacity of the mycobacteriology laboratories and the number of specimens that would be anticipated by the number of patients, (2) questions from Taiwanese physicians and public health officials about collecting valid respiratory specimens for mycobacteriological testing after patients have become free of productive cough because of successful treatment, (3) the need to monitor treatment success for each patient, and (4) WHO guidance about confirming "cure" at the end of treatment by testing sputum specimens.

Discussion and conclusions

The review team discussed the problems, reached several conclusions, and left some issues open. First, the burden on the mycobacteriology laboratories has to be ameliorated. The current burden on the laboratories confers the risk of impairing laboratory performance, and it should be corrected by submitting only the necessary number of specimens from each patient. Simultaneously, laboratory capacity should be increased either by adding infrastructure, such as equipment and space, or by extending the service hours, which might require more personnel.

The burden to laboratories could be lessened somewhat by decreasing the number of sputum specimens for initial diagnosis from three to two. More information is needed for determining precisely whether the excessive number of specimens stems from too many patients being evaluated for suspected TB or too many sputum specimens being collected from TB patients during or after their treatment.

Second, the procedures of sputum induction, bronchoscopy, and other interventions for specimen collection should be reserved primarily for medical indications when patients cannot spontaneously expectorate sputa. The reasons for doing these procedures should be related to patient care: the confirmation of an initial TB diagnosis and especially the isolation of *Mycobacterium tuberculosis* for susceptibility testing. Sputum induction and other interventions should not be done for purely programmatic reasons. For managing pulmonary TB, the submission of a monthly sputum specimen during treatment until the sputum-smear microscopy result or the culture result is negative is in keeping with standards of practice in some countries. Although this practice might be helpful in the medical management in some instances, for example, multidrug-resistant TB, the overall utility of routinely collecting monthly sputum is unknown.

Finally, in monitoring the response to treatment and documenting cure, the medical needs are different from the programmatic needs. This is especially true when it comes to collecting sputum at the end of a full treatment course, which is not necessary for medical care in most instances. The WHO guidance for program evaluation and cohort review was developed for resource-poor settings with a reliance on sputum-smear microscopy to diagnose TB and then to confirm the cure. A national TB program such as the one in Taiwan has the option of designing its own distinct indicators for program evaluation, in keeping with its resources and its technological capabilities.

Recommendations

The review team did not reach full consensus on all details, but a summary of recommendations, with points left open for discussion, follows:

1. Investigate the sources of the excessive number of specimens. This could be done from the laboratory focus, from the clinical-care focus, or from both. The “Bayesian approach,” which is patient centered, is the preferred method. Use the findings of these investigations to design interventions for standardizing specimen-collection practices and reducing unnecessary submissions to laboratories.
2. Consider reducing the number of initial specimens for diagnosis from three to two as a temporary measure while reducing the burden caused by excessive specimens during treatment.
3. On the basis of medical judgment, use sputum induction, bronchoscopy, and other interventions for ascertaining the TB diagnosis and obtaining an *M. tuberculosis* isolate for drug susceptibility testing. Sputum induction and the other methods confer health risks to the patient and infection control risks, which should be taken into account. These interventions should not be used routinely when the response to treatment is satisfactory.
4. For managing pulmonary TB, collect sputum specimens for mycobacterial culture at the end of the second month of treatment. This is important for assessing the efficacy of treatment and for adjusting the treatment regimen (i.e., either the medications or the duration). Sputum induction is not necessary for routine sputum collection at 2 months. If there are indications the treatment may not be working satisfactorily, and the patient cannot produce an adequate sputum specimen, then sputum induction might be medically indicated for selected cases.
5. Collect expectorated sputum specimens during treatment as recommended by current treatment guidelines in Taiwan, while avoiding excessive numbers of specimens. The panel reached consensus that, for pulmonary TB patients who display signs or symptoms suggesting that the response to treatment is unsatisfactory, sputum specimens should be collected at least monthly, which includes the possible use of sputum induction or other interventions when medically indicated, that is, to detect a potential treatment failure or relapse as early as possible. If a patient with pulmonary TB that is caused by drug-susceptible *M. tuberculosis* is observed to be adhering to treatment and responding well clinically, the need for subsequent routine collection of sputum samples is uncertain and considered unnecessary in some countries. In monitoring the response to treatment and documenting cure, the medical needs are different from the programmatic needs. This is especially true when it comes to collecting sputum at the end of a full treatment course which is not necessary for medical care in most instances. Taiwan should consider adopting different criteria for collection of sputum specimens during

the continuation phase of treatment in uncomplicated patients which could streamline clinical practices and moderate the burden on mycobacteriology laboratories.

6. Define “cure” or “completion of therapy” in Taiwan both for medical care and for program evaluation. Separate definitions might be needed for medical care and for program evaluation. The WHO definitions (i.e., those used for the standard registry, for a cohort review, and for program evaluation) offer the benefits of simplicity, rigor, and comparability across countries. but the definitions in Taiwan could differ from the WHO definitions. Adopting definitions that are designed for Taiwan could streamline clinical practices and moderate the burden on mycobacteriology laboratories.

Annex 2 ：External Review of "Halving TB in 10 Years Program in Taiwan, 2006-2015" Agenda and Photos

AGENDA AND ITINERARY

TIME	LOCATION	ACTIVITY
Feb. 24 (Sun.)		
17:00-17:30	TCDC	**Orientation & Chair election** **Host:Chang-Hsun Chen**, Director, Third division, TCDC
18:00-20:00	Restaurant	***Working group dinner***
Feb. 25 (Mon.)		
09:00-09:10	TCDC (video conference)	**Opening Remark** **Feng-Yee Chang**, Director-general, TCDC
09:10-09:40		**History of TB Control in Taiwan** **Jen Suo**, National Tuberculosis Association, Taiwan
09:40-10:00		**Discussion**
10:00-10:30		**Characteristics of Health System in Taiwan** **Chen-Yuan Chiang**, Director, Department of Lung Health and NCDs, IUATLD
10:30-10:50		**Discussion**
10:50-11:10	*Break*	
11:10-11:40	TCDC (video conference)	**Epidemiology of Tuberculosis in Taiwan** **Cheng-Yi Lee**, TB Surveillance Officer, EIC, TCDC
11:40-12:00		**Discussion**
12:00-13:30	*Lunch*	
13:30-14:00	TCDC (video conference)	**Situation Analysis and Future Direction** **Chang-Hsun Chen**, Director, Third division, TCDC
14:00-14:20		**Discussion**
14:20-14:50		**Epidemiology of TB-HIV Co-infection in Taiwan** **Chin-Hui Yang**, Director, Fourth division, TCDC
14:50-15:10		**Discussion**
15:10-16:00	*Break*	
16:00-16:30	TCDC (video conference)	**Contact Investigation and LTBI Treatment** **Pei-Chun Chan**, Medical officer, Third division, TCDC
16:30-16:50		**Discussion**
16:50-17:30		Time for Preliminary Draft Report
18:00-20:00	Restaurant	***Welcome Dinner***
Feb. 26 (Tue.)		
09:00-09:30	TCDC (video conference)	**Medical Care for Tuberculosis in the Elderly with Co-morbidity** **Pin-Hui Lee**, Medical officer, Third division, TCDC
09:30-09:50		**Discussion**
09:50-10:20		**TMTC Care System for MDR TB** **Jen-Jyh Lee**, President, National Tuberculosis Association, Taiwan

TIME	LOCATION	ACTIVITY
10:20-10:40		**Discussion**
10:40-11:00	*Break*	
11:00-11:30	TCDC (video conference)	**TB Control among Aboriginal Mountainous Districts in Taiwan** **Yen-Fang Huang**, Deputy director, Third division, TCDC
11:30-11:50		**Discussion**
11:50-13:30	*Lunch*	
13:30-14:00	TCDC (video conference)	**Tuberculosis Laboratory Program** **Ruwen Jou**, Research Fellow and Principal Investigator, R & D Center, TCDC
14:00-14:20		**Discussion**
14:20-14:50		**Quality Management of Clinical Mycobacteriology Laboratories** **Hwa-Jen Teng**, Section Chief, R & D Center, TCDC
14:50-15:10		**Discussion**
15:10-15:30	*Break*	
15:30-16:00	TCDC (video conference)	**DOTS strategy and Patient Support in Taiwan** **Kwei-Feng Wang**, Senior technical specialist, Third division, TCDC
16:00-16:20		**Discussion**
16:20-17:30		Time for Preliminary Draft Report
17:30-20:45	***THSR to Tainan*** ***Dinner***	
Feb. 27 (Wed.)		
07:30-08:00	***Transportation to Chest Hospital, DOH***	
08:00-08:30	Chest Hospital, DOH (located in Tainan City) / East District Health Center, Department of Health, Tainan City Government	**1. Overview of TB Control in Southern Territory** **2. A TB Outbreak in a Veteran Nursing Home** **Huai-Te Tsai**, Medical officer, Fourth branch, TCDC
08:30-10:40		**TMTC Care System: Visit to Chest Hospital, DOH** **(Drs. Shinnick, Cegielski, Watson & Wang)** / ***Visit to East District Health Center, Department of Health, Tainan City Government** **(Drs. Mori & Jereb)**
10:40-14:00	***Transportation to Kaohsiung Airport; Flight to Hualien;*** ***Lunch*** ***Transportation to Hualien County Health Bureau***	
14:00-14:30	Sioulin Public Health Station, Hualien County	**Epidemiology and Control of Tuberculosis in Eastern Taiwan** **Song-En Huang**, Medical officer, Sixth branch, TCDC
14:30-15:00		● **The Implementation of TB Control in Hualien County** **Hsiang Ming Hsu** Dr. P.H , Director General, Hualien County Health Bureau ● **Visit to Sioulin Public Health Station**

TIME	LOCATION	ACTIVITY
15:00-16:30		**Inspection of DOTS Medication Delivery**
16:30-17:30		Time for Preliminary Draft Report
Feb. 28 (Thu.)		
09:00-16:00	Hualien County	Time for Preliminary Draft Report
16:00-18:00	***Transportation to Hualien Airport; Flight to Taipei*** ***Dinner***	
Mar. 1 (Fri.)		
08:30-09:00	***Transportation to Wan Fang Medical Center***	
09:00-09:30	Wan Fang Medical Center	**Control of an outbreak of tuberculosis in a campus, 2011** **Jiunn-Shyan Wu**, Section Chief, First branch, TCDC
09:30-10:30		**Case Management in Hospitals** **Ming-Chih Yu,** Director, Medical Administration and Chief Pulmonary Medicine, Wan Fang Medical Center

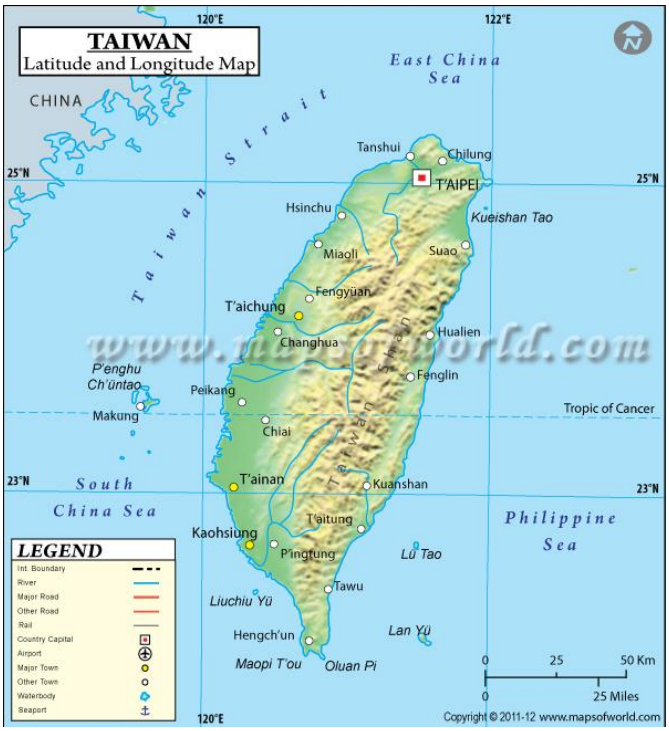
10:30-12:30	Wan Fang Medical Center	Kuming branch, Taipei City Hospital, Department of Health, Taipei City Government	**Visit to Wan Fang Medical Center** **(Drs. Shinnick, Cegielski, Jereb & Mori)**	**Visit to Division for Disease Control and Prevention, Department of Health, Taipei City Government** **(Drs. Waston & Wang)**
12:30-13:30	*Lunch*			
13:30-14:30	TCDC	Certified TB Lab	Public Health Bureau, Hsinchu City Government	*Transportation to TCDC*	*Transportation to Certified TB Lab*	*THSR to; Hsinchu; Transportation to Eastern District Health Center*
14:30-17:30				**Visit to Epidemic Intelligence Center, TCDC** **(Drs. Jereb & Mori)**	**Visit to Certified TB Labs** **(Drs. Shinnick & Cegielski)**	**Visit to Eastern District Health Center, Public Health Bureau, Hsinchu City Government Inspection of DOTS Medication Delivery** **(Drs. Wang & Watson)**

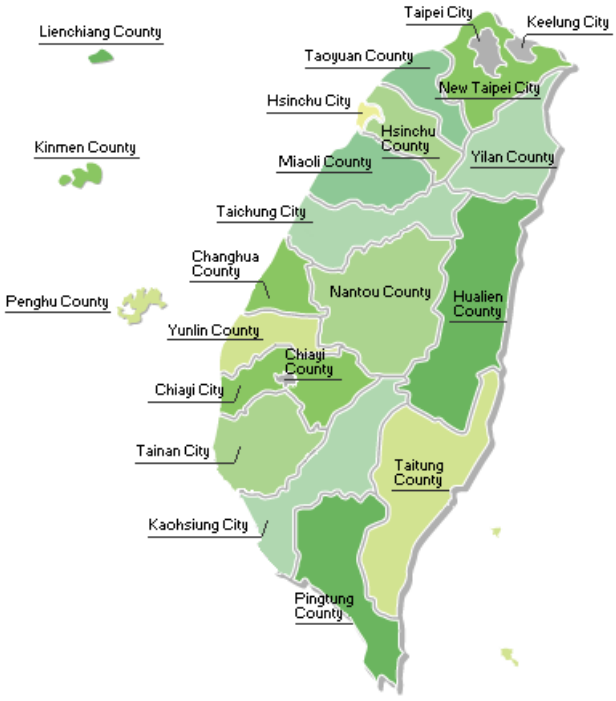
Mar. 2 (Sat.)		
09:00-12:00	TCDC	**Discussion on the Whole Agenda and Preparation for the Report (I)** **Experts of external review**
12:00-14:00	***Lunch***	
14:00-17:00	TCDC	**Discussion on the Whole Agenda and Preparation for**

TIME	LOCATION	ACTIVITY
		the Report (II) **Experts of external review**
Mar. 3 (Sun.)		
Mar. 4 (Mon.)		
09:00-12:00	TCDC (video conference)	**Final Report of External Review** **Experts of external review** (Moderator: **Feng-Yee Chang**, Director-general, TCDC)
End of the external review		

TCDC: Taiwan Centers for Disease Control
Third division: Third Division for TB/HIV Prevention and Control
Fourth division: Fourth Division for Emergency Preparedness
EIC: Epidemic Intelligence Center
R&D Center: Research & Diagnostic Center
First branch: supervising Health Bureaus of Taipei City, New Taipei City, Keelung City, Yilan County, Kinmen County and Lienchiang County.
Fourth branch: supervising Health Bureaus of Yunlin County, Chiayi City and Tainan City.
Sixth branch: supervising Health Bureaus of Hualien County and Taitung County.

Taiwan map





Feb. 24-25 Presentation

Discussion on the Whole Agenda and Preparation for the Report

Visit to Wan Fang Medical Center

Visit to Certified TB Labs

Visit to East District Health Center, Department of Health, Tainan City Government

Inspection of DOTS Medication Delivery

Visit to Sioulin Public Health Station


Visit to Division for Disease Control and Prevention, Department of Health, Taipei City Government

Visit to Certified TB Labs


Visit to Eastern District Health Center, Public Health Bureau, Hsinchu City Government

TMTC Care System: Visit to Chest Hospital, DOH

Final Report of External Review

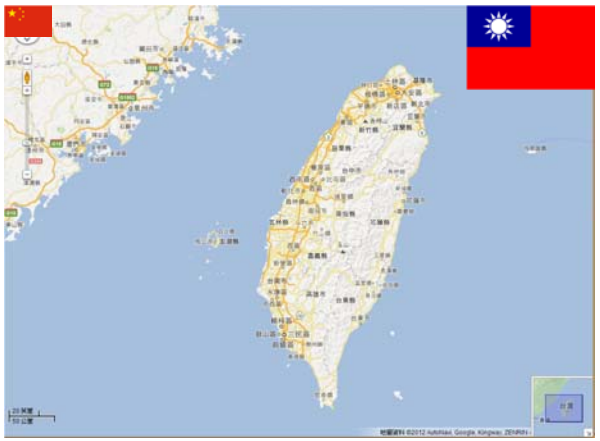
Annex 3 ：Presentation documents

History of TB Control in Taiwan, Republic of China

History of TB Control in Taiwan, Republic of China

- Background
- Tuberculosis control network
- BCG vaccination
- TB case finding
- Chemotherapy
- Case management
- Conclusion

Taiwan, the Republic of China



Taiwan located some 150 km east of the South China Coast.

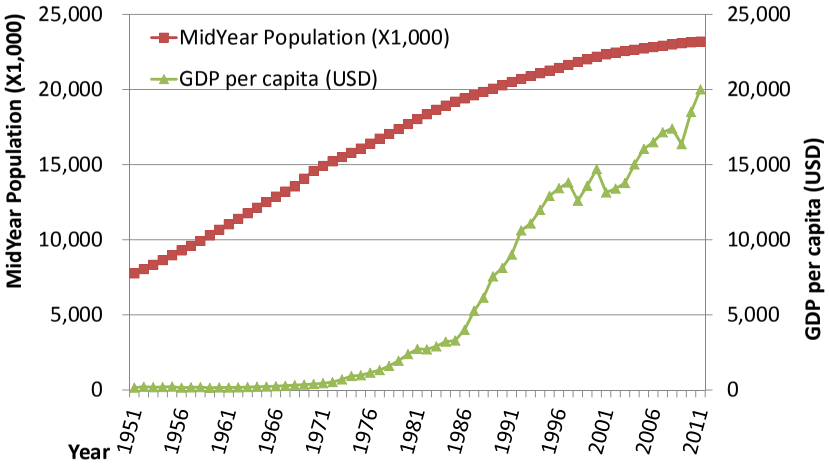
The territory is 36,193 km^2 (13,974 sq mi)

Population (2012 estimate) 23,305,021
Density 642/km^2 (1,664/sq mi)

Brief History of Taiwan, ROC

- 1683
  - Governed by the Qing Dynasty of China
- 1895
  - Taiwan was ceded to Japan in the Treaty of shimonoseki after the Sino-Japanese War
- 1912
  - the Republic of China (ROC) established in China
- 1945
  - Japan surrendered Taiwan to ROC military forces on behalf of the Allies.
- 1949
  - Following the Chinese civil war, the Communist Party of China took full control of mainland China and founded the People's Republic of China (PRC). The ROC relocated its government to Taiwan, and its jurisdiction became limited to Taiwan and its surrounding islands.
- 1971
  - the PRC assumed China's seat at the United Nations, which the ROC originally occupied. International recognition of the ROC has gradually eroded as most countries switched recognition to the PRC.

Mid-Year Population and GDP per Capita, Taiwan, 1951-2011



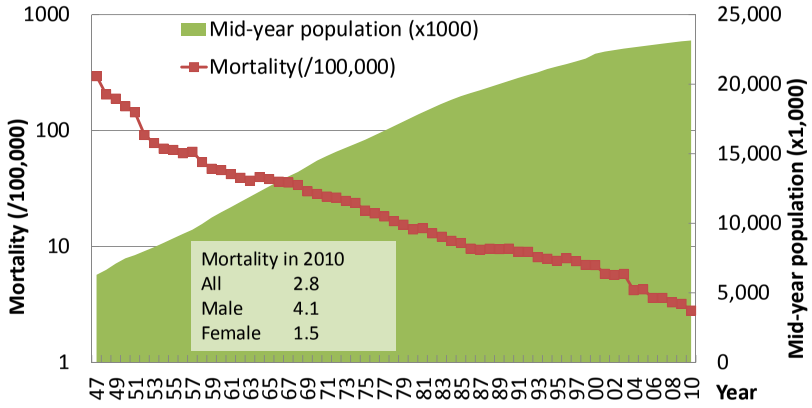
GDP: Gross domestic product

Source: National statistics, ROC (Taiwan)
http://www.dgbas.gov.tw

1895 – 1945 Sanatoriums

- 1915
  - Taipei
    Sungshan sanatorium
- 1945
  - Tainan
    Chingfeng sanatorium

Mid-year Population and Tuberculosis Mortality, Taiwan, 1947-2010

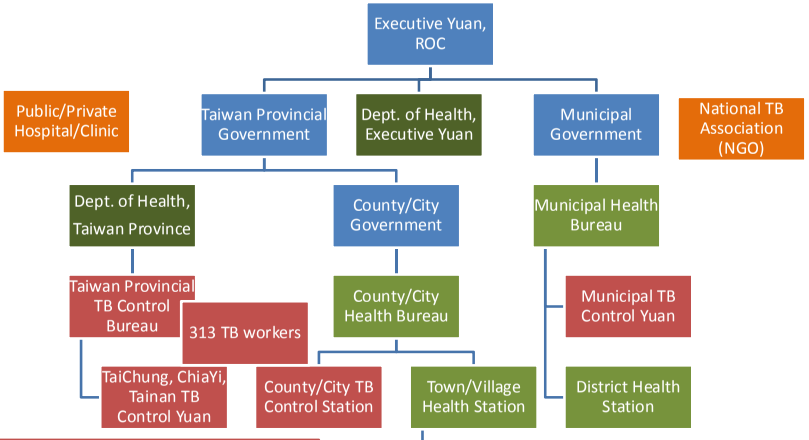


* Include Kinmen and Matsu since 1994

TB Control Network in Taiwan

- 1950-1967
  - TB control committee, Dept. of Health, Taiwan Province.
  - Taipei, Tainan, Chayi, Taichung TB Control Centers
  - City/County TB Control Stations
  - Township/village Health Stations/Rooms
- 1967
  - Establishment of Taiwan Provincial Tuberculosis Control Bureau in charge of National TB Control Program
- 1966-8
  - Employment of 313 TB workers assigned to each health station for TB control activities such as case finding and case holding
- 1989
  - TB Control Units were renamed Chronic Disease Control Units
  - TB control activities was integrated into usual health workers in local health station

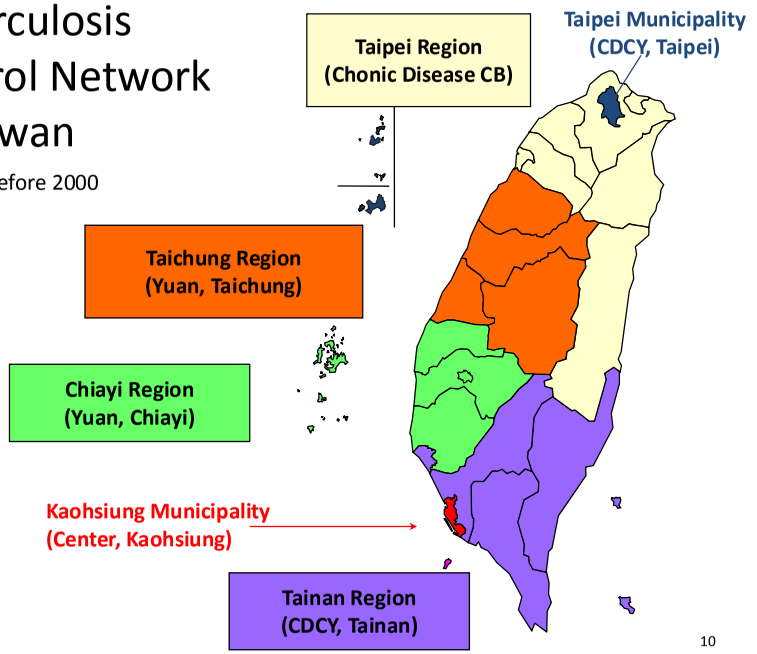
Health Organization in Taiwan



- 25 health bureaus
- 398 health stations
- 496 health rooms In 1998

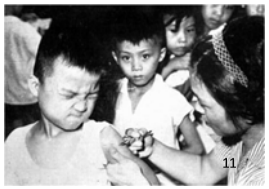
Tuberculosis Control Network in Taiwan

Before 2000



BCG vaccination in Taiwan

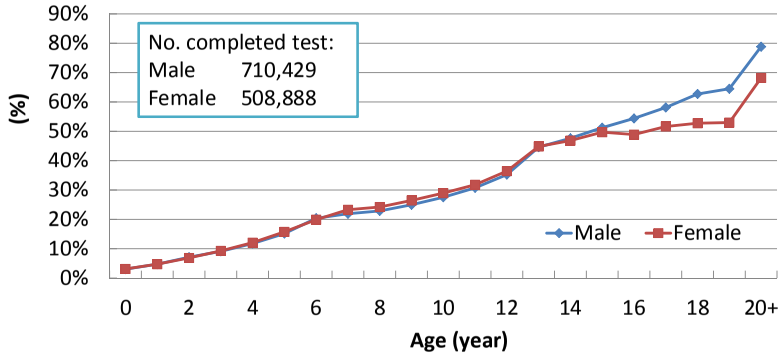
- 1950 Pilot program
- 1952 Primary school children with negative TST
- 1956 Primary school entrants and leavers
- 1963 Preschool children
- 1965 Simultaneous vaccination with BCG and smallpox vaccine in newborn infants
- 1971 Stop revaccination for primary school entrants
- 1980 Stop smallpox vaccination
- 1997 Stop all revaccinations



BCG vaccination in Taiwan, 1997-

- Tokyo 172 strain Freeze-dried BCG vaccine
- 0.05mg/0.1ml intradermal
- Left upper arm near the centre of deltoid muscle
- New born, as soon as possible after birth.
- BCG coverage: 98%
- No revaccination.

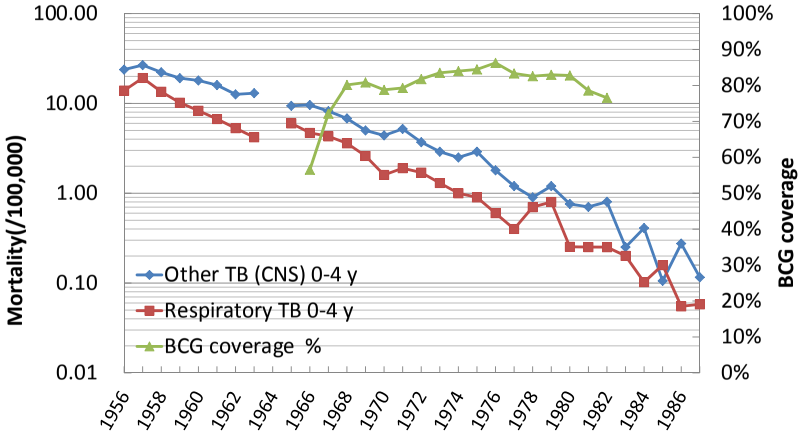
Percentage of reactors to tuberculin by sex and age, Taiwan, 1951-2



PPD RT22 5tu/0.1ml, Mantoux

Source: Taipei Provincial Tuberculosis Control Center. Annual Report 1952[13]

Newborn BCG coverage and TB mortality in children age 0-4 in Taiwan, 1956-87



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Case Finding

- Bacteriological examinations
  (sputum smear, sputum culture, and laryngeal swab culture)
  - 1955
    Central mycobacteriology laboratory set up at Taipei TB Control Center. Subsequently, a mycobacteriology laboratory was established at each TB Control Center and district TB dispensary.
  - 1966-8
    313 TB workers were hired and each was assigned to one township/village health station to carry out TB control activities including identification of individuals with suspected TB in the community by household visits and sputum smear examination.

Chiang CY. Integration of tuberculosis services in Taiwan, 2001: challenges and opportunities. 2012. University of Bergen. Norway

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Case Finding

- Mass chest X-ray survey
  - 1949 First mobile radiography unit.
  - 1954 Mobile teams established for mass chest X-ray screening in communities, institutes, prisons, workplaces, military conscripts, schools, …etc.
  - 1957 The first TB prevalence survey island wide.
- Contact examinations
- 1991 Enhance TB reporting by hospital/clinic

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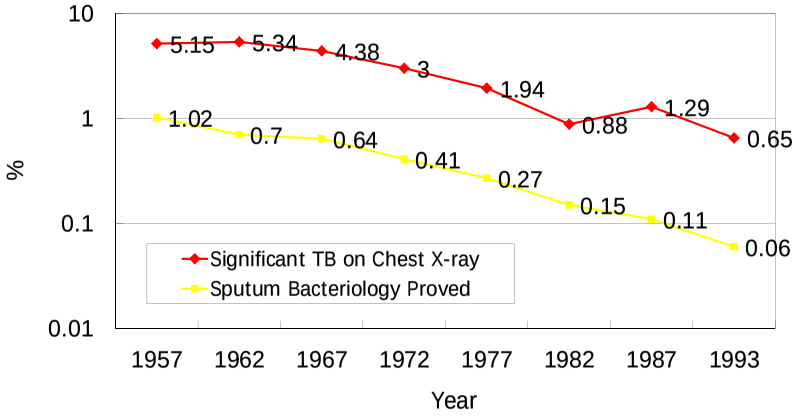
TB Prevalence for Taiwan Adults, 1957-1993



Free Domiciliary Chemotherapy and TB case registration

- 1957-1958
  - INH (Isoniazid) alone
- 1959-1967
  - INH + SM (Streptomycin) or INH + PAS (Para-Aminosalicylate)
    12HS/12H or 12HP/12H
- 1968-1976
  - INH + SM + Thiacetazone(T)
    2HST/10H2S2/12H or 2HST/10HT/12H (2years)
- 1977/2-1978/9
  - INH + SM + Ethambutol (E)
    3 HES/9 HE/12 H (2years)

Free Domiciliary Chemotherapy and TB case registration

- 1978/10-1990/11
  - 5 HER(Rifampin)/5H (10 m)
- 1990/11 – 1992/7
  - 2HERZ/4HER (6m) or
  - 9HER
- 1992/7-
  - Introduction of Fixed dose combination Rifater (HRZ) and Rifinah (HR) ◦

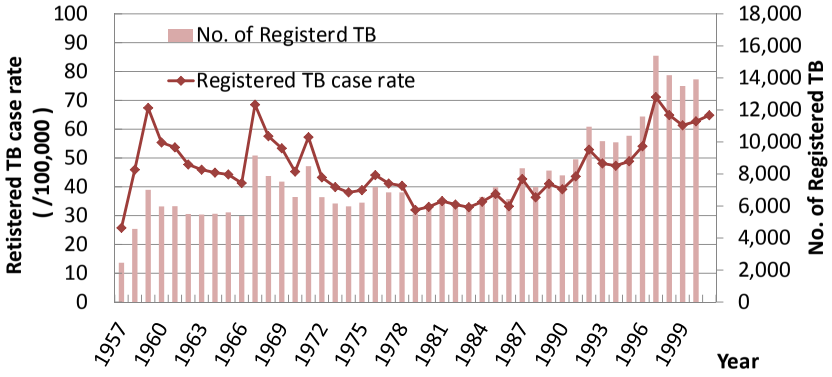
- 1979.9 -
  - Treatment expenses were covered by the Labor insurance for patients with the insurance

H: Isoniazid	E: Ethambutol	R: Rifampin	Z: Pyrazinamide

TB Central Registration

Year	Criteria for case registration and free chemotherapy
1957	Sputum smear positive cases
1969	+ Cavitary pulmonary TB
1974	+ Far advanced pulmonary TB
1978	+ TB Pleurisy
1981	+ Other extrapulmonary TB (pathological or bacteriological diagnosed)
1984	+ Moderately advanced pulmonary TB in indigenous area, high prevalence area, and those detected in contact examination
1988	+ Minimal pulmonary TB in indigenous area
1991	All form of pulmonary TB and extrapulmonary TB

Number and rate of registered TB case, Taiwan, 1957-2000



- Prevalence Surveys 1957; 1962; 1967; 1972; 1977; 1982; 1987; 1993
- 1995 National Health Insurance (NHI) launched
- 1997 NHI No-notification-no-reimbursement policy

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Strategy for case finding , 1990-

- Passive case finding through examination of individuals who present themselves for examination at the health services.
- A tuberculosis “suspect” recommended for examination is any person with a cough for a duration longer than 3 weeks.
- Such an individual is recommended to have chest x-ray and sputum examination, and notified to the county health bureau.

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Strategy for case finding , 1990-

- An expert from the Chronic Disease Control Bureau then reviews each case (with clinical information, chest radiograph and sputum status).
- Passive case detection is supplemented with active case-finding in target groups (aborigenes, prisons, long-term care and mental institutions), using mass miniature radiography.

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Notification & Registration

- All of the confirmed and suspect patients should be notified ,regulated by
  - Communicable disease control law
  - National insurance policy
- Notified case will be confirmed by the health agencies, mainly by experts from the Chronic Disease Control Bureau and Yuans
  - Review of CXR, clinical, microbiological and pathological data

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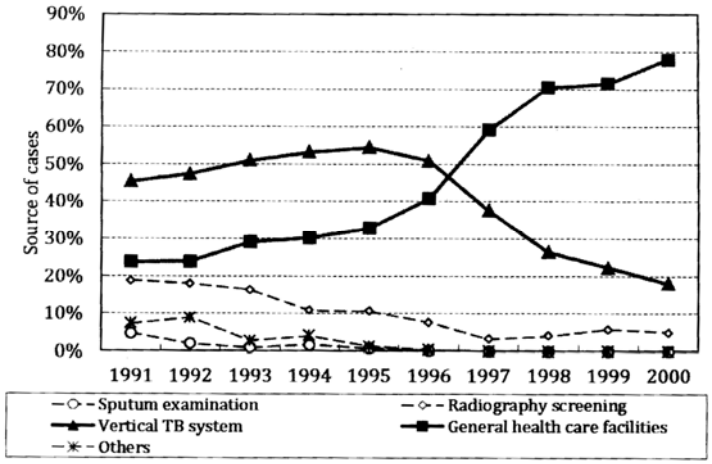
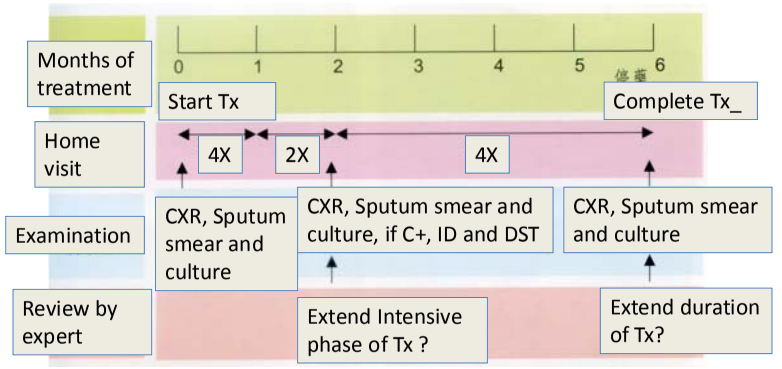
Source of registered TB cases in Taiwan, 1991-2000



Source: CDC, DOH, Taiwan. TB Control Report 2010

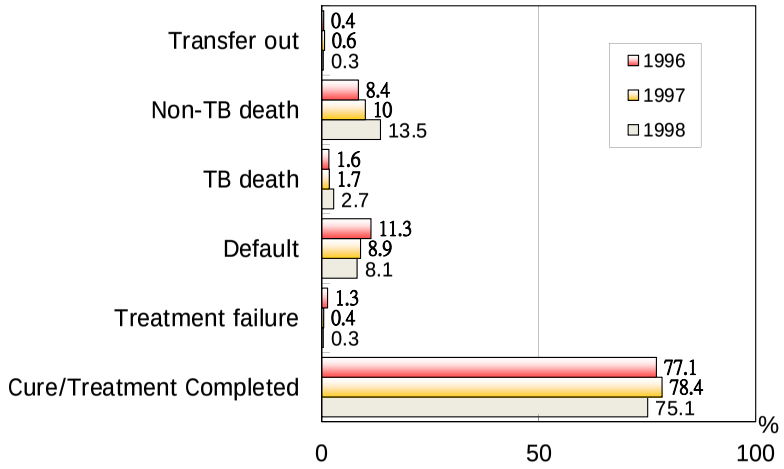
Case Management

- Self-administered treatment (SAT) with supervision by home visits and telephone interviews



Taiwan Provincial Chronic Disease Control Bureau. TB Statistics, 1999

Outcomes of Newly-diagnosed TB Patients, Taiwan, 1996-1998



Taiwan Provincial Chronic Disease Control Bureau. TB Statistics, 1997; 1998; 1999

Direct Observed Treatment, Short-course (DOTS)

- 1995.4 -
  - Hospital DOTS: Hospitalization for patients from indigenous villages during the first 2 months of treatment
- 1997.3 -
  - Pilot community-based DOTS for patients in Indigenous villages

Taiwan Provincial Chronic Disease Control Bureau. TB Statistics, 1999

Isoniazid Preventive Therapy (IPT)

- 1988-1990
  - 6 months isoniazid treatment for children (<6y/o) in indigenous villages with tuberculin skin test (TST) ≥ 10mm with no visible BCG scar; or TST ≥ 15mm with BCG scars.
- IPT for close contact (<12y/o) by decision of individual clinicians.

Major Events in Taiwan TB Control, 1950-2000

Year	Events
1950	BCG vaccination programs
1954	Mobile X-Ray team for mass chest x-ray screening
1955	Mycobacteriology laboratory network
1957	TB case central registration and free drug treatment The first tuberculosis prevalence Survey
1966-8	Employment of 313 TB workers in each health station for TB control activities
1978	Short-course free regimen containing rifampin
1989	TB control activities of TB workers was integrated into usual health care of public health nurses in the health station
1991	Enhance TB reporting by hospital/clinic
1997.7	No-notification-no-reimbursement policy by National Health Insurance
2000	Establish of Taiwan Centers for Disease Control

Thank You for Your Attention

http://l.yimg.com/f/xp/tw-travel.yahookimo.com.tw/20111221/12/3916641454.jpg

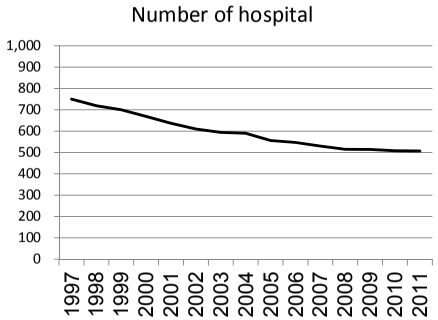
International Union Against Tuberculosis and Lung Disease

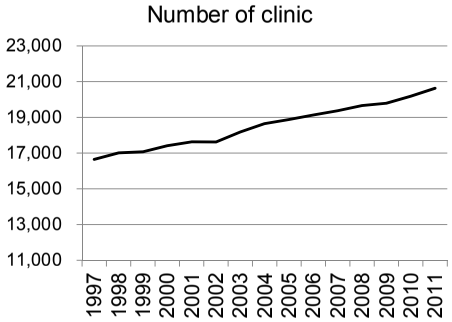
Health solutions for the poor

Characteristics of Health System in Taiwan

CHIANG Chen-Yuan MD, MPH, DrPhilos
Director, Department of Lung Health

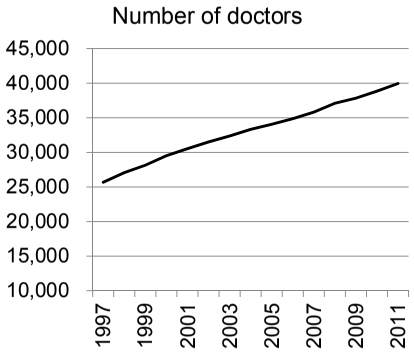
Number of hospitals and clinics, 1997-2011, Taiwan

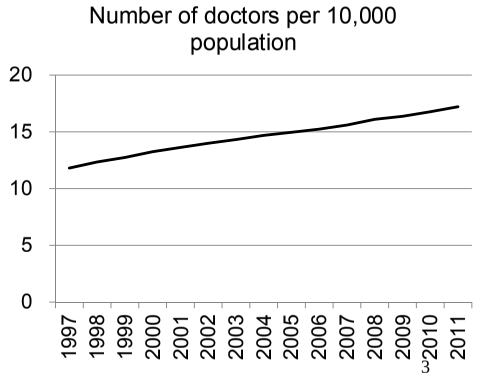




Source of information: Department of Health, Executive Yuan, ROC

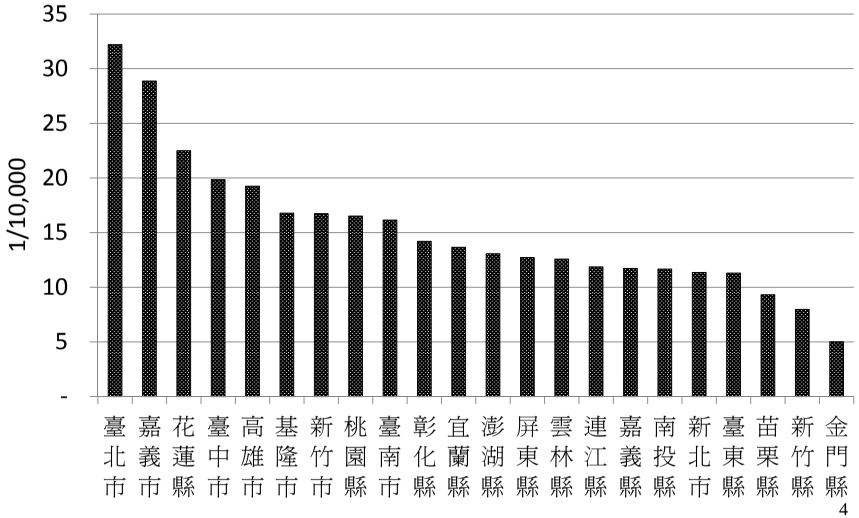
Number of doctors, 1997-2011, Taiwan





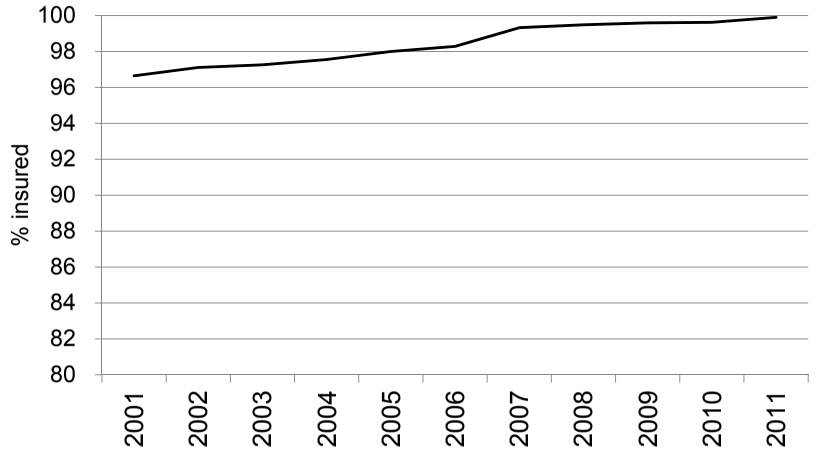
Source of information: Department of Health, Executive Yuan, ROC

Number of doctors per 10,000 population, 2011, by county/city, Taiwan



Source of information: Department of Health, Executive Yuan, ROC

National health insurance program, percentage of population insured, 2001-2011, Taiwan



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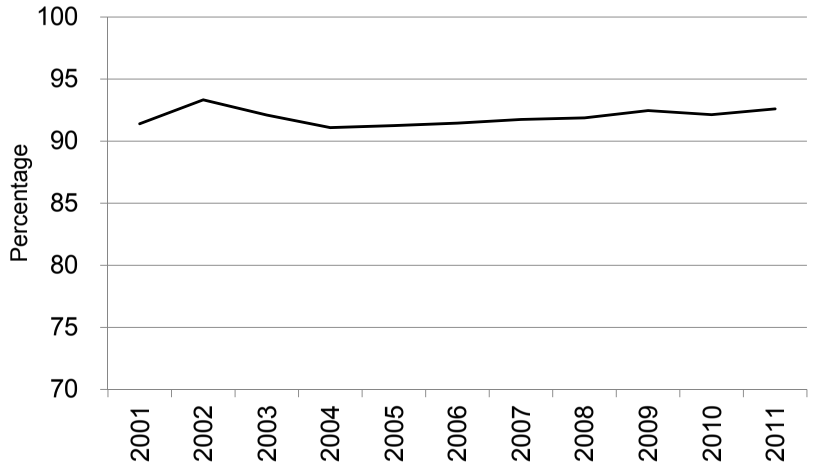
Source of information: Department of Health, Executive Yuan, ROC

National health insurance program, percentage of health care facilities contracted, 2001-2011, Taiwan



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Source of information: Department of Health, Executive Yuan, ROC

Health care system in Taiwan

- a market-oriented system regulated by the laws of supply and demand
  - health providers are free to set up their practice
  - patients are free to seek health services from any clinician.
- tiered referral procedures were not mandatory

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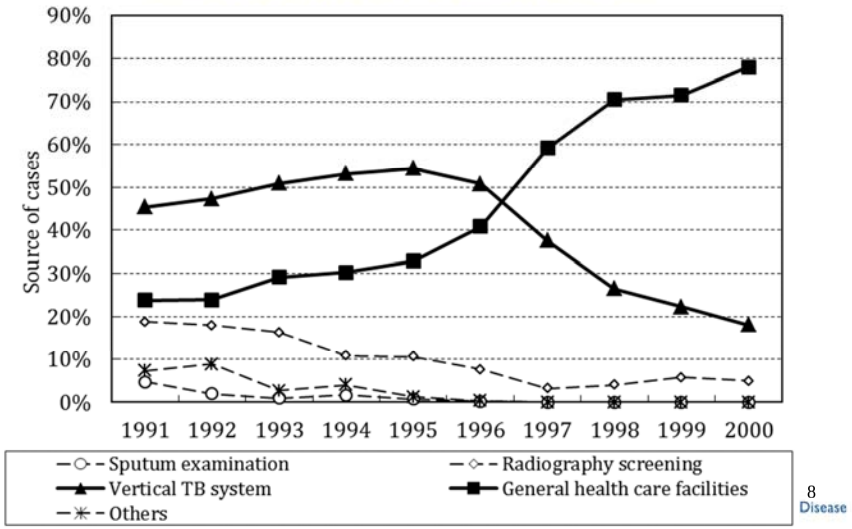
Source of registered tuberculosis cases in Taiwan, 1991-2000

Chronic Disease Control Bureau



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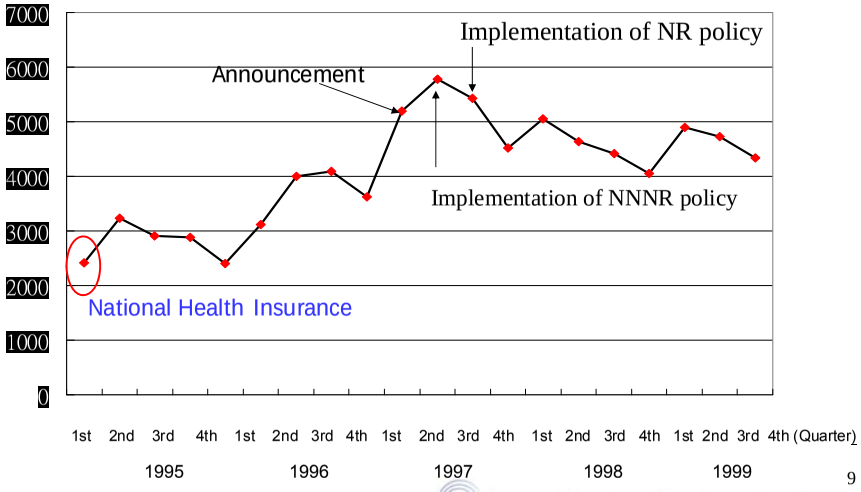
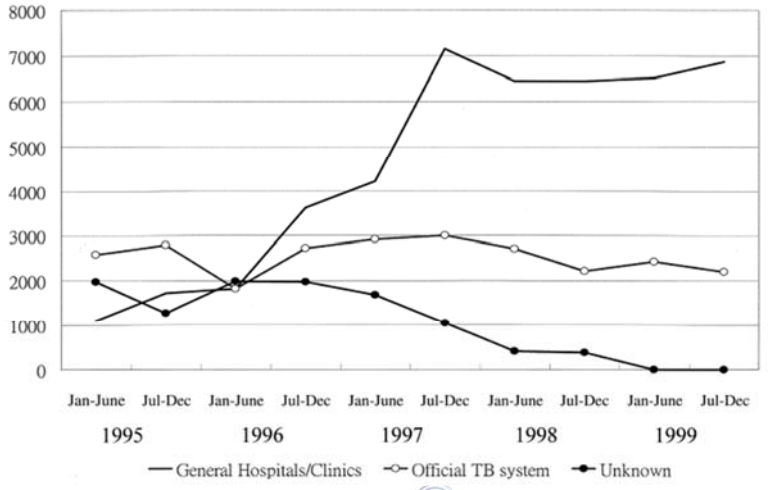
Quarterly Reported Tuberculosis Cases in Taiwan, 1995-1999



Chiang C-Y, et al. Int J Tuberc Lung Dis 2002;6:974-9

Biannually reported tuberculosis cases in Taiwan, 1995–1999, by source



Chiang C-Y, et al. Int J Tuberc Lung Dis 2002;6:974-9

Procedure of clinical investigation leading to a decision to start treatment in 1126 TB patients

CXR: immediate start of treatment after CXR, based solely on CXR findings	**45.5%**
Smear: start of treatment after CXR and a positive AFB smear	19.0%
Other: start of treatment after further investigations	23.2%
Culture: start of treatment after positive sputum culture	12.3%

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Chiang C-Y, et al. Int J Tuberc Lung Dis 2008;12:441-446.

Factors associated with clinicians' decision to stop anti-tuberculosis treatment before completing a full course

	Change diagnosis		Adjusted OR (95% CI)
	No	Yes	
	Number (percent)		
Overall	970 (86.2)	156 (13.9)	
Basis of diagnosis			
Chest X-ray findings	436 (85.2)	76 (14.8)	2.2(1.1-4.4)
Positive smear	199 (93.0)	15 (7.0)	0.9 (0.4-2.3)
Other findings	207 (79.3)	54 (20.7)	3.2 (1.6-6.7)
Positive culture	128 (92.1)	11 (7.9)	1

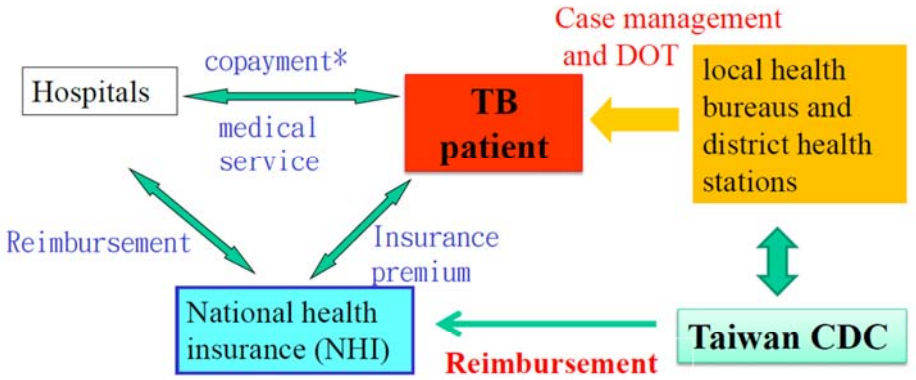
Chiang C-Y, et al. Int J Tuberc Lung Dis 2008;12:441-446.

Accuracy of classification of notified tuberculosis cases in Taiwan, 2003

- 68 (8.7%) of the 782 bacteriologically confirmed cases were misclassified as non-notifiable
  - 4.1% by a clinician
  - 4.6% by administrative coding.
- 72 (43.1%) of the 167 cases in whom NTM were isolated were misclassified as TB cases.
- 31 (12.1%) of the 257 untreated suspects were questionably classified as newly diagnosed cases.

Chiang C-Y, et al. Int J Tuberc Lung Dis 2007;11:876-81

Medical care system and TB control in Taiwan



*Copayment, cost of isolation, and patients without NHI were reimbursed to NHI by the budget from Taiwan CDC

Courtesy Dr. Li PH.

Pay for performance, Tuberculosis, Taiwan

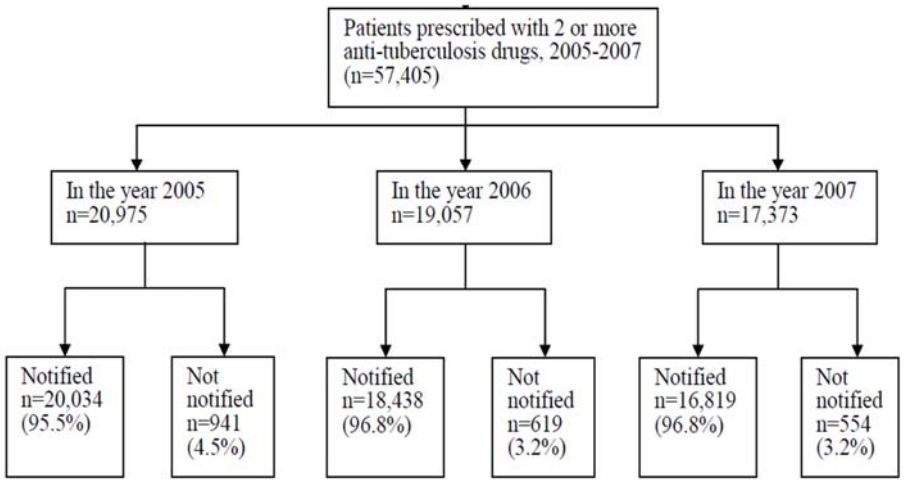
- Notification: 750 reimbursement points
- Case management for 3 months: 1500 reimbursement points (upto one year)
- Successful treatment: 2000 reimbursement points
- TB case manager: full time in hospital notified 100 or more TB cases, part time in <100 TB cases

Source of information: Taiwan CDC

Health care service and surveillance system of tuberculosis in Taiwan

- Access to care: National Health Insurance program
  - Operated by government under the principle of mandatory and universal enrollment
  - Maintain a large patient-based reimbursement database
- Reporting of tuberculosis: mandatory by law
- Surveillance of tuberculosis:
  - TB registry: electronic and patient-based
  - TB notification system: web-based
- Public-private mix
  - Public: Public health nurses and DOT observers
  - Private: TB case managers at hospitals funded by Taiwan CDC

Completeness and timeliness of tuberculosis notification in Taiwan, 2005-2007



Lo H-Y et al. BMC Public Health 2011, 11:915

Timeliness of notification of tuberculosis in Taiwan, 2005-2007

	Number of patients (%)		New cases					
			2005		2006		2007	
			n	(%)	n	(%)	n	(%)
Total	55,291	100.0	18,662	100.0	17,135	100.0	15,696	100.0
0-7 days	45,250	81.8	15,176	81.3	14,181	82.8	13,196	84.1
8-30 days	8,006	14.5	2,771	14.8	2,362	13.8	2,040	13.0
31-90 days	1,630	2.9	555	3.0	477	2.8	399	2.5
≧ 91 days	405	0.7	160	0.9	115	0.7	61	0.4

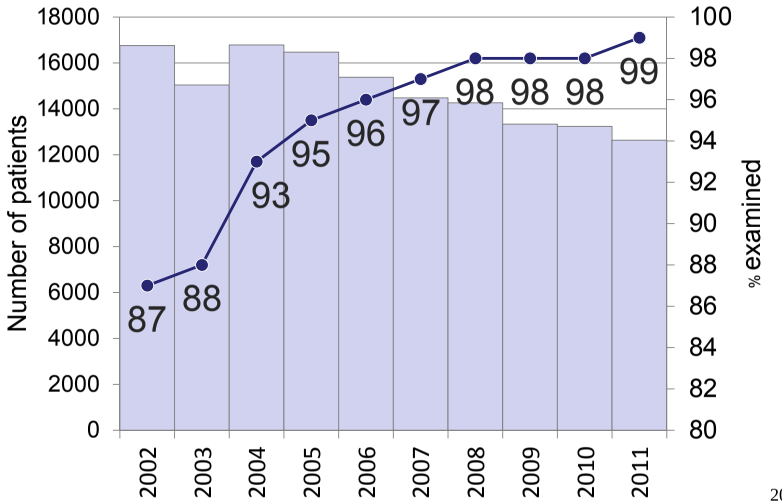
Lo H-Y et al. BMC Public Health 2011, 11:915

Notification of confirmed Tuberculosis cases, 2011, Taiwan

	Number of TB patients	%
Total	12634	100
Medical Center (n=22)	4578	36.2
Regional hospitals (n=58)	4667	36.9
District Hospitals (n=168)	2791	22.1
Clinics (n=59)	598	4.7

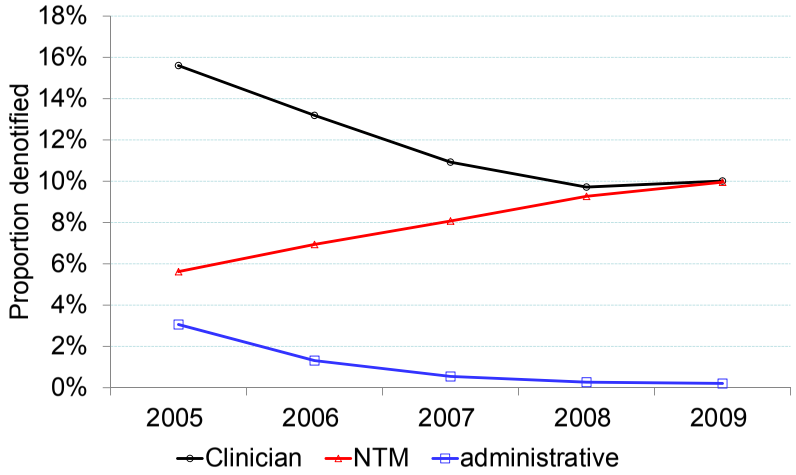
* 248 out of 507 hospitals and 59 out of 20628 clinics in Taiwan notified tuberculosis in 2011

Proportion of tuberculosis patients with sputum examinations, 2002-2011, Taiwan



Source of data: Taiwan CDC

Proportion of notified tuberculosis patients de-notified, 2005-2009, Taiwan



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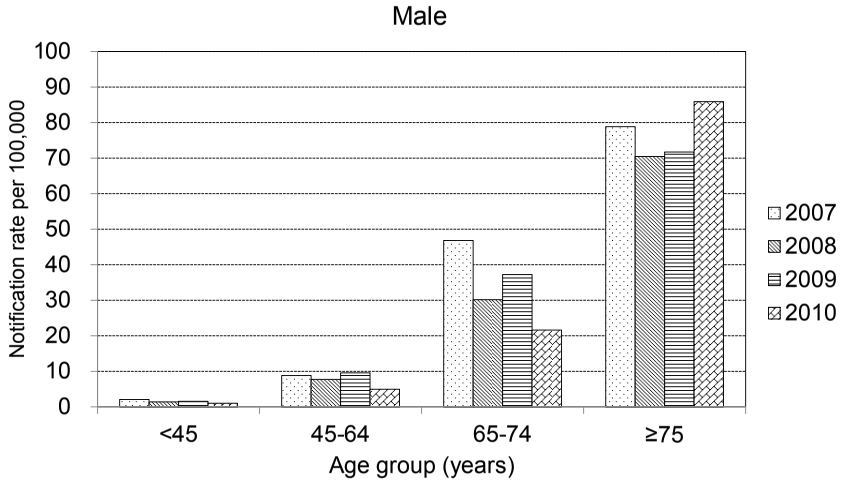
Source of information: Taiwan CDC

Reported case rate of nontuberculous mycobacterium among male in Taipei City, 2007-2010, by age group (per 100,000 inhabitants)



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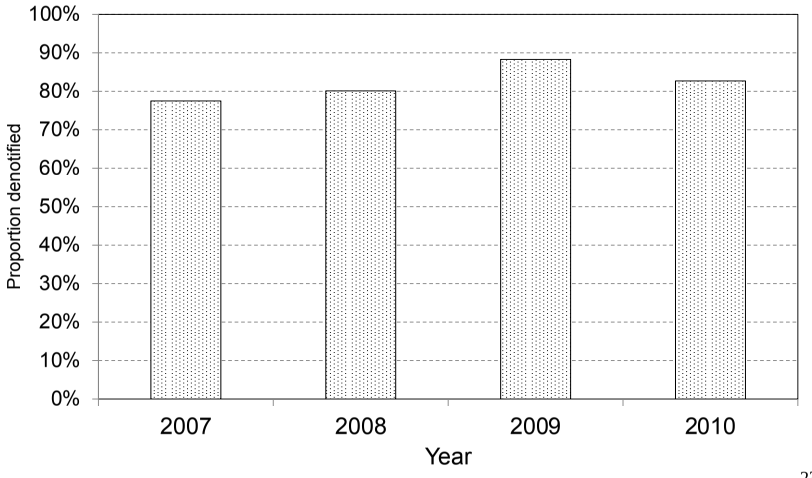
Chiang C-Y, et al. Preparing manuscript

Proportion of notified nontuberculous mycobacterium cases denotified, 2007-2010, Taipei City



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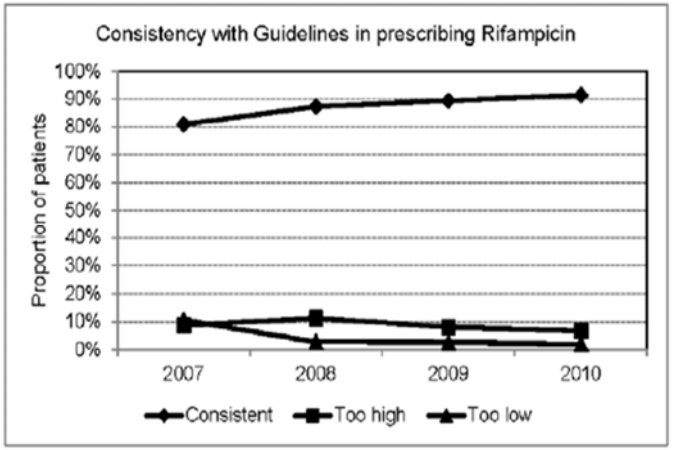
Chiang C-Y, et al. Preparing manuscript

Improved Consistency in Dosing Anti-Tuberculosis Drugs in Taipei, Taiwan



Chiang C-Y, et al. PLoS ONE 7(8):e44133. doi:10.1371/journal.pone.0044133

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International Union Against Tuberculosis and Lung Disease

Patient and health system delays in the diagnosis and treatment of tuberculosis in Southern Taiwan, 2003

- Median patient delay: 7 days.
- Median health system delay : 23 days,
  - 13 for smear-positive patients
  - 37 for smear negative patients
- Median total delay:44 days

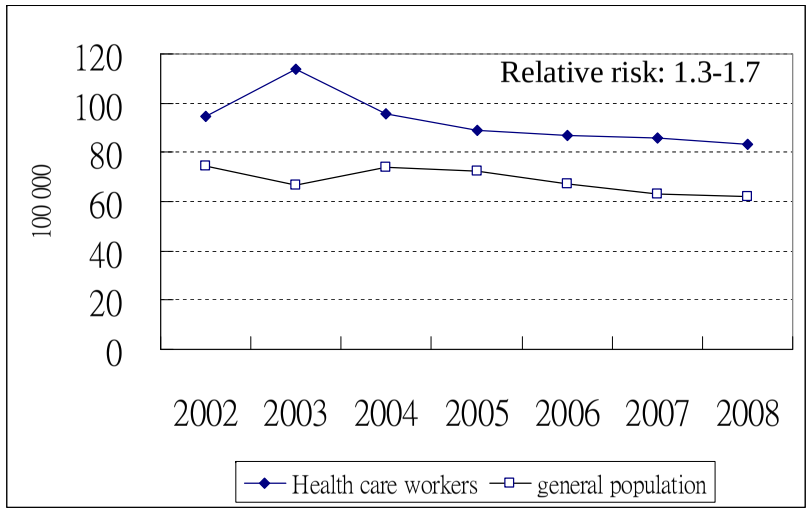
Chiang C-Y, et al. Int J Tuberc Lung Dis 2005;9:1006-12

Delay in the diagnosis and treatment of tuberculosis, 2005, Taiwan

- a population-based study using National Health Insurance claims data
- Path to the diagnosis of TB
  - Frequency of medical consultations(mean): 12.8
  - Number of health care facilities visited (median): 6
- Health system delay (median): 53 days (inter-quartile range, 12-147 days)

Karen Lai. Thesis for MPH 2007

Notification rate of tuberculosis, 2002-2008, Taiwan



Source of information: Taiwan CDC

Epidemiology of Tuberculosis in Taiwan

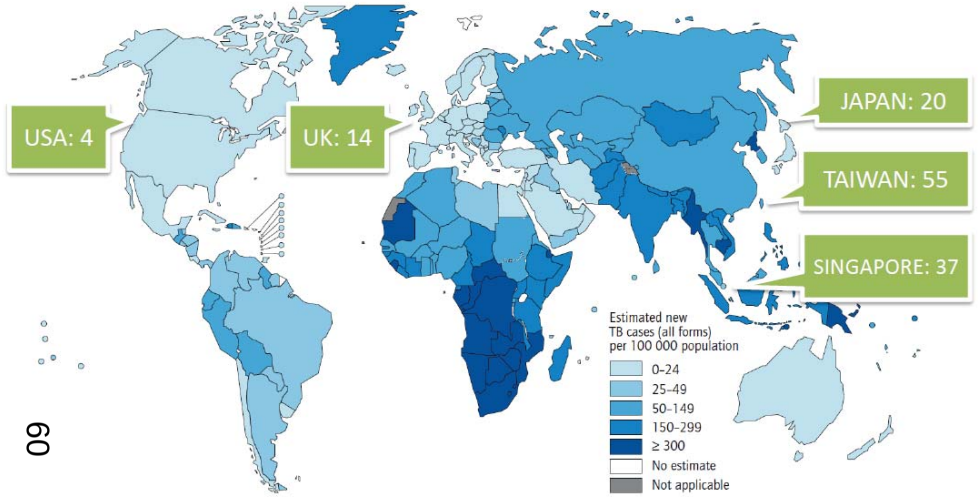
Cheng-yi Lee, MSc, PhD Candidate.
TB Surveillance Officer
Epidemic Intelligence Center
Taiwan CDC

Presentation Outline

- Case notification and incidence
  - Case detection
  - By age and sex
  - Sputum status
- Mortality
- Drug-Resistant TB
- Pulmonary and Extra-pulmonary TB
- Implementation of DOTS program
- TB/HIV co-infection
- Treatment outcomes
- TB in remote areas
- Challenges and solutions

Incidence of tuberculosis, 2011

FIGURE 2.5 **Estimated TB incidence rates, 2011**



Data sources: WHO, Global TB Control -2012

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Demographic of population and TB in Taiwan

	2005	2006	2007	2008	2009	2010	2011
Population (persons)	22,729,753	22,823,455	22,917,444	22,997,696	23,078,402	23,140,948	23,193,518
≧65 yrs	2,183,639	2,251,917	2,315,060	23,726,56	2,429,934	2,472,770	2,508,071
Aging index	50.5	53.6	56.6	59.8	63.3	66.8	70.4
% of ≧65 yrs cases of population	9.6	9.9	10.1	10.3	10.5	10.7	10.8
New TB cases	**16,472**	**15,378**	**14,480**	**14,265**	**13,336**	**13,237**	**12,634**
Relative risk (≧65 yrs vs. <65 yrs)	9.8	10	9.5	9.5	9.6	9.4	7.4
Incidence rate of ≧65 yrs	385	356.5	323	314	291.3	283.1	237.7
Incidence rate of <65 yrs	39.2	35.7	34	33	30.3	30.2	32.0
Case no. (≧65 yrs)	8,408	8,029	7,477	7,451	7,078	7,000	6009
% of ≧65 yrs among new TB cases	51	52.2	51.6	52.2	53.1	52.9	52.3

Case notification of TB, 2005-2010

		2005	2006	2007	2008	2009	2010
New cases	**Total**	**16,472**	**15,378**	**14,480**	**14,265**	**13,336**	**13,237**
	Smear(+)	5,748	5,542	5,734	5,559	5,210	5,027
	Smear(-)/unknown	9,396	8,815	7,944	8,065	7,526	7,630
	EPTB	1,328	1,021	802	641	600	580
Retreatment cases	Relapse	108	715	646	580	490	510
	Others	1,135	419	1,128	1,341	1,254	1,108
% of smear(+) among new pulmonary cases		38	39	42	41	41	40
% of lab confirmed among new pulmonary cases			71	77		80	81

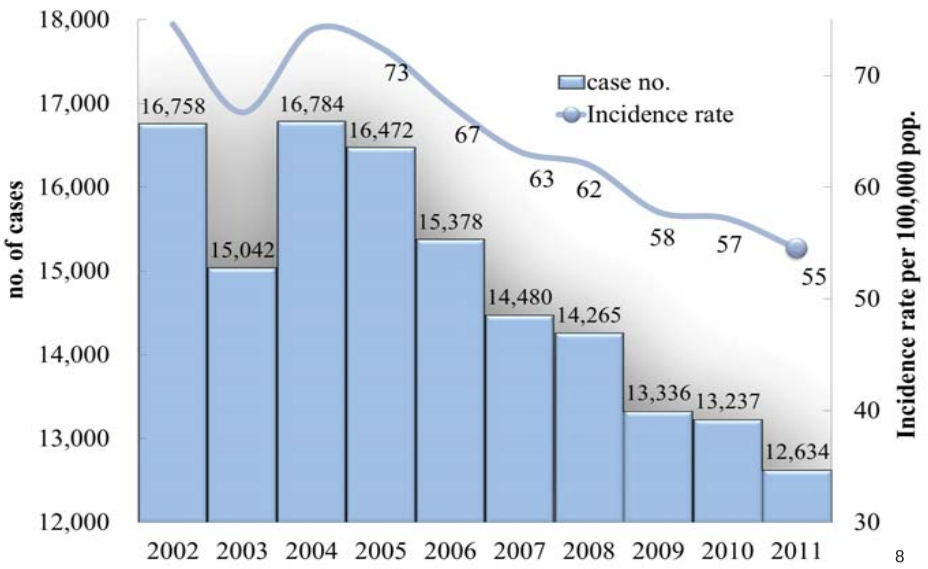
Estimated case detection rate of TB, 2005-2010

	case detection rate (all new cases)	case detection rate (new ss+ cases)
2005	77%	139%
2006	77%	90%
2007	74%	63%
2008	74%	75%
2009	71%	107%
2010	76%	79%

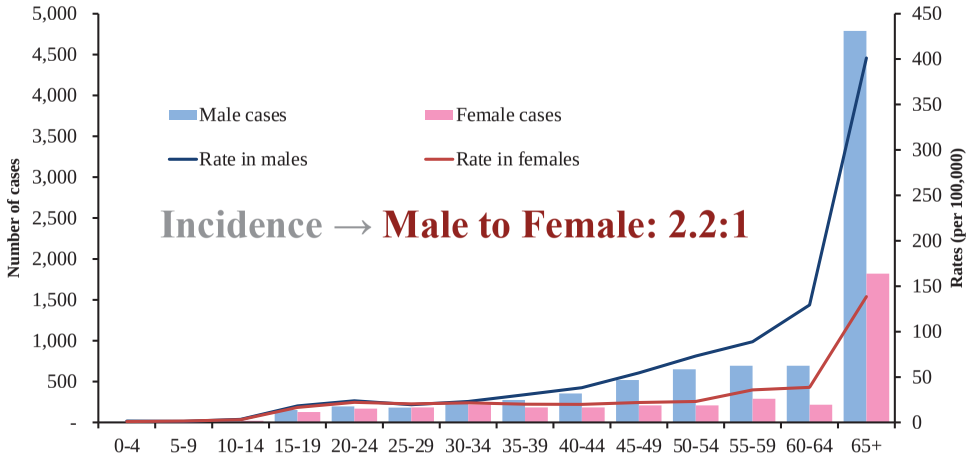
Measured by WHO TB impact index equation. Estimated incidence = Deaths / proportion of incident case that die.
Reference: http://www.who.int/tb/en; Dye C et al, Global burden of TB: estimated incidence , prevalence and mortality by country. JAMA (1999); Global TB control: a short update to the 2009 report. ; Global TB control 2011.

Incidence

Tuberculosis cases and rates, 2002-2011

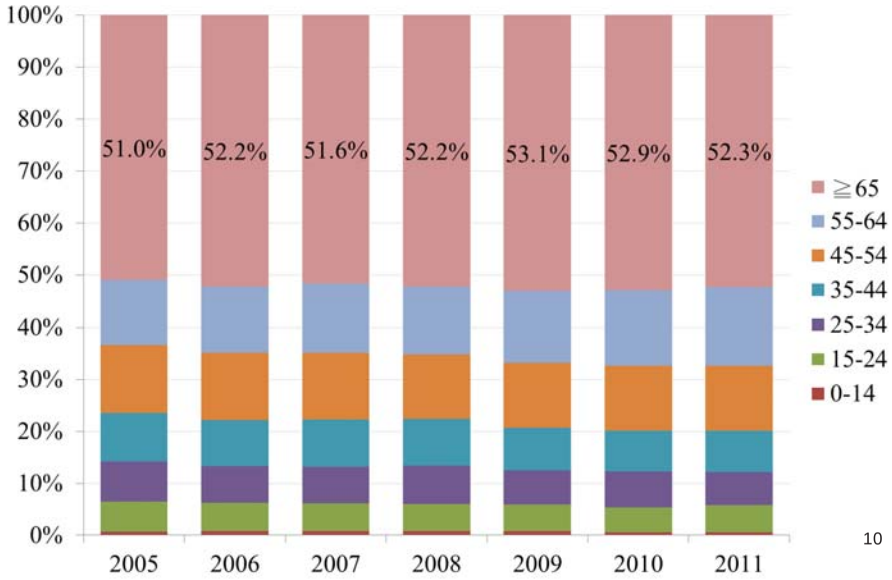


Tuberculosis cases and rates by age and sex, 2011



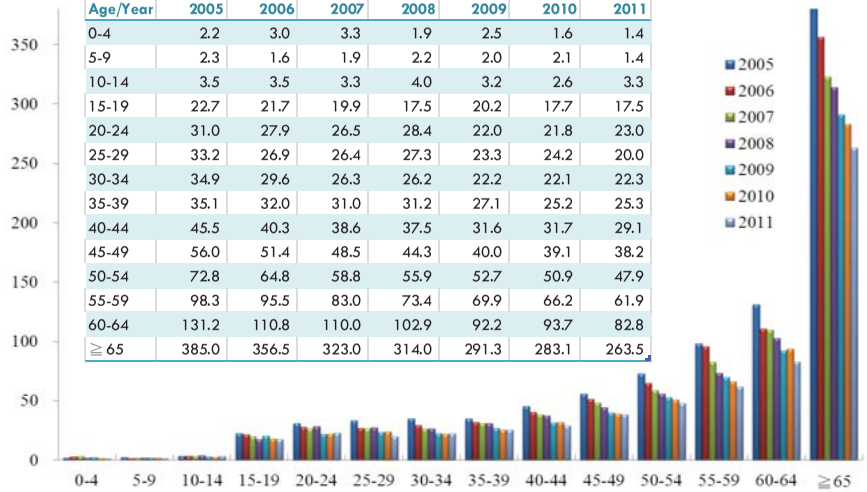
Incidence of males were 74.5 cases per 100,000 population and females were 33.4 cases per 100,000 population.

Cases proportion among incident TB cases, by age, 2005-2011

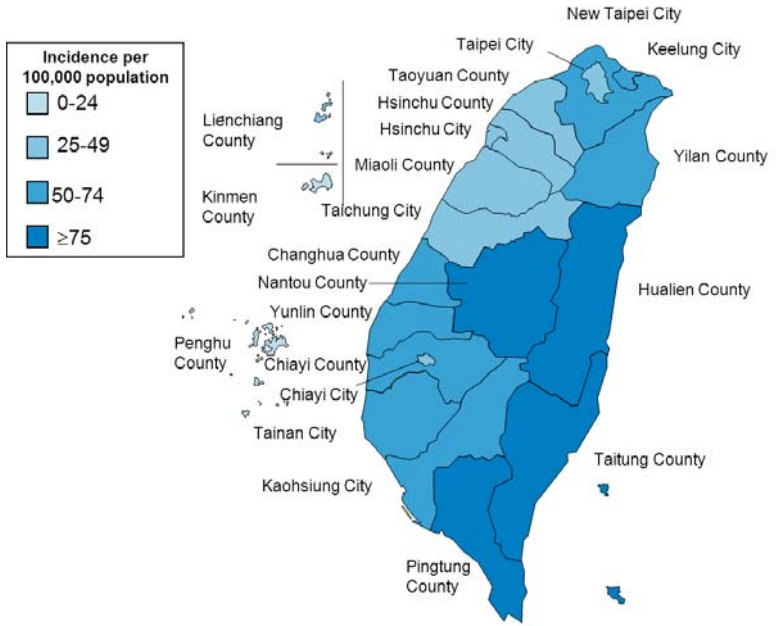


TB incidence by age, 2005-2011

Age/Year	2005	2006	2007	2008	2009	2010	2011
0-4	2.2	3.0	3.3	1.9	2.5	1.6	1.4
5-9	2.3	1.6	1.9	2.2	2.0	2.1	1.4
10-14	3.5	3.5	3.3	4.0	3.2	2.6	3.3
15-19	22.7	21.7	19.9	17.5	20.2	17.7	17.5
20-24	31.0	27.9	26.5	28.4	22.0	21.8	23.0
25-29	33.2	26.9	26.4	27.3	23.3	24.2	20.0
30-34	34.9	29.6	26.3	26.2	22.2	22.1	22.3
35-39	35.1	32.0	31.0	31.2	27.1	25.2	25.3
40-44	45.5	40.3	38.6	37.5	31.6	31.7	29.1
45-49	56.0	51.4	48.5	44.3	40.0	39.1	38.2
50-54	72.8	64.8	58.8	55.9	52.7	50.9	47.9
55-59	98.3	95.5	83.0	73.4	69.9	66.2	61.9
60-64	131.2	110.8	110.0	102.9	92.2	93.7	82.8
≧65	385.0	356.5	323.0	314.0	291.3	283.1	263.5



Incidence of TB in Taiwan, 2011

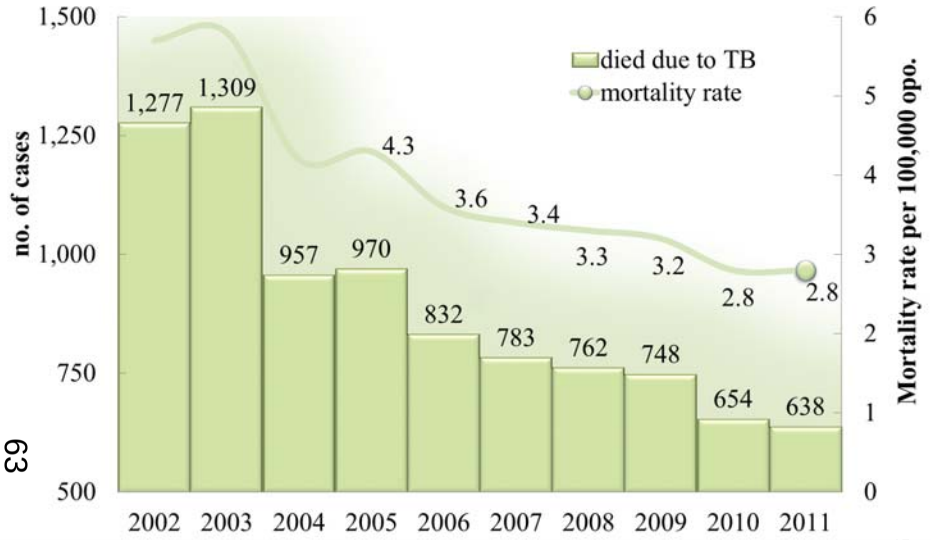


Sputum smear or culture positive rate of TB cases, 2005-2011

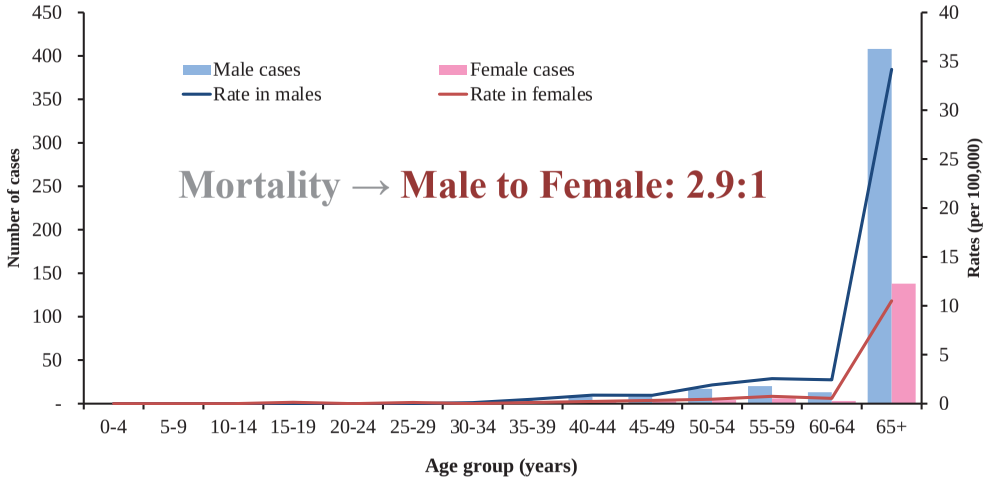
	No. of PTB	No. of ss+	%	No. of ss+/cul+	%
2005	15,262	5,748	**37.7%**	10,649	**69.8%**
2006	14,357	5,542	**38.6%**	10,261	**71.5%**
2007	13,678	5,734	**41.9%**	10,544	**77.1%**
2008	13,624	5,559	**40.8%**	10,826	**79.5%**
2009	12,736	5,210	**40.9%**	10,232	**80.3%**
2010	12,657	5,027	**39.7%**	10,310	**81.5%**
2011	12,069	4,559	**37.8%**	9,780	**81.0%**

Mortality

TB mortality rate, 2002-2011



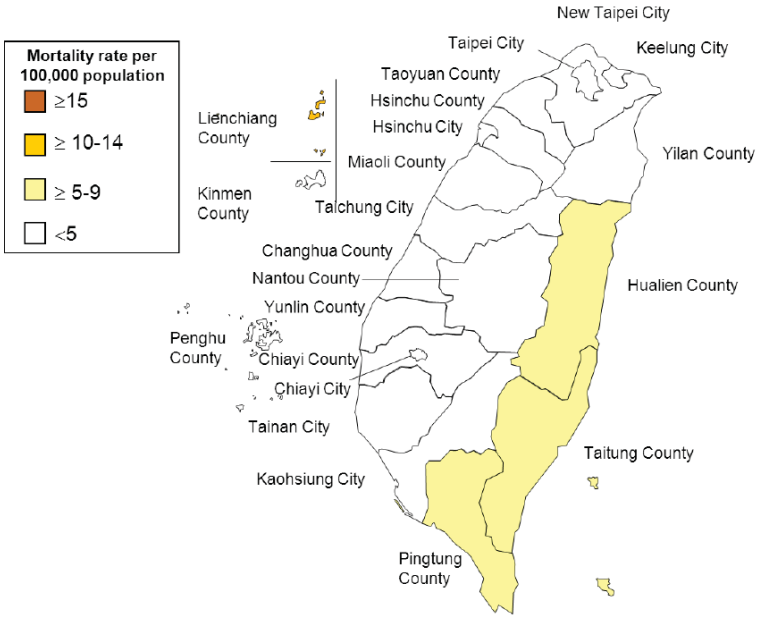
Tuberculosis mortality by age and sex, 2011



Male mortality rate were 4.1 cases per 100,000 population;
Female were 1.4 cases per 100,000 population.

Proportion of TB death, by age, 2005-2011

Mortality rate of TB in Taiwan-2011



Drug-Resistant TB

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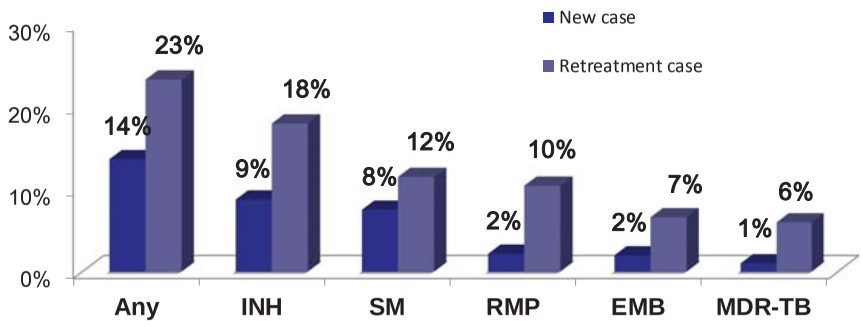
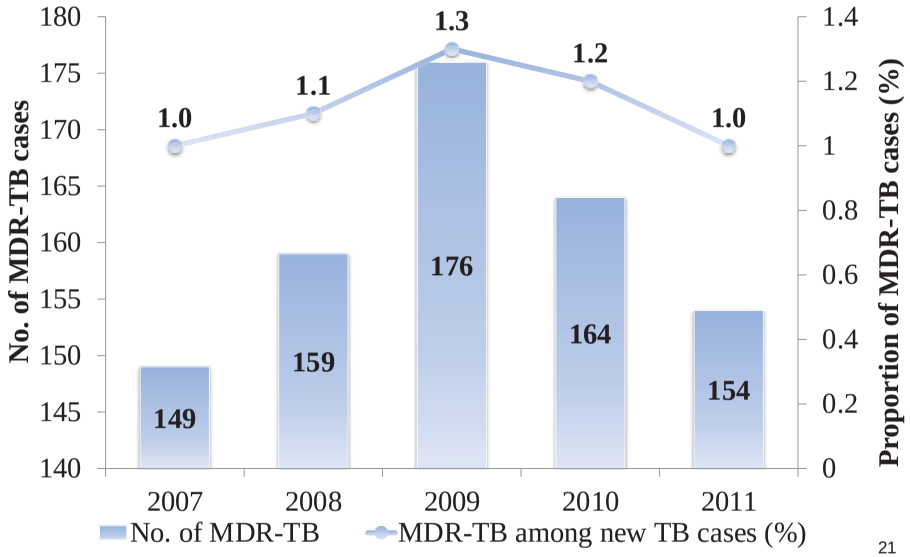
Drug-Resistant TB



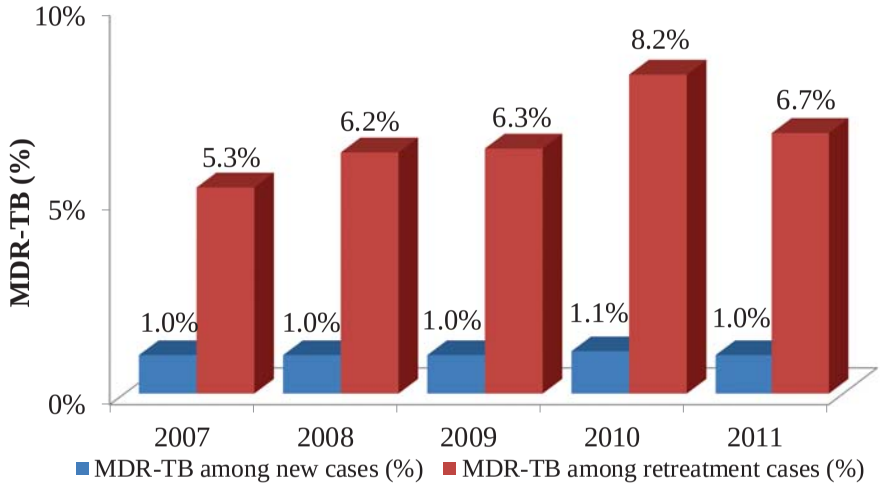
Time Period : 2009/7/1 to

MDR-TB among all new TB cases



21

MDR-TB among new and retreatment cases, 2007-2011



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Pulmonary Tuberculosis (PTB) & Extra-pulmonary Tuberculosis (EPTB)

65

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Proportion of PTB and EPTB, 2005-2011

	Total	PTB	%	PTB+EPTB	%	EPTB	%
2005	**16,472**	13,413	**81.4**	1,849	11.2	1,210	7.3
2006	**15,378**	12,329	**80.2**	2,028	13.2	1,021	6.6
2007	**14,480**	11,588	**80.0**	2,090	14.4	802	5.5
2008	**14,265**	11,548	**81.0**	2,076	14.6	641	4.5
2009	**13,336**	10,582	**79.3**	2,154	16.2	600	4.5
2010	**13,237**	10,435	**78.8**	2,222	16.8	580	4.4
2011	**12,634**	10,027	**79.4**	2,042	16.2	565	4.5

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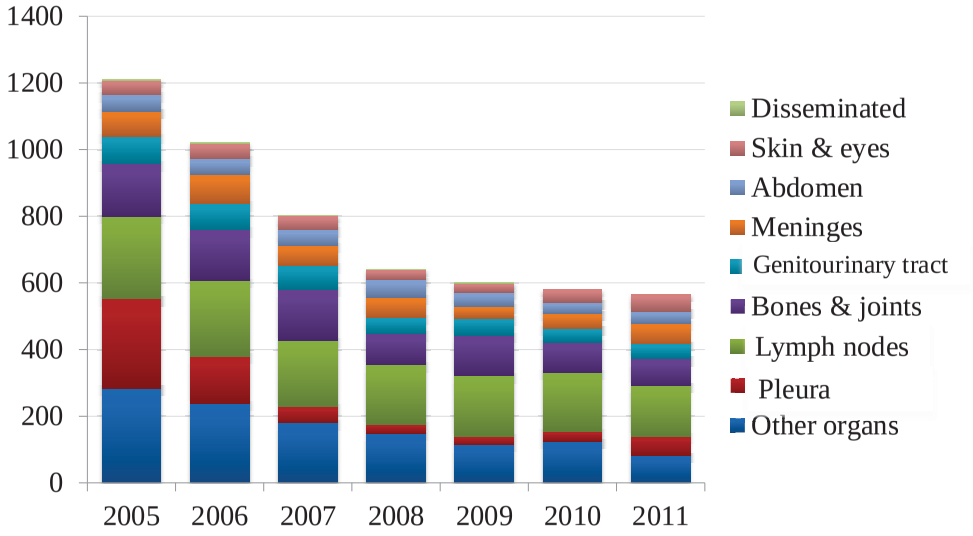
Sites of EPTB, 2005-2011



EPTB in young age, 2005-2011 (1)

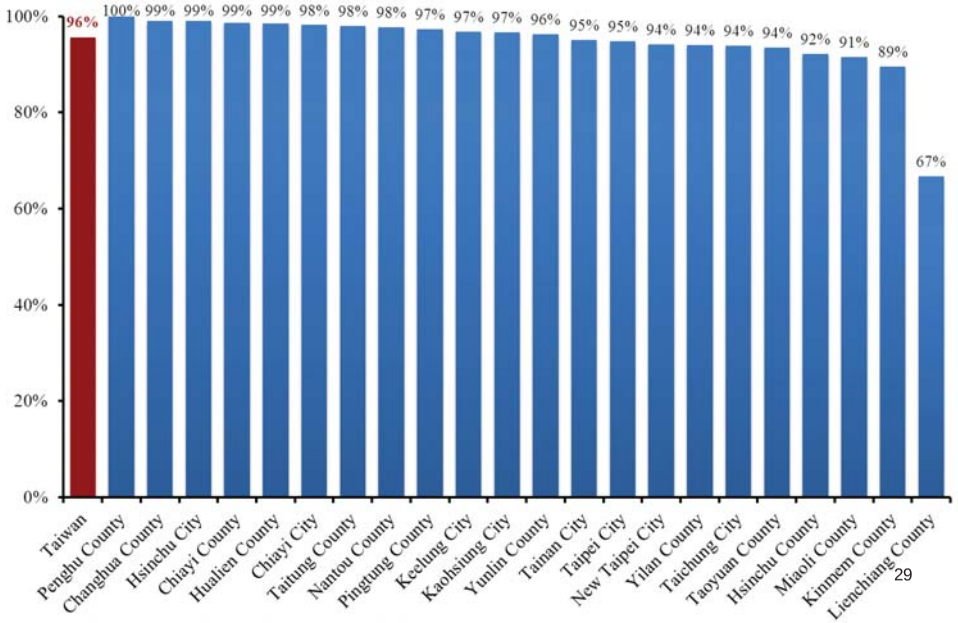
Year	Total	Cases <15 y/o	% in children	Total EPTB	Cases <15 y/o	% in children
2005	16,472	118	**0.7**	1,210	33	**2.7**
2006	15,378	114	**0.7**	1,021	35	**3.4**
2007	14,480	115	**0.8**	802	50	**6.2**
2008	14,265	112	**0.8**	641	29	**4.5**
2009	13,336	100	**0.7**	600	31	**5.2**
2010	13,237	81	**0.6**	580	30	**5.2**
2011	12,634	77	**0.6**	565	23	**4.1**

EPTB in young age, 2005-2011 (2)

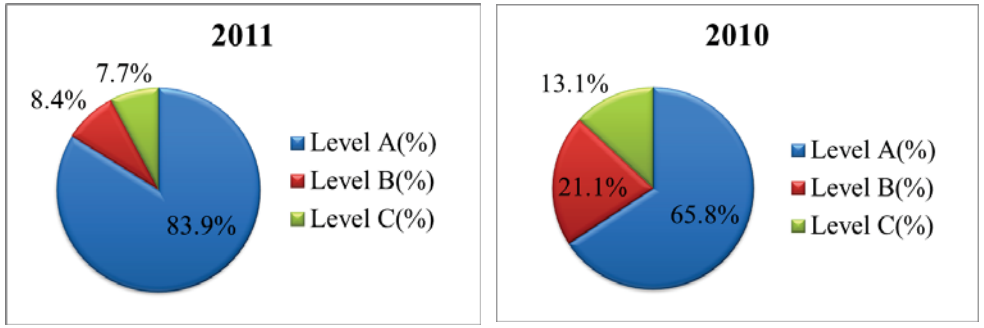
	2005	2006	2007	2008	2009	2010	2011
Total	**33**	**35**	**50**	**29**	**31**	**30**	**23**
Lymph nodes	**11**	**13**	**21**	**21**	**19**	**20**	**11**
Bones & joints	6	6	11	0	6	2	3
Skin & eyes	3	5	4	2	1	0	2
Meninges	3	1	3	1	0	2	1
Pleural effusion	0	0	0	0	0	0	1
Genitourinary tract	0	0	0	0	0	0	0
Abdomen	0	1	2	0	0	0	0
Disseminated	0	0	0	0	0	0	0
Other organs	10	9	9	5	5	0	5

Directly observed treatment, short-course, (DOTS)

Proportion of DOTS implementation



DOTS implementation among smear or culture positive cases



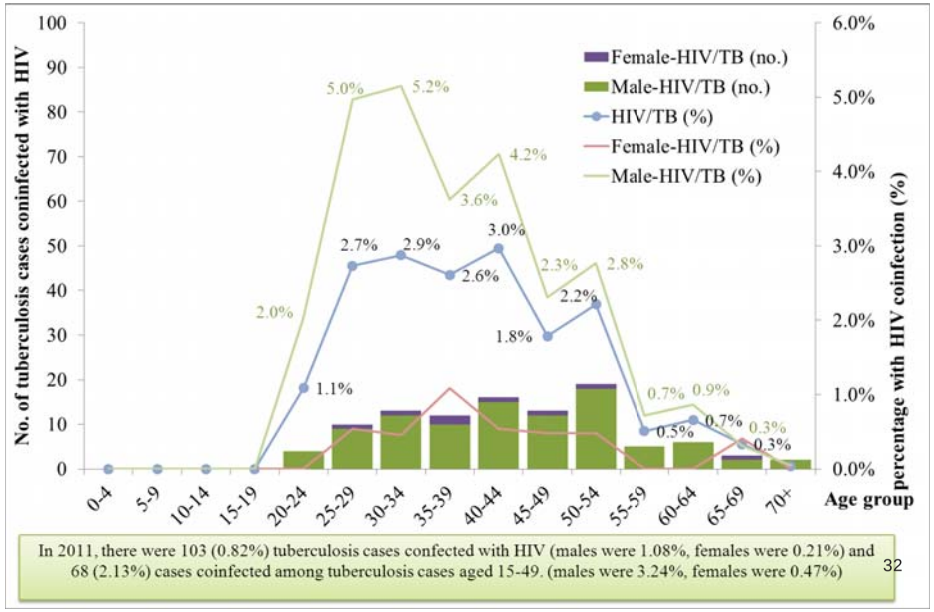
Level A: The proportion of days during which an official DOT observer witnessed treatment was >70% in the initial 2 month, **AND** observer witnessed was ≥ 60% during whole treatment period.

Level B: Observer witnessed was ≥ 60% during whole treatment period.

Level C: Others.

TB/HIV, HIV/TB co-infection

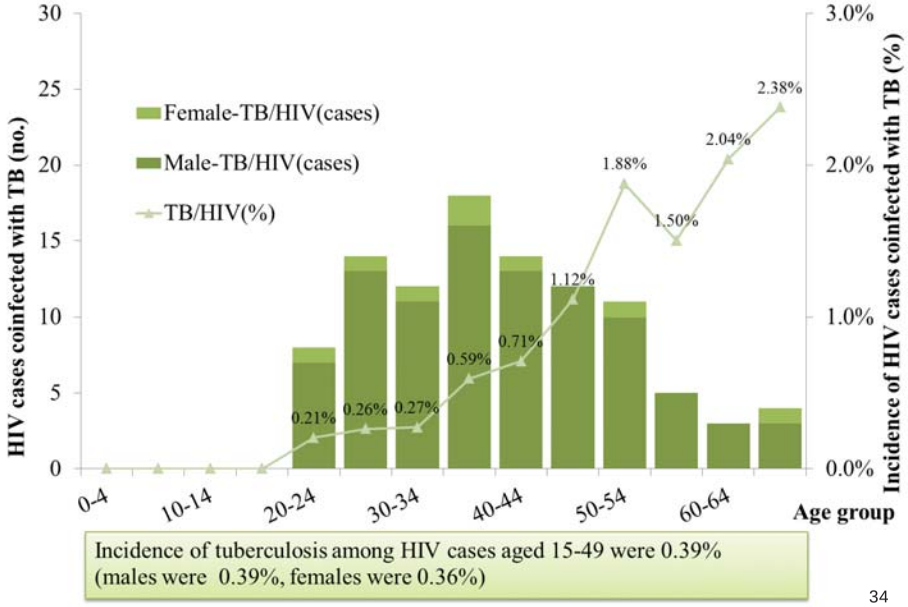
TB cases and percentage with HIV co-infection by age group, 2011



Characteristics of TB with HIV co-infection, 2011

	New TB	HIV/TB		Non HIV/TB		P value
	No.	No.	(%)	No.	(%)	
Total	12,634	103		12,531		
Abnormal Chest X-ray	11,641	86	83.5%	11,555	92.2%	<0.01
AFB positive	4,559	42	40.8%	4,517	36.0%	0.319
Positive sputum bacteriology	9,780	76	73.8%	9,704	77.4%	0.377
Extra-pulmonary TB	2,607	42	40.8%	2,565	20.5%	<0.001

TB co-infection with HIV, 2011



Treatment outcomes

Treatment outcomes of 12 month follow-up, 2005-2010 (1)

%	2005	2006	2007	2008	2009	2010
Success	69.2	71.8	71.0	70.4	70.0	71.1
Died	19.6	16.8	17.8	19.2	20.0	20.2
Failed	1.0	1.4	2.0	3.2	3.4	2.9
Defaulted	2.7	2.3	2.0	2.2	1.6	1.7
Transferred	0.1	0.4	0.3	0.1	0.1	<0.01
Not eval'd*	7.4	7.2	6.8	4.9	4.9	4.2

*Patients still on treated/followed-up after full 12 months treatment.

Adopted WHO definitions of tuberculosis treatment outcomes. Reference: http://www.who.int/tb/publications/global_report/2007/table_5/en/index1.html

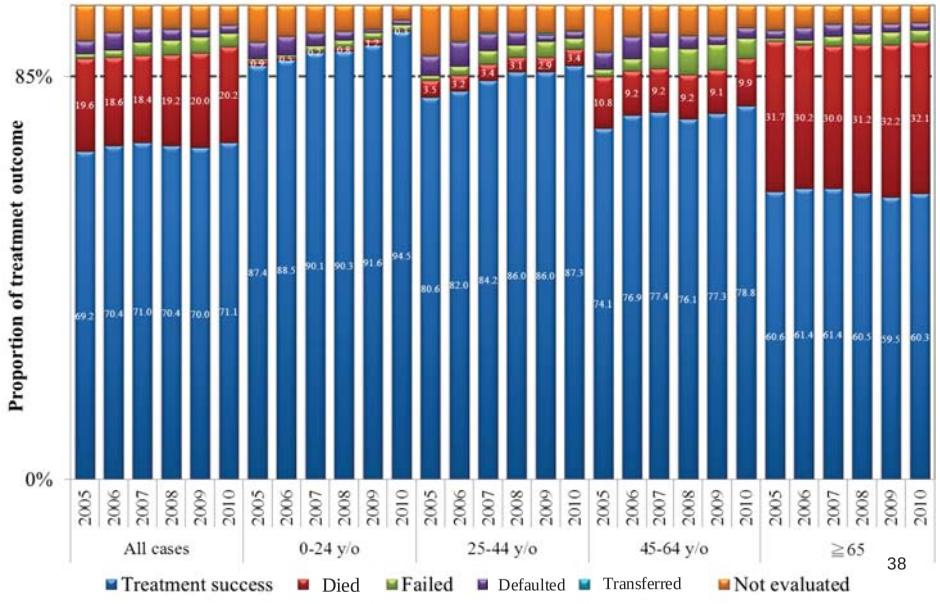
Treatment outcomes of 12 month follow-up, by age, 2005-2010 (2)

%	2005	2006	2007	2008	2009	2010
<50 y/o						
Success	80.5	82.5	84.5	85.1	85.3	86.9
Died	3.9	3.5	3.4	3.7	3.9	3.8
≧50 y/o						
Success	64.3	65.3	65.6	64.3	64.4	65.6
Died	26.4	24.9	24.4	25.6	25.8	25.9

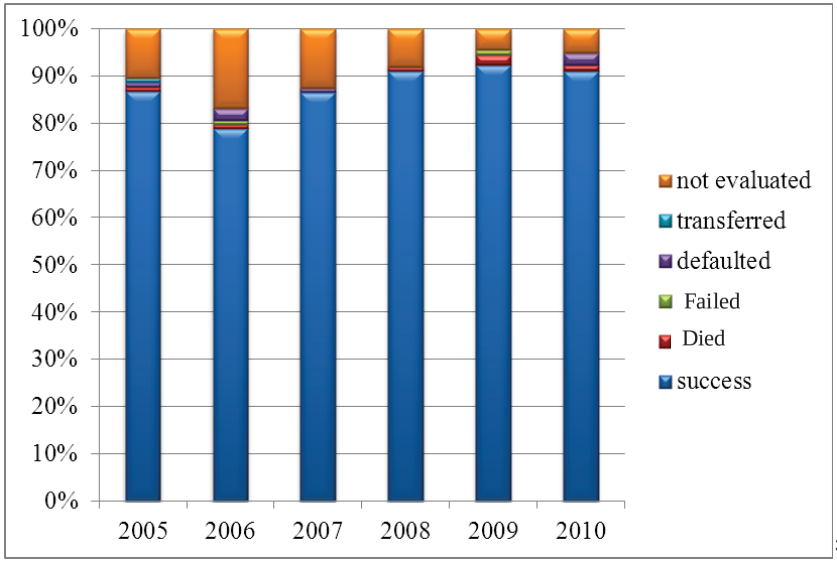
*Patients still on treated/followed-up after full 12 months treatment.

Adopted WHO definitions of tuberculosis treatment outcomes. Reference: http://www.who.int/tb/publications/global_report/2007/table_5/en/index1.html

Treatment outcomes of 12 month follow-up, by age, 2005-2010 (3)



Treatment outcomes of 12 month follow-up among young age(<15 y/o)



Cases relapse within 2 years

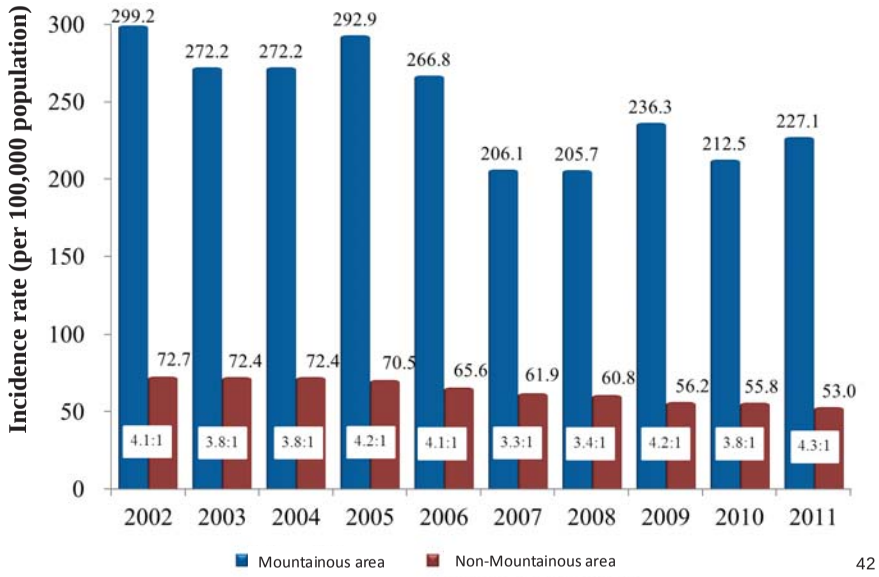
Cases relapse within 2 years, 2005-2010 cohort

	2005		2006		2007		2008		2009		2010※	
	no.	(%)	no.	(%)	no.	(%)	no.	(%)	no.	(%)	no.	(%)
New cases	16,472		15,378		14,480		14265		13,336		13,237	
Treatment success	12,968		12,205		11,521		11311		10,430		10,326	
Relapse within 2 years	175	**1.3**	125	**1.0**	87	**0.8**	78	**0.7**	73	**0.7**	47	**0.5**
<65y/r	99		57		51		42		45		29	
≧65y/r	76		68		36		36		28		18	

※ data date: 2012/9/28

TB in mountainous area

TB incidence rate in mountainous area



Prevalent cases* of TB by township

As of Feb.21, 2013

Category	Prevalent cases	Total MDR	%	MDR	XDR
Total	**8630**	**234**	**2.7**	**224**	**10**
General area	8067	204	2.5	194	10
Sub-Mountain area	252	8	3.2	8	-
Mountain area	311	22	7.1	22	-

1. A total of 368 townships are included in Taiwan, divided to general areas (313), mountain areas (30), and sub-mountain areas (25).
2. Mountain areas generally indicate to Remote areas with limited medical resources and mainly residents are aboriginals.
3. *Prevalent cases refer to TB cases under management and still receiving treatment on the designated date.

Challenges and solutions

- Static database management
- Development of information application such as smart phone apps with standard report search function
- Advance ISO certification of TB system
- Proceed personnel training, cooperate with national organization and establishment of standardization materials

Thank you for your attention!

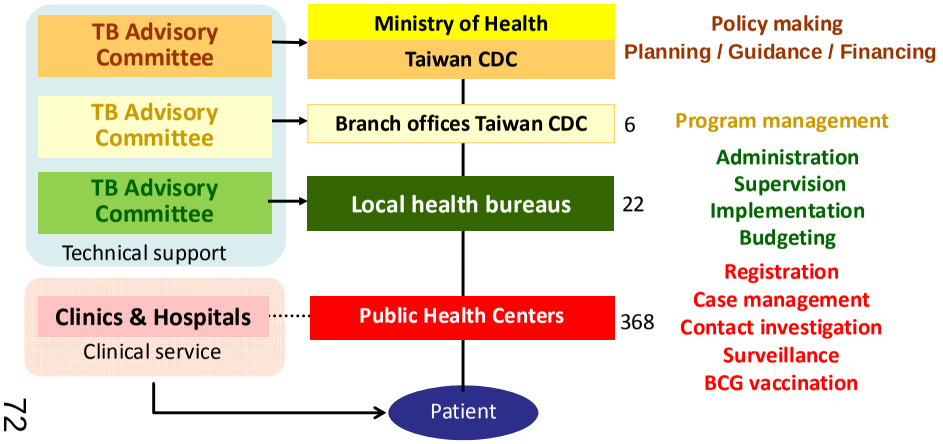
Situation Analysis and Future Direction

Chang-Hsun Chen, Director
Third division
Taiwan CDC

Outline

- Governance architecture
- Legal authorization for TB control
- National TB Program
- Manpower resources and budgeting
- Case identification and confirmation
- Case management
- Other important components
- Status Quo & progress
- Future direction

Governance Architecture



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Legal authorization for TB control (1)

- Communicable Disease Control Act
  - Article 3
    - Tuberculosis: Category 3 communicable diseases
    - MDR TB: Category 2 communicable diseases
  - Article 39
    - Reporting of cases mentioned in the preceding Paragraph shall be made
      - for category 2 communicable diseases, within 24 hours
      - for category 3 communicable diseases, within one week
  - Penalty
    - Article 65

Legal authorization for TB control (2)

- Article 43
  - Patients or suspected patients with communicable diseases and relevant personnel shall not refuse, evade or obstruct the laboratory testing, diagnosis, investigation and management mentioned in the preceding paragraph
- Article 44
  - patients with category 2 and category 3 communicable diseases, when necessary, may be placed under isolation care in designated isolation care institutions
- Penalty
  - Article 67、69

National TB Program

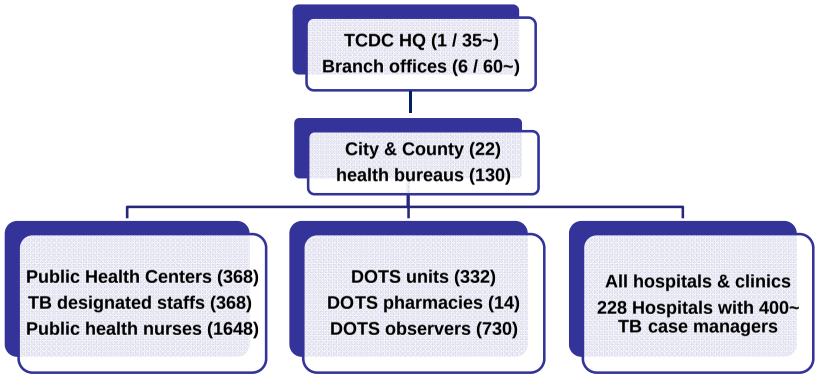
Mobilization Plan to Halve Tuberculosis Incidence in Ten Years

- Approved by the Executive Yuan on July 7, 2006
- Duration of implementation: 2006-2015
- Goal: to reduce the incidence to 36 per 100,000 by 2015

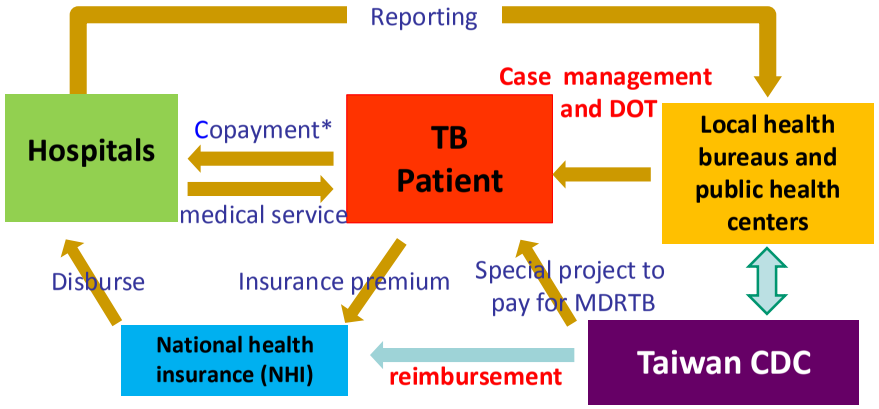
Action Plans

- Plan 1— Case finding campaign
- Plan 2— Laboratory capacity improvement
- Plan 3— Directly Observed Treatment Short-Course (DOTS)
- Plan 4— Hospital Care Enhancement & infection control
- Plan 5— MDR-TB project (DOTS-Plus)
- Plan 6— Air Travel control
- Plan 7— Surveillance and database
- Plan 8— National Health Insurance related issues
- Plan 9— Local government evaluation
- Plan 10— LTBI treatment program
- Plan 11— Contact tracing plus pilot project
- Plan 12— New immigrant program
- Plan 13— BCG evaluation
- Plan 14— IC and R&D
- Plan 15— Mandatory isolation implementation

Manpower allocation for TB control program



Medical care system and TB control



*TCDC pays for MDRTB and reimburses NHI to cover following expenditure :

1. Copayment for all TB patients
2. Medical expense of uninsured patients
3. Expense of isolation

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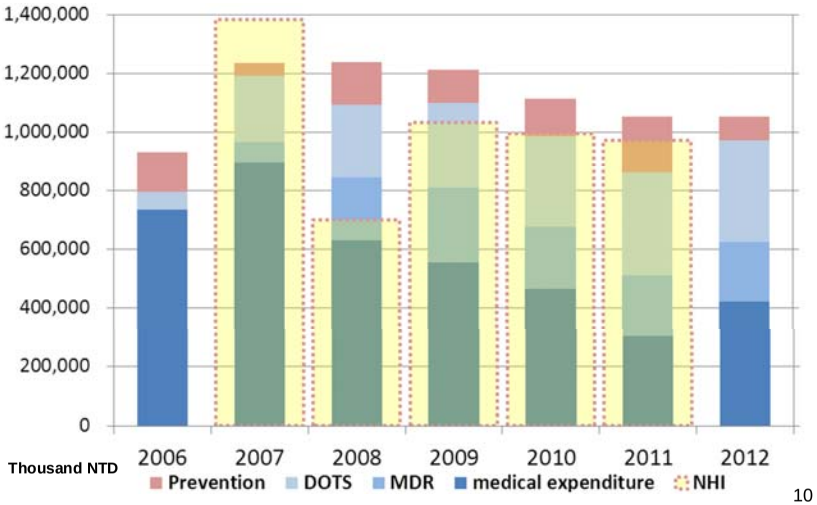
Allocation of Government's budget 2006-2012



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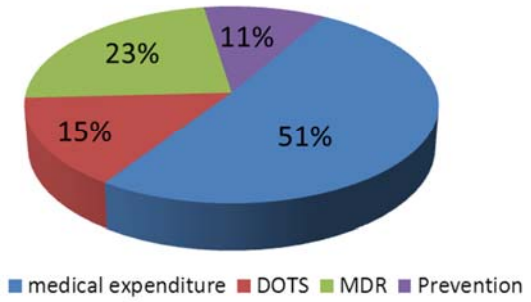
Budgeting, 2006-2012



A total of 7,842,472 thousand NTD (261 million USD)

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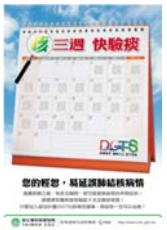
Case Finding

- Public health sectors (4.5%)
  - Public education
    - Symptom screening (7 scores)
    - check sputum, think of TB if cough> 3 week
  - Contact investigation
  - Active case finding among the high risk groups
    - Mountainous area, indigenous populations, prisons and jails, homeless people, etc.
- Private sectors (clinics/hospitals) (95.5%)
  - Medical attendance of the symptomatic
- Screening policy for foreigners
  - Foreign permanent residency (foreign spouses and foreign nationals, ROC nationals without Household Registration, People from Mainland China Area, or Hong Kong and Macau Area Residents)



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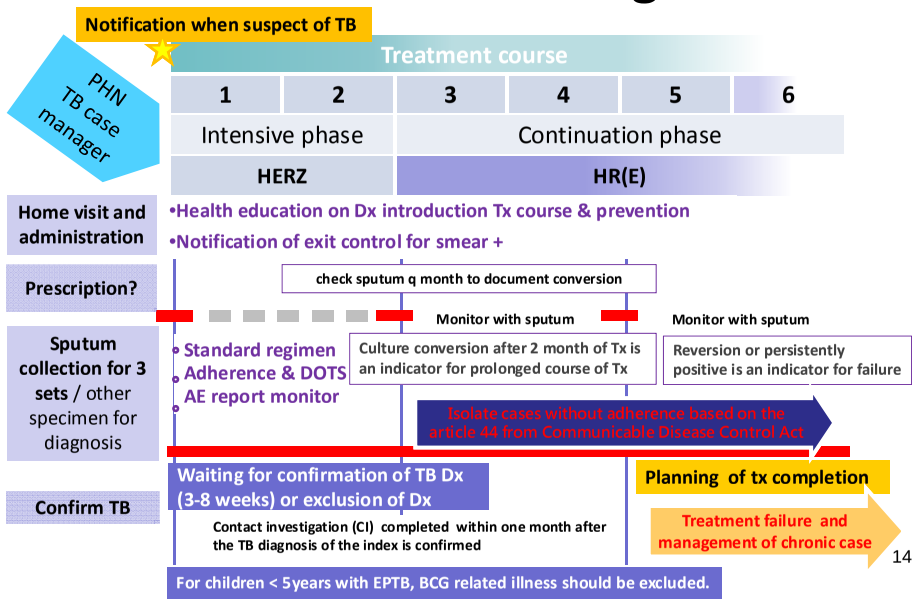
How to identify suspected TB cases

- Radiographic examination
  - CXR、CT
- Laboratory Diagnosis
  - AFS、culture / MGIT、ICT
    - 325+1 Policy
      - 3 sets of sputum initially no more than 2 sets during follow-up
      - check sputum at the end of2nd month, 5th month & Tx completion
      - recommend to check sputum every month until conversion documented, if feasible
  - DST
    - MDRTB should be confirmed by National ref. lab
    - Second-line DST provided by National ref. lab
  - Rapid test for MDR-TB high risk groups (GenoType®)
  - Genotyping
    - *M. bovis*, *M. bovis*-BCG, NTM
    - Spoligotyping, MIRU,RFLP

Timeline of case management



Restriction of infectious tuberculosis patients from boarding public aircraft for going abroad

- In line with the second edition of WHO publication "Tuberculosis and Air Travel"
- Based on Article 43 of Communicable Disease Control Act
- Target group
  - To prevent infectious PTB patients from traveling by flight on a journey exceeding 8 hrs
  - MDR-TB patients must postpone any air travel until that they are no longer infectious, i.e. culture-negative.

IHR : since June 15, 2007

Plan 6

Mandatory isolation implementation

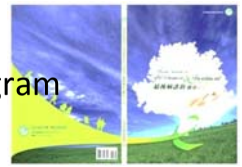
- Criteria for Compulsive isolation
  - Infectious TB case (sputum positive)
    - Remove isolation on ① negative conversion of sputum ② exclusion of TB ③ sputum remains positive but regular medication under DOTS
    - Continue isolation
      - Potential jeopardy to public health
        - » Household members including children <13 years or immuno-compromised hosts
        - » Comorbid with psychiatric diseases, HIV/AIDS
        - » Homeless

      And – uncooperative patient
        - » Incompliance of treatment course and pose threat to public
        - » Evadeing public health nurse's visit
        - » Sputum remains positive but refuse DOTS
- A total of 137 hospitals designated for isolation (1,504 beds)
- 17 of them with the capacity of taking care of TB cases comorbid with psychiatric diseases

Plan 15

Hospital Care Enhancement & infection control (1)

- Taiwan guidelines for TB diagnosis & treatment (Fifth Edition, 2012)
- Medial-care quality enhancement program
- Collaboration with NHI
  - Review of adequacy of anti-TB regimen & intervention through NHI
- Supply and management of 2nd-line drugs



Plan 4

Hospital Care Enhancement & Infection Control (2)

- Pursuing NHI special project--Medial-care quality enhancement program, encourage case management enrollment and improve treatment success rate
- Requirement in hospital accreditation

  <on-site inspection of infection control>
  - At least one TB case manager for every 100 TB cases
  - Documentation of monthly, in-hospital meetings regarding diagnosis and treatment of TB cases
  - Enhancement of CI of in-hospital contacts (both exposed health care workers and patients in the same room)

Plan 4

Hospital Care Enhancement & infection control (3)

- Provide incentives through disbursement system
- TB related medical expenditure pay by governmental budgets
  - TB medical expenditure co-payment (include LTBI treatment and contact exam)
  - Medical expenditure of mandatory isolation
  - C2：≦14 days hospitalized medical expenditure of S(+) cases
  - C3：≦ 30 days hospitalized medical expenditure of TB cases with side effects of TB drugs
  - C4：medical expenditure of TB cases who were NHI uninsured (include LTBI treatment and contact exam)
  - Diagnosis and ward fee of chronic TB cases
    - A total of 14 designated hospitals for chronic TB cases
    - Encourage admission to the designated hospitals with incentives (20 USD per day)
  - 2nd-line drug

Plan 4

Hospital Care Enhancement & infection control (4)

The Introduction of Reducing disbursement from NHI to Improve the Inadequate Regimen for TB Care

Duration :

March to December, 2008

Total :

199 charts (selected by branches)

-- 50.3% (100) were appropriate

-- 49.7% (99) were inappropriate

Result of Review	Number	percentage (%)
Inappropriate	99	
Non-standardized regimen in combination	28	28.3
Inadequate/over dosage	32	32.3
Inappropriate frequency	19	19.2
Others	9	9.1
Inadequate dosage combined with inappropriate frequency	4	4
Inappropriate frequency combined with non-standardized regimen	2	2
Inadequate dosage combined with non-standardized regimen	4	4
Inappropriate frequency, inadequate dosage, combined with non-standardized regimen	1	1

Li YP et al. The Introduction of Reducing of Reimbursement from National Health Insurance to Improve the Inadequate Regimen for TB Care. (40th Union World Conference on Lung Health poster, 2009)

OPEN ACCESS Freely available online PLOS ONE

Improved Consistency in Dosing Anti-Tuberculosis Drugs in Taipei, Taiwan

Chen-Yuan Chiang[1,2,3], Ming-Chih Yu[2,3], Hsiu-Chen Shih[4], Muh-Yong Yen[4], Yu-Ling Hsu[5], Shiang-Lin Yang[5], Tao-Ping Lin[6], Kuan-Jen Bai[2,3]*

August 2012 | Volume 7 | Issue 8 | e44133

- **Methodology**
  - Medical audit of TB case management files to collect pretreatment body weight and regimens prescribed at commencement of treatment of all notified culture positive TB cases in 2007–2010. Dosages prescribed were compared with dosages recommended and difference in prescribing practice of anti-TB drugs in Taipei City. between 2003 and 2007–2010 evaluated.
- **Principal Findings**
  - The proportion of patients with recorded pre-treatment body weight was 64.5% in 2003, which increased to 96.5% in 2007–2010 (p<0.001)
  - The proportion of patients treated with consistent dosing
    - 3-drug FDC increased from 73.9% in 2003 to 87.7% in 2007–2010 (p<0.001)
    - 2-drug FDC from 76.0% to 86.1% (p = 0.024)
    - rifampicin (RMP) from 62.8% to 85.5% (p<0.001)
    - isoniazid from 87.8% to 95.3% (p<0.001)

Medical care system for MDR-TB

- **Taiwan MDR-TB Consortium (TMTC)**
  - Launched On May 2007
- Goal
  - To provide medical care services to MDR-TB
  - Expanded to cases with RMP mono-resistance or resistance to any 3 anti-TB drugs or more more anti-TB drugs since 2011
- Requirement
  - Qualified staff & facilities
- Effect
  - 90% MDR-TB cases were enrolled in DOTS-plus program up to Feb. 2013
  - Treatment success rate (24 months) reached 78%

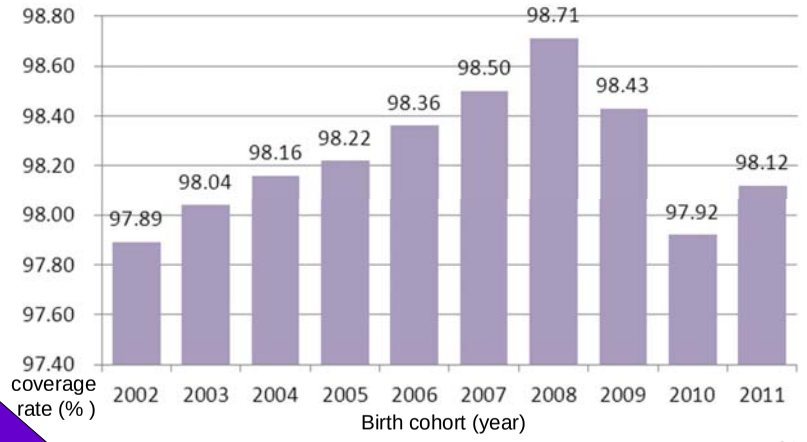
Plan 5

BCG Vaccination

- Routine BCG immunization in infancy
  - Coverage exceeding 98%, 2005-2011
- Surveillance of BCG injury
  - For children<5 years, specimens or strains of MTB complex are collected to exclude BCG relatedness
- Subcontract to related academic societies for training or evaluation of BCG and TST injection technical and reading proficiency
  - A total of 1145 accredited nurses for BCG and TST on duty(as of 2011)
  - 1221 received educational course; 207 passed evaluation and 47 Seed trainers (in 2012)

Plan 13

The coverage of BCG immunization in infancy 2002-2011



Plan 13

Completion of molecular diagnosis and the number of confirmed BCG in extra-pulmonary TB cases aged under 5, notification year 2002-2012

Year of notification	Completion of molecular diagnosis	Osteitis /Osteomyelitis	Cellulitis	Disseminated	LAP &Others
		(No. of molecular Dx / No. confirmed BCG related)			
2005	28%	6(3/1)	6(1/1)		6(1/1)
2006	24%	9(3/3)	8	1(1/1)	3(1/1)
2007	19%	10(2/2)	10(1/1)	1	6(2/2)
2008	89%	2(2/1)	13(11/1)		13(12/5)
2009	92%	14(14/9)	6(6/1)		17(14/9)
2010	86%	12(12/10)	7(6/1)	2(1/0)	46(38/6)
2011	91%	11(10/4)	6(6/3)		50(45/16)
2012	74%	8(8/7)	3(3/3)		54(37/24)
Total	73%	72(54/37)	57(34/11)	4(2/1)	195(150/64)

Plan 13

330 notification, 240 completion of Dx, 113 confirmed BCG; Data : chart review and TCDC

Adverse effects of BCG birth cohort 2003~2012

Incidence (/10^7)

Birth cohort (year)	No. of immunization	Osteitis /Osteomyelitis No.	Osteitis /Osteomyelitis Incidence	Cellulitis No.	Cellulitis Incidence	Disseminated No.	Disseminated Incidence
2005	211296	3	14.2	0	0	0	0
2006	209006	0	0	1	4.8	0	0
2007	206772	3	14.5	1	4.8	0	0
2008	198820	11	55.3	0	0	0	0
2009	194737	10	51.4	4	20.5	0	0
2010	169462	4	23.6	1	5.9	0	0
2011	196290	5	25.5	1	5.1	0	0
2012	212703	0	0	0	0	0	0

1. Global estimation of AE/million dose of BCG (WHO2000)- Osteitis：**1-700**
2. Data：TCDC , surveillance ~ 2013/1/14

Plan 13

New immigrant program-1

- **Cascades for foreign workers (labor) health checks**

Accredited hospital (in home country) → *Designated hospitals for health checks → *Designated CXR confirmation hospitals

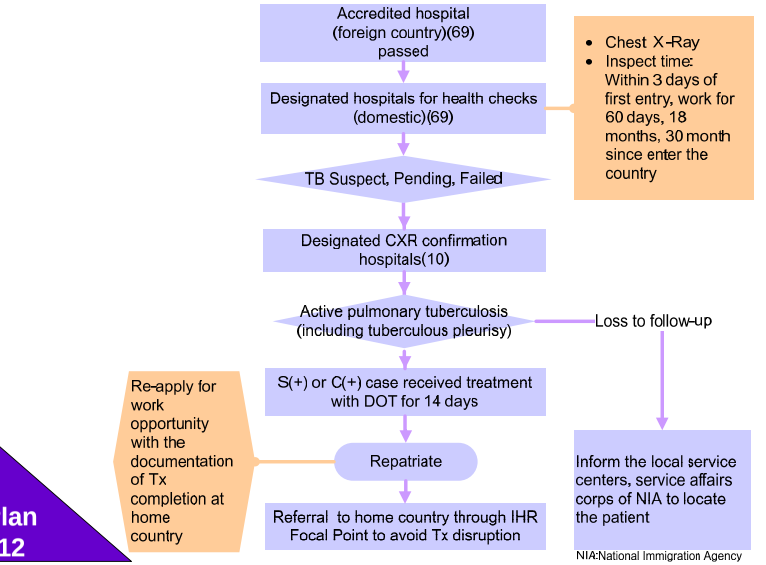
  - **Accredited hospital (foreign country) by DOH**
    - Indonesia (27)、Malaysia (15)、Philippines (12)、Thailand (6)、Vietnam (8)、Mongolia (1)
    - Provide health checks and certifications in mother countries for application of visa to Taiwan
  - **Designated hospitals for health checks (domestic): 69**
    - Provide service of health checks for the first-time arrived foreign workers and the following regular health checks
  - **Designated CXR confirmation hospitals: 10**
    - For confirmation of suspected TB diagnosis referred from designated hospitals for health checks

*quality reassurance program

Plan 12

New immigrant program-2

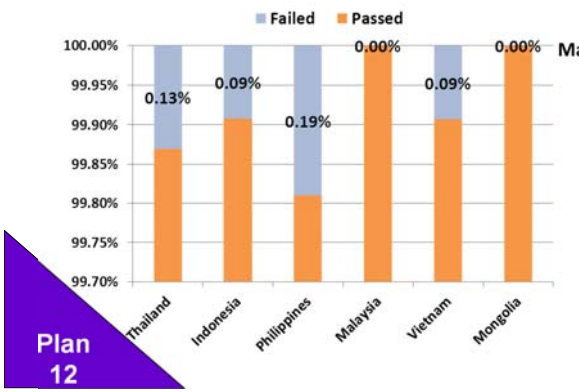
Regulations Governing Management of the Health Examination of Employed Foreigners



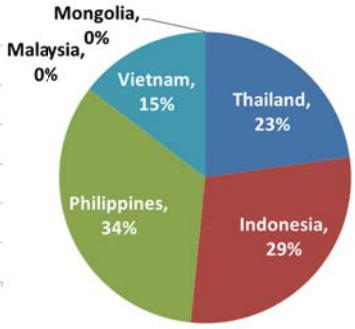
Plan 12

The analysis of CXR results of foreign workers (labors), 2006-2011

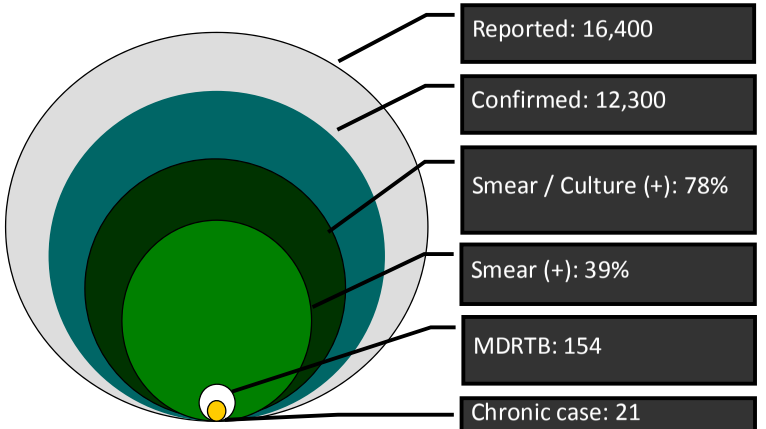
The cumulative failed rate stratified by nationalities, 2006-2011



The cumulative proportion of nationalities with failed results of CXR,2006-2011



Numbers of Reported and Confirmed TB Cases, 2012



In 2012, there were 12,300 newly confirmed TB cases and the estimated incidence rate was 53/10^5 persons.

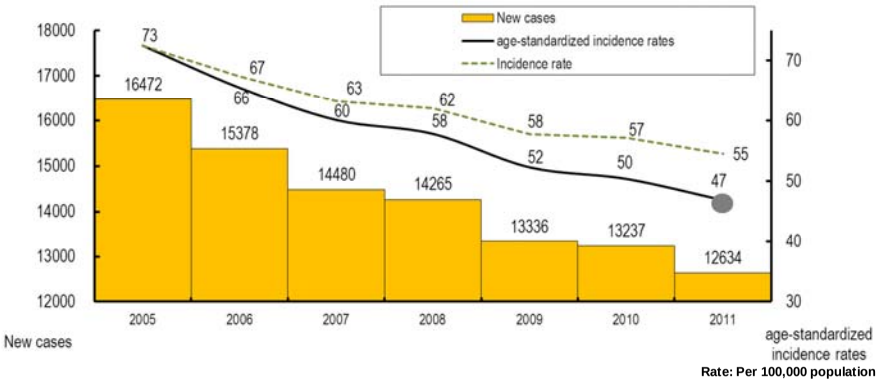
Progress of TB control in Taiwan

Period	Confirmed No.	Incidence rate (ID) ($1/10^5$)	The decrease in ID (%)	No. of Death	Mortality ($1/10^5$)	The decrease in Mortality (%)
2005	16,472	72.5		970	4.3	
2006	15,378	67.4	7.0	832	3.6	16.3
2007	14,480	63.2	6.2	783	3.4	5.6
2008	14,265	62.0	1.9	762	3.3	2.9
2009	13,336	57.8	6.5	748	3.2	3.0
2010	13,237	57.2	1.7	654	2.8	12.5
2011	12,634	54.5	5.0	638	2.8	0.0
2012	12,300	53.0	3.0	630	2.7	4.0

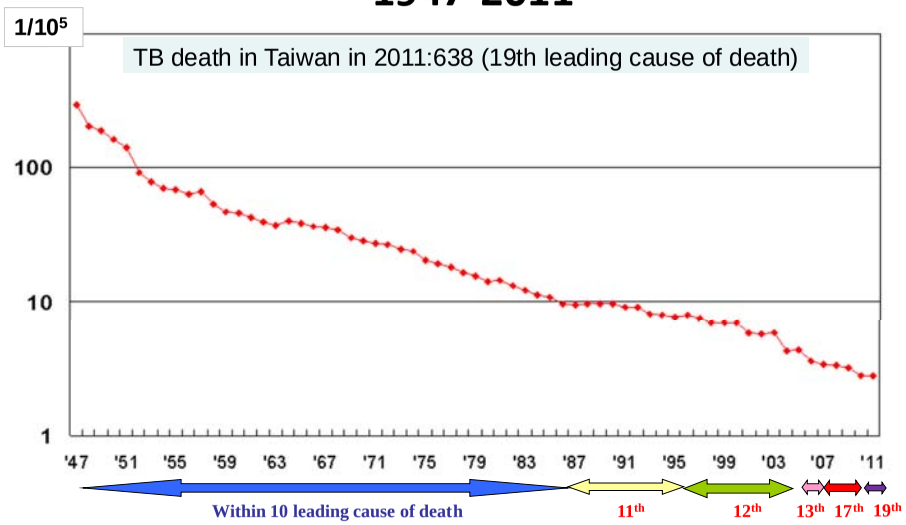
27%

37%

Age standardized incidence of new TB cases, 2005-2011

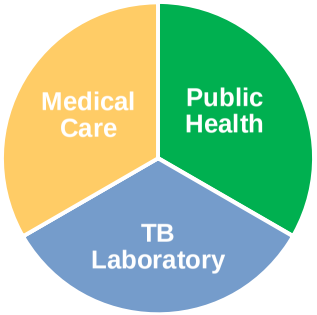


Trend of TB Mortality rate in Taiwan 1947-2011



Future direction

- Screening for TB among the high risk groups (DM, HIV, ESRD, smoking, RA …)
- Introducing short course therapy, short course LTBI treatment



- Coping with budget cuts
- Active case finding among the high risk group (DM, HIV, aboriginal, homeless, low SES…)
- Developing new vaccine to substitute BCG

- Improving lab quality and turn-around time
- The number of specimens to be examined for screening of TB cases can be reduced from three to two
- Revising protocol for MDR-TB genotyping

ON THE MOVE AGAINST TB

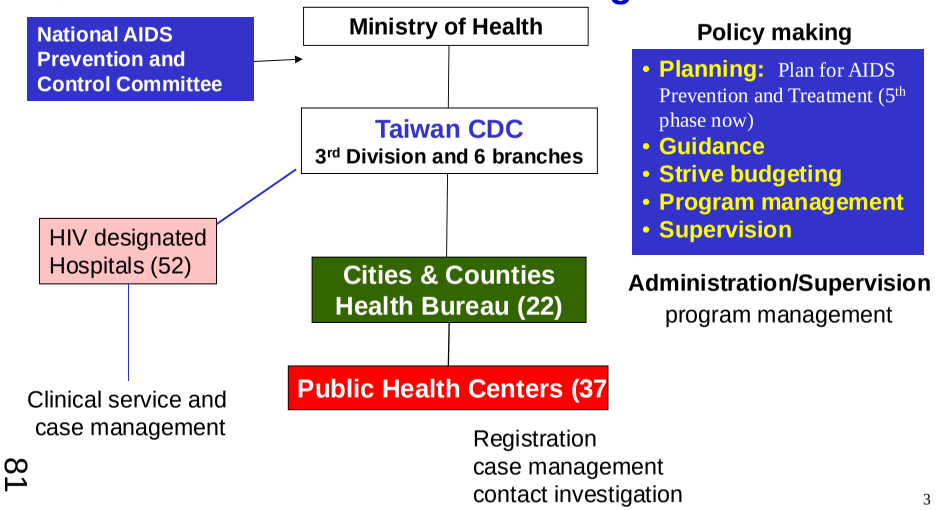
Epidemiology of TB-HIV Co-infection in Taiwan

Chin-Hui Yang, M.D., Director
Forth division
Taiwan CDC

Epidemiology of HIV in Taiwan

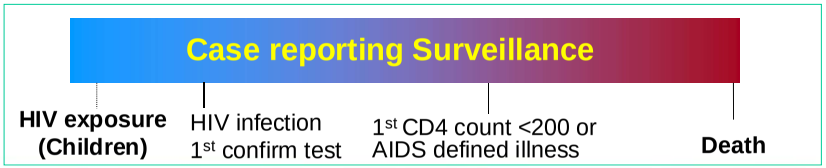
Increasing in young MSM and decreasing trend in IDUs

Structure of National HIV Program in Taiwan



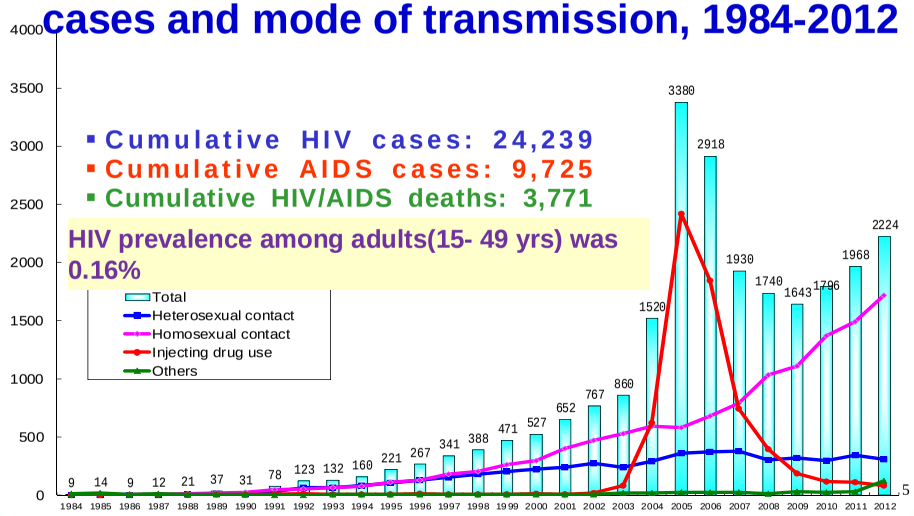
HIV/AIDS surveillance in Taiwan

- **Both HIV infection and AIDS were mandatory reportable diseases in Taiwan since 1984. All physicians are required to report all identified cases to Taiwan CDC within 24 hours.**
  - Patients' information included name, ID, date of birth, gender, home address, date of diagnosis, risk factors, and etc.



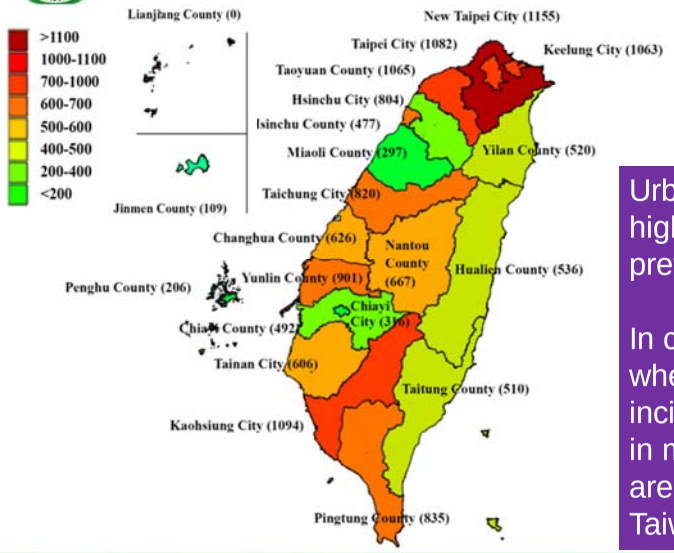
衛生署疾病管制局

Annual numbers of newly reported HIV cases and mode of transmission, 1984-2012



衛生署疾病管制局

Geographic distribution of HIV prevalence (1984-2012)

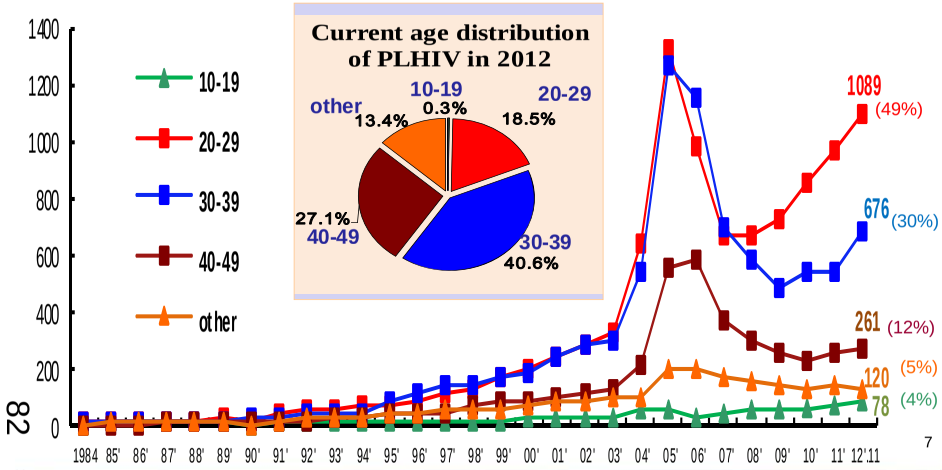


Urban area had higher HIV prevalence.

In contrast with TB where higher incidence occurred in mountainous areas and eastern Taiwan.

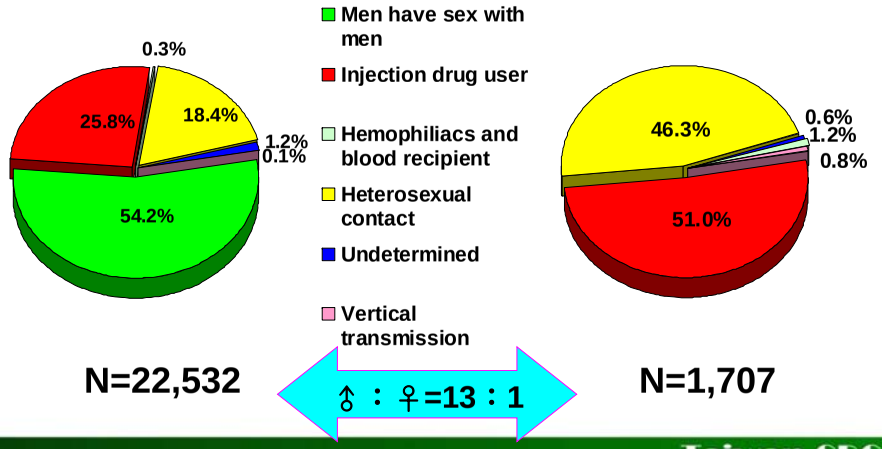
衛生署疾病管制局

Age distribution of reported HIV cases by year of diagnosis in Taiwan, 1984-2012

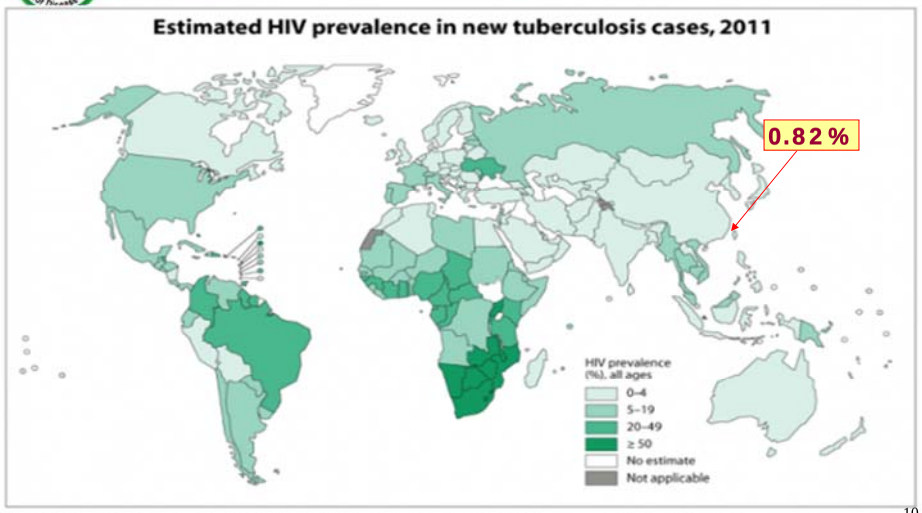


衛生署疾病管制局

Taiwanese Cases of HIV/AIDS by Exposure Category,Taiwan,1984-2012

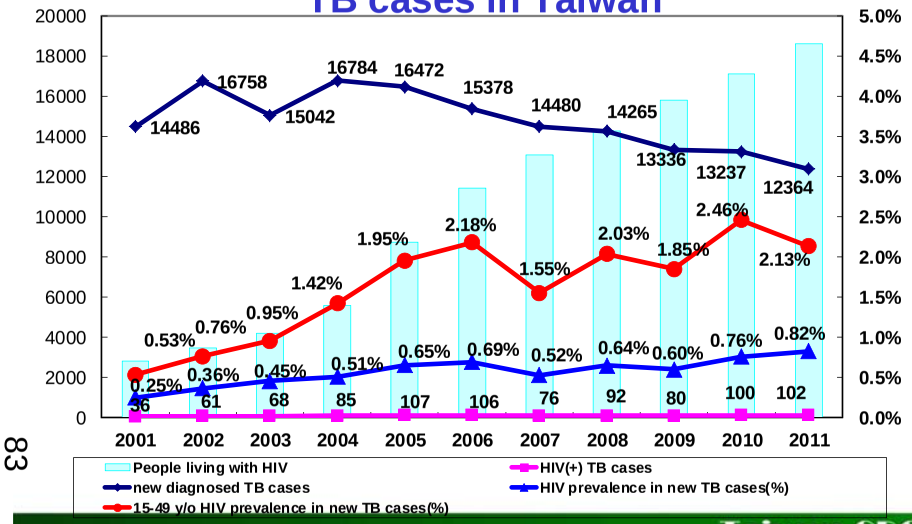


HIV/TB Co-infections in Taiwan



TB prevalence among HIV-infected individuals was 6.5 % in 2012.

Trend of HIV prevalence in new diagnosed TB cases in Taiwan



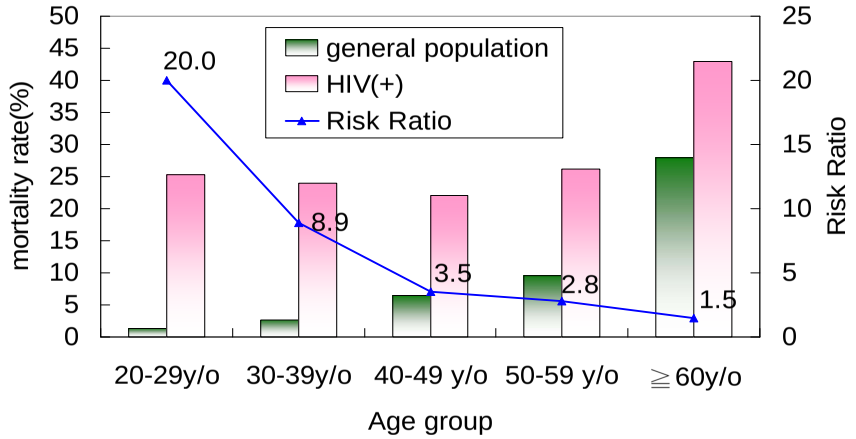
Culture-confirmed TB in HIV-infected patients in Taiwan

- **Objectives: To access the clinical characteristics and treatment outcome of TB-HIV co-infected patients**
- **Designs: Link registered HIV and TB dataset in Taiwan CDC from 1997 till 2006 to identify HIV-TB co-infected patients. Medical records were reviewed.**
- **Results:**
  - Among the 13,103 HIV-infected persons, 511 cases (560 episodes) were co-infected with tuberculosis.
    - 315 cases (**61.6%**) with **culture confirmed** tuberculosis (340 episodes, 22 cases relapse);
    - 73 cases (**14.3%**) with **positive AFS bacilli** finding through sputum or tissue smear;
    - 100 cases (**19.6%**) diagnosed by **chest X-ray** findings
    - 23 cases (**4.5%**) were diagnosed by **clinical** evidences

Culture-confirmed TB in HIV-infected patients in Taiwan

- **Results:**
  - Among the 315 patients with cultured-confirmed TB
    - Extra-pulmonary involvement was common : 53.7%
    - 21 patients(7.2%) had normal CxR though 8 of them had positive AFS bacilli finding and 15 patients had positive MTB sputum culture.
    - **Treatment outcome:** 218 patients (69.2%) had success treated, 90 patients(28.6%) died during anti-TB treatment and 7 patients (2.2%) defaulted.
      - 67 among the 90 deaths were interpreted as TB-related.
    - **MDR-TB accounted for 3.3%,** any drug resistant MTB accounted for 13.2%. Both drug resistance proportions were lower than the general population.

One-year TB Mortality, comparison of HIV-infected persons and general population in different age group



*data for general population was extract form the average of 2004 and 2005 cohort

TB fatality rate of HIV-infected persons in the HAART era

- **Designs:**
  - Linked the registered TB dataset in Taiwan CDC from 2002 to 2007 incorporated with National Health insurance HIV testing data and HIV registry data to confirm the HIV status of reported TB cases.
  - All the TB patients were classified as **HIV-infected**, **HIV-uninfected**(which means persons ever received HIV testing but not in HIV registry) and **unknown HIV status**(no HIV testing data).
  - Only included bacteriologic confirmed TB (positive AFS bacilli smear and/or MTB culture)

Table 1. Demographic characteristics of bacteriological diagnosed tuberculosis infection by HIV status between 2002 and 2007.

	HIV-infected persons (n=297)	HIV-uninfected (n=9,608)	HIV status unknown (n=47,452)
TB diagnosis Year*			
2002	50 {0.58%}	1,228 {14.2%}	7,380 {85.2%}
2003	39 {0.51%}	1,295 {16.8%}	6,381 {82.7%}
2004	53 {0.55%}	1,632 {16.8%}	8,035 {82.7%}
2005	55 {0.52%}	1,874 {17.7%}	8,635 {81.7%}
2006	50 {0.49%}	1,844 {18.1%}	8,321 {81.5%}
2007	50 {0.48%}	1,735 {16.6%}	8,700 {83.0%}
Age (yrs) at TB diagnosis, median [IQR]#	40 [33-48]	59 [41-76]	68 [50-78]
Sex#			
Male	280 (94.3)	6,964 (72.5)	33,641 (70.9)
Female	17 (5.7)	2,644 (27.5)	13,811 (29.1)
Extrapulmonary involvement#	97 (32.7)	426 (4.4)	1,287 (2.7)
Sputum acid-fast smear			
Positive	187 (63.0)	5,610 (58.4)	27,456 (57.9)
Negative	96 (32.3)	3,653 (38.0)	17,941 (37.8)
Not done	14 (4.7)	345 (3.6)	2,055 (4.3)
Sputum MTB culture			
Positive	217 (73.1)	7,265 (75.6)	34,980 (73.7)
Negative	26 (8.8)	868 (9.0)	4,579 (9.7)
Not done	54 (18.2)	1,475 (15.4)	7,893 (16.6)
MDR-TB$	4 (1.4)	126 (1.3)	336 (0.7)

Table 2. Factors associated with TB fatality rate.

Variable	HR (95% CI)	#Adjusted HR (95% CI)	†Adjusted HR (95% CI)
HIV-uninfected/unknown#†	1	1	1
HIV-infected under HAART	0. 834(0.635-1.095)	2.33(1.66-3.27)	1.62(1.15-2.29)
HIV-infected without HAART	2.52(1.63-3.91)	7.41(4.60-11.94)	5.45(3.37-8.81)
Age at TB diagnosis(per 10 year increase)	1.68(1.65-1.70)	1.72(1.70-1.75)	1.53(1.49-1.58)
Female (male as reference)	0.83(0.80-0.87)	0.91(0.87-0.96)	0.87(0.76-0.99)
Extrapulmonary involvement(no involvement as reference)	0.90(0.81-0.998)		
Positive sputum acid-fast smear (negative as reference)	0.88(0.84-0.91)	0.91(0.87-0.95)	
Positive sputum mycobacteria culture (negative as reference)	0.72(0.68-0.76)	0.70(0.66-0.74)	0.74(0.65-0.84)

Exclude cases not perform sputum smear or culture. Adjusted for age at TB diagnosis, sex, extrapulmonary involvement, sputum smear and culture status.

† Exclude cases with unknown HIV status, not perform sputum smear or culture. Adjusted for age at TB diagnosis, sex, extrapulmonary involvement, sputum smear and culture status.

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WHO-recommended collaborative TB/HIV activities

- **Establish and strengthen the mechanisms for delivering integrated TB and HIV services**
- **Reduce the burden of TB in people living with HIV(PLHIV) --the *Three I's for HIV/TB***
  - Intensify TB case-finding (ICF)
  - Isoniazid preventive therapy(IPT) and early ART
  - TB Infection control(IC) in health-care facilities and congregate settings
- **Reduce the burden of HIV in patients with presumptive and diagnosed TB**
  - Provide HIV testing and counselling to patients with presumptive and diagnosed TB

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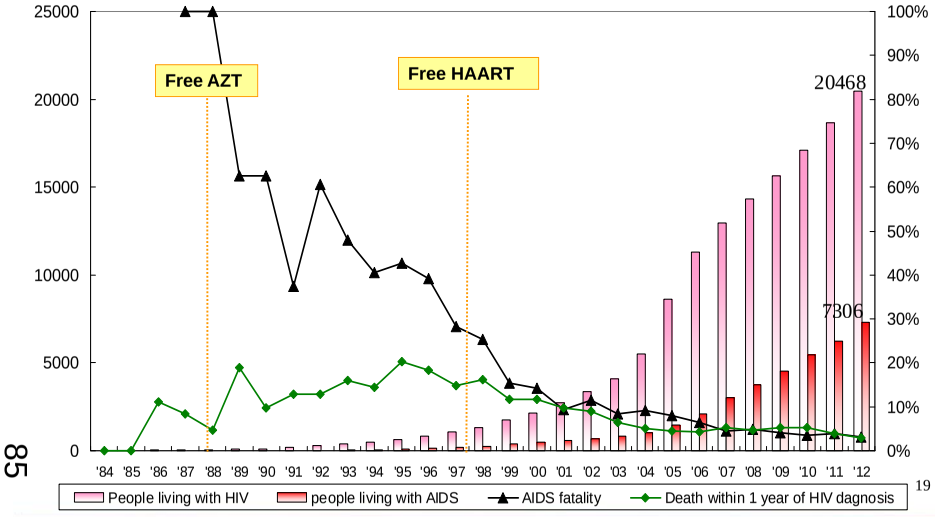
Interim policy on collaborative TB/HIV activities (WHO/HTM/TB/2004.330; WHO/HTM/HIV/2004.1, updated version in 2012)

Program achievements: care and treatment



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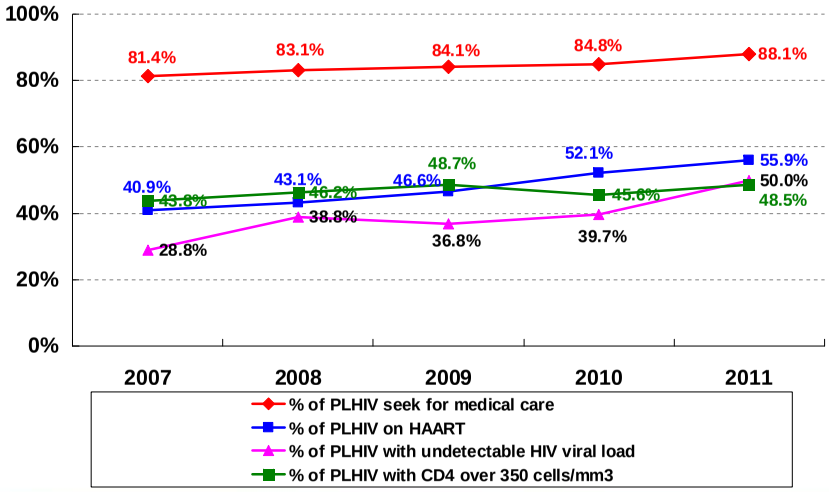
The provision of free HAART decreased HIV transmission by 53% (published in JID)

Clinical status of HIV-infected patients



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HAART coverage rate in PLHIV stratified by transmission routes

Transmission Route	People living with HIV	Considered should be treated	On HAART	ART CD4<350	On HAART/people living with HIV	On HAART /considered should be treated
MSM	**9,298**	**6,840**	**6,408**	**432**	**68.9%**	**93.7%**
Heterosexual	**3,508**	**2,679**	**2,556**	**123**	**72.9%**	**95.4%**
IVDU	**5,659**	**2,194**	**1,357**	**837**	**24.0%**	**61.9%**
Others	**193**	**110**	**99**	**11**	**51.3%**	**90.0%**
Total	**18,658**	**11,823**	**10,420**	**1403**	**55.8%**	**88.1%**

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Study population: people living with HIV/AIDS ever been prescribed or ever had CD4 count lower than 350 in 2011 and before that received ART in 2011

衛生署疾病管制局

LTBI diagnosis in BCG-vaccinated HIV-infected individuals

- **Objective:**
  - To evaluate the T-SPOT.TB and TST for the diagnosis of LTBI and the development of subsequent active TB, in BCG-vaccinated HIV-infected individuals.
- **Design:**
  - HIV-infected individuals without clinical suspicion of active TB or a past history of TB were offered both tests from 2008 to 2010
  - Followed up prospectively until 30 April 2012, for development of TB.
- **Results:**
  - Among the 909 participants, 25% had positive TST reactions with cut-off point of 5 mm and 15% had positive T-SPOT.TB results. Dual positive results was noted in 8.9% of participants.
  - After a median follow-up of 2.97 years, there were 5 cases developed culture-confirmed active TB (all had dual positive results), and the incidence was 0.17 per 100 person-years.

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Yang Ch, et al. in submission

Taiwan CDC http://www.cdc.gov.tw

衛生署疾病管制局

Number of patients for IPT by different criteria

- **Assuming a full protection of IPT, in our patient population, we would need to treat 35, 22 and 8 patients with positive TST results, a positive T-SPOT.TB and dual positive results to prevent 1 case of TB.**
  - Strategy: either positive TST or T-SPOT.TB→ 30.8% of the enrollee need treatment.
  - Strategy: positive TST → 25% of the enrollee need treatment.
  - Strategy: positive T-SPOT.TB→ 14.78% of the enrollee need treatment.
  - Strategy: dual positive results as criteria for IPT, then there were 8.9% of the enrollee need treatments.
- **IPT induced hepatotoxicity in HIV-infected patients co-infected with HBV or HCV!!!**

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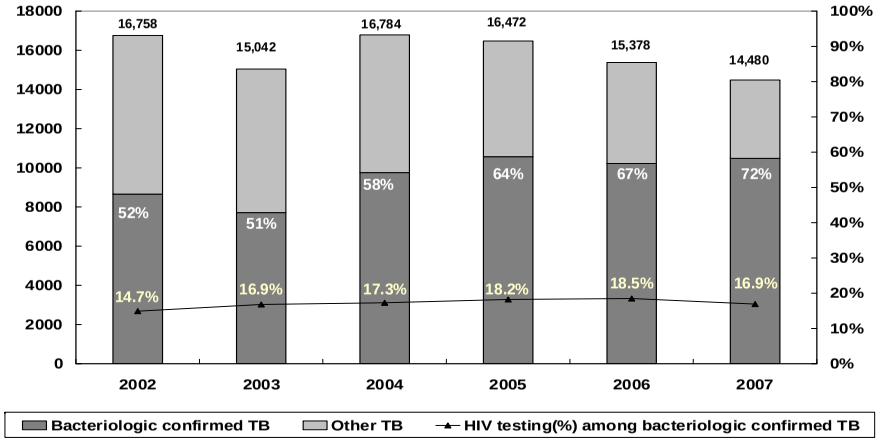
Yang Ch, et al. in submission

Taiwan CDC http://www.cdc.gov.tw

衛生署疾病管制局

Trend of HIV testing rate among annual new report TB cases



The overall HIV testing among new TB report cases from 2002-2007 was 17.1%.

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Yang CH, et al. Poster presentation at 2009 49th ICAAC, Abstract H-234

Taiwan CDC http://www.cdc.gov.tw

The rates of HIV testing and number of new HIV infections found among TB patients stratified by age groups(2004-2007)

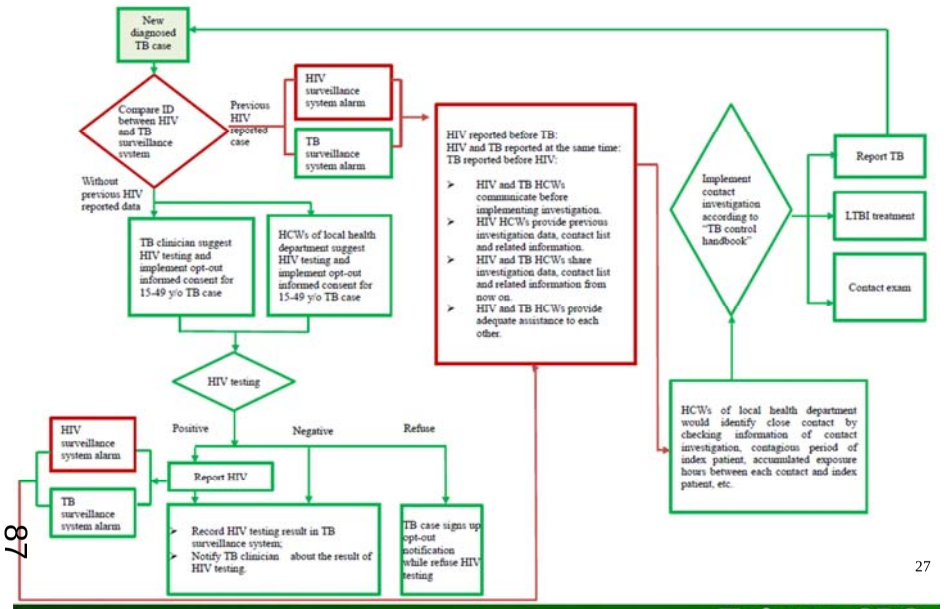
Age at TB diagnosis	TB reported case, N	Confirmed HIV infection, N(%)	Received HIV testing, N(%)	New HIV infection found among HIV testing#, N(%)
<20 years	1,952[3.1%]	0	301(15.4%)	0
20-39 years	9,390[14.9%]	223(2.4%)	2,697(28.7%)	112(4.3%)
40-59 years	15,543[14.6%]	149(0.95%)	3,125(20.1%)	79(2.6%)
≧60 years	36,226[57.4%]	30(0.08%)	5,131(14.2%)	23(0.4%)
Total	63,114[100%]	402(0.63%)	11,254(17.8%)	205(1.8%)

The denominator is the number of TB patients received HIV testing, exclude cases with known HIV infection.

The goal and principles of collaborative management for HIV/TB co-infected cases (draft)

- **To provide opt out HIV tests for every TB patients aged 15-49 years**
- **Administrative preparation**
  - Notify and discuss with related stakeholders in terms of the policy
  - Revise “TB control handbook” and “HIV/AIDS control handbook”
  - Designated collaborative window of contacts in each health department
  - Campaign to all levels and operational research for results

Principles of collaborative management for HIV/TB co-infected cases (draft) flow chart



Challenges and solutions

- **TB/HIV collaborative activities**
  - Identified those who defaulted from HIV program, linking to care
  - Government and non-government cooperation
  - Cooperation between chest physicians and infectious disease specialist
- **Evaluation of the need and the obstacles for Isoniazid Preventive Therapy (IPT)**
  - Protocol to detect LTBI in HIV population??
  - Relatively high HCV and HBV prevalence among HIV-infected individuals
  - Resistance from physicians
- **Need for further HIV testing for all TB cases?**
  - Suggestions ?

Thank You for Your Attention!!

Contact Investigation and LTBI Treatment

Anita, Pei-Chun Chan, Medical officer
Third division
Taiwan CDC

Outline

- Introduction of contact investigations & LTBI treatment in NTP
- Indicators for CI and LTBI
- Challenges

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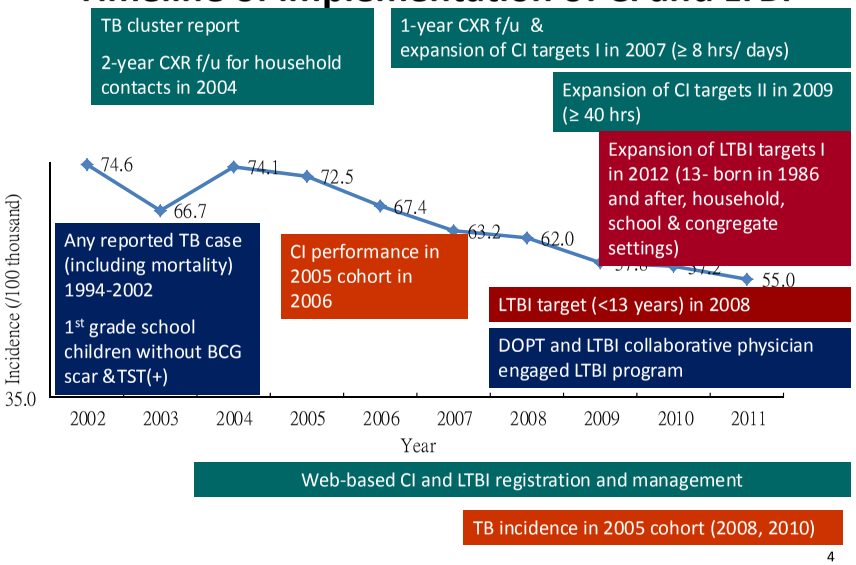
INTRODUCTION OF CONTACT INVESTIGATIONS & LTBI TREATMENT IN NTP

Timeline of implementation of CI and LTBI



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Contact investigation for tuberculosis in Taiwan contacts aged under 20 years in 2005

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SUMMARY

OBJECTIVE: To measure the tuberculosis (TB) incidence rate and assess the relative risk of TB disease in contacts based on the tuberculin skin test (TST) and sputum status of index cases.

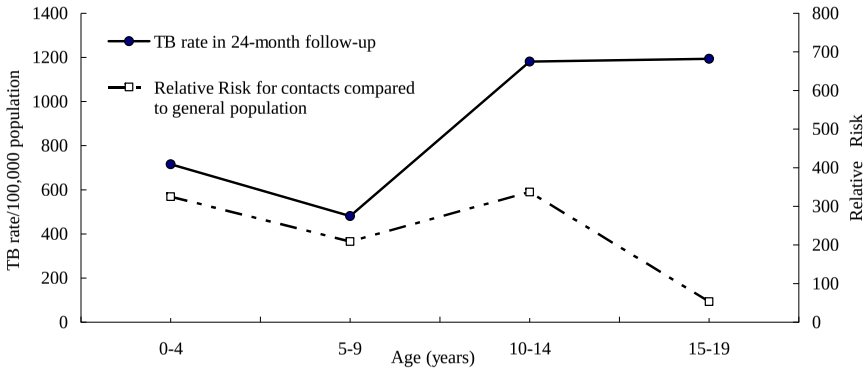
DESIGN: All contacts aged <20 years who were exposed to a TB case in 2005 were cross-matched using an electronic surveillance system to estimate TB incidence over a 24-month follow-up period.

RESULTS: Among 6959 contacts there were 67 secondary cases (1%). The incidence was highest in the first year after exposure and decreased by half in the second year ($P = 0.001$). The relative risks of developing TB in contacts aged 0–4, 5–9, 10–14 and 15–19 years were respectively 325, 209, 337 and 53 times greater than for the general population. The hazard ratio of developing TB among contacts with a TST ≥ 15 mm induration was 12 times higher than for those with a TST < 5 mm ($P = 0.003$).

CONCLUSIONS: The relative risk of developing TB disease within 24 months of exposure was approximately 200–300 times greater for contacts aged <15 years. The majority developed TB within 12 months of exposure.

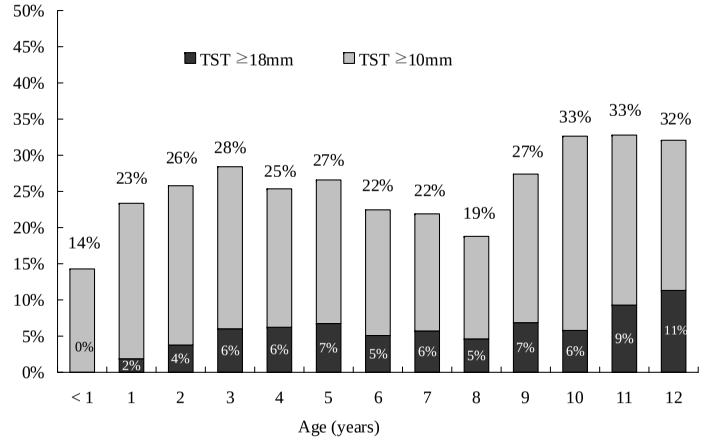
KEY WORDS: contact investigation; latent TB infection; active case finding; infant and children; tuberculosis

Relative risks of TB incidence in contacts compared to general population



The TB incidence rate of general population in 2005 were 2.18, 2.31, 3.53, 22.68/100,000 for 0-4 year, 5-9 year, 10-14 year and 15-19 year, respectively

Distribution of the positive rates of tuberculin skin test (TST) in different age groups (n=2410).

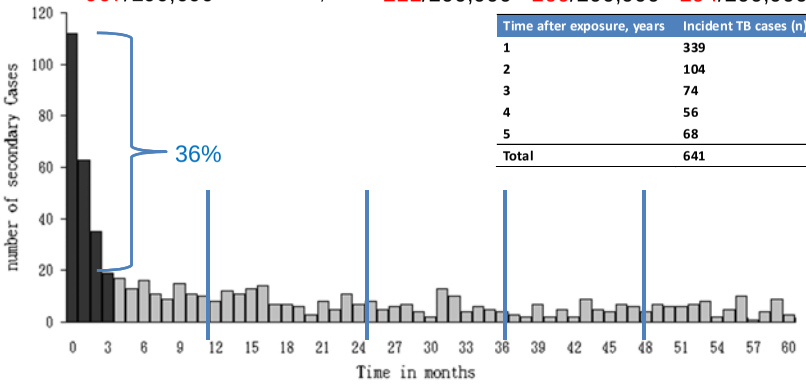


The tuberculosis risk in 0-12-year-old contacts according to the induration size of the first tuberculin skin test (TST) applied

TST size mm	Total at risk n	TB cases n	TB rate/100 000 (95%CI)	HR (95%CI)*
0-4	1,343	2	149 (0-355)	Reference
5-9	439	0	0	-
10-14	366	1	273 (0-808)	1.68 (0.15-18.55)
≥15	262	5	1908 (252-3564)	12.16 (2.32-63.67)‡
Total	2,410	8	332 (103-561)	

TB Incidence among contacts
5 year follow-up of 2005 cohorts

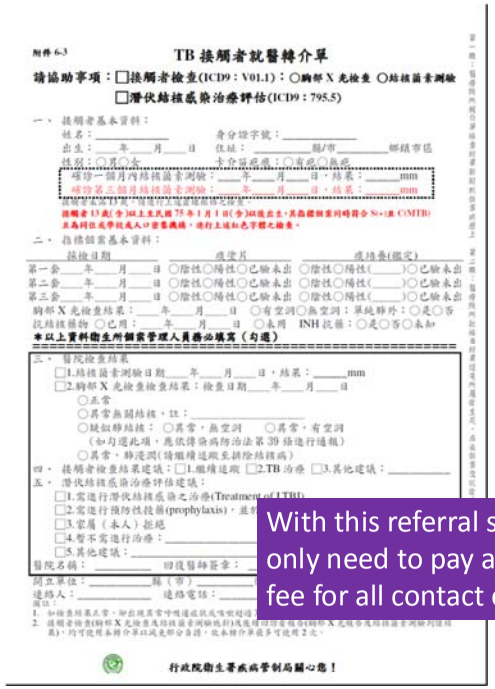
967/100,000 297/100,000 211/100,000 160/100,000 194/100,000



Time after exposure, years	Incident TB cases (n)	(%)
1	339	52
2	104	16
3	74	12
4	56	9
5	68	11
Total	641	100

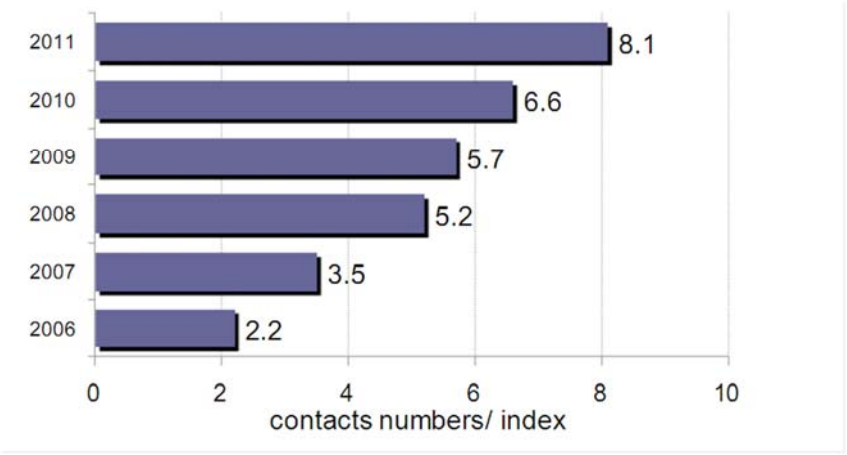
Timing of diagnosis of 641 coprevalent and incident TB cases following diagnosis in the index case during 60-month follow up. The black bar reveals coprevalent cases found directly by contact investigations

Lin DL et al. Tuberculosis contact investigation in Taiwan : a 5-year follow-up study. (Oral presentation at 2010 Annual Meeting of Taiwan Society of Pulmonary and Critical Care Medicine, Taipei, 20121210


TB 接觸者就醫轉介單

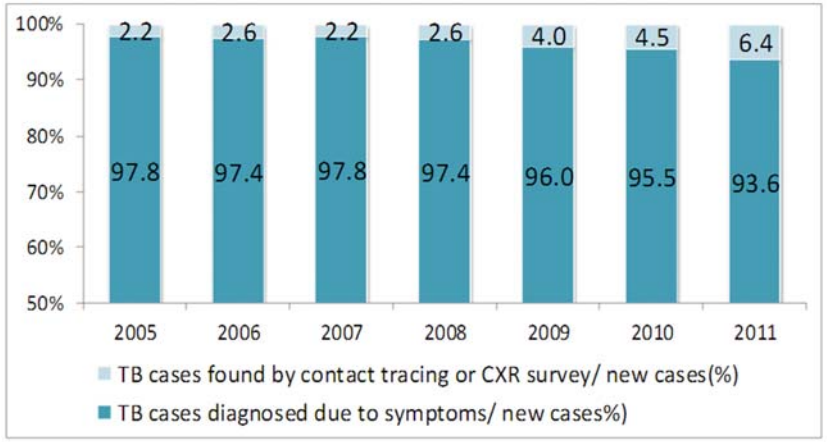
With this referral sheet, contacts only need to pay administration fee for all contact examinations

Average contact numbers per TB cases



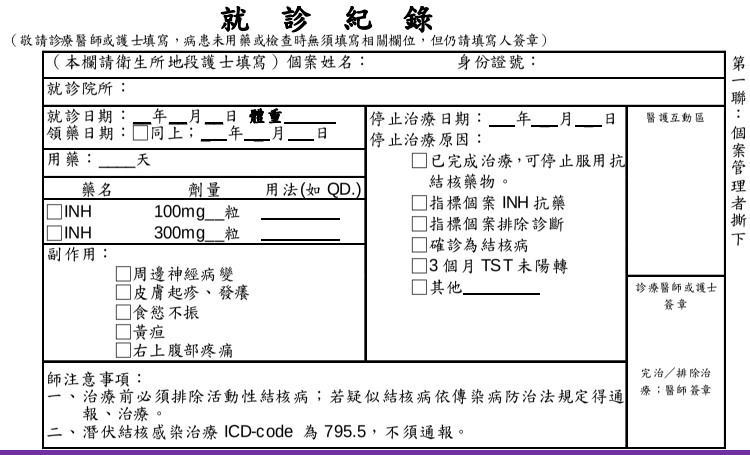
With implementation of several public health strategies, average contact numbers per TB case increased to 8.1 per index case in 2011.

The Proportion of cases found through active case finding process vs. total TB cases



With this LTBI booklet, contacts only need to pay administration fee for LTBI treatment

15



就 診 紀 錄

（敬請診療醫師或護士填寫，病患未用藥或檢查時無須填寫相關欄位，但仍請填寫人簽章）

（本欄請衛生所地段護士填寫）個案姓名：　　身份證號：

就診院所：

就診日期：__年__月__日 體重_____
領藥日期：□同上；___年___月___日

停止治療日期：___年___月___日
停止治療原因：
□已完成治療，可停止服用抗結核藥物。
□指標個案 INH 抗藥
□指標個案排除診斷
□確診為結核病
□3 個月 TST 未陽轉
□其他_____

用藥：____天

藥名	劑量	用法(如 QD.)
□INH	100mg__粒	_____
□INH	300mg__粒	_____

副作用：
□周邊神經病變
□皮膚起疹、發癢
□食慾不振
□黃疸
□右上腹部疼痛

醫護互動區

診療醫師或護士簽章

完治／排除治療：醫師簽章

師注意事項：
一、治療前必須排除活動性結核病；若疑似結核病依傳染病防治法規定得通報、治療。
二、潛伏結核感染治療 ICD-code 為 795.5，不須通報。

第一聯：個案管理者撕下

Inside of the booklet, there are spaces for both regimen prescribed (frequency and amount) & adverse events encountered, a way designed for communication between collaborative physicians and public health sectors.

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INDICATORS FOR CI AND LTBI

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Populations and settings

- Definitions
  - All confirmed cases including re-registered TB cases
  - Contacts including nationalism and foreigners
- LTBI treatment
  - Calendar year of contacts when the index case was diagnosed
    - Children contacts <13 years
    - Contacts 13- born in 1986 & after

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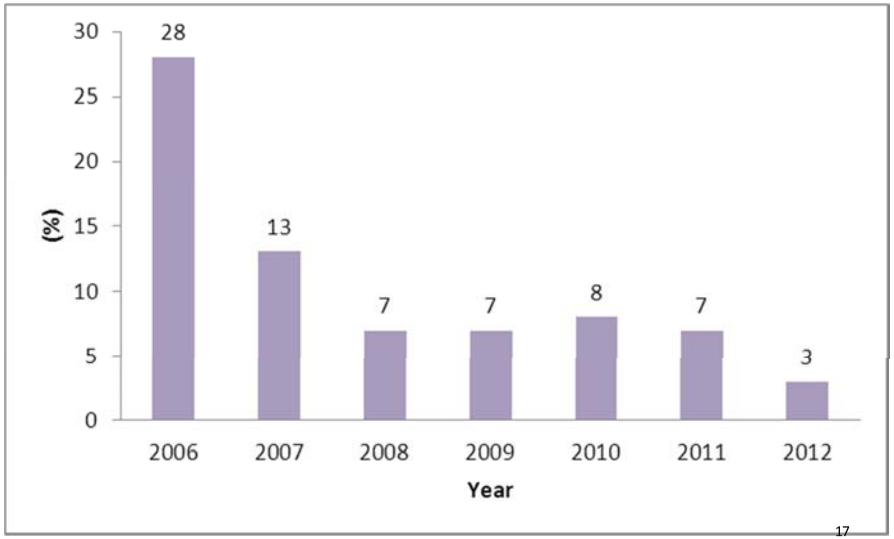
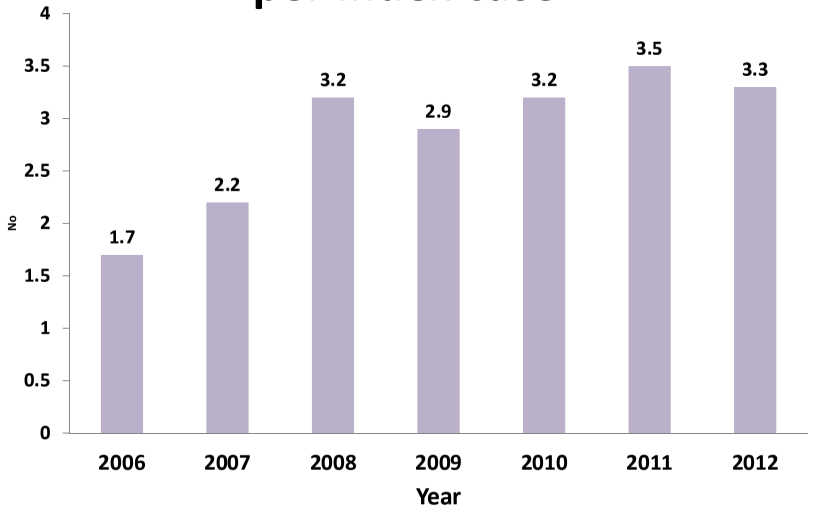
Proportion of zero contact registered



17

Average household contact number per index case



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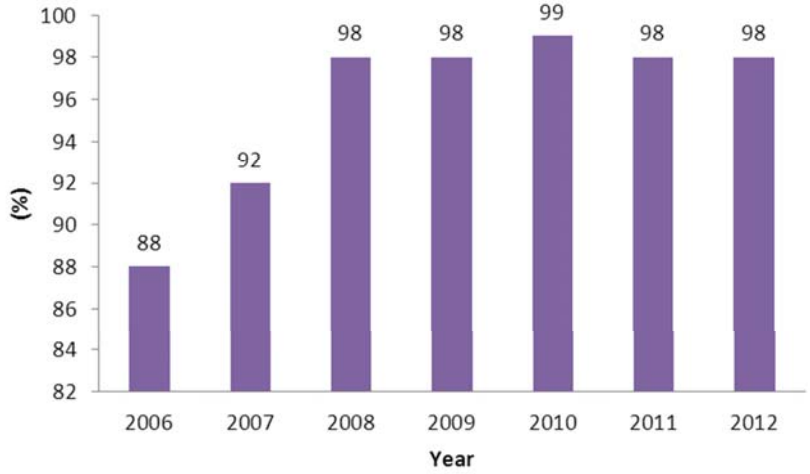
CI completion within the first month



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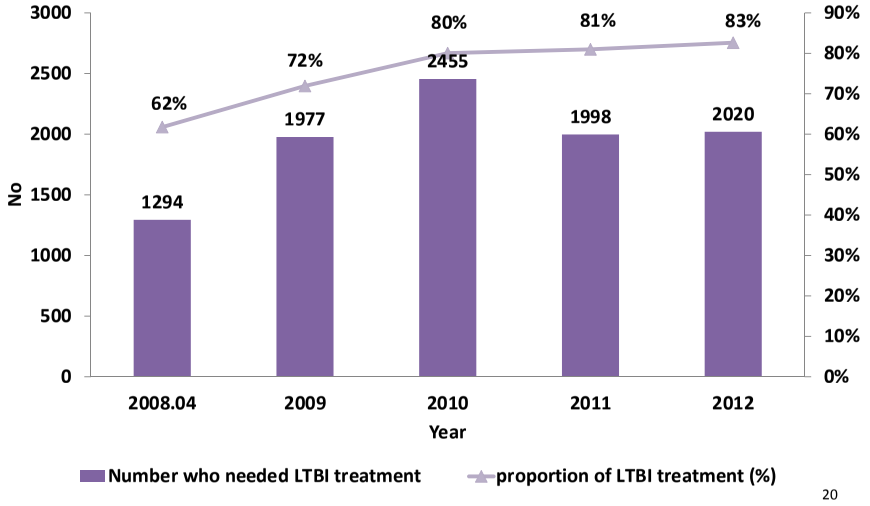
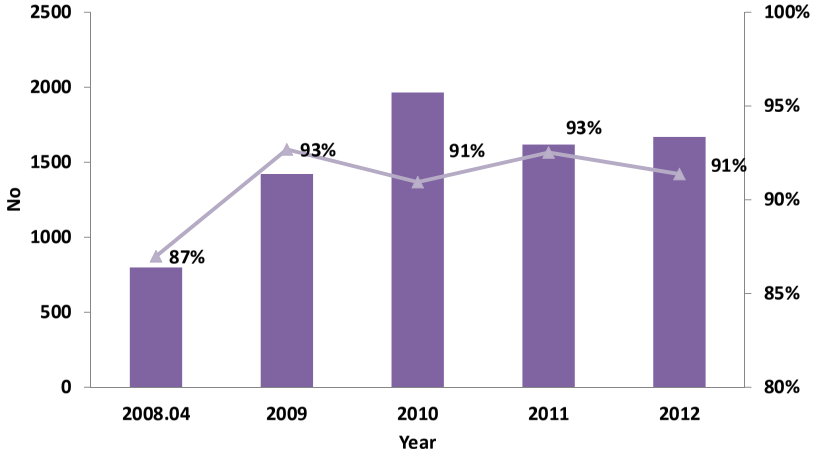
Coverage of LTBI treatment among TST positive contacts aged <13y/o

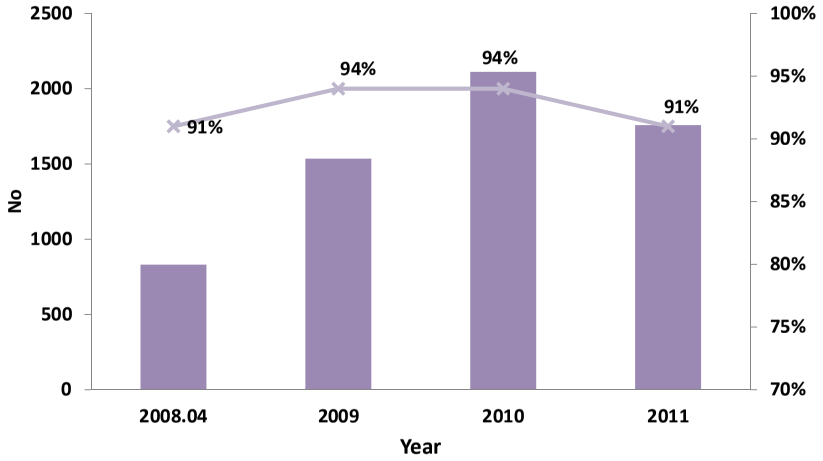


20

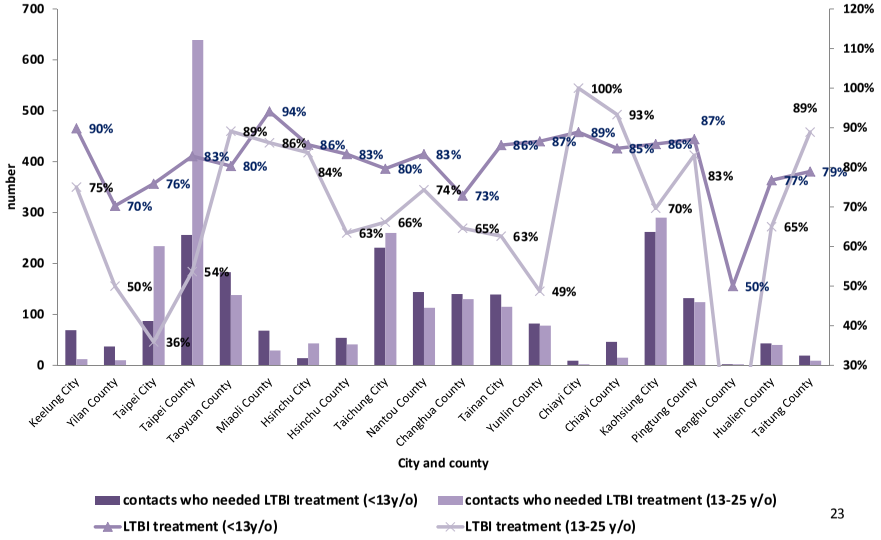
DOPT rate of LTBI treatment among contacts aged <13y/o



Treatment completion rate of LTBI contacts aged <13 y/o

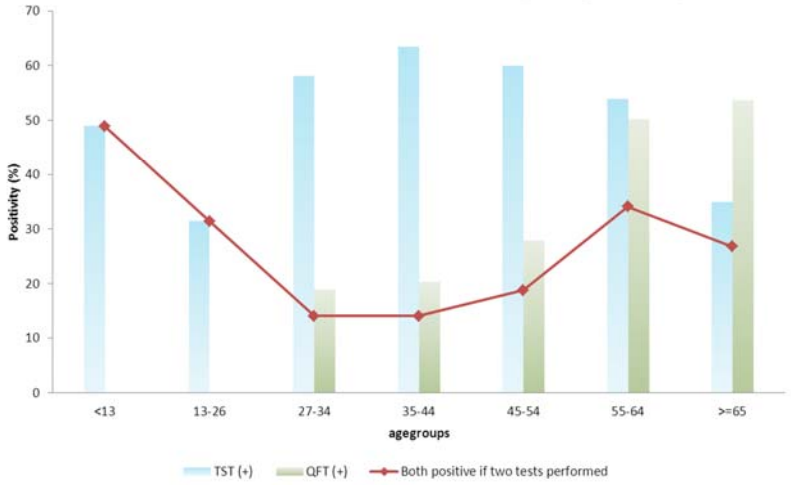


Comparison of coverage of LTBI treatment between <13 y/o and 13-25 y/o in year 2012



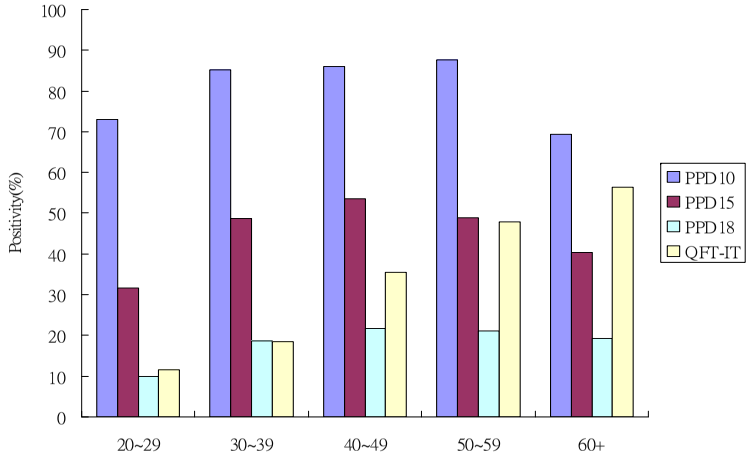
CHALLENGES

Positivity of TST and/or QFT-IT among contacts in different age groups



Pilot program for CI and LTBI treatment conducted in 2010-2012[25]

Positivity classified with QFT-IT(+) and TST among HIV negative male inmates (non contact)



N=2384, Chan PC et al. Lower prevalence of tuberculosis infection in BCG vaccinees: a cross-sectional study in adult prison inmates. Thorax. 2012 Sep 27. [Epub ahead of print]

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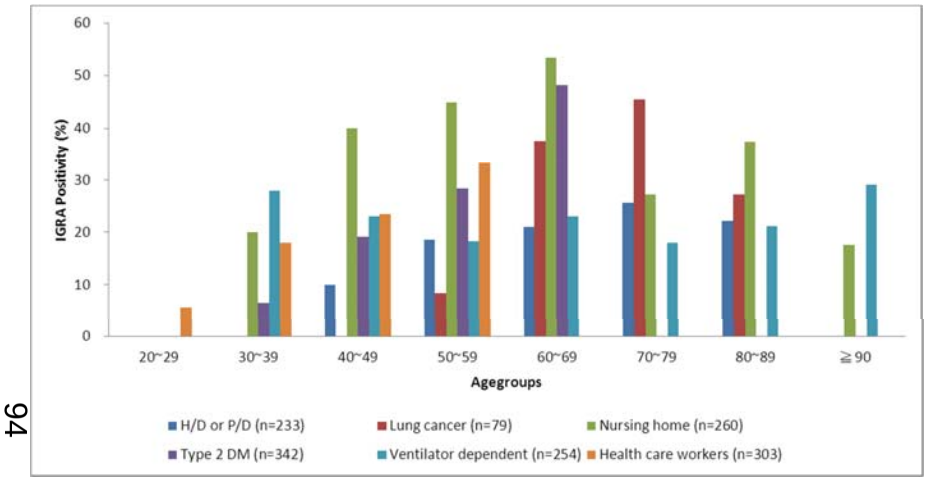
LTBI survey by IGRA in high-risk populations other than contacts



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Challenges and solutions

- **Further expansion of different target groups in contacts**
  - Age? outbreak settings? Immuno-compromised contacts?
  - Lack of TB risks among contacts with different comorbidities
- **Medical aspect**
  - Not specific enough for PPV of TB in the future (Diagnostic tool)
  - Possible hepatotoxicity encountered during IPT (more carriers for NAT-2 slow acetylator)
  - Time consuming to persuade healthy LTBI contacts receiving IPT (long duration + no sense of disease)
  - New regimen including 3Rpt
- **Realistic cost-effectiveness for LTBI treatment through CI**
  - Manpower burden in CI and LTBI conjugated with DOPT
  - Efficacy or effectiveness?

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Acknowledgement



- Mei-Yu Chiou, Bao-Yun Lu & Yu-Hsun Huang
- Du-Lin Ling
- EIC & 3rd Division

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Medical Care for Tuberculosis in the Elderly with Co-morbidity

Stephne, Pin-Hui Lee, MD, MSc
Medical officer
Third division
Taiwan CDC

Outline

- Epidemiology of TB in aging population in Taiwan
- Challenges in TB care among the elderly
- At-risk population and LTBI prevalence
- Summary and future perspectives

Demographics and TB incidence in Taiwan

	2005	2006	2007	2008	2009	2010	2011
Population (persons)	22,729,753	22,823,455	22,917,444	22,997,696	23,078,402	23,140,948	23,193,518
≧65 yrs	2,183,639	2,251,917	2,315,060	23,726,56	2,429,934	2,472,770	2,508,071
% of ≧65 yrs cases of population	9.6	9.9	10.1	10.3	10.5	10.7	10.8
New TB cases	16,472	15,378	14,480	14,265	13,336	13,237	12,634
Relative risk (≧65 yrs vs. <65 yrs)	9.8	10	9.5	9.5	9.6	9.4	7.4
Incidence rate of ≧65 yrs	385	356.5	323	314	291.3	283.1	237.7
Incidence rate of <65 yrs	39.2	35.7	34	33	30.3	30.2	32.0
Case no. (≧65 yrs)	8,408	8,029	7,477	7,451	7,078	7,000	6009
% of ≧65 yrs among new TB cases	51	52.2	51.6	52.2	53.1	52.9	52.3

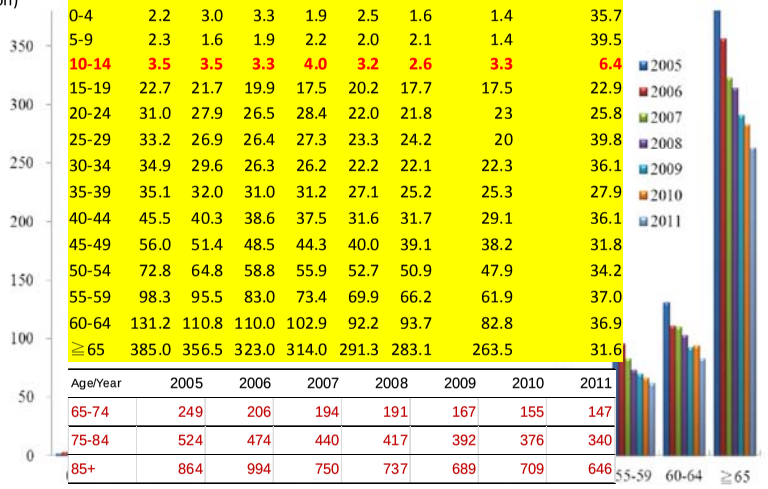
year	birth		death	
	number (1000 person)	crude rate (o/oo)	Crude rate (per 100,000)	standardized (per 100,000)
1991	321.9	15.7	511	670
1995	329.6	15.5	555	648
1996	325.5	15.2	562	641
2001	260.4	11.7	567	559
2006	204.5	9.0	592	495
2011	166.9	7.2	625	456
2012	196.6	8.5	656	462

http://www.doh.gov.tw/CHT2006/DM/DM2_2.aspx?now_fod_list_no=10238&class_no=440&level_no=1

TB incidence, by age group, 2005-2011

Rate (per 100,000 population)

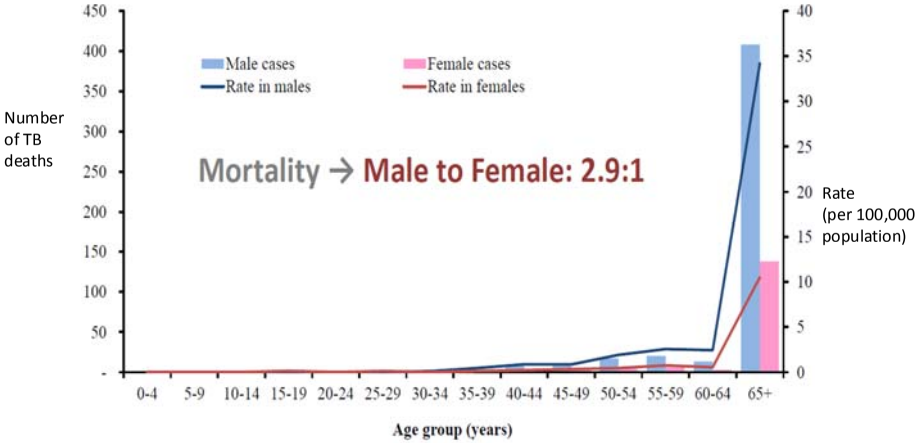
age(yr)	2005	2006	2007	2008	2009	2010	2011	incidence reduction(%)
0-4	2.2	3.0	3.3	1.9	2.5	1.6	1.4	35.7
5-9	2.3	1.6	1.9	2.2	2.0	2.1	1.4	39.5
10-14	3.5	3.5	3.3	4.0	3.2	2.6	3.3	6.4
15-19	22.7	21.7	19.9	17.5	20.2	17.7	17.5	22.9
20-24	31.0	27.9	26.5	28.4	22.0	21.8	23	25.8
25-29	33.2	26.9	26.4	27.3	23.3	24.2	20	39.8
30-34	34.9	29.6	26.3	26.2	22.2	22.1	22.3	36.1
35-39	35.1	32.0	31.0	31.2	27.1	25.2	25.3	27.9
40-44	45.5	40.3	38.6	37.5	31.6	31.7	29.1	36.1
45-49	56.0	51.4	48.5	44.3	40.0	39.1	38.2	31.8
50-54	72.8	64.8	58.8	55.9	52.7	50.9	47.9	34.2
55-59	98.3	95.5	83.0	73.4	69.9	66.2	61.9	37.0
60-64	131.2	110.8	110.0	102.9	92.2	93.7	82.8	36.9
≧65	385.0	356.5	323.0	314.0	291.3	283.1	263.5	31.6



Age/Year	2005	2006	2007	2008	2009	2010	2011
65-74	249	206	194	191	167	155	147
75-84	524	474	440	417	392	376	340
85+	864	994	750	737	689	709	646

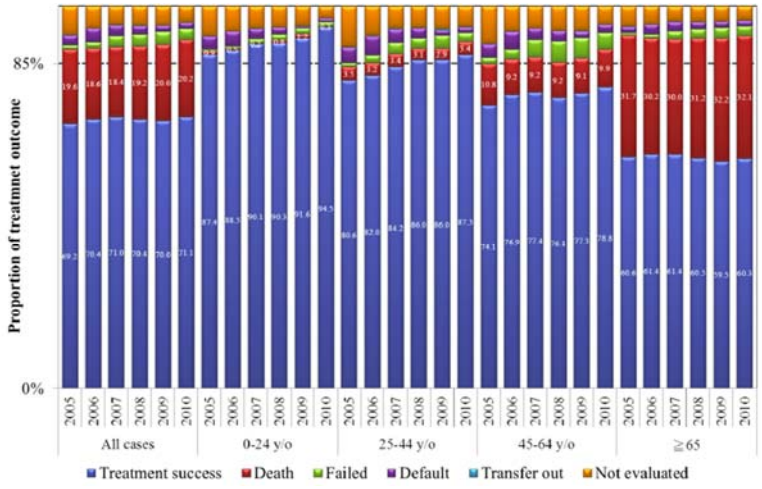
Age group (year)

TB mortality by age group and sex, 2011



In 2011, the TB mortality rate for males was 4.1 deaths per 100,000 males, higher than 1.4 deaths per 100,000 females.

Treatment outcome of 12-month follow-up, by age groups, 2005-2010



Co-morbidity among TB patients in Taiwan, 2006-2008 cohort

Table 3. Cases Comorbidities Distribution (N = 33 851)

Variable	Total	Percentage	<65 Years (n = 16 832) n	%	≥65 Years (n = 17 019) n	%	All Causes of Death (n = 5584) n	%	P
Total (any one of comorbid diseases*)									<.001
No	14 225	42.0	9715	57.7	4510	26.5	970	17.4	
Yes	19 626	58.0	7117	42.3	12 509	73.5	4614	82.6	
COPD									<.001
No	25 877	76.4	14 511	86.2	11 366	66.8	3894	69.7	
Yes	7974	23.6	2321	13.8	5653	33.2	1690	30.3	
DM									<.001
No	26 214	77.4	13 792	81.9	12 422	73.0	3939	70.5	
Yes	7637	22.6	3040	18.1	4597	27.0	1645	29.5	
Cancer									<.001
No	29 312	86.6	15 368	91.3	13 944	81.9	4133	74.0	
Yes	4539	13.4	1464	8.7	3075	18.1	1451	26.0	
Stroke									<.001
No	29 593	87.4	16 227	96.4	13 366	78.5	3972	71.1	
Yes	4258	12.6	605	3.6	3653	21.5	1612	28.9	
Chronic liver disease and cirrhosis									<.001
No	31 117	91.9	15 385	91.4	15 732	92.4	4938	88.4	
Yes	2734	8.1	1447	8.6	1287	7.6	646	11.6	
Chronic kidney disease									<.001
No	32 089	94.8	16 104	95.7	14 983	88.0	4863	87.1	
Yes	1762	5.2	728	4.3	2036	12.0	721	12.9	
HIV									.84
No	33 687	99.5	16 674	99.1	17 013	99.96	5556	99.5	
Yes	164	0.5	158	0.9	6	0.04	28	0.5	

Risk Factors Associated With Death in a 12-Month Cohort Analysis of Tuberculosis Patients. Asia Pac J Public Health. 2011 Dec 23.

Comorbidities and death within one year after TB notification

- 16.5% of new TB patients died within one year after reporting
  - Death often occurred(48.5%) in the first 2 months after TB registration
- Cancer was the leading cause of death
- Predisposing factors of death within one year among age ≥65 years:
  - male gender, positive sputum bacteriology, pulmonary TB, and eastern Taiwan residential area
  - Comorbidities: CKD, stroke, cancer, and chronic liver disease/cirrhosis

Asia Pac J Public Health. 2011 Dec 23.

Initial presentations of TB predicting mortality in Taiwan

- A prospective observational study in 5 medical centers
- Nearly one-third (62/195, 31.8%) of the deaths occurred before or within 30 days of treatment initiation
- Factors associated with overall mortality:
  - older age
  - malignancy
  - renal insufficiency
  - constitutional symptoms: Fever and anorexia

PLoS One. 2011;6(9):e23715

Hepatitis during anti-TB treatment (HATT)

- A prospective survey of 360 TB patients in a medical center in northern Taiwan
- Concomitant infection :
  - HBV carrier: 11.7%
  - HCV carrier: 6.7%
- HATT: 18.9%
- Patients with age above 65 years did not have significantly higher drug-related or virus-related HATT than age ≤ 65 years

TB guideline in Taiwan: screening of HBV, HCV and HIV before initiating anti-TB treatment, and follow-up for liver function at the week 2, 4, and 8 of anti-TB tx

J Infect. 2011 Jun;62(6):448-55.

Ethambutol-induced optic neuropathy

Table 2 Adjusted ORs for optic neuropathy in relation to medical comorbidities

Variable	Model 1 OR (95% CI)	Model 2 OR (95% CI)
Sex		
Female	1.00 (reference)	1.00 (reference)
Male	0.94 (0.69 to 1.29)	0.96 (0.70 to 1.32)
Age		
20–39 years	1.00 (reference)	1.00 (reference)
40–64 years	1.96 (1.17 to 3.30)	1.76 (1.03 to 3.01)
≥65 years	2.48 (1.51 to 4.08)	1.93 (1.12 to 3.32)
Diabetes mellitus		
No	1.00 (reference)	1.00 (reference)
Yes	0.71 (0.46 to 1.08)	0.58 (0.37 to 0.90)
Hypertension		
No	1.00 (reference)	1.00 (reference)
Yes	1.64 (1.19 to 2.26)	1.62 (1.16 to 2.26)
Renal diseases		
No	1.00 (reference)	1.00 (reference)
Non-ESRD	2.17 (1.07 to 4.40)	2.11 (1.02 to 4.35)
ESRD	4.00 (1.96 to 8.17)	3.73 (1.79 to 7.74)
Malignant illness		
No	1.00 (reference)	1.00 (reference)
Yes	0.58 (0.33 to 1.03)	0.63 (0.35 to 1.13)

ESRD refers to end-stage renal diseases.
Model 1 was adjusted for age and sex.
Model 2 was additionally adjusted for variables listed in this table.

Table 4 ORs for optic neuropathy in relation to duration of ethambutol prescription

	Controls (n=924) %	Optic neuropathy cases (n=231) %	OR (95% CI) Model 1	OR (95% CI) Model 2
Duration of prescription, months				
≤3 months	436 (47.2)	88 (38.1)	1.00	1.00
>3 months	488 (52.8)	143 (61.9)	1.38 (1.02–1.86)	1.35 (0.99–1.83)

Model 1 was adjusted for age and sex.
Model 2 was additionally adjusted for hypertension and renal diseases.

TB guideline: stop EMB after DST: all susceptible to 1st line drugs
Monthly check VA and color discrimination while using EMB

Br J Ophthalmol 2012;96:1368–1371.

Pneumonia and concomitant pulmonary TB

- 1635 pneumonia patients were enrolled(mean age: 73 years) in the multi-center retrospective study
- Concomitant pulmonary TB:
  - 3% of HCAP (healthcare-associated pneumonia)
  - 2.7% of CAP (community-acquired pneumonia)
- HCAP with concomitant TB
  - higher respiratory failure, intensive care, and in-hospital mortality than those without TB
- Lower TB testing on admission in HCAP patients (27% vs. 40%)

PLoS ONE 7(5): e36832.

Factors associated with in-hospital diagnosis delay (IHDD) of TB

- Age > 65 years
- Other predisposing factors:
  - Negative sputum smear
  - Non-cavitary lesions on chest radiographs
  - Admission to hospital departments other than chest medicine/infectious diseases
  - Exposure to fluoroquinolones before anti-TB Tx
  - Underlying malignancy
- Death attributed to TB was associated with positive sputum smear but not prolonged In-hospital diagnosis delay(IHDD)

J Formos Med Assoc. 2010 Apr;109(4):269-77.

Medical care for comorbidity

- Covered by NHI
- Basically "fee for service" → need to control care quality
- Pay for performance (**P4P**), disease specific:
  - TB (now included in global budget system)
  - DM (now included in global budget system)
  - Asthma
  - CKD (early CKD, pre-ESRD)
  - Chronic hepatitis B & C
  - Cancer (only breast and cervical cancer)
  - Hypertension
  - Schizophrenia
- More reimbursement **points** as the incentives for health care providers

Pay for performance (P4P) program, TB care

- If not reported, no reimbursement from NHI since 1997
- P4P since 2002 and included in the global budget system of NHI
- Case managers in clinical care system
  - Improving bacteriological diagnosis for TB and follow-up (key in patient's bacteriologic results and regimen into the web-based reporting and case management system)
  - Monitoring regimen, dosing, and side effects
  - Educating and supporting TB patients

P4P program, DM care

- Estimated DM prevalence : 6.4% (1.47 million of population)
- Estimated only 30% of DM patients were enrolled
- Indicators in the program: Need to send the results to NHI server !
  - HbA1c, lipid profile(LDL), renal function, microalbuminuria, annual check for retinopathy
- NTP continues to communicate with diabetes medical association and NHI
  - To promote the awareness of TB suspect and referral
  - Screening for TB still not integrated into P4P of DM care

TB guideline in Taiwan: screening DM at the time of TB diagnosis

JFMA 2012; 111, 599-604

17

CKD care

- Early CKD and pre-ESRD in P4P:
  - Monitoring albuminuria
  - Glycemic control of comorbid DM patients
  - Nutrition education
- Dialysis:
  - Not included in P4P
  - NHI only reimburses to qualified dialysis care facilities
  - Accreditation by the medical association of Nephrology
  - Annual CXR has been the indicator for dialysis patient care (for infection control)

18

Chronic hepatitis B & C care

- Incentives for care providers
- Purpose:
  - Regular liver function and abdominal sonography follow-up (every 6 months)
  - Early diagnosis of hepatocellular carcinoma(stage I and II)
- NHI has a pilot program to covers anti-viral medication and interferon for selective patients with chronic hepatitis B and C

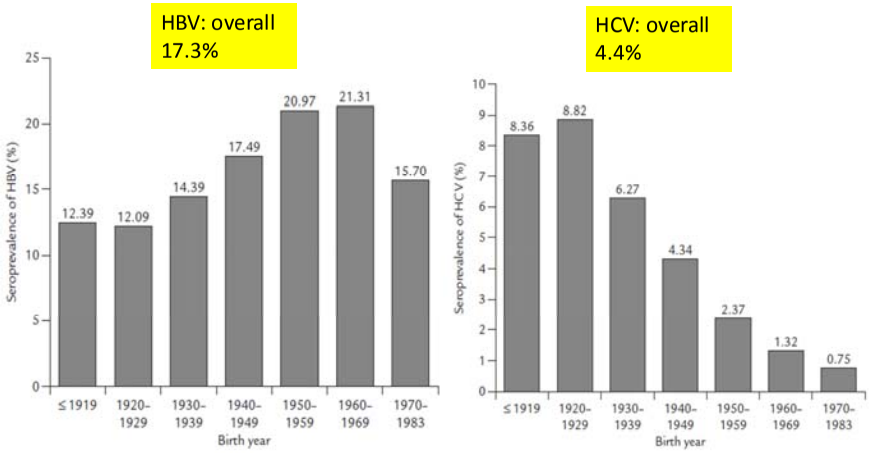
100

19

seroprevalence of HBV and HCV for adults ≥ 18 y/o, by birth-year

HBV: overall 17.3%

HCV: overall 4.4%



J Formos Med Assoc | 2007 • Vol 106 • No 2

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Confirmed TB outbreaks in long-term care facilities

The confirmation rate of TB suspected outbreaks in Taiwan by institutional category from 2007 to 2011
N=Number of confirmed outbreaks
*Workplace (non-medical care)

	2007 N (%)	2008 N (%)	2009 N (%)	2010 N (%)	2011 N (%)	Overall N (%)
Respiratory care wards	2 (15.4)	2 (16.7)	1 (12.5)	1 (14.3)	0 (0.0)	1(11.8)
Long-term care facilities	4 (9.3)	4 (5.9)	7 (26.9)	1 (3.6)	7 (10.0)	5 (11.1)
Others*	2 (66.7)	0 (0.0)	2 (100.0)	1 (20.0)	2 (13.3)	1 (40.0)
Schools	2 (25.0)	7 (87.5)	2 (33.3)	5 (55.6)	9 (27.3)	5 (45.7)
Health care workplaces (hospitals)	1 (33.0)	0 (0.0)	1 (20.0)	1 (11.1)	3 (10.0)	1 (14.8)

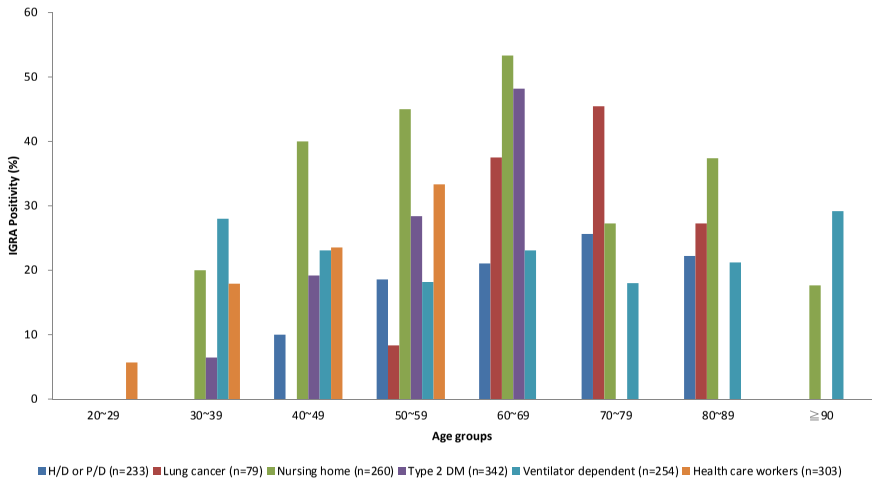
Taiwan Epidemiol Bull 2012;28: 244-251

TB incidence among at-risk population in Taiwan

- Kidney transplantation recipients:
  - 638/100,000
- ESRD with dialysis:
  - 300/100,000
- DM:
  - age-standardized : 191/100,000
- Hematological malignancies:
  - 120/100,000
- Gastric cancer/gastrectomy:
  - 788/100,000

Transpl Infect Dis. 2012 Oct;14(5):502-9.
Clin Microbiol Infect 2011; 17: 1646–1652
Chou et al. Tuberculosis Incidence and Survival Analysis in Diabetes Cohort-Using Secondary Database. http://ndltd.ncl.edu.tw/cgi-bin/gs32/gsweb.cgi?o=dnclcdr&s=id=%22096NTU05722007%22.&searchmode=basic
BMC Infect Dis. 2011 Nov 23;11:324.
Gastric Cancer. 2011 Aug;14(3):257-65.

Age-specific LTBI* prevalence among high risk population in Taiwan



*: IGRA positive
Institute for Biotechnology and Medicine Industry (IBMI) 2011 report

LTBI prevalence among high risk population in Taiwan

Risk population	Sample size	Age, mean (year)	IGRA (+) (%)	Indeterminate (%)	LTBI Tx in IGRA (+) patients (%)	Predisposing factors for IGRA (+)	Active TB in IGRA positive (%)
RA with TNFα inhibitors*[1]	242	54.7	18.6	3.7	?		8.1
Lung cancer[2]	191	69	30	9	0	COPD	1.6
Hematologic malignancy[2]	50	55.3	12	18	50		33
CKD[2]	703	61	27 (dialysis) 14 (severe CKD)	2	1.1	Serum albumin level	0
DM[2]	939	55	25.3	?	39		0

*: risk management plan
1. *Ann Rheum Dis* 2012;**71**:231–237.
2. Institute for Biotechnology and Medicine Industry (IBMI) 2012 report

Challenges and future perspectives for TB control among elderly (1)

- Delay of TB diagnosis and treatment, especially in the elderly
- Need more sensitive and specific diagnostic tools to shorten turn around time (TAT)
  - Use molecular methods to improve TAT of diagnosis and provide treatment as early as possible
  - Decreasing unnecessary treatment (i.e., NTM) and mortality of true TB
  - NHI's reimbursement influences the clinical use of molecular methods!
- Combined active case finding strategies for risk population
  - Partnership with NHI, Bureau of health promotion, and medical societies

25

Challenges and future perspectives for TB control among elderly (2)

- Strengthening the infection control in congregating settings for the elderly
- Prioritizing the populations for LTBI treatment based on available LTBI prevalence studies and follow-up of TB incidence among risk population
- Need more transmission dynamic studies for the impact of high TB incidence among the elderly to Taiwan's epidemic
  - especially social network for elderly TB patients
  - Cost effectiveness analysis for resource allocation

26

Thanks for your attention!

27

TMTC Care System for MDR TB

Jen-Jyh Lee
President, National Tuberculosis Association, Taiwan

Outcome of Pulmonary Multidrug-resistant Tuberculosis: A Six Year Follow-Up Study

C-Y. Chiang, D.A. Enarson, M-C. Yu, K-J. Bai, R-M. Huang, C-J. Hsu, J. Suo and T-P. Lin

Eur Respir J 2006;28:980-985

- A retrospective study was performed to determine factors associated with the outcome of pulmonary multidrug-resistant tuberculosis (MDR-TB) in Taipei, Taiwan.
- All patients newly diagnosed with pulmonary MDR-TB in a referral center from 1992-1996 were enrolled and their outcome over the subsequent 6 yrs was determined.

Eur Respir J 2006;28:980-985

- A total of 299 patients were identified.
- Out of the 299 patients, 153(51.2%) were cured, 31(10.4%) failed, 28(9.4%) died, and 87(29.1%) defaulted. Of the 125 patients receiving second-line drugs with ofloxacin, 74(59.2%) were cured.

Eur Respir J 2006;28:980-985

In May 2007, Taiwan CDC launched a new treatment program for MDR-TB, named Taiwan MDR-TB Consortiums (TMTC).

The program was a hospital-initiated and patient-centered treatment program.

- Taiwan was divided into 5 areas.
- Five medical teams were chose to provide the care for MDR-TB patients.
- More than 80% of MDR-TB cases in Taiwan were enrolled in the TMTC program.

Taiwan CDC offered the financial resources (NT 1 million for one MDR-TB patient each year) to be used flexibly by medical teams.

All 5 medical teams must comply with the WHO guidelines. Every MDR-TB patient should undergo rigorous treatment for 2 years.

9

Guidelines for the programmatic management of drug-resistant tuberculosis
WHO/HTM/TB/2006.361

The Low Default Rate Improved Treatment Outcome of MDR-TB in Taiwan

10

Purpose

Aims of this study were to describe the management and treatment outcomes of patients with MDR-TB in Taiwan and to identify the risk factors associated with poor treatment outcomes.

11

The target population was MDR-TB cases managed from May 2007 to April 2012 in Taiwan. All MDR-TB patients newly diagnosed since May 2007 and previously diagnosed MDR-TB patients with persistent positive culture after Jan 2007 were included in this study.

12

Our program uses individualized MDR-TB treatment regimens.

The initial MDR-TB regimens were designed by a panel of chest specialists based on a thorough review of patients' clinical characteristics and prior anti-tuberculosis treatment history before the drug susceptibility test (DST) results for second-line drugs became available in 3-8 weeks. The initial regimens included at least four anti-tuberculosis agents which were deemed to be effective.

13

The typically combination consisted of an injectable drug, a fluoroquinolone, first line drugs to which isolates were susceptible and other second-line oral drugs.Subsequently, regimens were adjusted according to the DST result for the second-line drugs.

14

Treatment was given for a period of 18–24 months, including at least 18 months after culture conversion. The actual duration of treatment was determined individually. The injectable drug was given for at least six months if feasible.

15

The six mutually exclusive treatment outcome categories recommended by WHO, namely, cure, treatment completion, transfer out, default, death, and treatment failure, were used in outcome assessment. Cure and treatment completion were classified as successful outcome; death, defaulted, failure and transferred out were considered as poor outcomes.

16

Treatment outcome definitions for Category IV treatment

Cured. **A Category IV patient who has completed treatment according to the programme's protocol and has at least five consecutive negative cultures from samples collected at least 30 days apart in the final 12 months of treatment.**

Treatment completed. **A Category IV patient who has completed treatment according to the programme's protocol but does not meet the definition for cure because of lack of bacteriological results (i.e. fewer than five cultures were performed in the final 12 months of treatment).**

Died. **A Category IV patient who dies for any reason during the course of MDR-TB treatment.**

17

Guidelines for the programmatic management of drug-resistant tuberculosis
WHO/HTM/TB/2006.361

Treatment outcome definitions for Category IV treatment

Failed. **Treatment will be considered to have failed if two or more of the five cultures recorded in the final 12 months of therapy are positive, or if any one of the final three cultures is positive.**

Defaulted. **A Category IV patient whose treatment was interrupted for two or more consecutive months for any reason.**

Transferred out. **A Category IV patient who has been transferred to another reporting and recording unit and whose treatment outcome is unknown.**

18

Guidelines for the programmatic management of drug-resistant tuberculosis
WHO/HTM/TB/2006.361

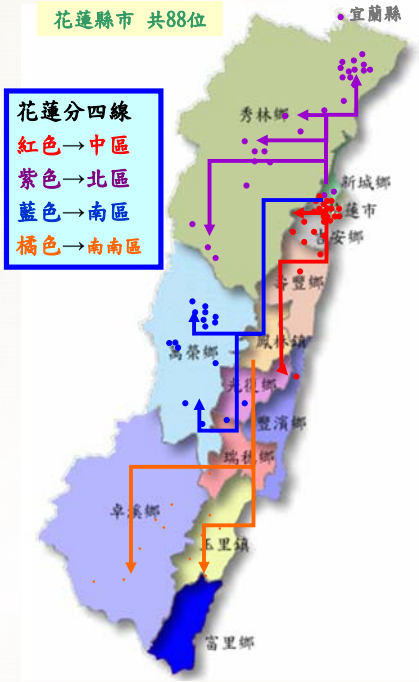
MDR-TB case management

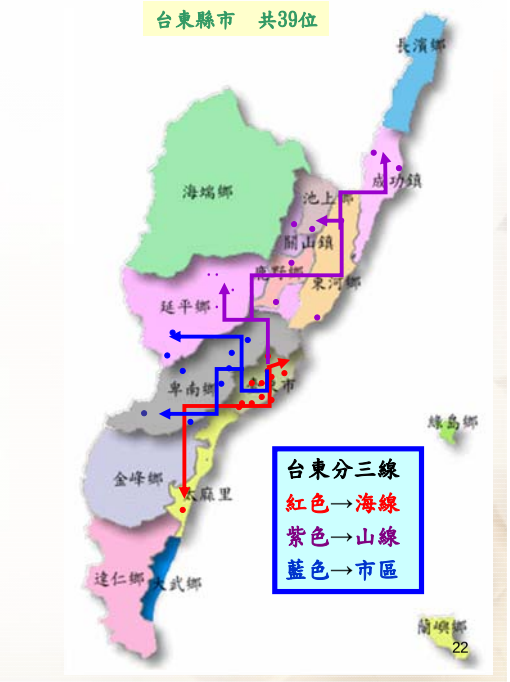
Several measures were adopted to safeguard effective treatment support: (1) recruitment of highly motivated individuals committed to providing community-based DOT, (2) special training of the public health nurses on providing psychosocial, cultural, and financial support, (3) providing enablers and incentives to patients, which included transportation fee, lunch boxes, various amount of money for daily expenses if patients were unable to work, social visits by clinicians, holiday and birthday gifts, and (4) closely monitor and careful management of adverse drug effects. Treatment support was consistently provided throughout the entire treatment period.

19

Seven cars were rented in order to perform community-based treatment of MDR-TB. Each car has one DOTS worker (driver and body guard) and one nurse. They would deliver the drugs to patients' homes or workplaces. Nurses managed ambulatory treatment including giving injection, observing for adverse events, and providing directly observed therapy twice a day from Monday to Friday. On weekends, patients administer their medications.

20



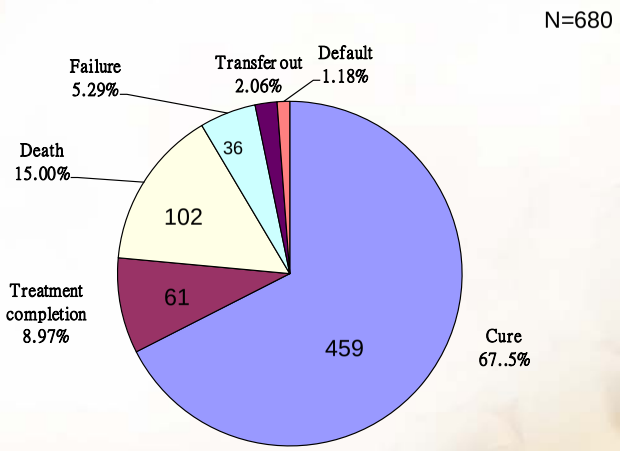


RESULTS

From May, 2007 to April, 2012, a total of 859 patients with bacteriologically confirmed pulmonary MDR-TB were identified. Of the 859 MDR-TB cases, 680 had final outcome and 179 were still receiving treatment.

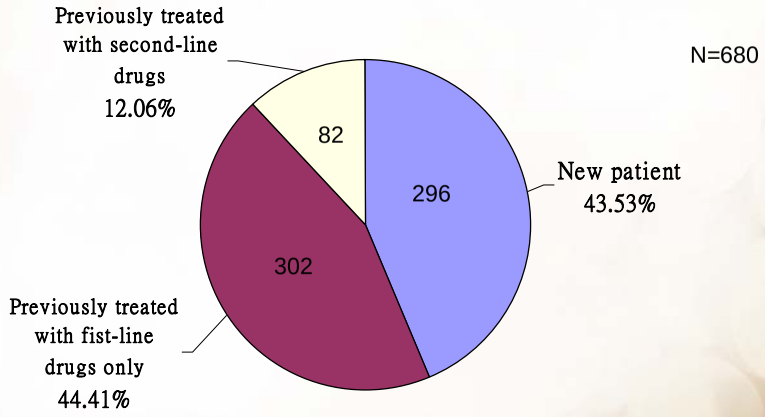
Of the 680 patients, 459 (67.5%) were cured, 61 (9.0%) completed therapy (76.5% has successful treatment), 102 (15.0%) died, 36 (5.3%) failed, 14 (2.1%) transferred out and 8 (1.2%) defaulted (23.5% had poor outcomes).

Treatment outcome



494 (72.6%) were men. The mean age was 53.1 years (range 13-93) for men and 47.4 years (range 12-96) for women. 32 (4.7%) patients had extra-pulmonary TB.

Among the 680 MDR-TB patients, 296 (43.5%) were new cases, 302 (44.4%) have been previously treated with first-line anti-TB drugs, and 82 (12.1%) second-line drugs



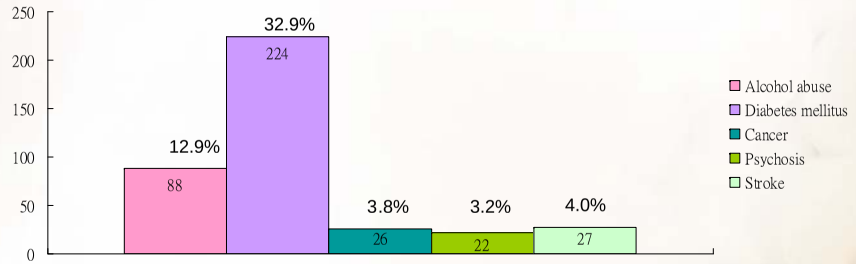
Among these 680 patients, 329 (48.4%) were smear positive, 314 (46.2%) had cavitation on chest radiograph; Serological tests for HIV were performed in 477 patients and were positive in 5. Of the 203 patients with unknown HIV serology status, all were free of AIDS defined illness during follow up.

29

The most common co-morbidities were diabetes mellitus (224, 32.9%), stroke (27, 4.0%), cancer (26, 3.8%), and psychosis (22, 3.2%). The mean body mass index was 21.7 kg/m2.

30

co-morbidities



31

In total, 443 (65.1%) were admitted to hospital. The mean of the hospital stay was 90.3 days (range 1-910 days). 37 patients (5.4%) had surgical resection.

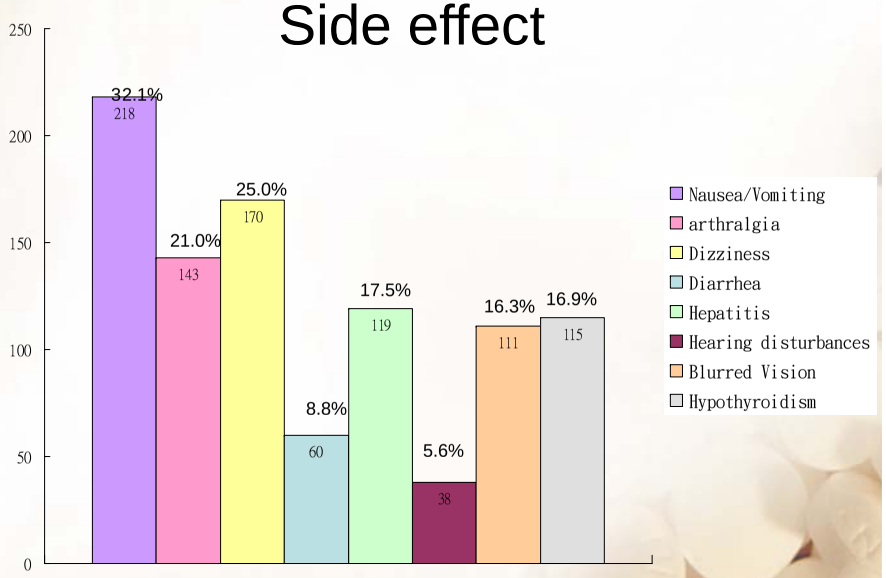
32

All 680 patients received a fluoroquinolone (levofloxacin in 228 and moxifloxacin in 549) and 637 (93.7%) patients received an injectable agent.

52 (7.6%) patients did not achieve sputum culture conversion. These included 36 patients who failed treatment, 15 patients who died with positive sputum culture, and 1 patient was transferred out before sputum conversion. Among the 628 patients who were converted, the mean conversion time was 41.9 days (range 0–885). Of the 680 patients, 327 (48.1%) had negative culture at the onset of MDR-TB treatment, 603(603/649, 92.9%) had sputum conversion in 3 month and 573 (573/618, 92.7%) in 6 months after treatment.

552 (81.2%) patients reported at least one adverse drug effect. Most adverse drug effects were minor. No patient stopped treatment permanently, but adverse drug effects resulting in permanent withdrawal of one or more drugs were seen in 390 (57.4%) patients. The five most common adverse events were nausea/vomiting (32.1%), dizziness/vertigo (25.0%), arthralgia (21.0%), hepatitis (17.5%) and hypothyroidism (16.9%).

Side effect



In this study, we found 99 strains (14.6%) resistant to both isoniazid and rifampicin but susceptible to all other tested drugs; 32 strains resistant to KM, but susceptible to fluoroquinolones, 21 strains were identified as XDR-TB.

In addition to INH and RMP resistance, 390/461 (84.6%) were resistant to rifabutin, 247/653 (37.8%) to streptomycin,222/609 (36.5%) to ethambutol, 49/147 (33.3%) to moxifloxacin, 63/226 (27.9%) to levofloxacin, 119/492 (24.2%) to ofloxacin, 110/552 (19.9%) to ethionamide, 63/570 (11.1%) to PAS, 51/585 (8.7%) to kanamycin and 20/454 (4.4%) to capreomycin

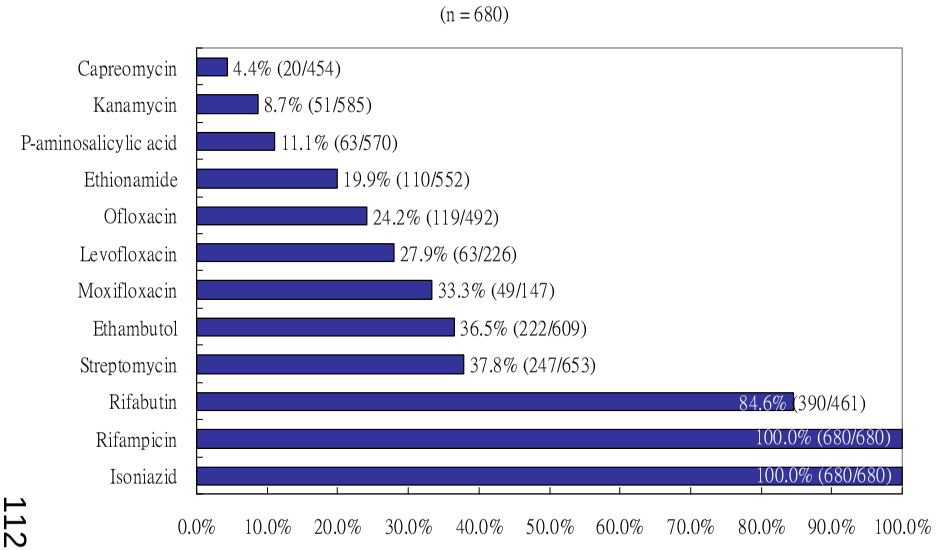


Table 1 Factors associated with outcomes of treatment

	Total (n)	Treatment success (%)	N	Poor outcome (%)	N	p
Sex						p=0.650
Male	494	380(76.9%)		114(23.1%)		
Female	186	140(75.3%)		46(24.7%)		
Age(yr)						p<0.001
≦ 45	251	217(86.5%)		34(13.5%)		
> 45	429	303(70.6%)		126(29.4%)		
Aboriginal						p=0.207
No	555	419(75.5%)		136(24.5%)		
Yes	125	101(80.8%)		24(19.2%)		
Sputum smear result						p=0.314
M+	329	246(74.8%)		83(25.2%)		
M-	351	274(78.1%)		77(21.9%)		
Cavitation on CXR						p=0.028
Yes	314	228(72.6%)		86(27.4%)		
No	366	292(79.8%)		74(20.2%)		
BMI						p=0.125
< 18.5	156	110(70.5%)		46(29.5%)		
18.5~24	376	295(78.5%)		81(21.5%)		
> 24	147	115(78.2%)		32(21.8%)		
Alcohol abuse						p=0.124
Yes	88	73(83.0%)		15(17.0%)		
No	592	447(75.5%)		145(24.5%)		
Diabetes Mellitus						p=0.048
Yes	224	161(71.9%)		63(28.1%)		
No	456	359(78.7%)		97(21.3%)		
FQN resistance						p<0.001
Yes	123	73(59.3%)		50(40.7%)		
No	409	320(78.2%)		89(21.8%)		
Unknown	148	127(85.8%)		21(14.2%)		
Patient category						p=0.144
New patient	296	233(78.7%)		63(21.3%)		
Previously treated with first line drugs only	302	231(76.5%)		71(23.5%)		
Previously treated with second line drugs	82	56(68.3%)		26(31.7%)		

There were no significant statistical differences between the patients with successful outcomes and the patients who had poor outcomes in sex, race, body mass index, alcohol abuse, bacterial smear result and MDR-TB patient categories (Table 1). There were significant statistical differences between the patients with successful outcomes and the patients who had poor outcomes in age, x-ray cavitations, comorbidity of diabetes and FQN resistance.

41

DISCUSSION

In this study, we had achieved good compliance to the DOTS-Plus treatment strategy with a treatment success rate of 76.5%, much better than our earlier strategies of achieving 51.2% treatment success rate with 9.4% death, 29.1% default, and 10.48% failures in a group of 299 MDR-TB patients enrolled from 1992 to1996 in northern Taiwan. The significant difference in these two studies was the default rate which fell from 29.1% to 1.2%, that could explain the difference of the treatment success rates.

42

The recent systematic review by Orenstein et al of 33 studies on MDR-TB treatment outcomes reported a successful outcome in only 62%. The most important cause of this poor results was attributed to default from treatment which is a serious global threat in the treatment and control of MDR-TB with rates over 15% in many countries, including Korea (32.2%) [8], Taiwan (29.1%) [6], South Africa (21%) [9], Russia (20%) [12], Argentina (19.9%) [10], Peru (19%) [11], India (18%) [13], Nepal (17%) [14], Italy (16.6%)

43

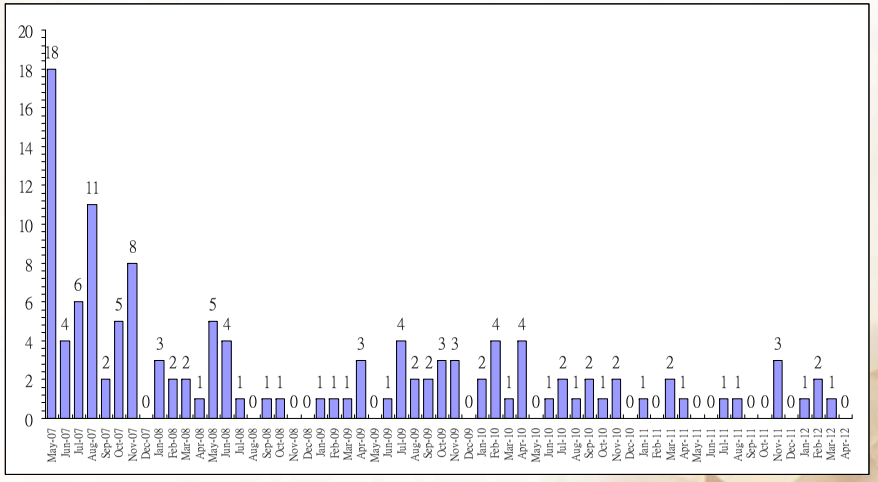
Team work and frequently scheduled interactions with the nurses can ensure a high level of treatment compliance and prompt identification and timely treatment of adverse drug events. Continuous psychosocial support was also provided in our study to assist patient to resolve both medical and non-medical problems that may result in non-compliance.

44

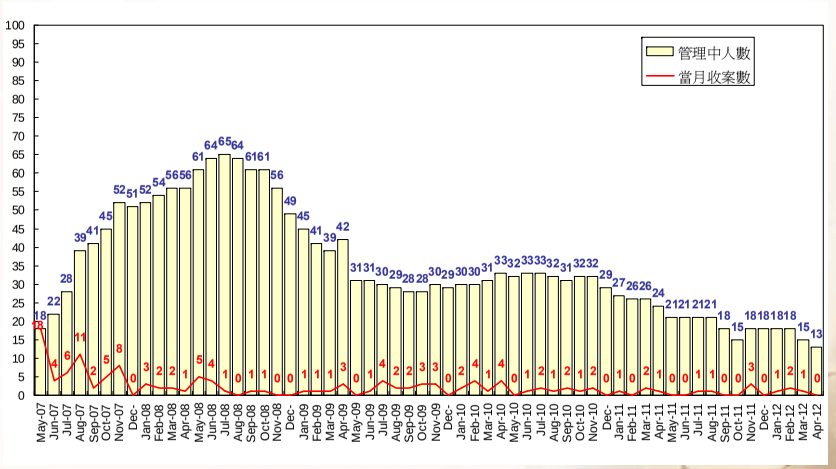
To build a friendly relationship with trust, compassion, and respect is the most important element in our treatment program. Cellular phones were provided for the patients to allow free access between them and their caring nurses for any medical, social, and financial problem that may arise. These measures could be key factors in achieving a low rate of default in our program.

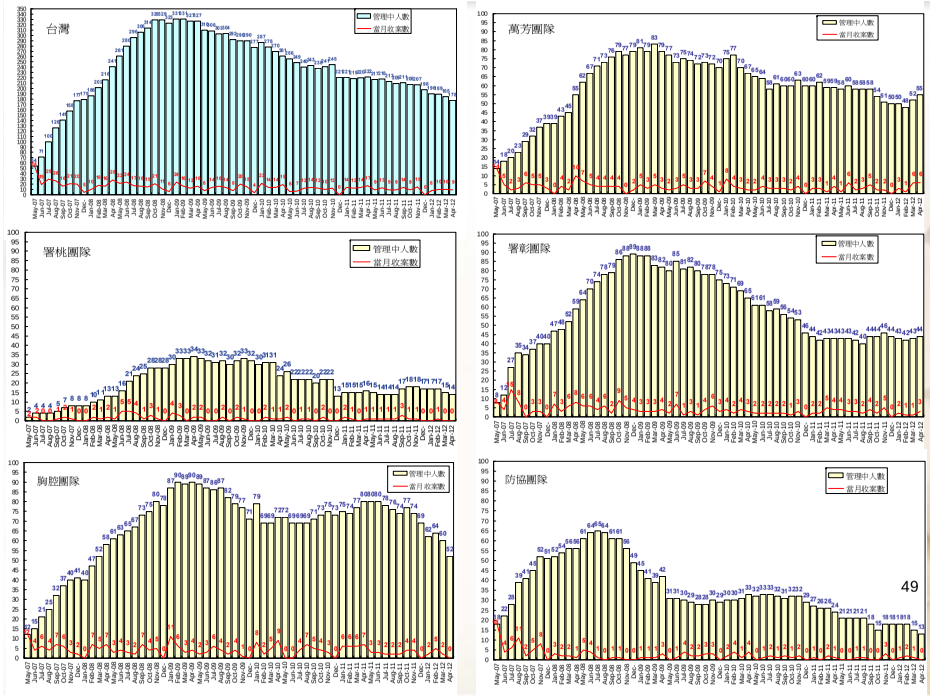
Side-effects were promptly managed to relieve symptoms. Drugs suspected to cause the adverse reactions were discontinued and replaced by an alternative drug after consultation with the physician.

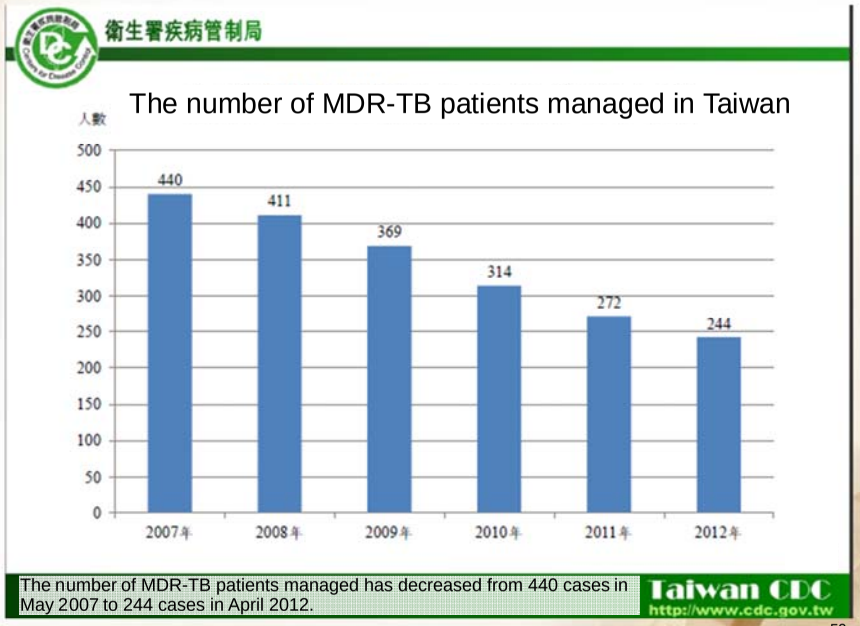
Number of MDR-TB patients enrolled in Eastern Taiwan

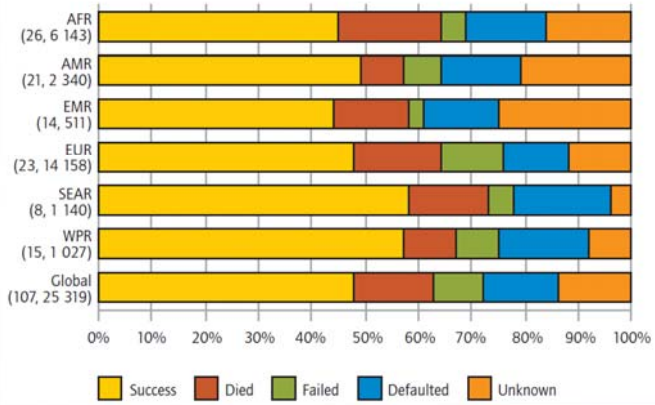


Total number of MDR-TB patients managed in Eastern Taiwan









GLOBAL TUBERCULOSIS REPORT 2012

In summary, this is a preliminary analysis of the treatment outcome in 680 of 859 patients enrolled in this study by adopting the DOTS-Plus programme in treating MDR-TB patients in Taiwan. We reported our successful experience in adding other enforcement measures to achieve a low default rate to increase the treatment success rate to 76.5%.

This DOTS-Plus programme provides an important model to give a high standard of care to patients with MDR-TB. The scale-up of such models might be needed to confront the threat of MDR-TB.

53

54

TB Control among Aboriginal Mountainous Districts in Taiwan

Yen-Fang Huang, Deputy director

Third division

Taiwan CDC

Outline

- Aboriginal population in Taiwan
- TB control strategies for aboriginal mountainous districts
- Performance
- Future perspectives

Aboriginal population in Taiwan

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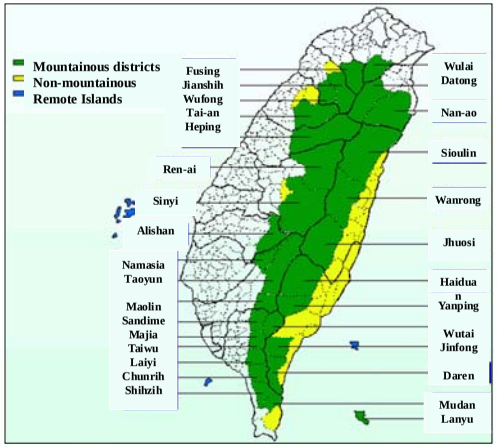
Distribution of aboriginal tribes in Taiwan

from Council of Indigenous Peoples

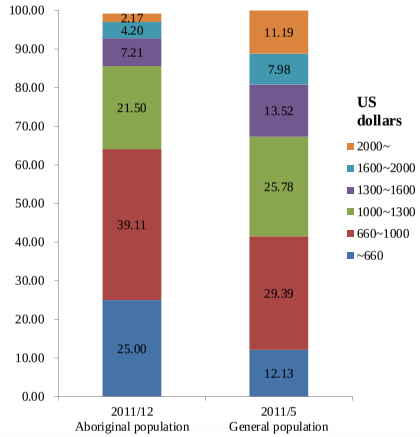
Distribution by districts of residence

- 30 aboriginal mountainous districts (indicated green)
- 25 aboriginal non-mountainous districts (indicated yellow)

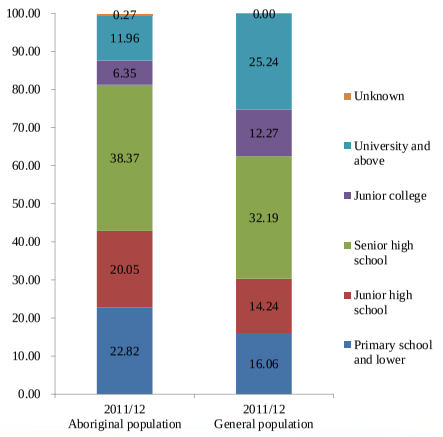


Socio-economic status

Monthly income

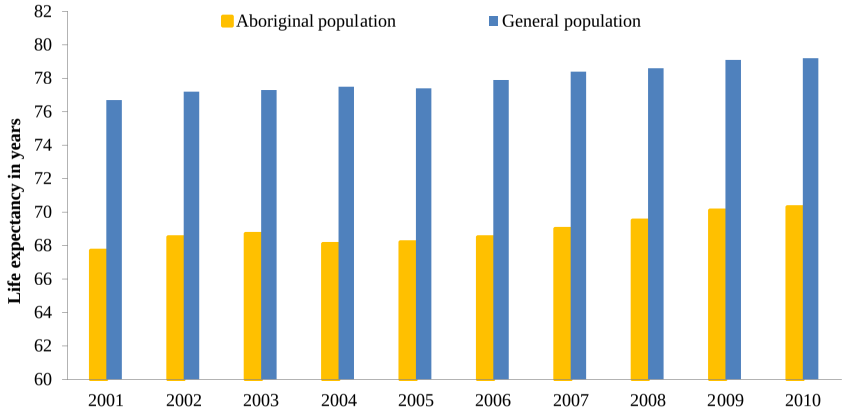


Educational level



from Council of Indigenous Peoples, Employment Status Survey of Indigenous People, 2011

Life expectancy in 2010



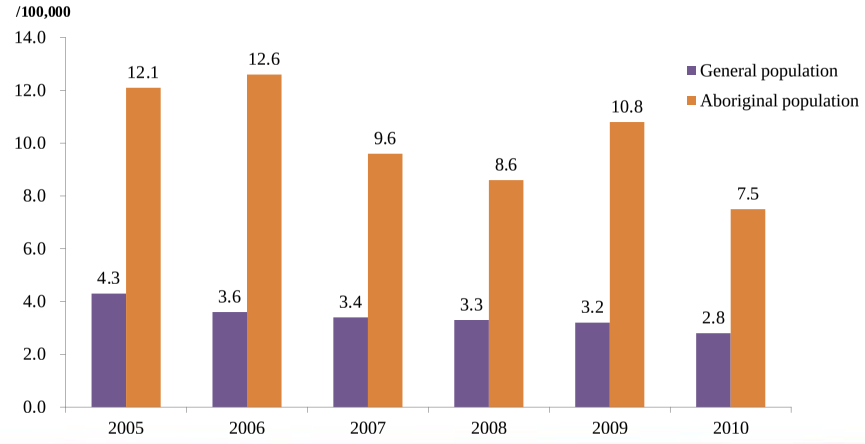
from Council of Indigenous Peoples, Executive Yuan , Annual Report of Health Statistics of the Aborigines in Taiwan 2010

Standard mortality ratio(SMR) among aboriginal population

Standardized Mortality Ratio; SMR				
	2006		2007	
	Male	Female	Male	Female
SMR	2.10	1.82	2.05	1.85
95% CI	2.01 – 2.19	1.73 – 1.92	1.96 – 2.14	1.75 – 1.94

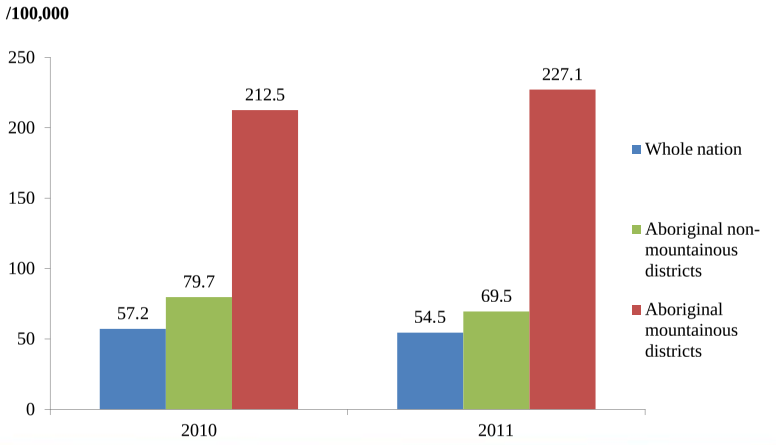
from Council of Indigenous Peoples, Executive Yuan , Annual Report of Health Statistics of the Aborigins in Taiwan 2007

TB mortality, 2005-2010

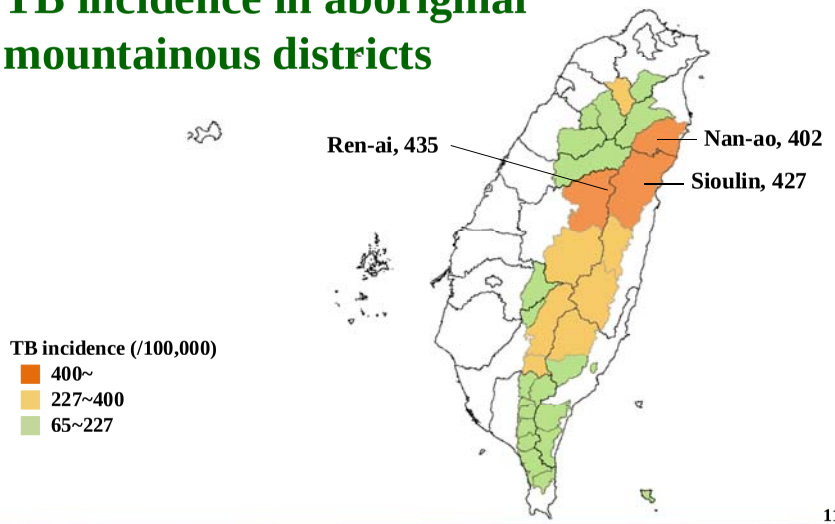


from Council of Indigenous Peoples, Executive Yuan

TB incidence, 2010-2011



TB incidence in aboriginal mountainous districts



Average TB incidence in mountainous districts = 227/100,000

Health literacy about TB

- **Knowledge and attitude**
  - Inherited
  - TB disease is a food-born disease
    - ✓Alcohol consumption can get TB disease
    - ✓Transmitted by sharing plates, etc.

Factors associated with adherence among aboriginal TB cases

- **Systematic factors**
  - Lack resources of medical care, long distance of transportation
  - Public health system
    Getting health information rely on local public health staffs or DOTS observers, but had language barrier
- **Individual factors:** low education level
- **Family support**
- **Stigma to the TB disease**

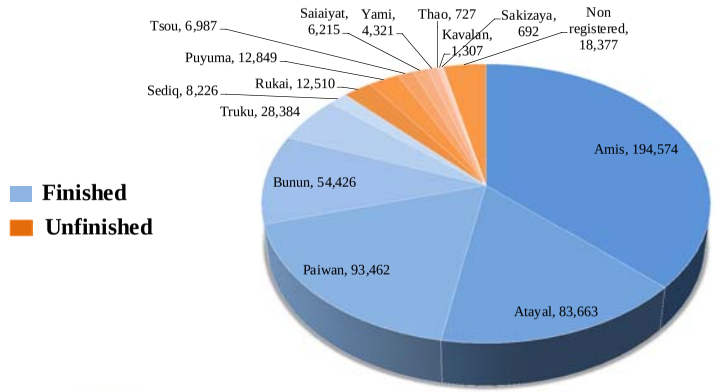
TB control strategies in mountainous districts

TB control strategies in mountainous districts

- **TB education integrated with native culture**
- **Strengthen active case finding**
- **Enhance case management**
- **Improve accessibility of medical care**
- **Inter-ministerial collaboration**

TB education integrated with native culture

- **Educational material with native culture and language**
- **Training community workers for TB education**



Educational material, animation





Strengthening active case finding (1)

- **The number of annually X-ray screening in mountainous districts**

Year	No.of screenings
2004	6,324
2005	26,965
2006	21,750
2007	28,470
2008	22,929
2009	24,906
2010	30,273
2011	54,357

Strengthening active case finding (2)

- **CXR in mountainous districts in 2011**

County	No. of screenings	No. of registered population	No. of Confirmed TB cases	Proportion of screenings / registered population (%)	TB prevalence (/100,000)
New Taipei	417	5194	0	8.03	0.00
Yilan	3284	10390	16	31.61	487.21
Taoyuan	3534	9171	10	38.53	282.97
HsinChu	3545	10347	11	34.26	310.30
Miaoli	1561	5146	1	30.33	64.06
Taichung	2603	9765	12	26.66	461.01
Nantou	8644	30006	12	28.81	138.82
Chiayi	2075	5573	2	37.23	96.39
Kaohsiung	2542	8590	3	29.59	118.02
Pingtung	12070	40164	7	30.05	58.00
Hualian	8637	26554	30	32.53	347.34
Taitung	5331	17147	9	31.09	168.82
total	54243	178047	113	30.47	208.32

Strengthening active case finding (3)

- Active surveillance for students aged 16-18 who registered residence in mountainous districts in 2011
  - Coverage 35%
  - Detection rate 131/100,000
  - Rate ratio: 6.5 times of the age-specific incidence in general population (20.2/100,000)
  - The incidence of TB in the population lived in mountainous districts at childhood and moved to urban areas for study, is similar to the age-specific incidence in mountainous districts (85.2/100,000) .

Case management (1)

- **DOTS in mountainous districts**
  - Pilot projects implemented in all mountainous districts since March 1997
  - DOTS had been implemented since April 2006
  - Manpower required: two-times more of general townships
  - On site DOTS (TB patients go to designated sites for taking medicine): providing the transportation fees
  - Coupons for nutrition support

Case management (2)

- **Incentives for TB treatment completion**
  - 170 USD/patient covered by the Council of Indigenous Peoples (CIP)
- **Helping patients transporting to health care facilities**
  - If distance of transportation is more than 20KMs, CIP offers the fee for transportation

Improving accessibility of medical care

- **Inviting pulmonologist or TB specialist to help TB diagnosis and treatment in local health station**

Shortening turn-around time for diagnosing MDR-TB

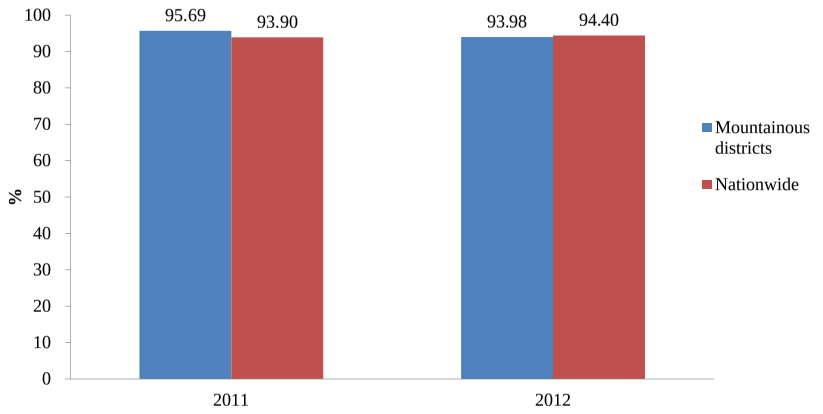
- **Using Hain test since 2010**
- **Targets:**
  - MDR-TB outbreaks in mountainous districts: Xiu-lin, Zhuo-xi, and Wan-rong in Hualien county
  - MDR-TB contacts
  - Failed, defaulted, and relapsed patients

Multi-departments collaboration

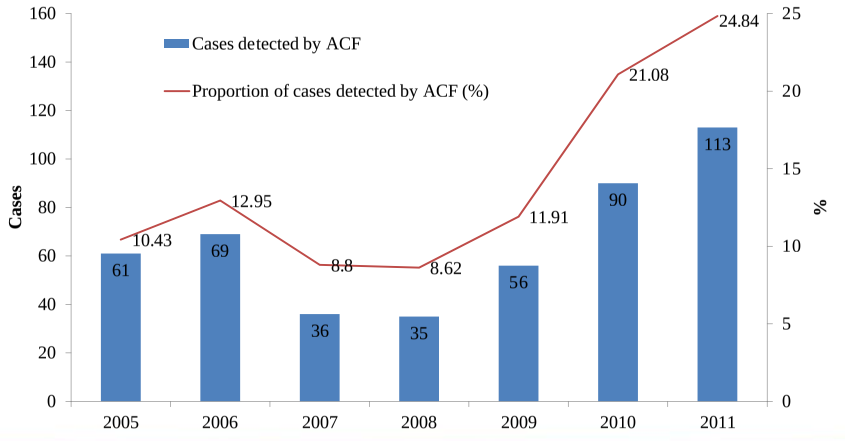
- **Central government**
  - Council of Indigenous Peoples (CIP)
- **Local government**
  - aboriginal peoples bureaus & health bureaus
  - Township offices and health stations
- **To improve KAP about TB, to provide TB education during festivals, and to translate the educational materials into native language**

Performance of TB control in mountainous districts

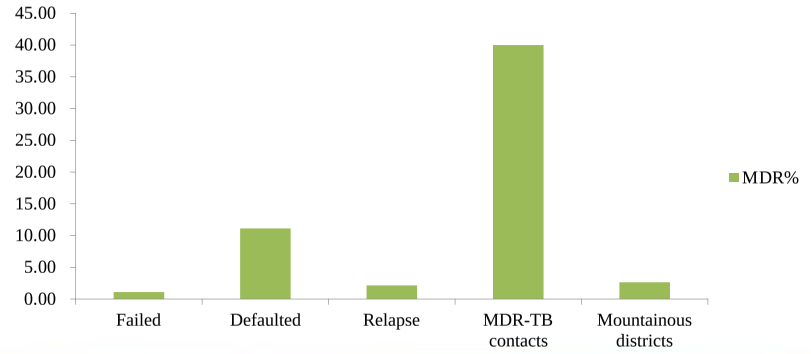
DOTS coverage in mountainous districts



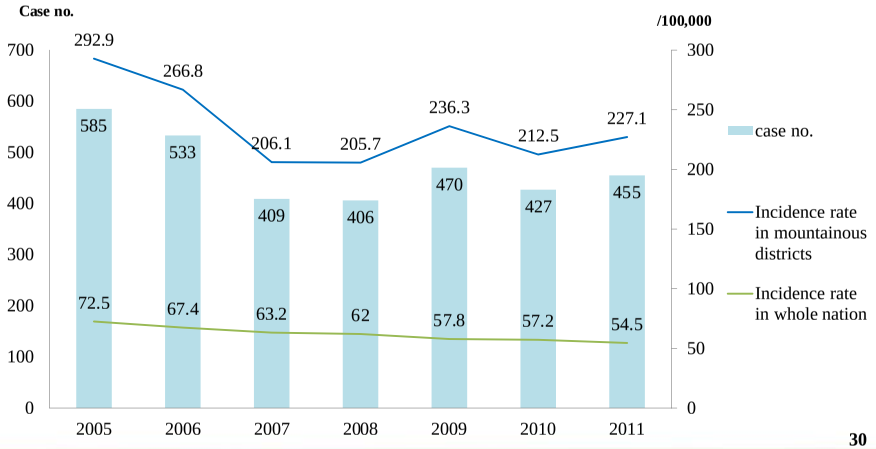
The proportion of TB cases detected through active case finding (ACF) in mountainous districts, 2005-2011



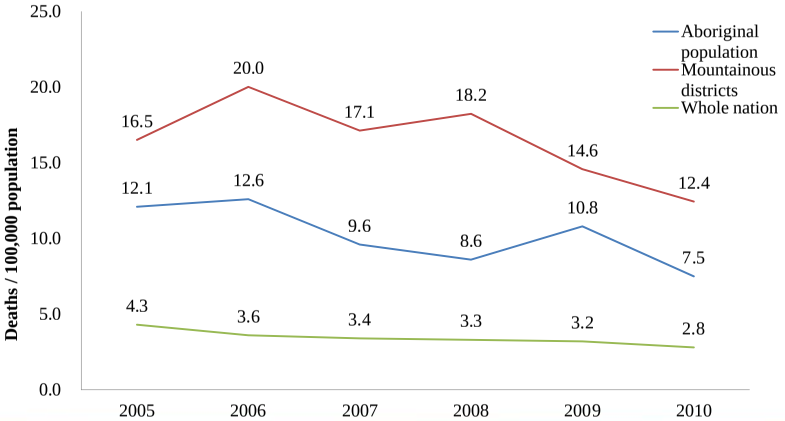
The proportion of MDR-TB cases detected through Hain test among smear positive patients, by patients' classification, 2012



Performance of TB control in mountainous districts (1): TB incidence



Performance of TB control in mountainous districts (2): TB mortality



Future perspectives

Future perspectives (1)

- **Promoting TB Health literacy among aboriginal population**
  - Integrate TB education with native culture and native language into community activities
- **Establish e-database for monitoring effectiveness of X-ray screening in aboriginal population**

Challenges and future perspectives (2)

- **Strengthen active case finding**
  - Increase education and screening for people registered residence in mountainous districts but living in urban areas
  - Define frequency of X-ray screening for each aboriginal case
- **Resource allocation**
  - Continue to collaborate with other government departments

Thank you for your attention !

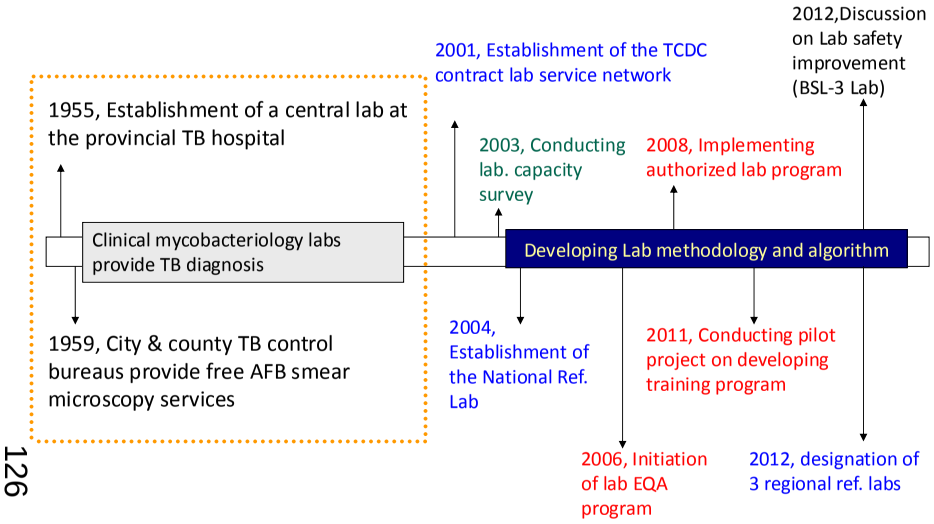
Tuberculosis Laboratory Program

Ruwen Jou, PhD
Reference Laboratory of Mycobacteriology
Research and Diagnostic Center
Taiwan CDC

Outline

- TB laboratory system
- TB laboratory service network
  - Clinical laboratory diagnosis
  - External quality assessment
  - Drug-resistance surveillance
  - Genotyping program
- Challenge and prospective

Development of TB laboratory program



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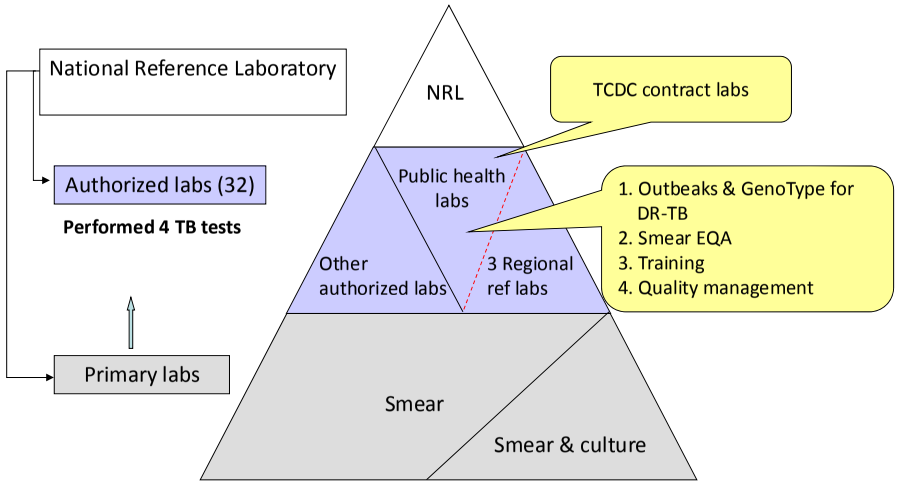
Estimated capacity of clinical laboratory diagnosis

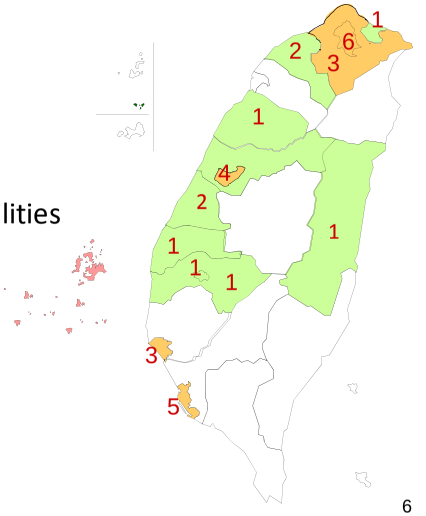
Year \ Test	AFB smear	Culture	Identification	DST
2009	755,000	750,000	65,000	Approx. 30,000
2011	**834,000**	**827,000**	**88,000**	Approx. 30,000

Levels of TB laboratory diagnosis

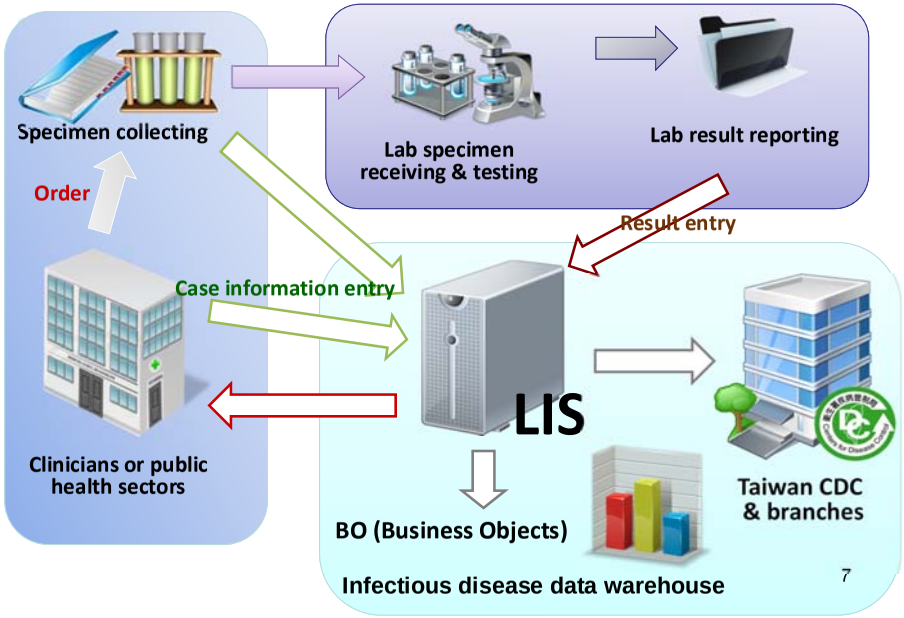


Distribution of authorized tuberculosis laboratories

- 32 authorized labs
- 8 TCDC contract labs, 2013
- Biosafety level 2 (-) or BSL3 facilities
- Logistics



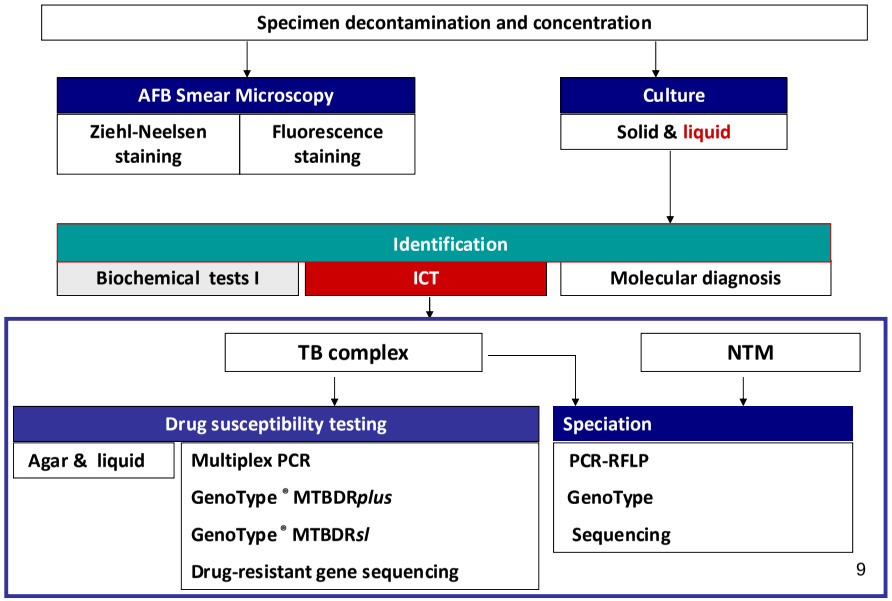
Management of laboratory information



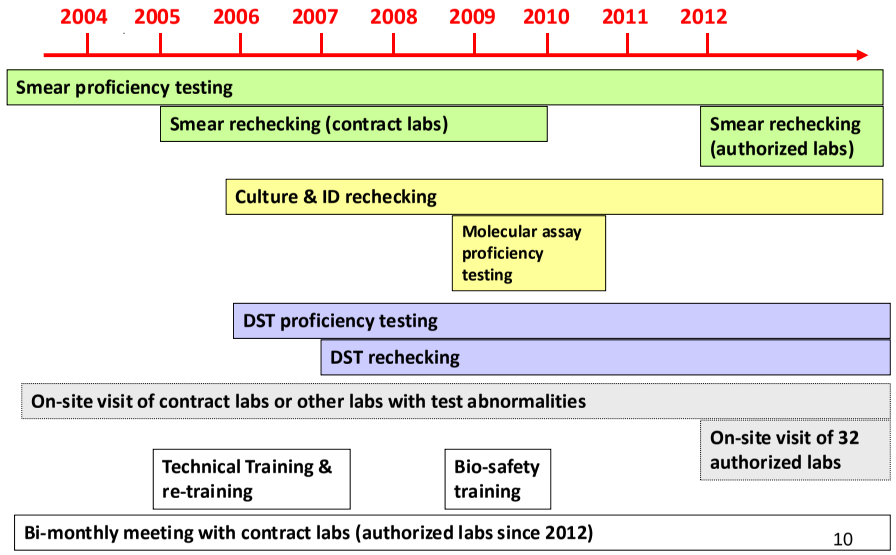
Implementation of new diagnostics

- Culture
  - Liquid TB culture
    - Implementation, 2007
    - All authorized labs has adopted liquid culture in Jan. 2013
- MTBC identification
  - Lateral-flow test
    - Implementation, 2011
- Drug susceptibility testing
  - Line-probe assay
    - Implementation, 2008

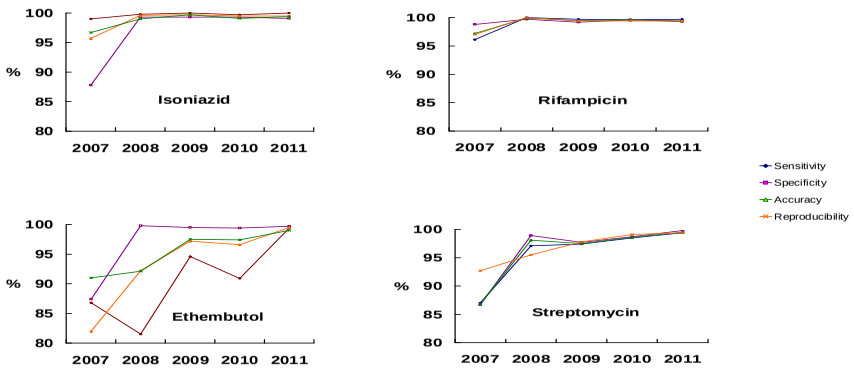
Algorithm of laboratory diagnosis



Timeline of the EQA program



Proficiency of drug susceptibility testing



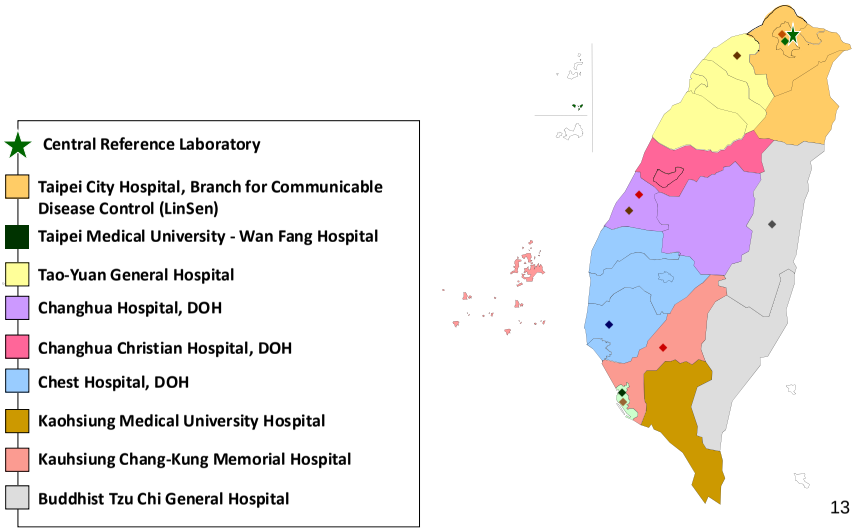
Overall, 16.7% (5/30), 85.7% (30/35), 86.1% (31/36), 82.4% (28/34) and 96.8% (30/31) of laboratories fulfilled the competency criteria for all drugs in 2007, 2008, 2009, 2010 and 2011, respectively.

Int J Tuberc Lung Dis, 17(1):1-7, 2013

Confirmation of MDR-TB

- All strains with INH and RMP resistance are required to be confirmed by National Reference Lab since May, 2007.
  - Molecular diagnosis is followed by conventional DST, if necessary
  - At least two sputum samples are confirmed by molecular diagnosis as MDR
- Molecular diagnosis directly on sputa of TB and/or MDRTB suspects is implemented in 2010 for those who are relapse, default, failure, or TB/MDRTB contacts

Laboratory-based surveillance system



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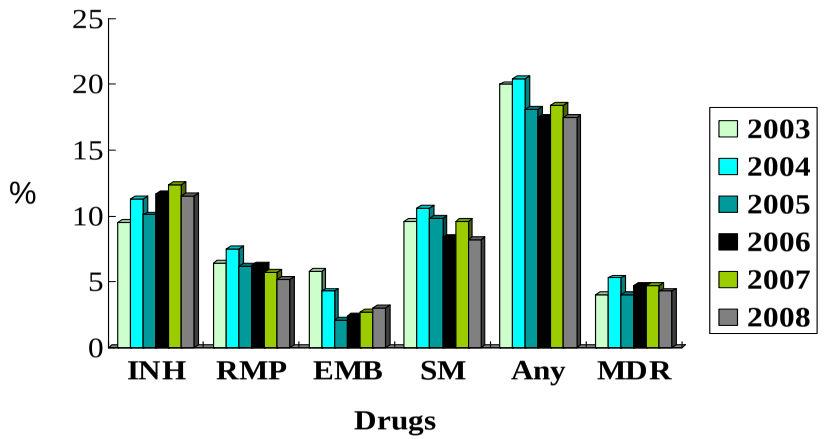
Combined TB drug resistance in Taiwan



The 21st European Congress of Clinical Microbiology and Infectious Diseases and the 27th International Congress of Chemotherapy, Milan, Italy, May 2011

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Applications of genotyping

- Differential diagnosis
  - *M. bovis*, *M. bovis*-BCG
- Re-activation or re-infection
- Outbreak investigation
- Laboratory cross-contamination
- Surveillance
- Other NTP needs

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Tokyo-172 BCG vaccination complications, Taiwan

Table. Characteristics *Mycobacterium bovis* BCG complication cases, Taiwan, 2005–2007*

Patient no.	Sex/age at diagnosis, y	Year reported	Specimen	Diagnosis and site of involvement
1	F/2	2005	Biopsy sample	BCG osteitis/osteomyelitis, right ankle
2	M/1	2005	Bacterial isolate	Subcutaneous abscess, left anterior chest wall
3	M/2	2005	Bacterial isolate	Severe combined immunodeficiency, disseminated BCGitis
4	M/9	2005	Bacterial isolate	Suppurative lymphadenitis
5	F/1	2005	Bacterial isolate	Injection-site abscess
6	M/1	2005	Biopsy sample	Suppurative lymphadenitis
7	M/2	2006	Bacterial isolate	BCG osteitis/osteomyelitis, right distal femoris
8	M/2	2006	Bacterial isolate	BCG osteitis/osteomyelitis
9	F/1	2006	Bacterial isolate	BCG osteitis/osteomyelitis, left distal femoris
10	F/1	2006	Bacterial isolate	BCG osteitis/osteomyelitis, left distal radius
11	F/2	2007	Bacterial isolate	BCG osteitis/osteomyelitis, right knee
12	M/1	2007	Bacterial isolate	Subcutaneous abscess, left wrist
13	M/2	2007	Biopsy sample	BCG osteitis/osteomyelitis, right ankle
14	F/1	2007	Bacterial isolate	Suppurative lymphadentitis
15	M/2	2007	Bacterial isolate	BCG osteitis/osteomyelitis, left proximal tibia

*BCGitis, disseminated BCG infection.

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Emerg Infect Dis, Vol 15, No 9, 1525-1526, 2009

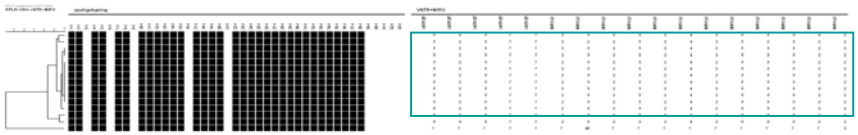
Differential diagnosis of *M. bovis*-BCG, 2010-2012

Year	*Case no. (%)	Positive, case no. (%)				Negative, case no.(%)
		M. bovis-BCG	*M. bovis* Family	*M. tuberculosis*	*M. tuberculosis* complex	
2010	43 (100)	21 (48.8)	1 (2.3)	5(11.6)	4(9.3)	12(27.9)
2011	51 (100)	30 (58.8)	0 (0.0)	2 (3.9)	1 (2.0)	18 (35.3)
2012	56 (100)	33 (58.9)	0 (0.0)	2 (3.6)	1 (1.8)	20 (35.7)

* Extra-pulmonary TB cases younger than 5 years old

In 2008, Taiwan CDC initiated a laboratory-based comprehensive BCG adverse events following immunization surveillance program.

Mycobacterium bovis infected human cases, Taiwan



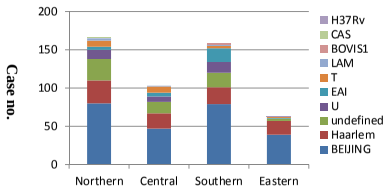
SpolDB4 ST 864

In a 2-year retrospective study, fifteen (0.4%) *Mycobacterium bovis* were identified among 3,321 isolates from human tuberculosis cases.

Only one contagious bovis sublineage, spoligotype ST 864, was recognized. Indigenous clonal expansion of one major strain was demonstrated.

Emerg Infect Dis, Vol 14, No3, 515-517, 2008

Population structure of multidrug-resistant *Mycobacterium tuberculosis* in Taiwan



Summary: (1) The study highlighted Beijing and Haarlem lineages were predominant among MDR-TB;(2) suggested LAM and EAI lineages had epidemic potential of XDR; (3) active transmission in eastern Taiwan.

Infect Gene and Evol, 11:633-639, 2011

Laboratory Investigation of a Nosocomial Transmission of Tuberculosis at a District General Hospital

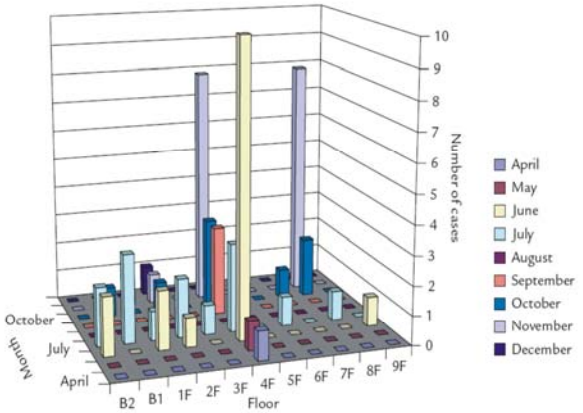


Figure 1. Trends over 62 notified tuberculosis cases on different floors of the main building and three cases from other buildings in the hospital complex from April to December 2003. One case was identified on the 8th floor of the main building in March 2004.

J Formos Med Assoc, Vol 106, No 7, 2007

Challenge and prospective

- Resources to support substantial development
  - Human
  - Finance
- International laboratory program
  - Partnership
- Research & development
  - laboratory directed
  - Operational *vs* cutting- edge research

Thank you for your attention!

Communication
Cooperation
Coordination
Collaboration

Quality Management of Clinical Tuberculosis Laboratories

Hwa-Jen Teng, Ph.D
Section of Laboratory Quality Assurance and Biosafety
Research and Diagnostic Center
Taiwan CDC

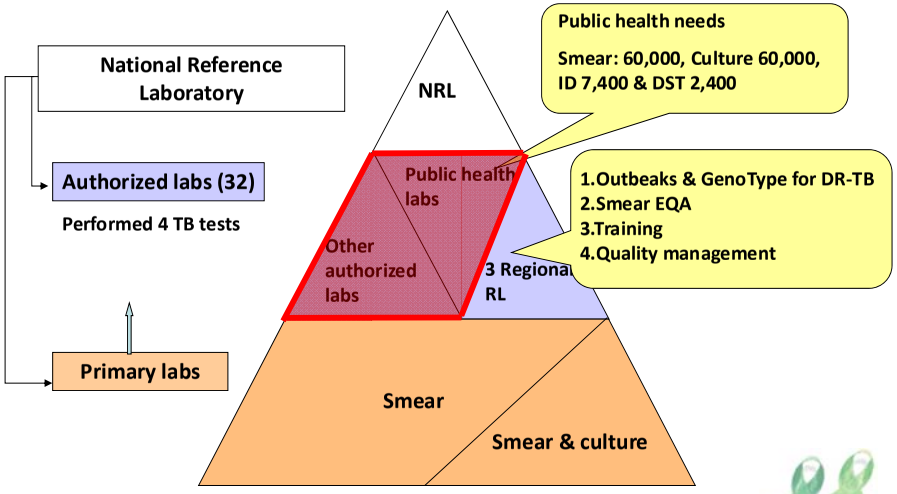
Outlines

- Background
- Timeline of TB quality management
- Quality indicators from 2008 to 2012
- Conclusion and future challenge

Background

- TB control responsible unit change in 2001
  - → Poor lab quality management
  - → In Oct. 2001, TCDC set up 9 TB contract labs to standardize lab SOP and report to meet the public health needs
- Laboratory contamination events
  - →Reagent contamination in March 2009
  - →Personnel operation/environmental contamination in November 2009

Levels of TB laboratory diagnosis



Lab definition

- **Accredited labs**

  Labs accredited by international accreditation organization e.g. TAF, CAP

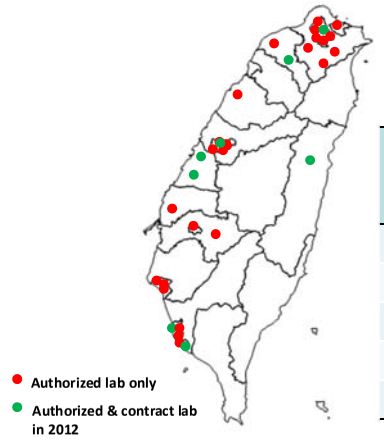
- **Authorized labs (by DOH)**

  Accredited labs or labs passing related proficiency tests with an approved SOP for a 4-year term certificate

- **Contract labs**

  Accredited and authorized labs contracted by TCDC to provide lab services for public health needs

Clinical tuberculosis laboratories

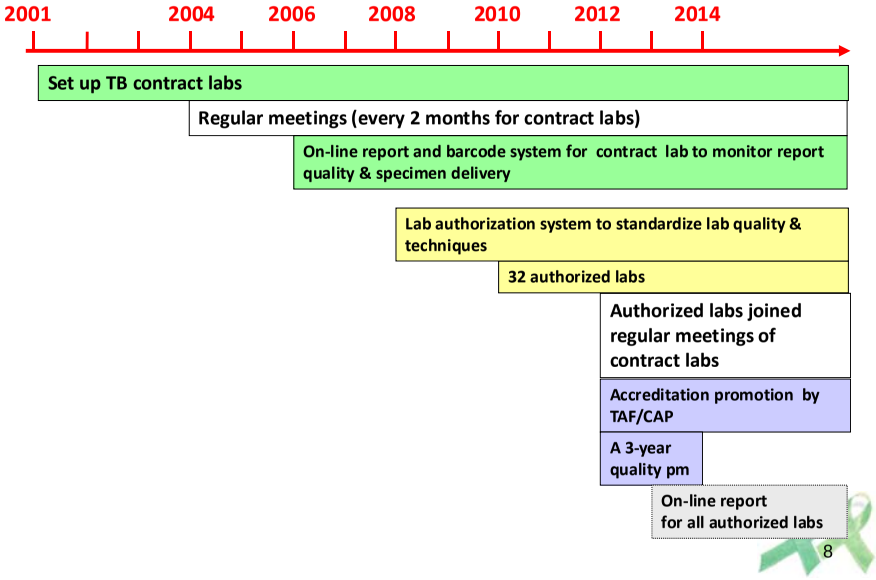


Year	TCDC contract lab no.	Authorized lab no.	Accredited lab no. by TAF/CAP
2008	9	10	
2009	9	31	
2010	9	32	
2011	9	32	25
2012	8	32	31

Objectives of TB quality management

- To improve the quality of all clinical mycobacterium laboratories to provide real-time and accurate reports to assist patient treatment, eventually TB control
- To prevent laboratory contamination and early detection on this incident, if it occurs

Timeline of quality management



Quality management plan since 2004

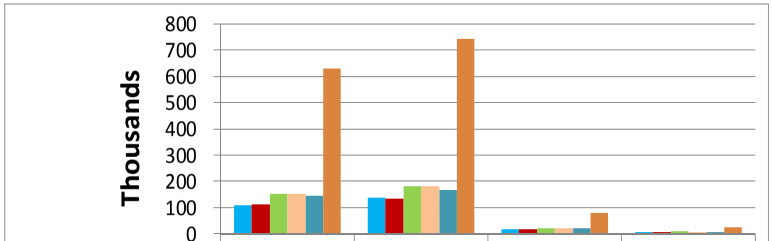
- Monitoring smear positive rates and culture positive rates biweekly using on-line report data.
- Holding bimonthly meetings to check 8 quality indicators for each lab.
- Authorizing every 4 years and checking proficiency test every 2 years to all TB labs.
- Set up "Quality Assurance Requirements" to require reporting wrong reports by fax within 3 days.
- Conducting on-site visiting and certifying smear personnel.
- Conducting DST proficiency test yearly by TCDC reference lab.

8 quality indicators

- Smear positive rate
- Culture positive rate
- Contamination rate (first L-J culture)
- TAT accomplishing percentage
  - Smear within 24 hours
  - Positive culture within 21 days
  - ID-MTBC within 7 days
  - DST within 28 days
- Specimen delivery within 3 days

2008-2012 quality indicators

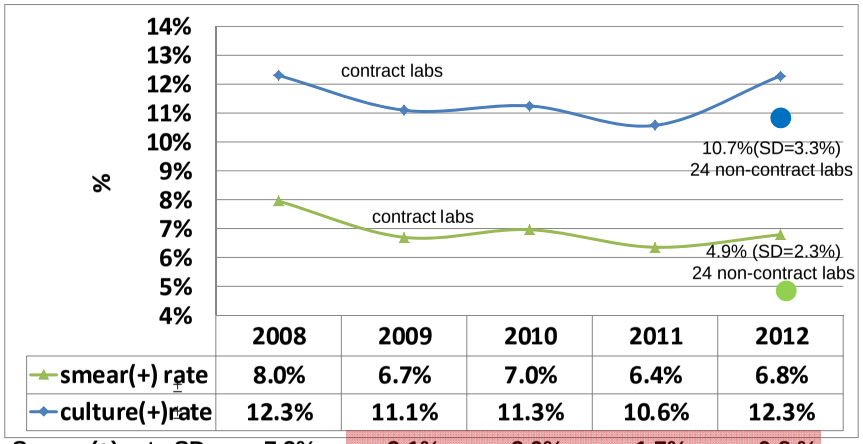
Total number of specimen in 2008-2012



	Smear	Culture	ID	DST
2008 (contract labs)	110,107	137,795	18,873	7,052
2009 (contract labs)	111,785	132,704	16,842	6,493
2010 (contract labs)	151,488	183,077	22,788	8,668
2011 (contract labs)	152,049	181,716	22,212	8,137
2012 (contract labs)	146,783	165,988	23,074	6,294
2012 (All 32 labs)*	629,292	742,776	79,668	24,996

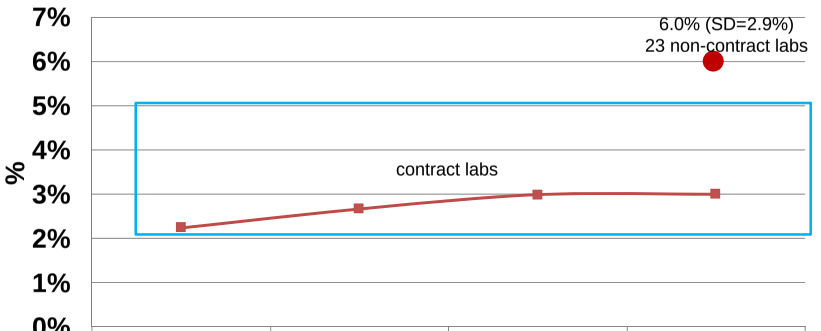
* Data shown here were estimated values .

Positive rate



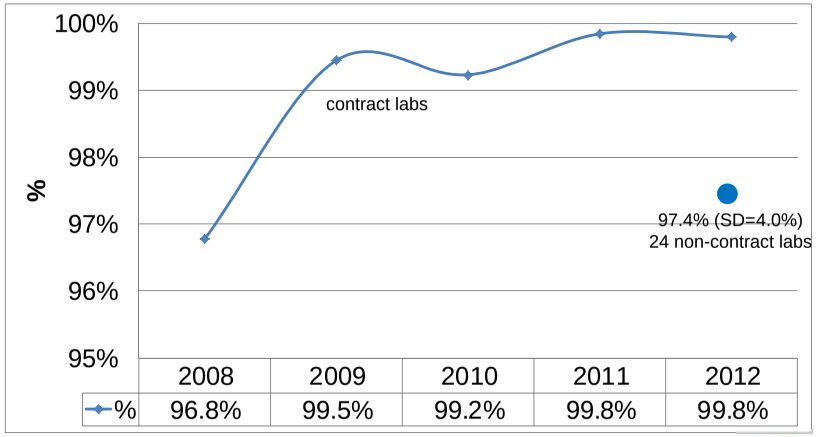
	2008	2009	2010	2011	2012
smear(+) rate	8.0%	6.7%	7.0%	6.4%	6.8%
culture(+)rate	12.3%	11.1%	11.3%	10.6%	12.3%
Smear (+) rate SD	7.3%	2.1%	2.0%	1.7%	0.8 %
Culture (+) rate SD	9.9%	2.6%	3.4%	3.5%	2.1%

Contamination rate (first L-J culture)



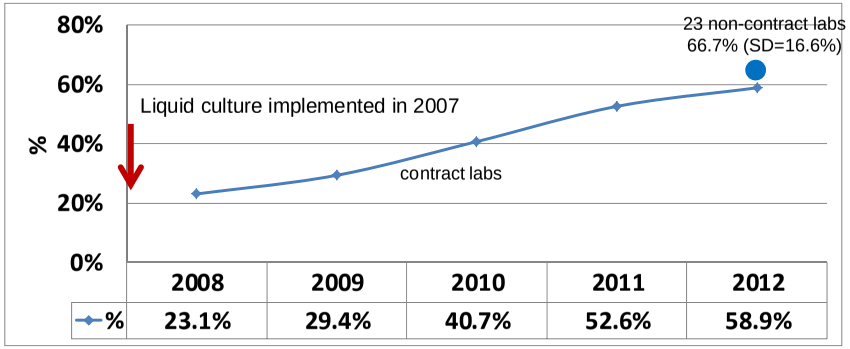
	2009	2010	2011	2012
%	2.2%	2.7%	3.0%	3.0%
SD	0.9%	1.3%	3.0%	1.1%

TAT accomplishing percentage of smear within 24 hours



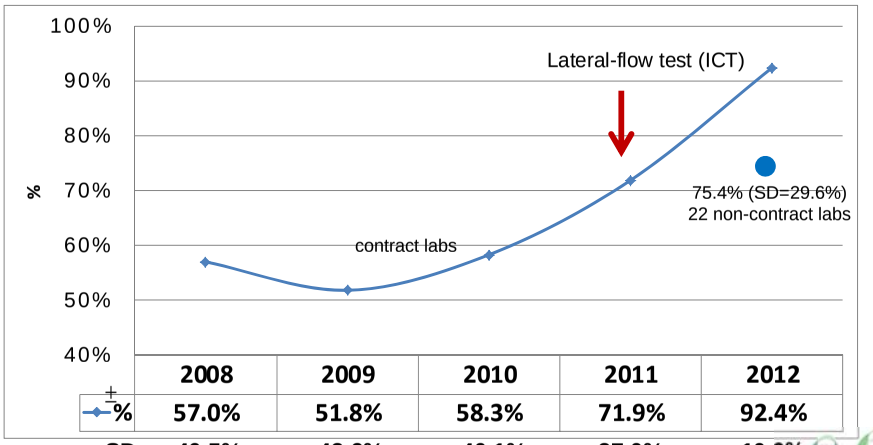
	2008	2009	2010	2011	2012
%	96.8%	99.5%	99.2%	99.8%	99.8%
SD	3.4%	0.4%	1.2%	0.2%	0.4%

TAT accomplishing percentage of culture (+) within 21 days



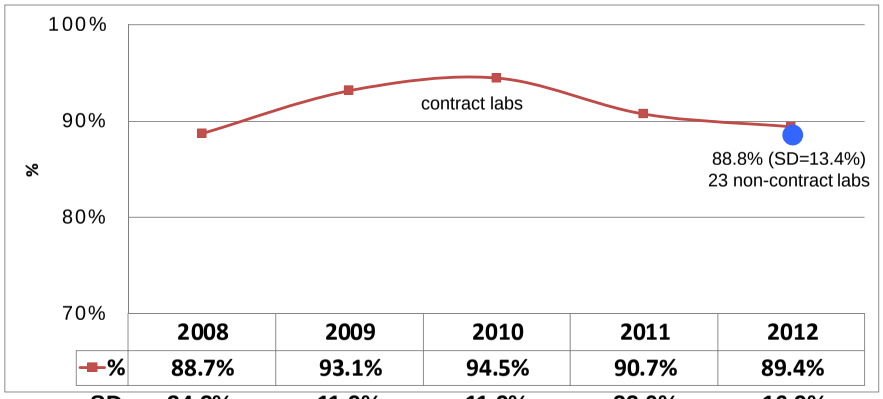
	2008	2009	2010	2011	2012
%	23.1%	29.4%	40.7%	52.6%	58.9%
SD	15.3%	11.4%	16.9%	17.4%	7.6%

TAT accomplishing percentage of ID-MTBC within 7 days (after culture positive)



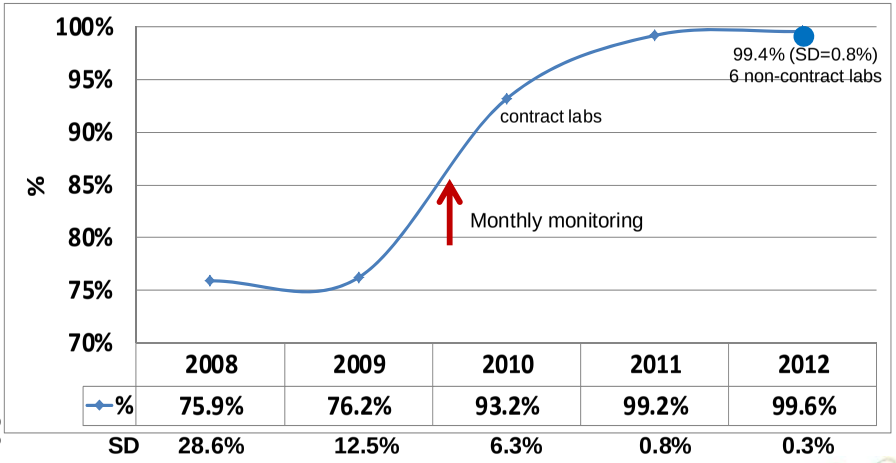
	2008	2009	2010	2011	2012
%	57.0%	51.8%	58.3%	71.9%	92.4%
SD	46.5%	43.9%	40.1%	37.0%	10.6%

TAT accomplishing percentage of DST within 28 days (after MTBC Identified)



	2008	2009	2010	2011	2012
%	88.7%	93.1%	94.5%	90.7%	89.4%
SD	34.2%	11.9%	11.9%	22.0%	16.9%

Specimen delivery within 3 days



	2008	2009	2010	2011	2012
%	75.9%	76.2%	93.2%	99.2%	99.6%
SD	28.6%	12.5%	6.3%	0.8%	0.3%

Conclusion

- TB diagnosis and quality management was standardized by contract labs and now are applying to all clinical tuberculosis labs.
- In contract labs, TAT on culture positive within 21 days (58.9%), ID-MTBC within 7 days (92.4%), and DST within 28 days (89.4%) varied widely among labs. Other indicators were stable with a small variation among labs.
- In other non-contract TB labs, smear positive rate (10.7% vs. 12.3%), culture positive rate (4.9% vs. 6.8%), contamination rate (6.0% vs. 3.0%), TAT of smear within 24 hours (97.4% vs. 99.8%) has rooms to improve.

Challenge

- Quality control on large quantity of specimen (≧740,000) in slow and time-consuming diagnostic methods
- Government budget restrain to support TB lab system
- No incentive to attract lab workers to work on TB diagnosis
- High biosafety requirements

Thank you for your attention!

DOTS Strategy and Patient Support in Taiwan

Kwei-Feng Wang,
Senior technical specialist
Third division
Taiwan CDC

Outline

- Introduction of TB patient support systems
- DOTS in Taiwan
- Indicators for DOTS
- Challenges and solutions

TB patient support

- ＊**Medical care**
  - @Free charge
  - @Pay for performance
  - @DOTS-plus
- ＊**Public health**
  - @Every patient has his/her own PHN
  - @DOT
- ＊**Social service**
  - @NGO
  - @Council of Indigenous Peoples

DOTS

(Directly Observed Treatment, Short-course)

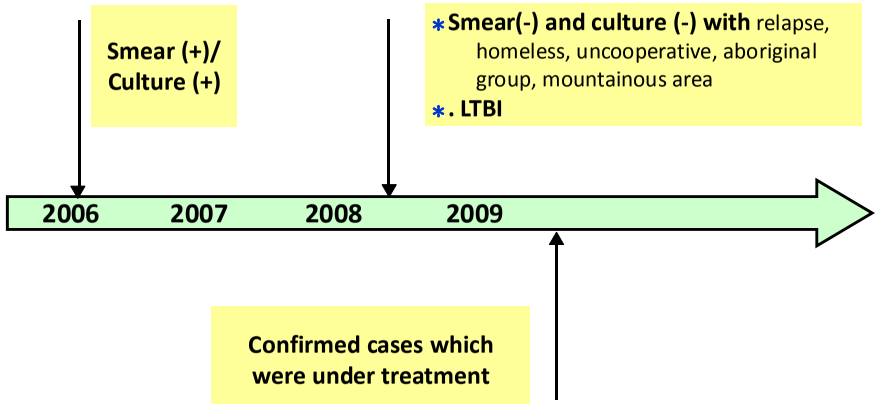
Large-scale implementation of DOTS program

- **Launched on 1 April 2006**
- **Each observer cares patient number**
  - Urban: 10-15 persons
  - Mountainous area: 5-10 persons

Purpose of DOTS

- **DOTS is a cost-effective strategy**
  - Attaining high cure or treatment completion rates
  - Reducing default
  - Avoiding emergence of drug resistance
  - Preventing relapse

Expanding DOT target groups



Resources of DOT

Years	DOT cases	Budget (US dollars, millions)	Observers
2006	4204	2	457
2007	12827	7.6	576
2008	14463*	8.3	673
2009	12003	9.6	652
2010	11914	10.3	680
2011	11312	11.7	694

* including DOPT of LTBI cases

Main tasks of different level of PH

- **Public health center**
  - TB case enrollment
  - Management of TB observer
  - Medication handling
  - DOT case management
  - Weekly conference
- **Local health bureau**
  - TB observer hiring
  - Medical consultation procedure
  - Supervision of public health center
  - Dealing with specific issue
  - Monthly meeting
  - Coordinate public health, medical and social sector
  - Education and training
- **TCDC branch**
  - Supervision of local health bureau
  - Coordinate public health and medical system
- **TCDC**
  - Policy making
  - Budgeting
  - Supervision

A health bureau director tries to persuade the patient to join the DOT program

Procedure of enrollment

DOT observer accompanies PHN to visit patients in the hospital

TB education and DOT program introduction

Meet patient at a designated site

Observation by pharmacist

Home visit

Tasks of DOT observer

- To deliver medication
- To watch patients taking pills
- To check side effects
- To report any event to the public health case manager
- To make documentation for each visit
- To assist patients with returning to the clinic on time
- To help patients getting social services

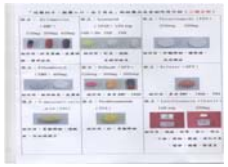
Training for DOT observers

- **Pre-service course: 16 hours**
  - TB basic knowledge
  - Introduction of DOTS program
  - Skill of building rapport with TB patients
  - Safety in the field work
  - Role play of DOT work
  - Communication skill
  - Orientation of the workplace
- **In-service course: 8 hours/year**
  - Anti-tuberculosis treatment and side effect
  - Case management
  - Sharing experience, especially difficult cases
  - Updated TB control policy

TB drugs storage in DOTS program

Cross check the medication

Anti-humidity cabinets



TB Drug instruction

Documentation of taking drug

Incentives in DOTS program

- **Purpose**
  - To breakdown the obstacles resulting in non-adherence
  - To encourage patients to retain in medical care
- **Examples**
  - Transportation vouchers
  - Grocery or food coupons
  - Food, powdered milk, meal box, bottled water

Transportation to hospital

Meal box and water

How DOTS program is monitored

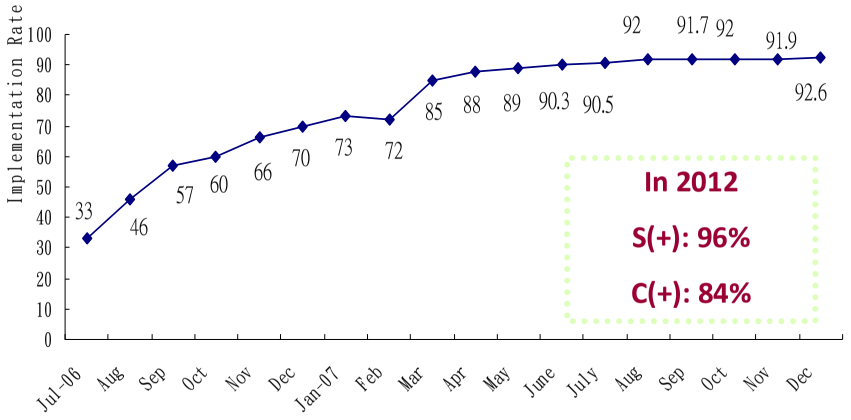
- **Weekly conference**
  - To review adherence, drug side effects, demand of social support, clinical and medical issues
  - To share information and experience, and give supports to team members
- **Evaluating program effectiveness by cohort analysis**
  - DOT coverage rate (the proportion of TB patients receiving DOT)
  - Proportion of each patient's medication administrated by DOT observer
  - Treatment completion rate
  - Sputum conversion within 3 months
  - Still on treatment after 6-9 months of anti-TB treatment
  - Number of Relapse/Treatment failure rate
  - Number of missed doses

Weekly DOT team meeting

Audit of DOTS program

- **Performed by staff of local health bureau and CDC branch offices**
- **Checking the DOT observers' schedule of drug delivery and records of DOT on the web-based system**
- **Randomly choose TB cases in DOT program through phone call to assess the satisfactory about DOT service**
- **On site evaluation**
  - Public health centers
  - Home visit

DOTS coverage rate for smear positive TB patients under management (Jul. 2006-Dec. 2007)



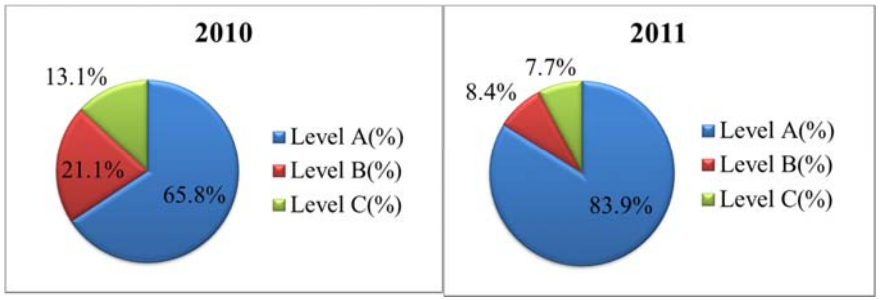
Evaluation of effect of DOT program

- Nation-wide TB patients who joined DOT program between 2007/1~2008/6
- Collaboration with US CDC
- A dose-response effect was found between proportion of DOT and these outcomes.

Proportion of days of DOT	Successful treatment	Unsuccessful treatment	Adjusted Odds Ratio
	n=9,344	n=2,184	
> 60% DOT	5,034 (53.9)	116 (5.3)	1.0
< 60% DOT	3,724 (39.9)	877 (40.2)	10.7 (8.7-13.1)
No DOT	586 (6.3)	1,191 (54.5)	73.1 (58.9-90.6)

E. Bloss et al. IJTLD 2012; 16(4):462-7

DOTS implementation quality in bacteriology confirmed cases



Treatment success rates among smear positive cases

Years (%)	2005	2006	2007
All cases	69.2	70.4	71.4
All S(+)	64.1	67.0	67.0
DOT		75	73
Non-DOT		49	32

Relapse within 2 years among new cases with complete treatment, 2005-2009

	2005		2006		2007		2008		2009	
	n	rate	n	rate	n	rate	n	rate	n	rate
New case	16,472		15,378		14,480		14,265		13,336	
Complete treatment	12,895		12,174		11,501		11,303		10,392	
Relapse within 2 years (all categories)	176	1.4%	126	1.0%	86	0.7%	76	0.7%	67	0.6%
<65y/o	100	1.4%	58	0.8%	52	0.8%	41	0.6%	39	0.7%
≧65y/o	76	1.4%	68	1.3%	34	0.7%	35	0.7%	28	0.6%
Relapse within 2 years/ smear positive case	119	2.8%	91	2.1%	54	1.2%	55	1.3%	51	1.3%
<65y/o	73	2.9%	44	1.8%	34	1.3%	32	1.3%	31	1.4%
≧65y/o	46	2.6%	47	2.6%	20	1.1%	23	1.3%	20	1.1%

Relapse in TB cases could be a proxy of efficacy for DOTS strategies.

Challenges and solutions

- **Efficiency and effectiveness of DOTS program**
  - Increasing the proportion of site DOT
  - E-DOT for younger population
- **Poor social supportive system**
- **Training public health nurses to figure out whether the TB patient need to be referred to social supportive system**
  - Incentives for public health nurses to report cases who need social support
  - Public communication
  - Integrating multi-disciplinary resources and communication with different units of government

Thanks for your attention!

衛生署疾病管制局

1. Overview of TB Control in Southern Territory
2. A TB Outbreak in a Veteran Nursing Home

Fourth Branch

Taiwan CDC
http://www.cdc.gov.tw

Southern Territory

- the Jurisdiction of the 4th Branch Office, TCDC

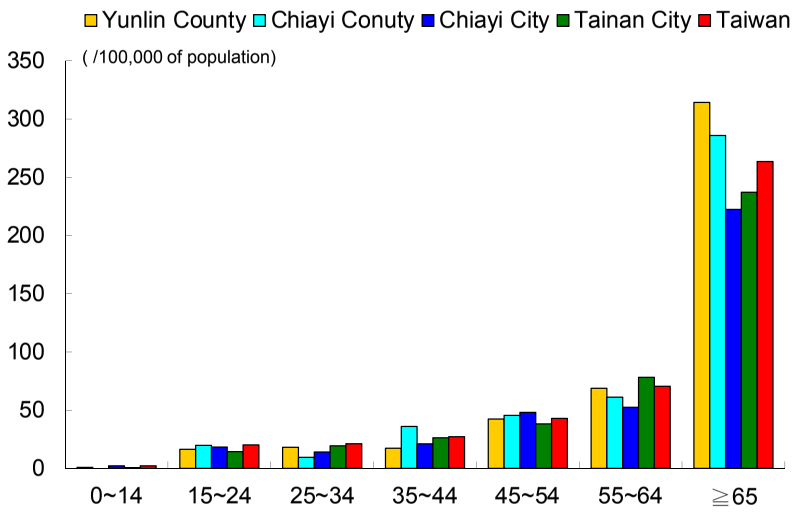
1. Overview of TB Control in Southern Territory

Demography of Southern Territory

	Yunlin County	Chiayi Conuty	Chiayi City	Tainan City
Population (person, x1,000)	711	534	271	1,880
Area (km^2)	1,290.8	1,903.6	60.0	2,191.7
Elderly Population [≥65 year-old] (x1000), (%)	110 **(15.4%)**	85 **(16.0%)**	31 (11.4%)	221 (11.8%)
Employed Population (x1,000)	327	255	118	885
Industry (%)	32.5	29.9	27.5	42.2
Service trade (%)	46.6	47.1	70.5	52
Agriculture, forestry, fishery and animal husbandry (%)	**20.9**	**23**	2	5.8

The elderly population in Taiwan is around 11%.

TB Incidence in Southern Territory by age groups, 2011



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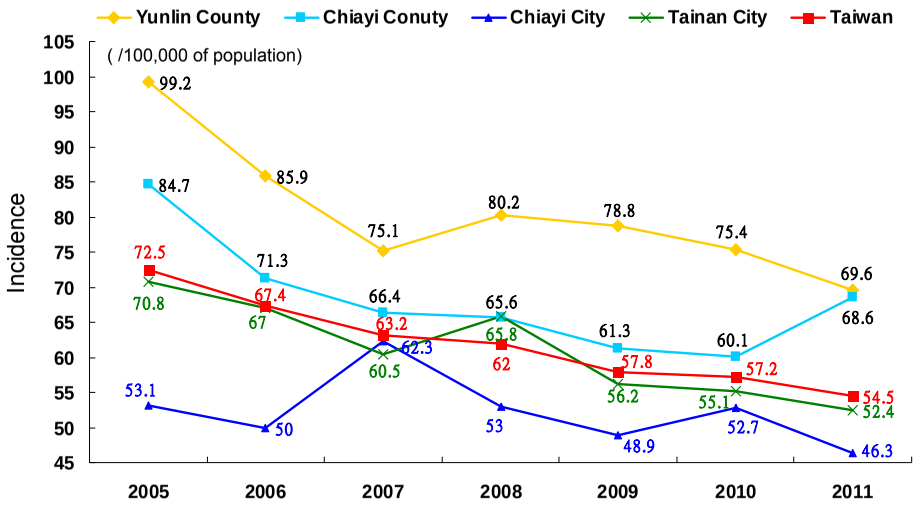
TB Incidence in Southern Territory, 2005~2011



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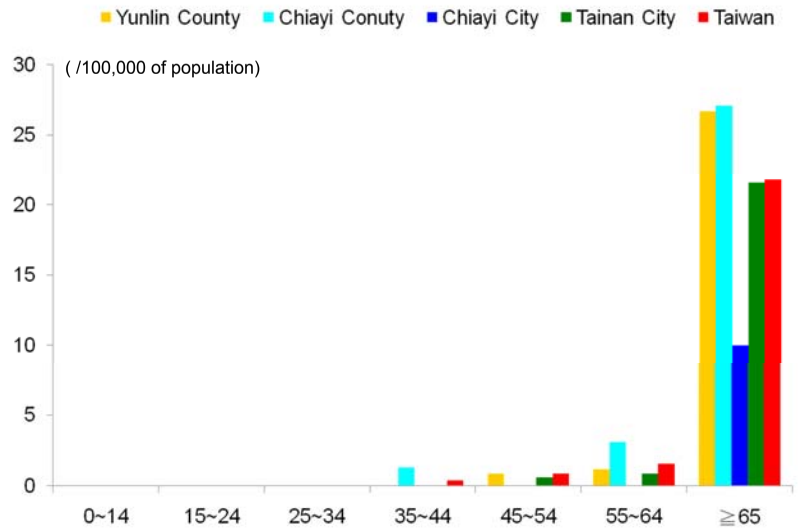
Age-specific Mortality, Southern Territory, 2011



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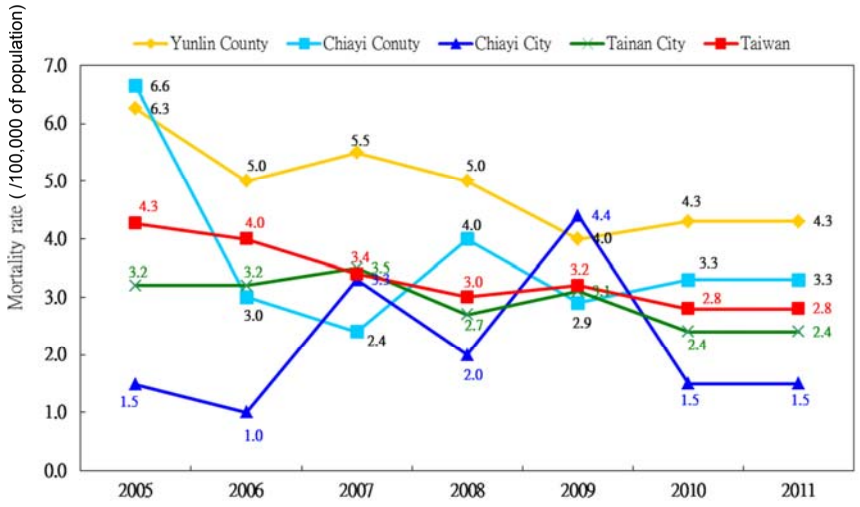
TB Mortality Rate in Southern Territory, 2005~2011



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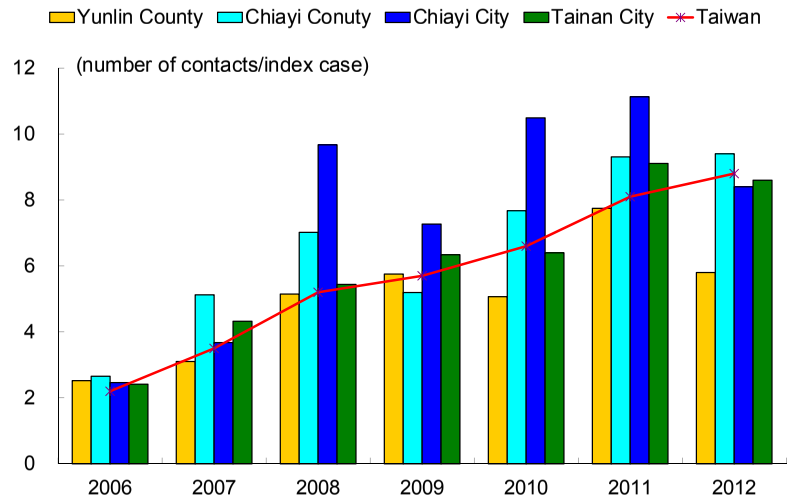
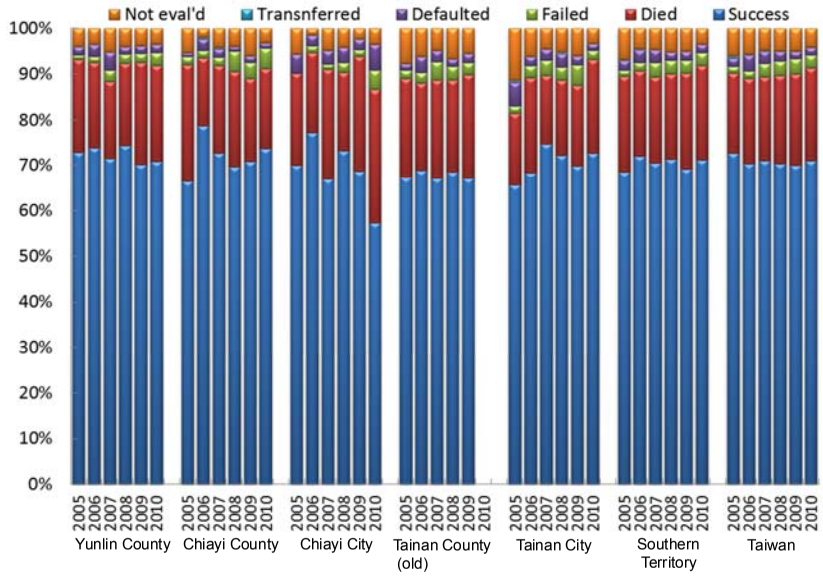
Contact investigation in Southern Territory, 2006~2012



Quality of DOTs in Southern Territory, 2010~2012

(DOTs: Directly Observed Therapy, short course)

Outcomes of TB treatment at 12th months, 2005~2010 Cohort



Challenges and solutions

Our growing elderly population

- Active case finding among patients with co-morbid diseases
- Creating the resident health database (Chiayi County)
  - may help future integration of active case finding among risk population

Pilot program in TB case finding among elderly DM patients (1)

- A cross-section survey in 2012 (Sep. to Nov.)
  - 3,087 participants with age ≥ 65 years comorbid with DM were enrolled
- Screening tool: CXR
  - Following confirmed TB: 6 cases, and 4 TB suspects
- Estimated incidence: 777.5/100,000
- Glycemia control among cases and non-cases: no significant difference

Unpublished data from Chiayi Chang Gung Memorial Hospital

Pilot program in TB case finding among elderly DM patients (2)

- Cost: ~41,000 USD
  - CXR screening: ~13 USD for each participants
  - Incentives for each participants
  - 4,100 USD needed to find one suspect TB
- Number needed to screen (NNS) = 551
- More operational research needed for further case finding strategies

Unpublished data from Chiayi Chang Gung Memorial Hospital

2. A TB Outbreak in a Veteran Nursing Home

"C" Veteran Hospital

- Total capacity: 658 beds; Staffs: ~600 persons
  - General wards: Acute 250, Chronic 53 (beds)
  - 8 Psychiatric wards: Acute 50, Chronic 175 (beds)
- Ancillary nursing home: 246 beds in 5 wards
  - Resident average age: 85 years old
- Residents and staffs of the Nursing home and Psychiatric wards
  - Staffs: Doctors: 10~14; Nurses: 58; Nurse aides: 58~60
  - Nursing home residents: 240~246
  - Psychiatric ward patients: 145~155

Outbreak scale

- Feb., 2010 to Nov., 2012
  - Residents of the nursing home: 33 confirmed cases (average: 80 y/o)
  - Psychiatric patients who are long-term cared
    - Patients: 14 confirmed cases (average: 51 y/o)
    - Nurses: 1 confirmed case (28 y/o, with the same genotype of some residents)
- Incidence: 3,233/100,000

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Molecular Genotyping

- Strain A: 2 residents of nursing home
- Strain B: 2 residents of nursing home
- Strain C: 2 residents of nursing home
- Strain D:
  - 3 residents of nursing home
  - 9 patients and 1 nurse of psychiatric wards
  - No solid epidemiological links between all of the TB patients from nursing home and psychiatric wards
- Poor ventilation was found while outbreak investigation

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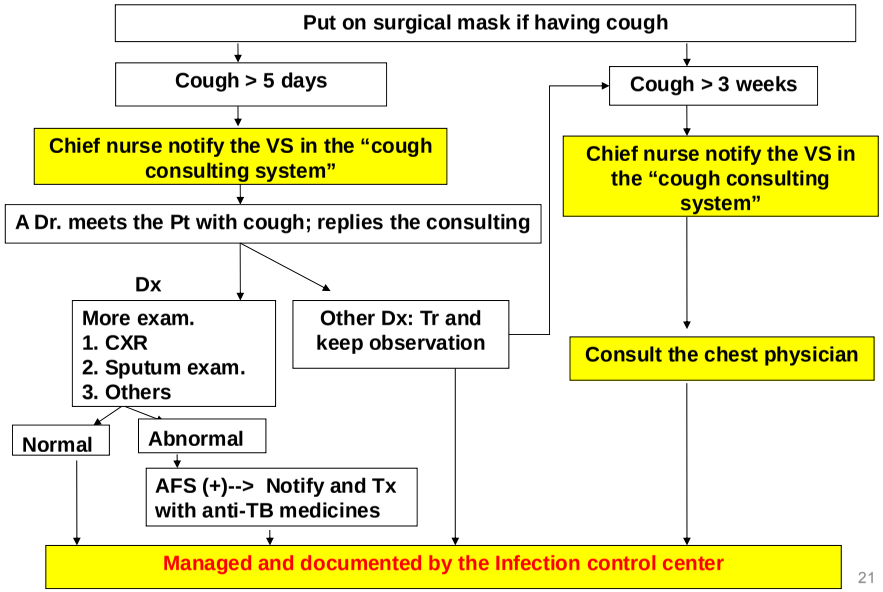
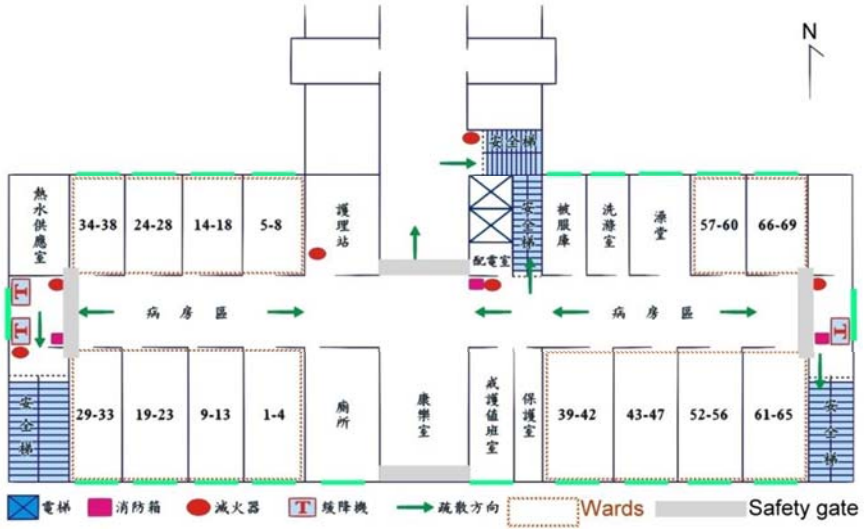
Cough surveillance in this hospitsl



Annual CXR examination

- Residents and patients: May ~ July
- Staffs: September
- Outsourcing staffs: July
- CXR: read by the radiologist
  - turn around time was not good enough, e.g., 1 patient was diagnosed almost 4 months after his clinical signs and CXR showed suspect TB
  - After the outbreak, pulmonologists provide second opinion, if needed

Ward Layout



149

精32-33
6FC

精神科第四病房


29


1115
6Fc
30


31


32

Mechanical ventilation before the TB outbreak

- Central air conditioning in every building
- Small indoor air-circulation conditioners in different rooms
- No effective ventilation in wards

33

34

35

36

The indoor air quality before the outbreak

One of the monitoring record

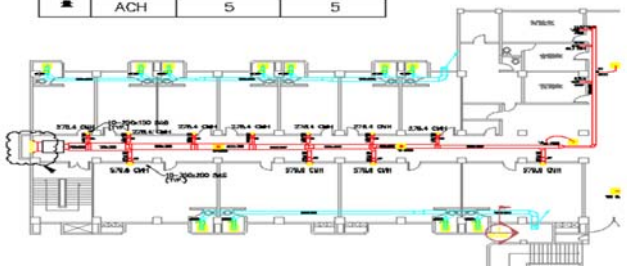
- Temperature: 25 ºC
- Relative humidity: 88%
- CO_2: 850 ppm (Standard: <1000; outdoor air: 300~500)
- TVOC (volatile organic compound): 1.5 ppm (Standard: <0.56)
- Bacteria: > 1000 CFU/m^3 (Standard: <1500)

Repairing and rebuilding the air conditioning systems

- Outdoor ACH ≥ 4 in the Building D
  - Automatically adjustment
- Outdoor ACH ≥ 2 in other buildings

		大病房	小病房
容積	M^3	144.9	69.6
外氣量	風量 CMH	579.6	278.4
	ACH	4	4
排氣量	風量 CMH	724.5	348
	ACH	5	5

- Measured room by room



Challenges and solutions

Infection control in long-term care facilities

- Cough surveillance is difficult in psychiatric patients
- Ventilation
  - Lack of environmental engineering expert
  - "Higher cost to maintain adequate ventilation" for "Lower risk of airborne disease transmission"
  - No national standards of ACH in health care facilities (currently, CO_2 concentration is the surrogate)

Acknowledgement

- Li-jing Zhang (張麗菁)
- Qiao-wen Lin (林巧雯)
- Dr. Pin-Hui Lee (李品慧醫師)
- Preventive Medicine Office, TCDC
- "C" Veteran Hospital

Thank you.

TB Control Strategy and Future Prospects in Tainan

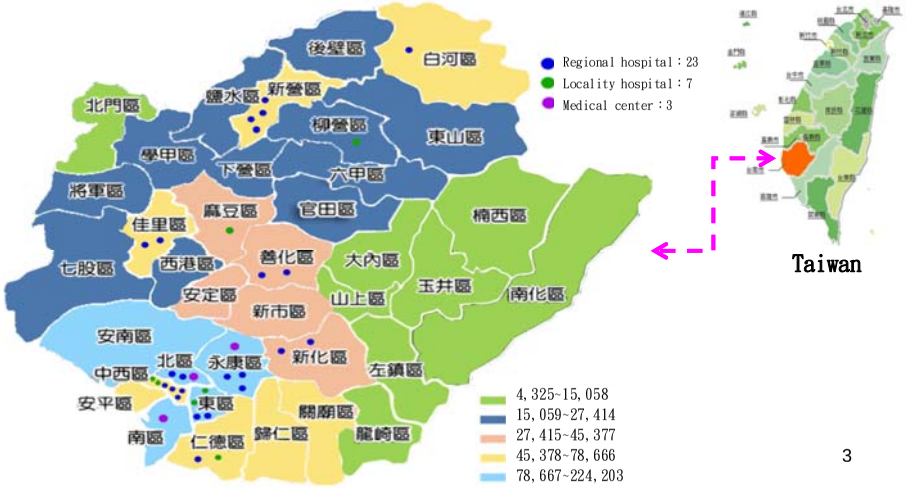
Sheng–Che Lin, Director
Department of Health,
Tainan City Government

Outline

- Current Status
  - -Incidence
  - -Mortality Rate
- Tuberculosis Control Strategy

The density of population and hospital in Tainan

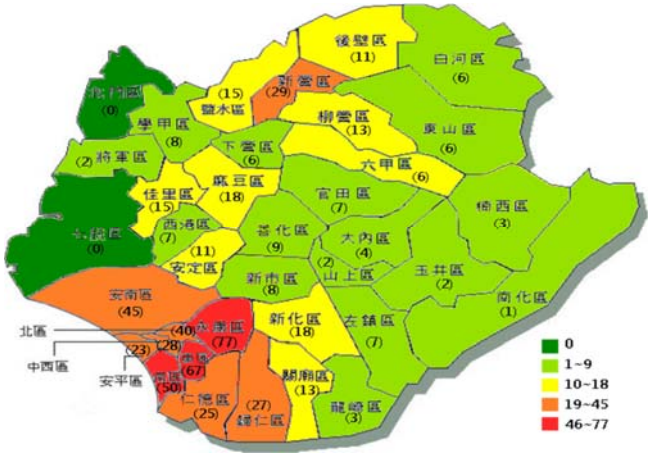
population：1,881,645



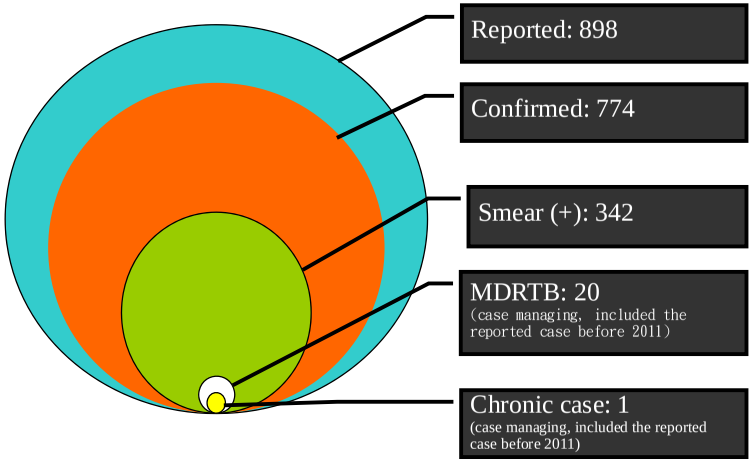
Managed Case Distribution

download date：2013/01/29

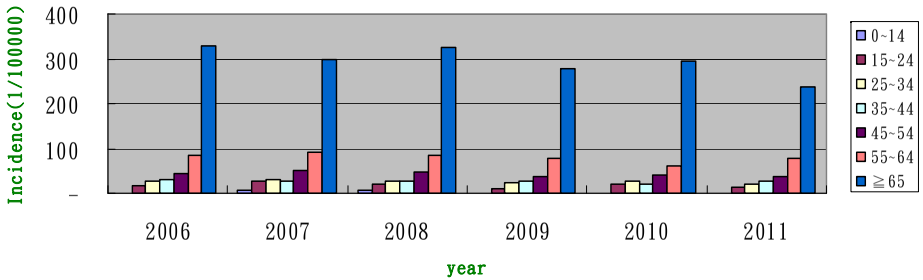
612 patient



Numbers of Reported and Confirmed TB Cases in Tainan, 2011

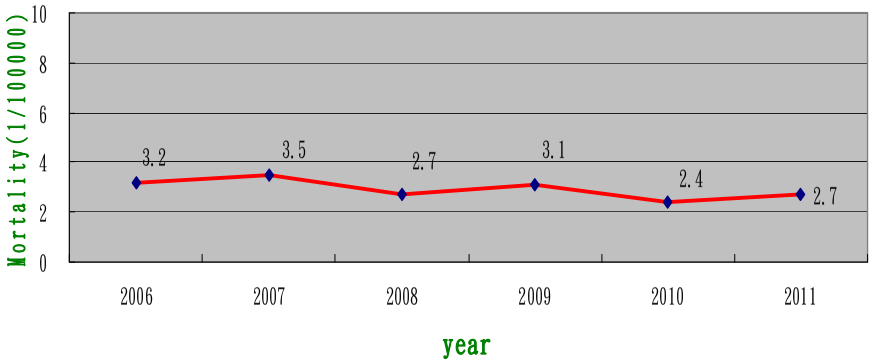


Age Distribution of Newly Confirmed Cases in Tainan, 2006-2011



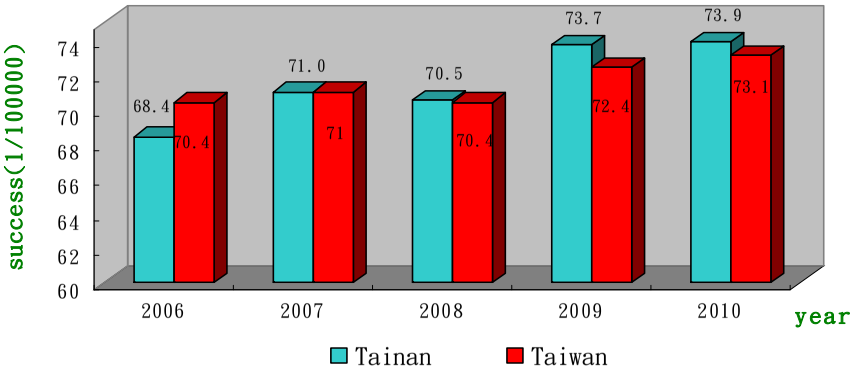
year	0~14	15~24	25~34	35~44	45~54	55~64	≧65
2006	0.7	18.4	25.5	29.6	45.4	84.8	328.2
2007	6.3	27.1	29.6	27.3	49.2	90.6	299.3
2008	6	19.3	27.2	26.1	46	85.8	324.4
2009	0.6	11.8	22.6	27.9	36.4	77.4	279.3
2010	0.8	19.7	28.4	20.8	42.3	61.2	294.3
2011	0.7	14.4	19.4	26.3	38.2	78.2	237.1

TB Mortality Trends in Tainan, 2006-2011

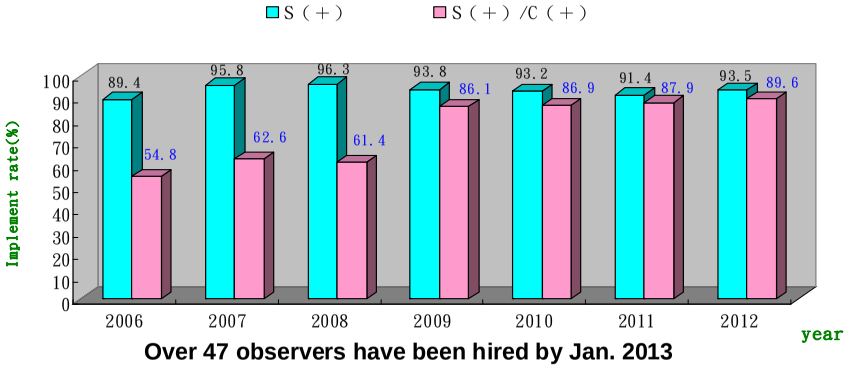


TB deaths in Tainan, 2011：51

The Treatment success rate contrast between Tainan and Taiwan, 2006-2010



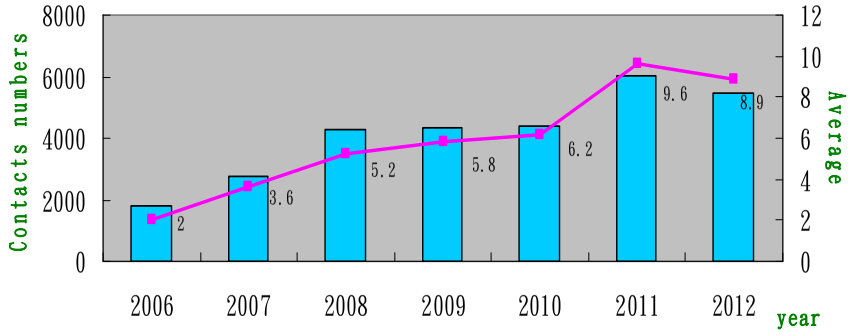
DOTs Coverage Rate for S(+) / S(+)C(+) TB in Tainan



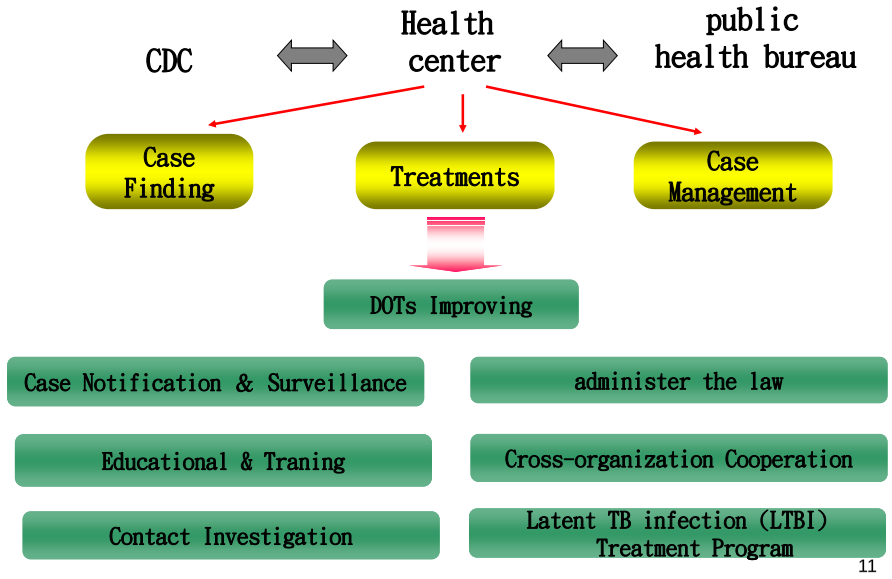
Over 47 observers have been hired by Jan. 2013

* In 2012, The DOTs coverage rate was at 93.5/89.6 in Tainan and the quality of treatment has greatly improved with constant supervision and reviews.
* In addition, treatment success rates for S(+) cases increased gradully.

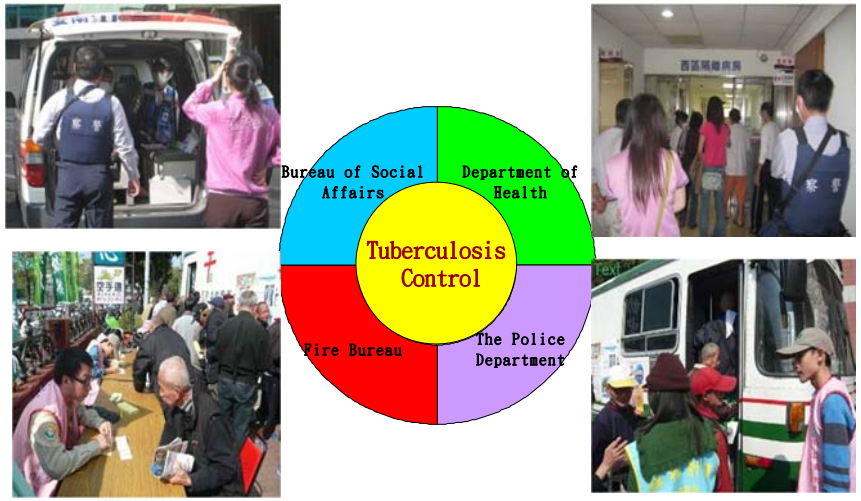
Contact Investigation Numbers per TB case in Tainan



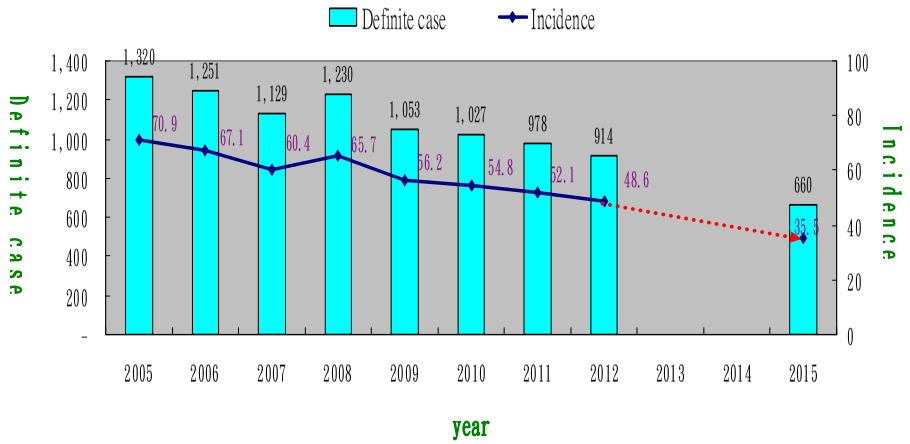
Tuberculosis Control Strategy



Cross-organization Cooperation



"Mobilization Plan to Reduce Tuberculosis by Half in Ten Years" Incidence in Tainan, 2006-2015



Halve the incidence rate(70.9 per 10^5 population→35.5 per 10^5 population)

Future Prospects

- Achieve annual reduction of new tuberculosis cases and lower the incidence rate to 36 per 100,000 population by year 2015.

Thank you for your attention

衛生署疾病管制局

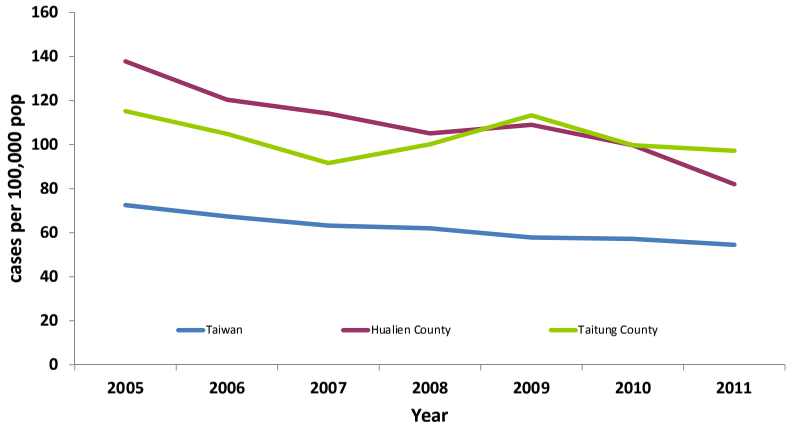
TB in Eastern Taiwan

Sixth Branch

Uniqueness of Eastern Taiwan

Characteristics	Hualien	Taitung	Taiwan
Area	4628 km^2	3515 km^2	36,193 km^2
Total population	336,485	226,252	23,315,822
Aboriginal	91,067 (27%)	79,437 (35%)	527,767 (2.3%)
Pop density	72/km^2	64/km^2	643/km^2
Ave. area per medical facilities	16.83 km^2	22.25 km^2	1.7 km^2

Incidence of tuberculosis in Eastern Taiwan, 2005 – 2011



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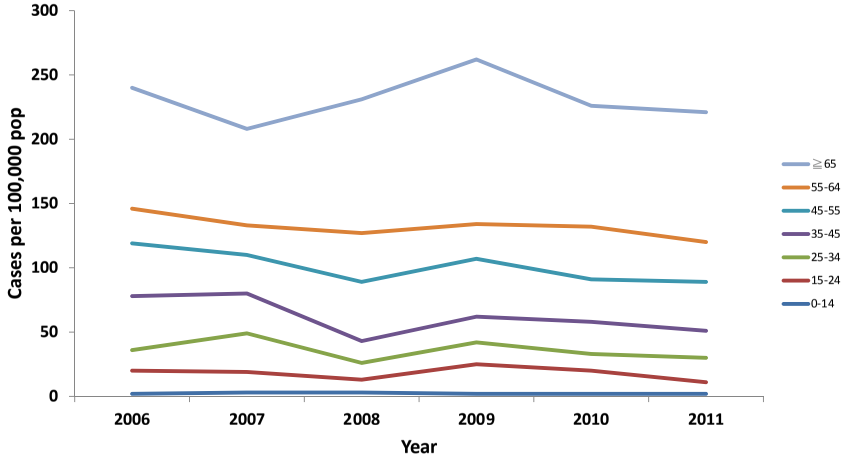
Incidence by age, Taitung, 2006 – 2011



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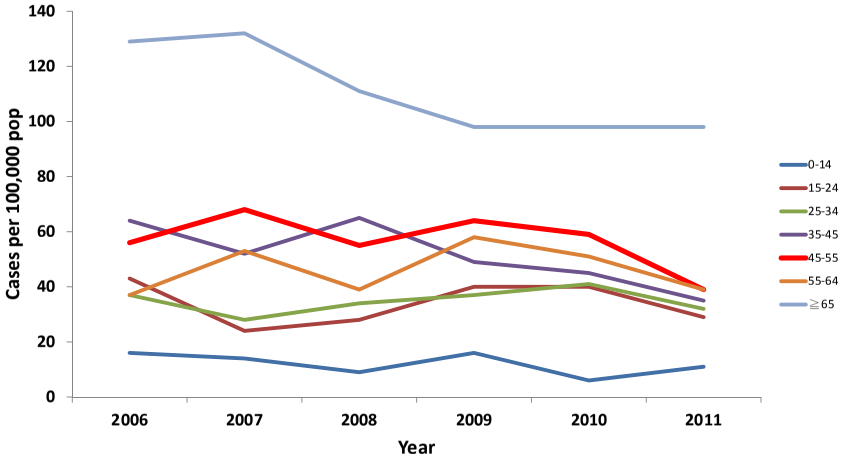
Incidence by age, Hualien, 2006 – 2011



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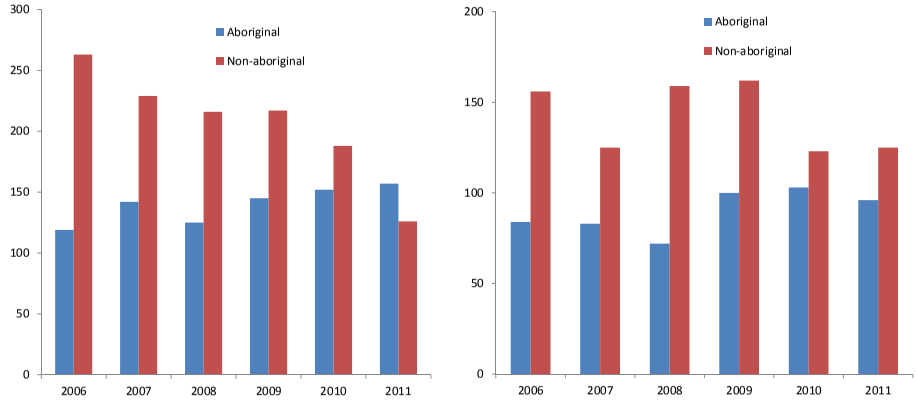
Aboriginal and Non-aboriginal cases in Eastern Taiwan, 2006 – 2011

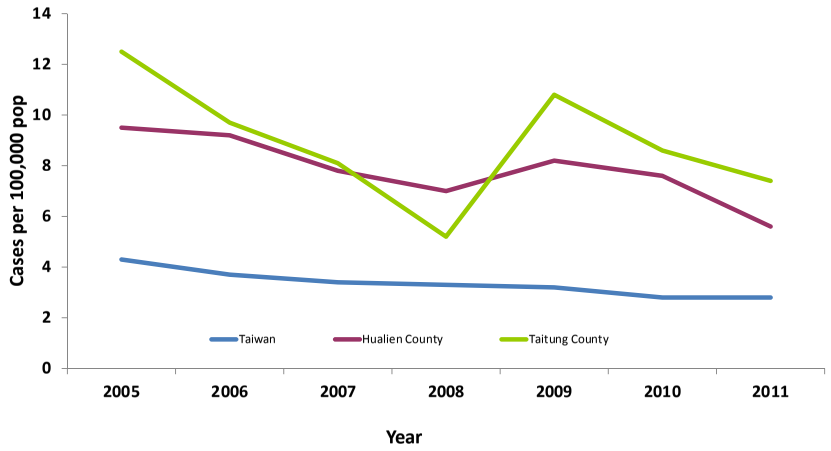


Hualien

Taitung

8

Tuberculosis mortality in Eastern Taiwan, 2005 – 2011



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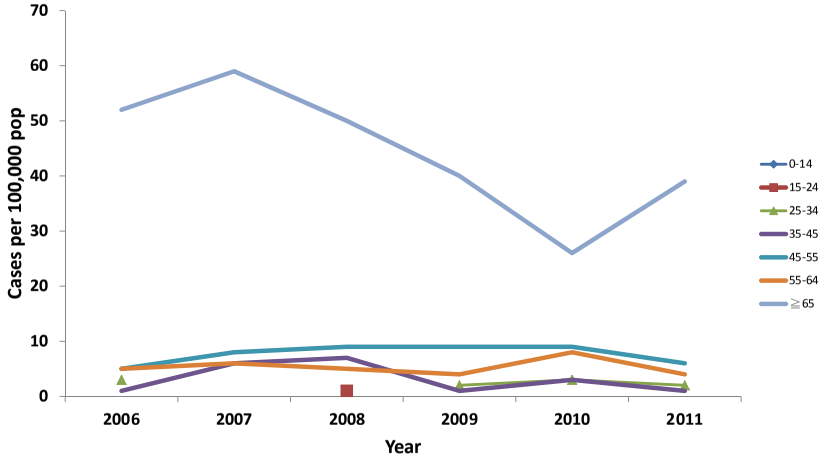
Mortality age distribution, Hualien, 2006 – 2011



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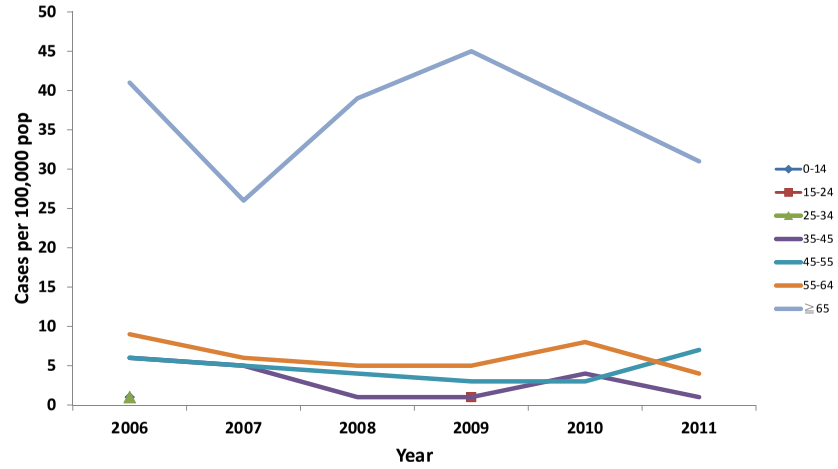
Mortality age distribution, Taitung, 2006 – 2011



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MDR-TB transmission in Hualien

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Current Status and Problems in Eastern Taiwan

- Highest incidence and mortality rates
- Slow decrease in incidence and mortality under TB Control Program
- Major public health problem among aboriginal people
- MDR-TB transmission
- Outbreak of tuberculosis in long term care facility

Tuberculosis outbreaks in long term care facilities

TB outbreak management manual

- Define clusters and outbreaks
- Surveillance
- Administrative process
- Cluster/Outbreak management

TB clusters and outbreaks definition

- Suspected clusters
  - Person: ≥2 confirmed cases
  - Place: in the same institution with close contact
  - Time: reported within one year
- Possible cluster
  - No genotyping available, and expert panel could not rule out epidemiologic linkage
- Outbreak
  - At least two cases with indistinguishable genotype by RFLP, VNTR-MIRU, or spoligotyping

Surveillance

- Case management system allows search by specified groups
  - Institutions
  - Schools
  - Other work places
- Index case investigation should include information on occupation and workplace
- Local health bureau should look for possible clusters every week

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Administrative process and division or work

- Local health bureau should complete initial investigation and submit report within 10 working days
- TCDC branch office to verify if the cluster is an outbreak within 5 days, and report to Third Division
- Third Division should coordinate inter-jurisdictional contact investigation

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Management of institutional outbreaks

- Onsite investigation: ventilation, contacts
- Contact investigation and LTBI treatment
  - Active case finding: CXR every 6 months for 2 years
  - LTBI treatment for those born after 1985
- Assessment of case isolation
- Rule out laboratory contamination
- Convene expert committee meeting to decide on extent of contact investigation

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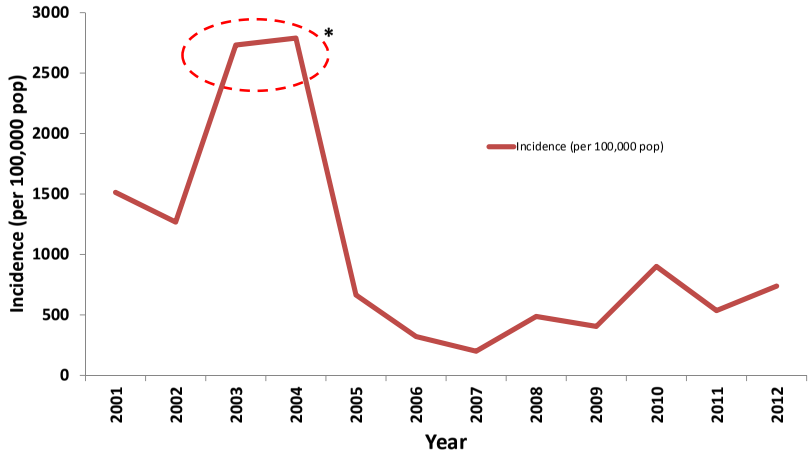
Hospital L

- 2796-bed hospital and nursing home
- Provide long term psychiatric care
- Designated a psychiatric hospital in 1985
- Expanded in 1989 to enhance and improve community medical services
- Average duration of admission: 10 years
- 45% of patients ≥65 years

20

Incidence of TB in Hospital L, Jan 2001–July 2012



*Han-Yu Huang et al. J Formos Med Assoc (2007.Vol 106.No 12)

Outbreak at Hospital L

- 8 cases reported during Dec 23-30, 2010
- Retrospective review
- During 2009–2012
  - 62 cases confirmed
  - 51 cases culture positive
- RFLP performed on 47 isolates
  - 20 isolates in 5 clusters, A (2), B (7), C (3), D (3), E (5)
- Frequent transfer within the hospital made epidemiologic linkage difficult to identify

Comparison of TB diagnosis time

Period (days)	Hospital L	Taiwan
CXR to sputum examination		
Mean	18.3	5.6
Median (min, max)	9.0 (0.0, 77.0)	2.0 (0.0, 418.0)
Sputum examination to diagnosis		
Mean	27.6	18.5
Median (min, max)	33.2 (2.0, 85.0)	20.6 (1.0, 55.0)
CXR to diagnosis		
Mean	37.0	13.2
Median (min, max)	35.0 (0.0, 128.0)	5.0 (0.0, 424.0)
Diagnosis to treatment initiation		
Mean	0.7	0.6
Median (min, max)	0.0 (0.0, 5.0)	0.0 (0.0, 288.0)

Summary

- Large outbreak of TB at a psychiatric hospital providing long term care
- Patients frequently transferred from one ward to another, making it difficult to establish epidemiologic linkage
- Significant delay in diagnosis
- Repeated contact with source patients

Intervention

- Active case finding
  - Semi-annual screening all staff and patients by CXR
  - Cough surveillance
- Infection control program with standard operation procedures
  - Administrative controls: transferring patients to isolation room as soon as possible
  - Maintain high level of suspicion of TB
  - Engineering controls
- LTBI diagnosis and treatment in targeted group?

Next steps?

The Implementation of TB Control in Hualien County

Hualien County Health Bureau

花蓮縣衛生局

Humanistic Background Data

花蓮縣衛生局 Hualien County Health Bureau

Area（proportion of Taiwan %）	4,628.5714 Km² (12.8%)
Administrative regions	1 City, 12 Townships, 177 Villages, 3,656 Neighborhoods
Population Density	72.42 people/Km²
Total amount of population (Aborigines %)	335190 people （27.14 %）
Men	172,064（51.3%）
Women	163,126（48.7%）
Crude Birth rate	9.93‰
Crude Death rate	9.40‰
Natural growth rate	0.53‰
Age>65 y/o	43365（12.94%）

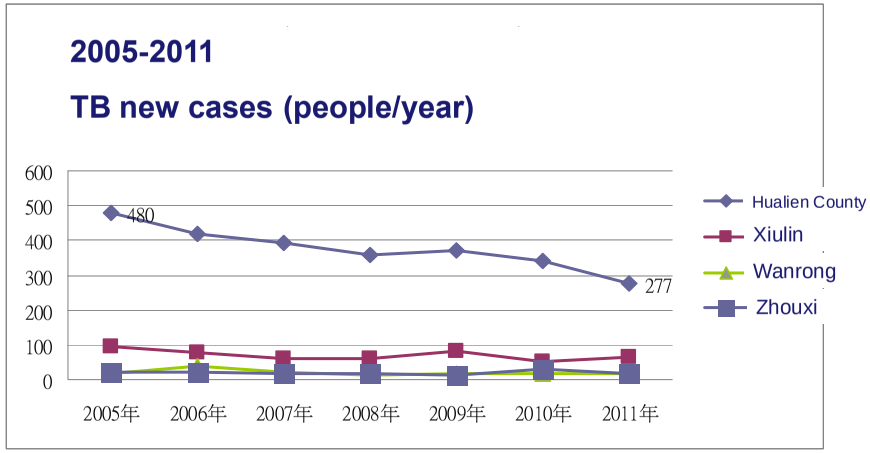
Data: till Dec., 2012

Maximal population density: Hualien City 3698people/km²

Minimal population density: Zhuoxi Township 6.10people/km²

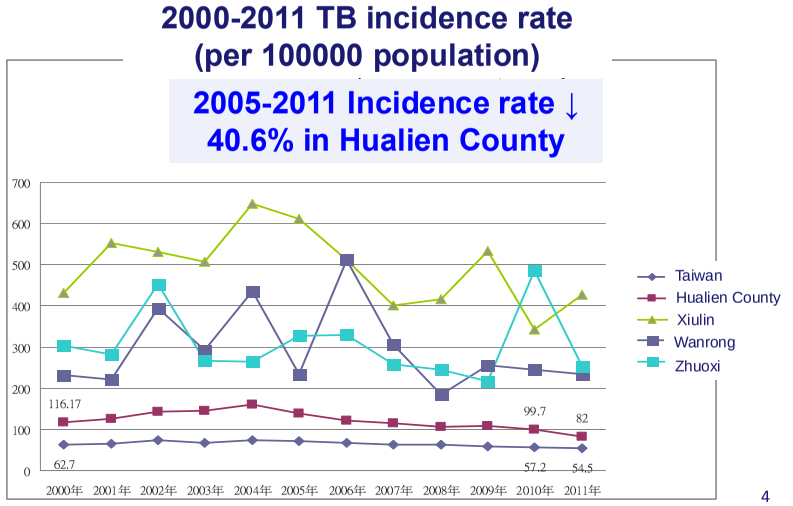
Our achievement in pushing TB prevention plans in last few years

花蓮縣衛生局 Hualien County Health Bureau



Our achievement in pushing TB prevention plans in last few years

花蓮縣衛生局 Hualien County Health Bureau



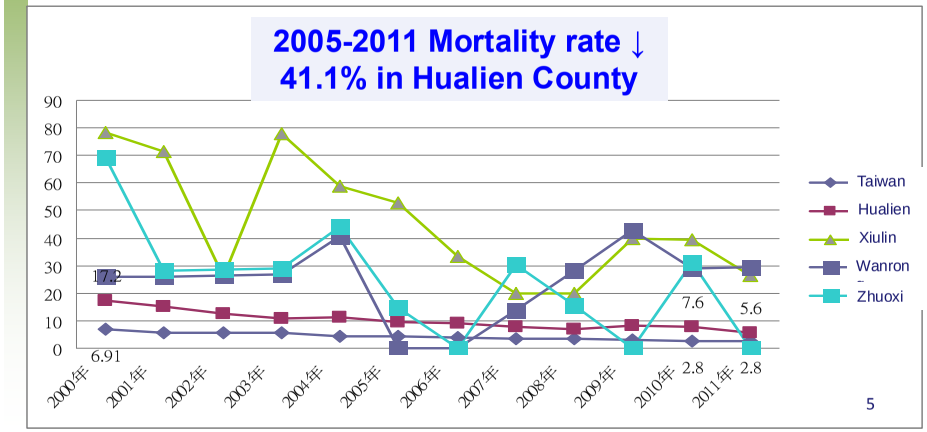
Our achievement in pushing TB prevention plans in last few years

Hualien County Health Bureau

2000-2011 TB mortality rate

(per 100000 population)

2005-2011 Mortality rate ↓ 41.1% in Hualien County

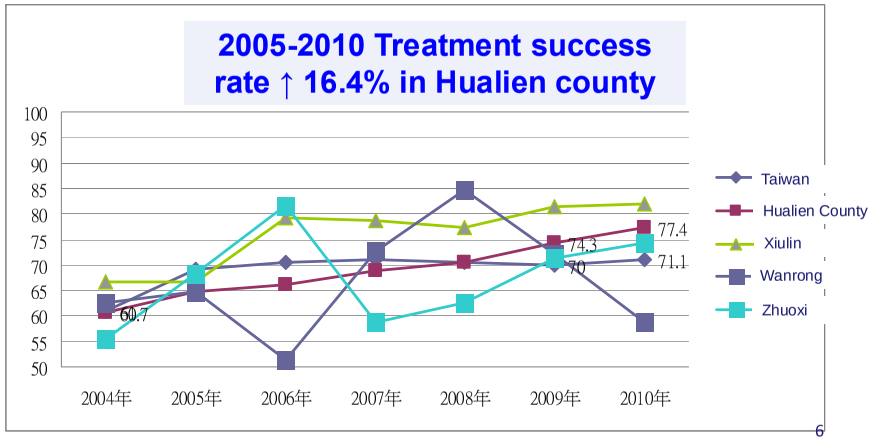


Our achievement in pushing TB prevention plans in last few years

Hualien County Health Bureau

2004-2011 TB treatment success rate (%)

2005-2010 Treatment success rate ↑ 16.4% in Hualien county



Promote TB Control Program

Hualien County Health Bureau

We applied "**3 levels and 5 grades**" on TB prevention in Hualien.

Susceptible Period	
Promote Health	Special Protection
1st Level Prevention	

Presymptomatic period	Clinical Period	Disability Period
Early Diagnosis Early Treatment		To Limit Disabilities
2nd Level Prevention		3rd Level Prevention

1st Level Program
- Recruit Community Volunteers
- Strengthen Community Health Education

2nd Level Program
- CXR Screening
- Referral
- Treatment

3rd Level Program
- DOTS

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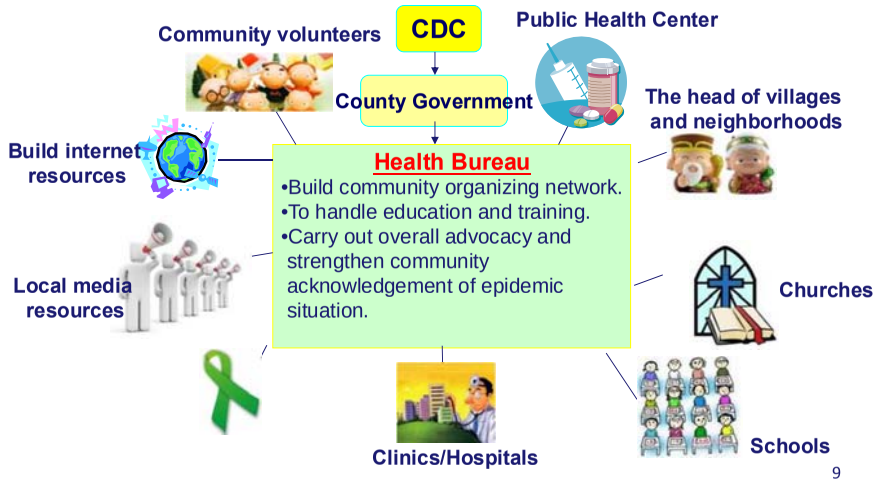
Cultural characteristics of Mountain Tribe

Hualien County Health Bureau

- Alcoholism
- Bad living environment
- Information was not universalized
- Unstable job and moved around→ not easy to F/U.

Combining Resources and Elevating the Power of Disease Prevention Comprehensively

Hualien County Health Bureau



Our Plans This Year

Hualien County Health Bureau

1. Find the source of infection: TB 7-point screening test

Our Plans This Year

Hualien County Health Bureau

Our Plans This Year

Hualien County Health Bureau

2. Arrange chest X-ray examination in every remote tribes

- X-ray truck

2. Arrange chest X-ray examination in every remote tribes

Hualien County Health Bureau

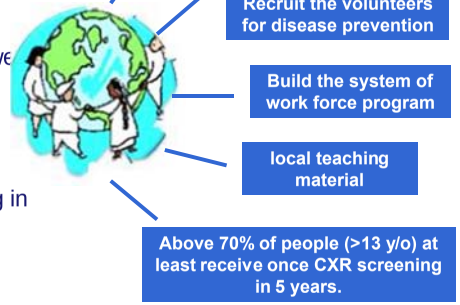
- Prior screenings in
  - High risk areas, worse living environment and other specific areas such as high incidence of TB occurrence.
- Specific population (economically disadvantaged groups)
- Follow up the screening schedules regularly.
- Combine with health education in each fa
- Strengthen the incentives
  - Public health center
  - The general public

Our Plans This Year

Hualien County Health Bureau

3. Upgrade the acknowledgement and build consensus

- Plan and promote the basic architecture of TB prevention league.
- Build the cooperative organizations for TB prevention.
- Build the system of work force program and push local labor powe
- Make and use local teaching material.
- Build CXR screening database.
- Above 70% of people > 13 y/o at least receive once CXR screening in 5 years.



Our Plans This Year

Hualien County Health Bureau

4. Cooperate with teachers and students in schools, community organization and churches to push TB prevention.

- Teach correct information about TB prevention in every tribe.
- Encourage people to receive TB screening regularly.
- Educate people in society to pay attention to people around themselves.

Our Plans This Year

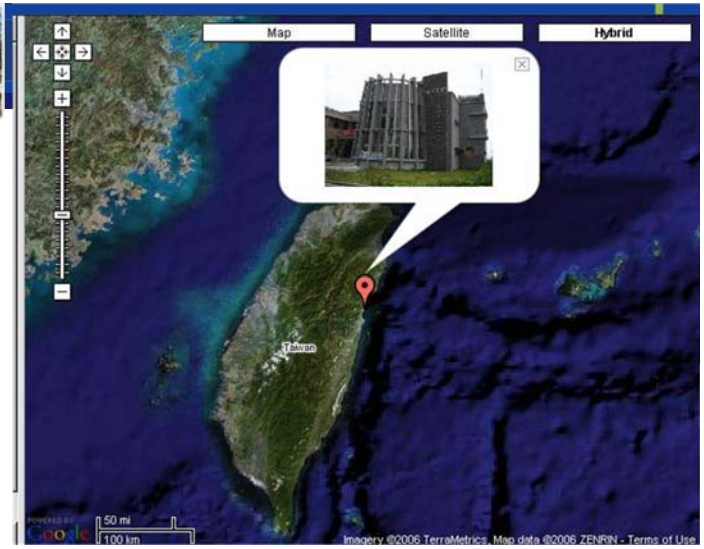
Hualien County Health Bureau

5. To push work force program in remote tribes.

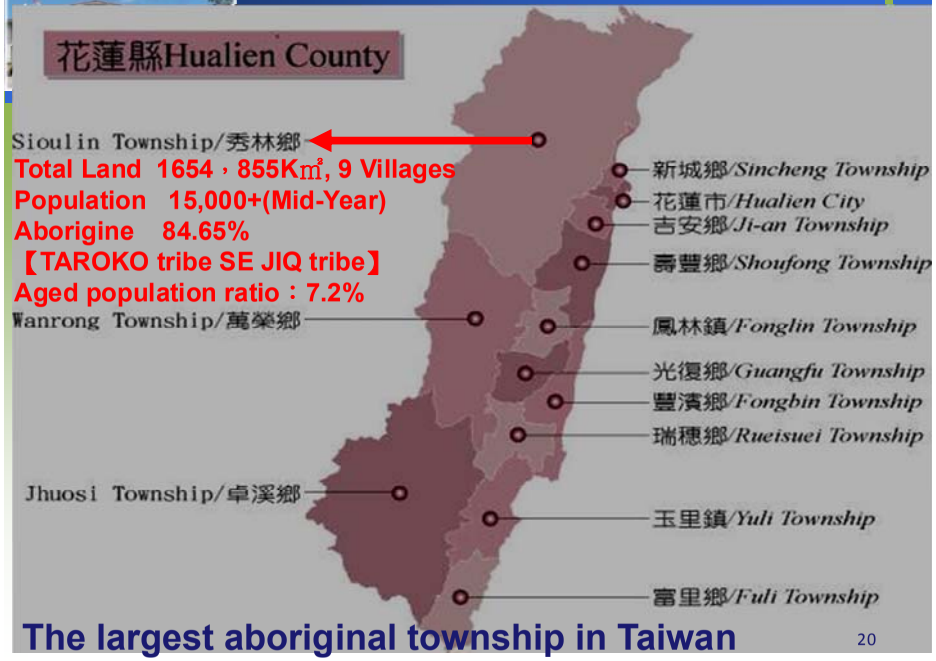
- We provide work subsidy for people in remote tribes.

Try to roll a snowball!

~Thanks for your listening~



Welcome to Sioulin Health Center



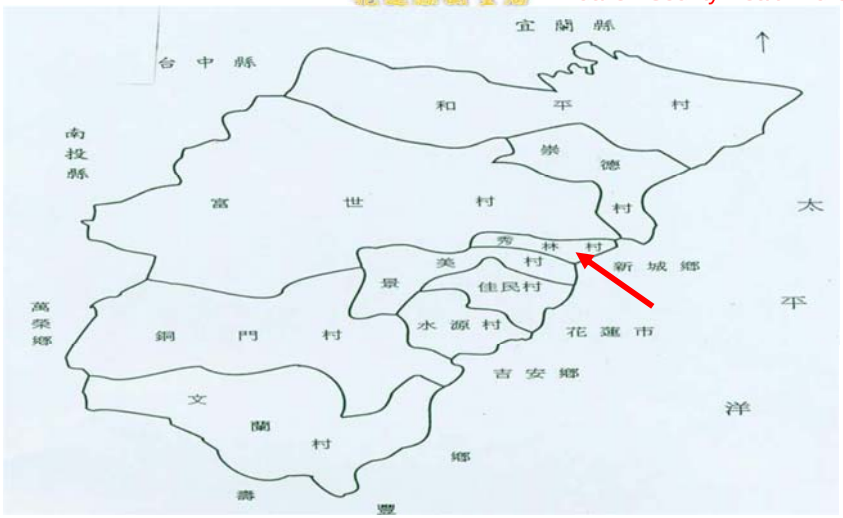
Vital Statistics

Hualien County Health Bureau

- The crude birth rate：12.2 ‰
- The crude death rate：12. ‰
- Natural growth rate：0.20‰
- Migratory rate：0 ‰
- Aged population ratio：7%
- Dependent population ratio：38.8%

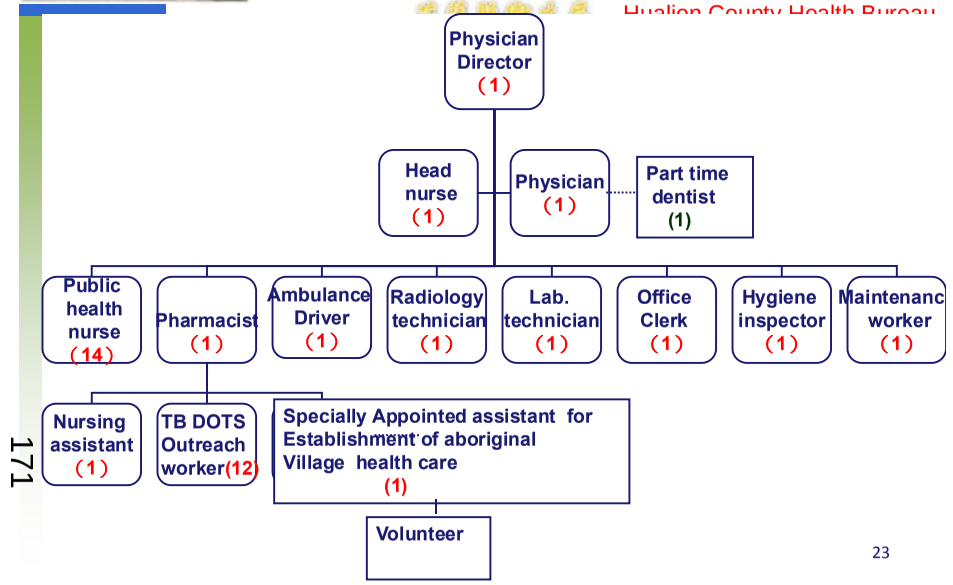
Health Center and 9 Health Units

Hualien County Health Bureau



Organization of Sioulin Health Center

Hualien County Health Bureau



Public Health Affairs

Hualien County Health Bureau

- Health promotion
- Epidemic prevention
- Medical practice
- Hygiene inspection
- Emergent care（Hehuan Mt. snow season medical service、transport of acute psychosis patients、holiday on call）
- Health administration

Health Promotion

Hualien County Health Bureau

- Family planning
- Mother & infant health
- Preschool age and School age health
- Long term care
- Health education
- Betel nut, tobacco and alcohol control
- Substance Use
- Chronic Disease prevention and control
- Cancer screen (oral ca, Cx ca,colon ca….)
- Establishment of aboriginal village health care

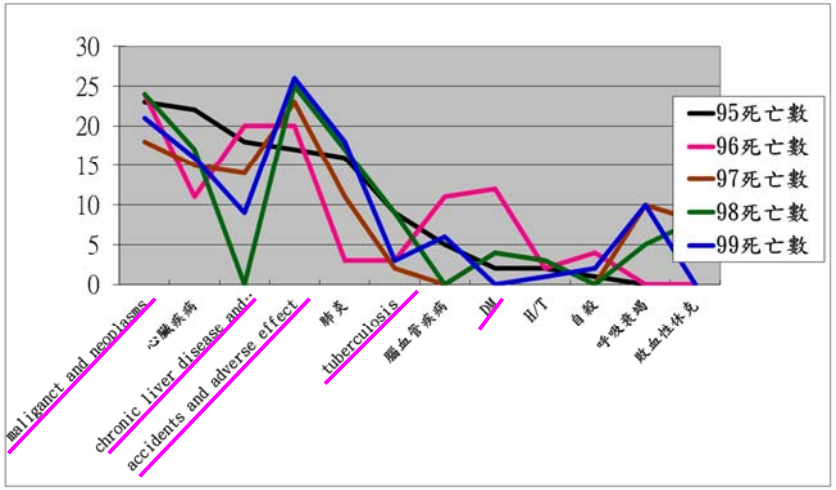
Medical Practice

Hualien County Health Bureau

time	Mon		Tue		Wen		Thu		Fri	
	Dr. Tien	Dr. Wang	Dr. Tien	Dr. Wang	Dr. Tien	Dr. Wang	Dr. Tien	Dr. Wang	Dr. Tien	Dr. Wang
AM 8:00 ~ 12:00	Health center	**Mobile Clinic**	**Mobile Clinic**	Health center	Health Center	**Mobile Clinic**	Health center	**Mobile Clinic**	Health center	**Mobile Clinic**
PM 1:30 ~ 5:30	**Mobile Clinic -village**	Health check up In village	Health center	**Mobile Clinic**	**Mobile Clinic**	Support Hulien Health center	**Mobile Clinic**	Health check up In village	Health center	**Mobile Clinic**

Cause of Death

Hualien County Health Bureau



IDS（Integrated Delivery System）

Hualien County Health Bureau

- NHI provide the reimbursement program
- To improve accessibility, equability, quality of medical services for areas without adequate medical resources
- Implemented in 48 remote mountainous areas and offshore islands since 1996
- Cooperation between hospitals and local medical resources
- General satisfaction over 90%

Medical Service of IDS

花蓮縣衛生局 Hualien County Health Bureau

- Rehabilitation twice a week
- Internal medicine（Chest and GI）once monthly
- Ophthalmologist once monthly
- Pediatric once a week
- Family practice 3 mobile clinics/week
- ENT once monthly
- Holiday emergency clinic every Sat and Sun
- Traditional Chinese medicine clinic every Tue

Other Service of IDS

花蓮縣衛生局 Hualien County Health Bureau

- Health promotion and education
- Referral
- Free medical service once per month
- Health care for women (Pap smear, pregnancy)
- Health care for children (screening and vaccination)
- Health care for adults (prevented medicine)

Incidence of Tuberculosis

花蓮縣衛生局 Hualien County Health Bureau

year	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Taiwan	62.7	64.84	74.6	66.7	74.1	72.5	67.4	63.2	62.0	57.8	59.12
Hualien	116.17	126.21	142.4	145	160.8	137.8	120.4	114.1	105.2	109	100.06
Sioulin	431.4	552.99	529.9	467.4	647.3	612	511.3	400.6	415.4	533.1	328

Process of TB Control in Sioulin【1】

花蓮縣衛生局 Hualien County Health Bureau

- Check new informed cases twice a day through internet to confirm new cases management
- To notify public health nurse and DOTS outreach worker
- Case and family visit for outbreak investigation and health education
- DOTS management for open TB
- X-ray examination for contactors
- Sputum AFB smear and culture monthly
- X-ray examination every two months

Process of TB Control in Sioulin 【2】

花蓮縣衛生局 Hualien County Health Bureau

- Force hospitalization process for uncooperative cases
- Records in medical chart, follow up sheet, and computer management system
- Case review by CDC and TB specialist monthly
- Send case follow up sheet to hospital
- Apply transport subsidies, complete treatment reward
- Health education to community,church , and school at least once a year
- Over 12 y/o chest x-ray screen
- LTBI

Changes after TB DOTS

花蓮縣衛生局 Hualien County Health Bureau

- Improving compliance of medication
- Increasing follow-up rate (sputum and X ray)
- First sputum follow-up 100%.
- Team approach: Medical professionals, TB DOTS outreach worker, Bureau Supervisor

Sabahda Elderly Day Care Center

花蓮縣衛生局 Hualien County Health Bureau

- The first aboriginal elderly day care center co-promoted by health unit, college and medical center in Taiwan
- Set up since 2005

Sabahda Elderly Day Care Center

花蓮縣衛生局 Hualien County Health Bureau

- Candidates : Age more than 65, disability, stroke patients. (66-93 years old, average 76.4)
- General satisfaction 9 9%
- Free service up to date (Financial support: manpower by Sioulin health center and donation)

Activities of Sabahda Elderly Day Care Center

花蓮縣衛生局 Hualien County Health Bureau

Time	Activity
0750-0820	**Welcome**
0820-0900	**BP, massage, warm-up**
0910-1000	**Physical activity**

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Activities of Sabahda Elderly Day Care Center

花蓮縣衛生局 Hualien County Health Bureau

1000-1100	**Leisure activity**
1100-1130	**Snack time**
1130-1200	**Group discussion** **Review activity**
1200-1230	**Sending home**

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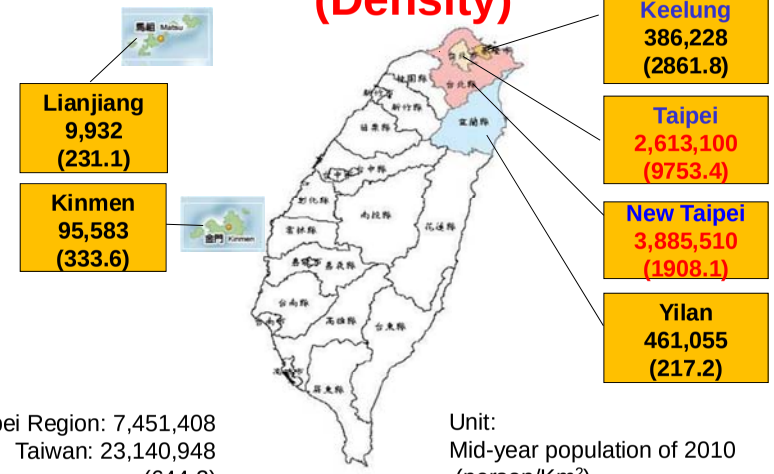
Control of an outbreak of tuberculosis in a campus, 2011

Jiunn-Shyan Julian Wu, Section Chief
First Branch (Taipei Region)
Taiwan CDC

Outline

- Demographics & Epidemiology
- Experience in Controlling Campus TB Clustering
- Lessons learned

Population (Density)



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Taipei Region: 7,451,408
Taiwan: 23,140,948
(644.2)

Unit:
Mid-year population of 2010
(person/Km^2)

Data Source: National Statistics, R.O.C.

Demographics

- **Population:** 1/3 of whole country.
- **High population density:** 3/5 of most populous counties/cities are located in Taipei Region.
- **Highest TB burden:** 27 – 29% of TB incidence cases reside in Taipei Region.
- Most **variable** levels of urbanization and ecology patterns.

Universities/Colleges, 2011

Region	Universities and Colleges	Students	Full-time Faculties
1st Branch	53	461,804	17,459
Taiwan	163	1,352,084	50,332
%	33%	34%	37%

(Data Source: Minister of Education, 2011）

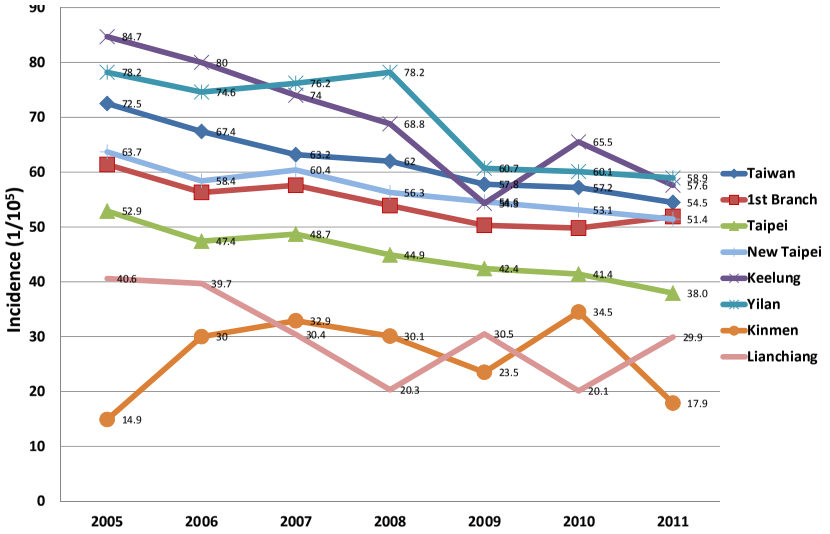
Human resources for TB control

	TB cases	TB PH staffs *	Case – Staff ratio	TB cases under DOTS	Observers	Case s under DOTS – observer ratio
Taipei	879	23	38.2	494	34	14.5
New Taipei	1691	192	8.8	1266	97	13.1
Keelung	184	36	5.1	154	11	14.0
Yilan	271	63	4.3	235	20	11.8
Kinmen	18	6	3.0	15	2	7.5
Lianchiang	4	5	0.8	4	0	2

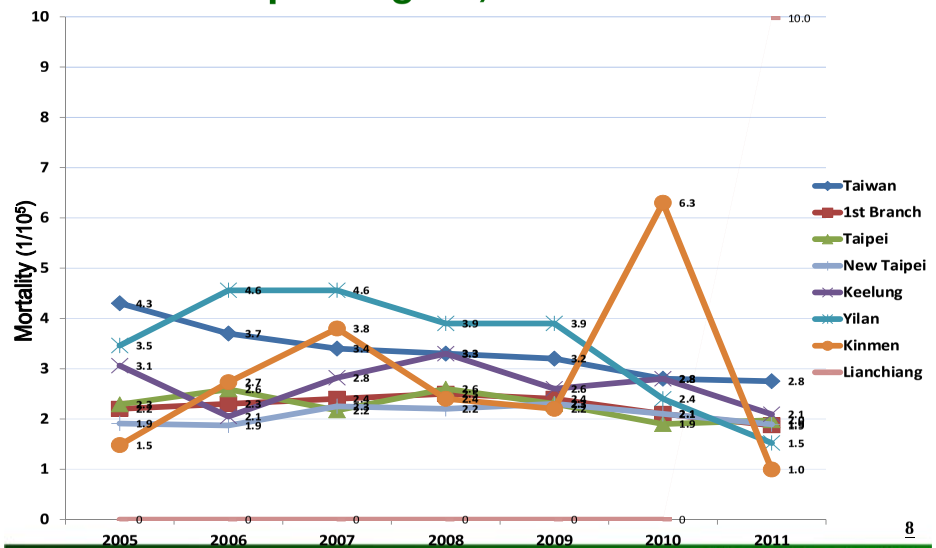
* TB public health staffs working in local health care unit.

Updated: 2011/12/01

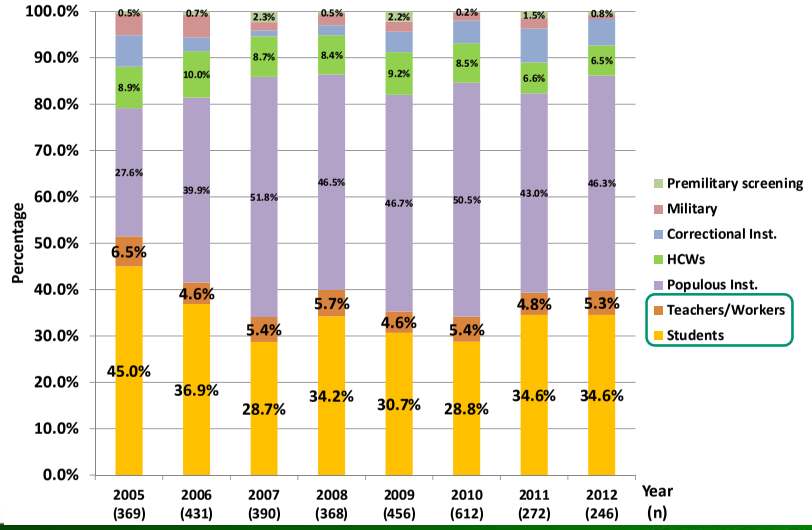
Incidence of TB in different counties/cities in Taipei Region, 2005 – 2011



Mortality of TB in different counties/cites in Taipei Region, 2005 – 2011



Proportion of each group among TB cases, 2005 – 2012



Proportion of confirmed TB clusters by institution type, 2007 – 2011

Year	2007	2008	2009	2010	2011	Average (%)
School	0	80	0	67	50	39
Workplace	0	0	100	0	50	30
Health Care Inst.	50	0	0	0	0	10
Nursing home	12	16	5	0	15	10

Data Source: Epidemiologic Information System

Control of an outbreak of tuberculosis in a campus, 2011

TB outbreak in Taipei school contained

TB OR NOT TB: The city health department's investigation said bad ventilation at Shih Hsin University dormitories could be why the standard screening process failed

STAFF WRITER, WITH CNA

A cluster outbreak of tuberculosis (TB) at a university in Taipei has been controlled, a senior Department of Health (DOH) official said yesterday.

Eight confirmed cases have been reported at Shih Hsin University since a student there was diagnosed with TB in September last year, the department said.

The September case has been confirmed as the origin of the outbreak, DOH Deputy Director-General Shih Wen-yi (施文儀) said, adding that all eight patients had been given medical treatment.

The department "believes the outbreak has been controlled," Shih said.

Taipei City Government's Department of Health has announced that it will launch a blanket health check targeting all 300-plus Shih Hsin students and teachers tomorrow and on Tuesday.

Shih said when the first infections were reported in September last year, the city carried out standard TB screening tests, which included X-rays and bacterial testing of family members or friends living with the patient.

Health checks were also carried out for people who had contact with the patient for at

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Identification of outbreak

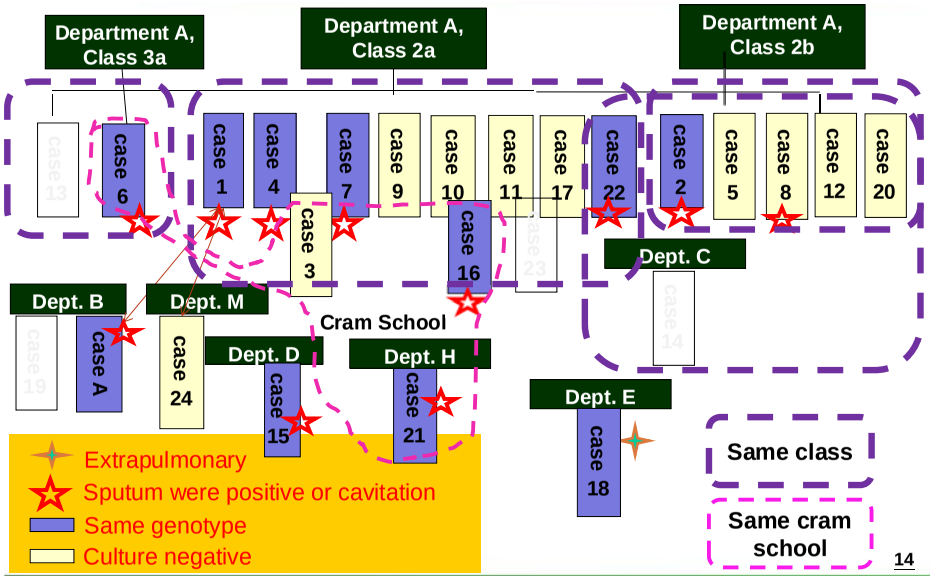
- **2010/11/29**
  - 1st case reported
  - Families confirmed on 2011/4/6 (Case A, sister of case 1, Dept. B 4th grade, same school), **same genotype**
- **2011/June - September**
  - 7 cases reported by physicians (Case 2 – 8, 4 symptomatic)
- **2011/9/27**
  - **Same genotype** of Case 1 and Case 2
- **2011/10/24-25**
  - 1st Extensive Contact Examination
- **2011/12/27**
  - 2nd Extensive Contact Examination

Overcrowded seats

Magnitude of outbreak

- Reported: 24
  Confirmed: 20 (11 with identical genotype)
  Excluded: 4
- Students were enrolled in five departments and one cram school.
- Twice extensive CXR examinations and TST tests in the campus
  - Close contacts: 892
  - Contact investigation
    - CXR: 892
    - TST: 500

Schematic Diagram of the Outbreak



Results of Contact Investigation (N=892)

Contacts	First CI	Second CI	Total	Note
Campus	431	281	712	6 diagnosed with TB
Non-campus	155	25	180	2 diagnosed as confirmed cases
Total	586	306	892	8 diagnosed with TB
TST	**First CI**	**Second CI**	**Note**	**Note**
TST	320	180	500	
TST Positive	162 (50%)	80 (44%)	242 (48.4%)	132 LTBI 18 withhold LTBI 92 refused LTBI

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Environmental Evaluation

Positive pressure in the classroom (air flew outside the classroom)

High CO_2 concentration (800 ppm) in this area

Ventilation Improvement

Modified Building A lobby

Stained glass wall, fixed

Change into screens, and open doors to improve ventilation and air-exchange volume.

Rearrangement of the Air Conditioning System

Modified air-conditioning system (A-building basements)

B1-3 flr. in A-building
(Front side is Exhaust port, and Air-Inlet port at backward)

Increased seats distance in the library

Partitions added.
Self-health management information posted on each table.

Challenges

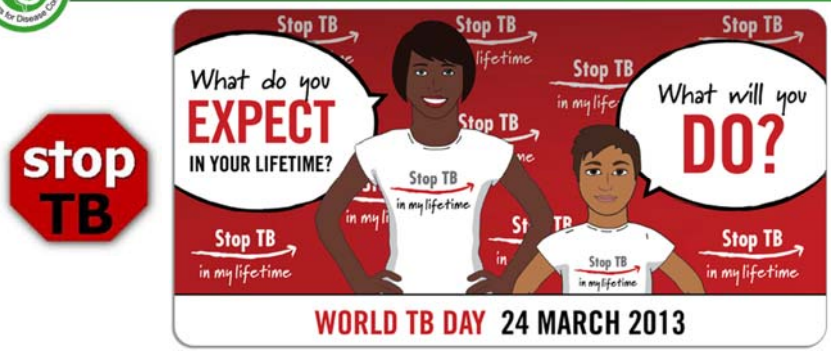
- Some contacts at high risk of progression to active TB **refused LTBI treatment**.
- Difficulties in **following up** of contacts who left school.
- **Media report** and public **panic**

Response Strategies

- In-person health education for contacts who refused LTBI treatment.
- Use all possible methods to contact students who left school.
  - Inter-jurisdictional/department cooperation
  - e-ways
- Use encouragement and law enforcement to have all contacts examined.
- Use media communication to turn media into partnership.

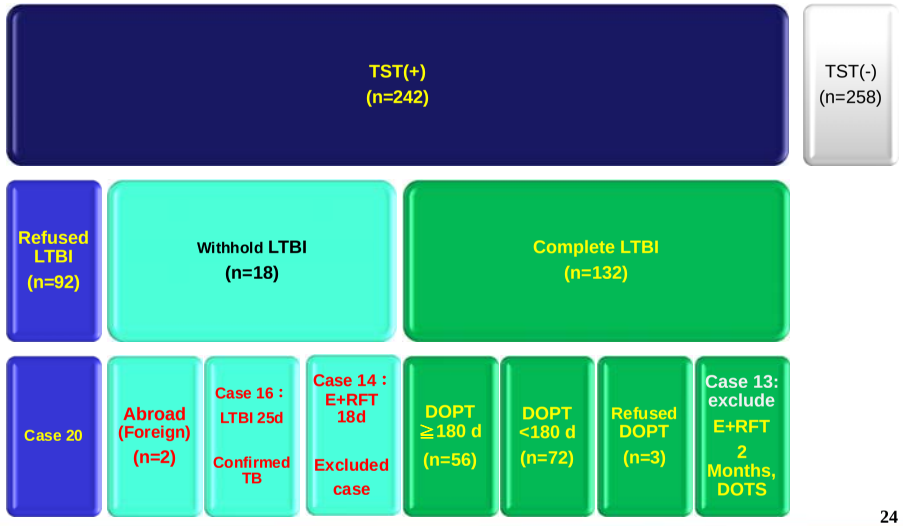
Lessons learned

- **Proper ventilation** of public areas helps **TB prevention and control**.
- Sincere media communication leads to positive support for disease control.
- Multiple methods targeting versatile **school** lifestyles is important in controlling TB outbreak in school.
- Timely comprehensive **epidemiologic investigation** and **contact examinations** are the keys to blockade transmission.



Thank you.

LTBI Treatment



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Halving TB in 10 Years Program in Taiwan

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Department of Health, Taipei City Government

Outline

- Organizational Framework and Manpower
- The Performance of TB Control
- The Further Prospection

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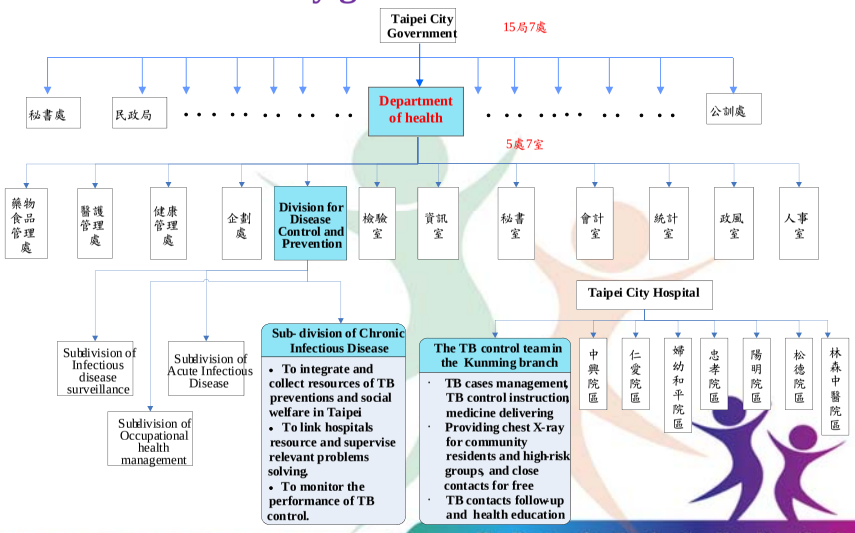
Organizational chart with regards to TB control at city government level



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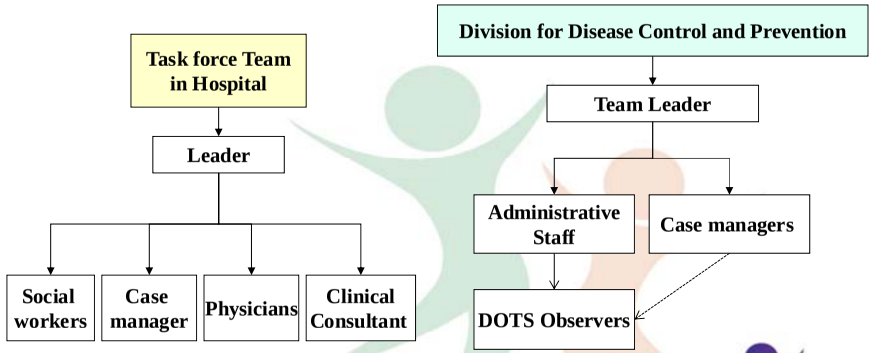
DOTS Group



Source：DOTS program in Taipei City

Manpower

Capacity \ District	Shilin	Datung	Peitou	Chungshan	Chungcheng	Wenshan	Wanhua	Taan	Sungshan	Hsinyi	Nankang	Neihu
Supervisor	2(Technical specialist、Chief of sub-division)											
Executive Officer	1(Undertaker)											
Case managers (TB section, Kunming branch)	1	1	2	1	1	2	1	1	1	1	1	1
DOTS Provider – Executive Officer	1											
DOTS Provider – Group leader	1			1			1			1		
DOTS Provider – Observer	4	1	3	3	2	2	3	3	2	3	1	3

Source：DOTS program in Taipei City

Outline

- Organizational Framework and Manpower
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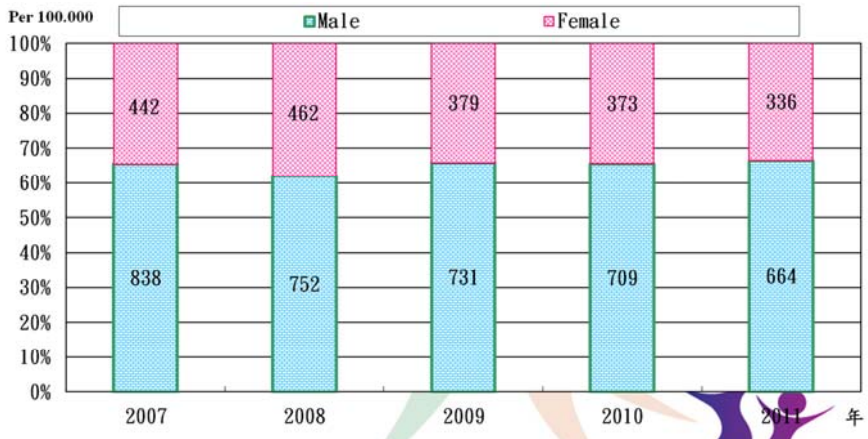
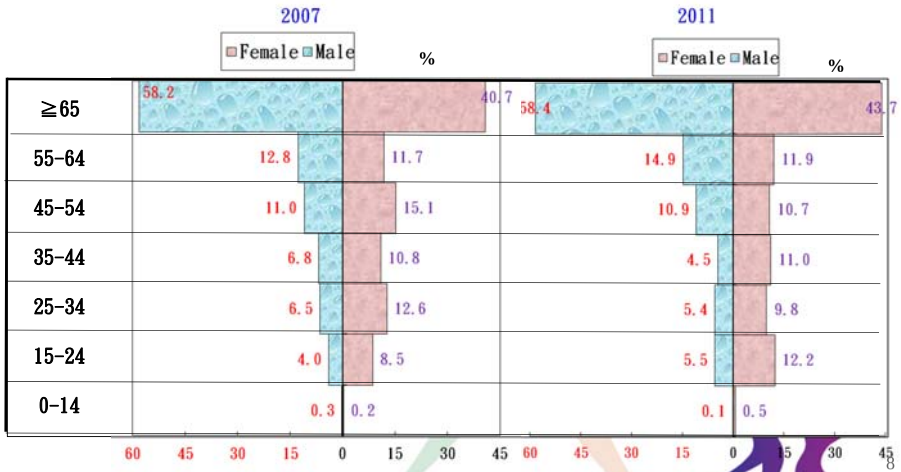
A Comparison of Notified TB Cases by Gender in Taipei from 2006 to 2011



Source: Data retrieved from Taiwan CDC

Age Structure of TB Cases by Gender in Taipei



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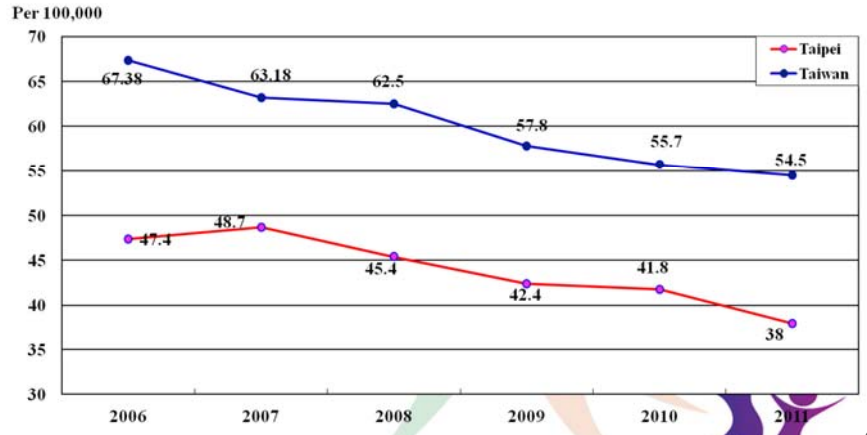
A Comparison of TB Incidence Rate between Taipei City and Taiwan



Source: Data retrieved from Taiwan CDC

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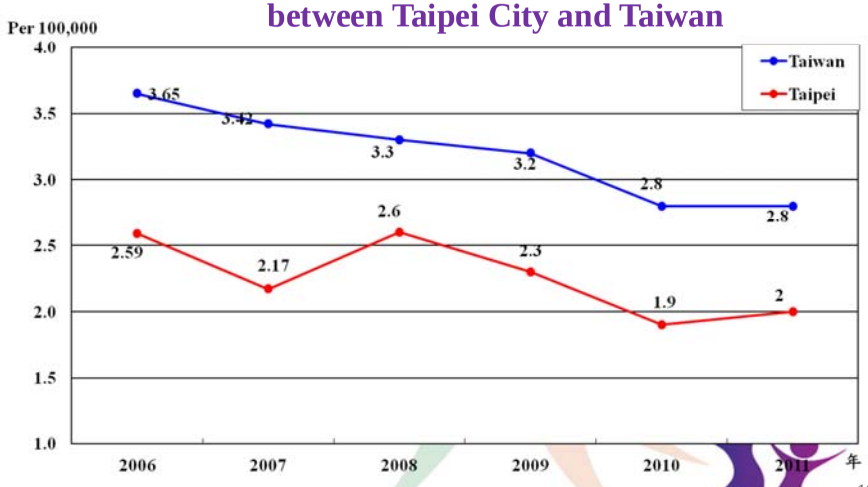
A Comparison of TB Mortality Rate between Taipei City and Taiwan



Source: Data retrieved from Taiwan CDC

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The Outcome of TB Cases Notified in 2005 to 2010 after 12 Months of Follow Up

Source: Data retrieved from Taiwan CDC

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Manageable Measures for DOTS quality Enhancement

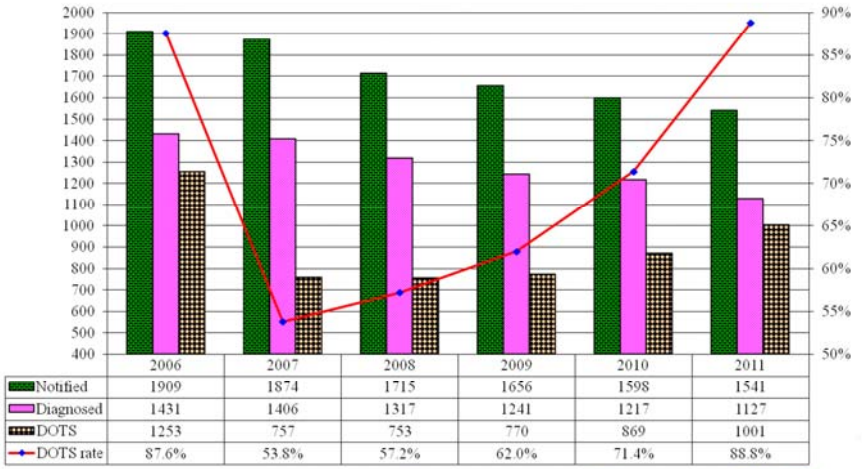
- **DOTS Auditing**
  - Auditing by task force (10 cases per person per month)
  - Auditing by group leader (10 cases per leader per month)
- **Medicine checking**
  - To ensure medicines are kept well and safety in the cabinet before delivering to patients.
- **Indicators monitoring**
  - Monitoring and evaluation indicators monthly regard lagging indicators
- **Frequently meetings**
  - Focus group discussion (weekly): Case conference, experience sharing, communication skill enhancement
  - Meeting (Monthly): Policies announcement, indicators inspection and improvement.

The effects of DOTS in Taipei

- **TB diagnosed cases: 671**
- **Under DOTS（Directly Observed Treatment Short-course）programme:**
  - **New cases of TB diagnosed: 91.5%（614/671）**
  - **New TB smear positive cases: 94.2%（436/463）**
  - **New TB culture positive cases: 95.4% (263/251）**
- **Under DOPT (Directly Observed Preventive Therapy) Programme:**
  - **LIBI（Latent tuberculosis infection）treated: 75**
  - **DOPT rate: 85.3% (64/75)**

Data accessed from TCDC on January 29, 2013

Newly Notified TB Cases and DOTS Coverage Rate from 2006 to 2011



	2006	2007	2008	2009	2010	2011
Notified	1909	1874	1715	1656	1598	1541
Diagnosed	1431	1406	1317	1241	1217	1127
DOTS	1253	757	753	770	869	1001
DOTS rate	87.6%	53.8%	57.2%	62.0%	71.4%	88.8%

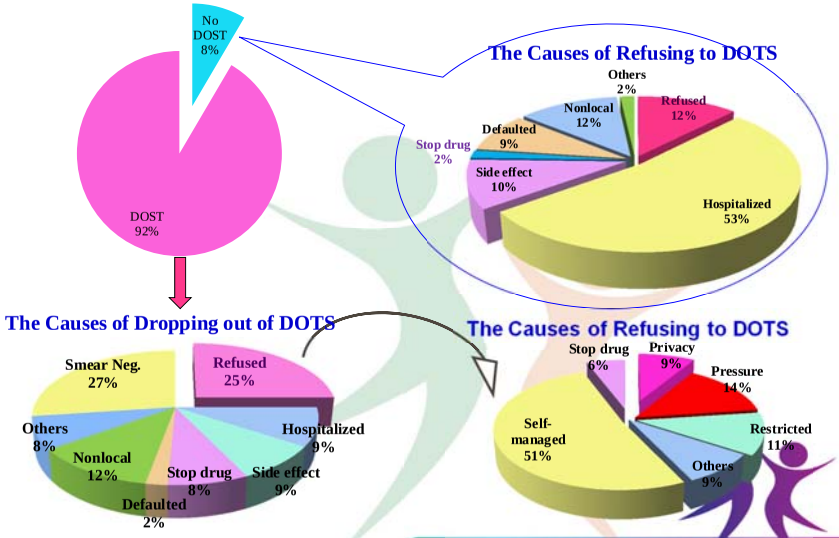
Source: Data retrieved from Taiwan CDC

LTBI program implemented in the TB contacts

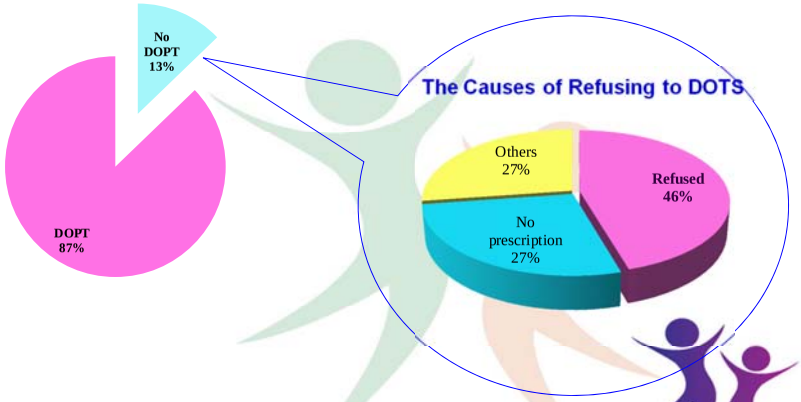
Notified date	Age	Case	Qualified	Under LTBI	Under DOPT	DOPT rate
2008	<13	329	96	43	37	86.0%
2009	<13	220	80	55	45	81.8%
2010	<13	240	97	74	55	74.3%
2011	<13	282	94	77	64	83.1%
2012	<13	253	88	76	47	61.8%
	13-25	-	217	69	46	66.7%

Source: Data retrieved from TCDC on Feb. 8, 2013
Note: A full course of TB prophylaxis regarding LTBI for age under 13 years old was started in 2008, and covering the birth cohort after 1986 from 2012.

The Cause Analysis of Rejection and Dropping Out of DOTS Program

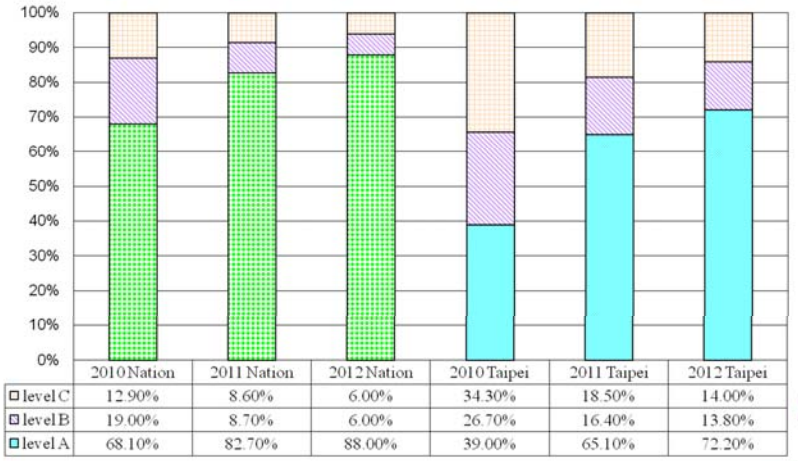


The Cause Analysis of the Rejection of DOPT Program



The Quality of DOTS – Close Care Rate

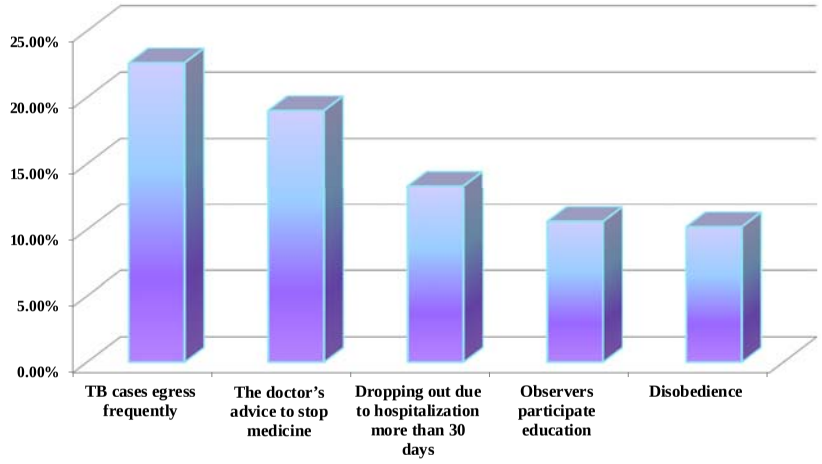
At level A, to closely watch patient taking medicine five days a week.



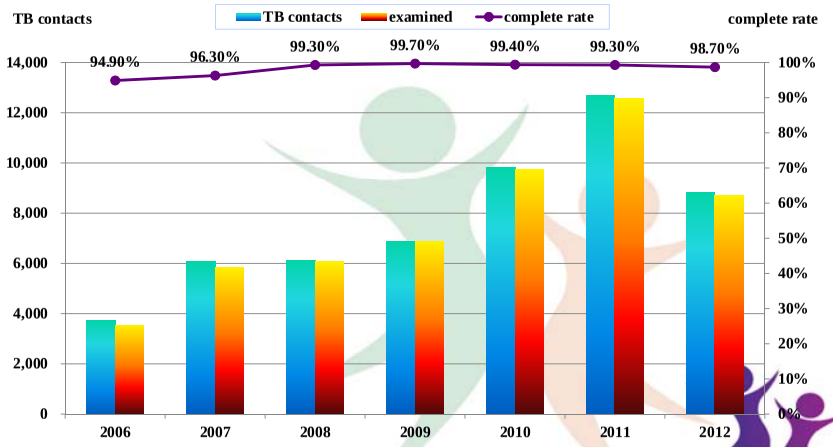
	2010 Nation	2011 Nation	2012 Nation	2010 Taipei	2011 Taipei	2012 Taipei
level C	12.90%	8.60%	6.00%	34.30%	18.50%	14.00%
level B	19.00%	8.70%	6.00%	26.70%	16.40%	13.80%
level A	68.10%	82.70%	88.00%	39.00%	65.10%	72.20%

Source: Data retrieved from Taiwan CDC

List of 5 Reasons Lead To DOTS Care with Poor Quality

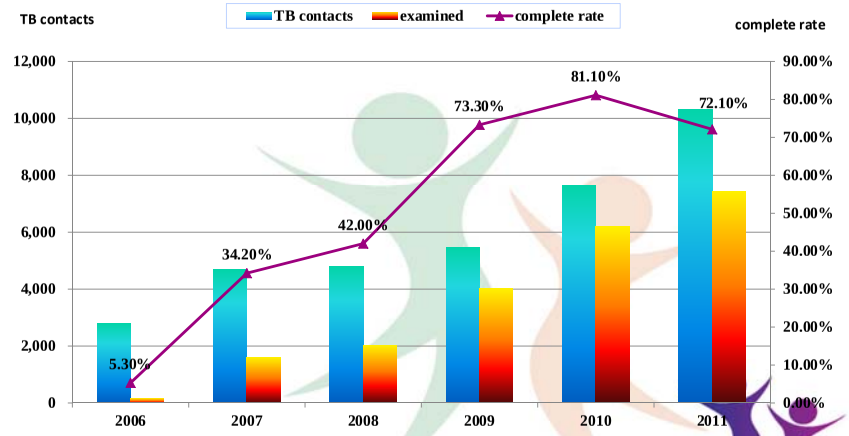


The implementation of TB contact examination at 1st month



Source: Data retrieved from TCDC on Feb. 8, 2013

The implementation of TB contact examination at 12-month



Source: Data retrieved from TCDC on Feb. 8, 2013

Outline

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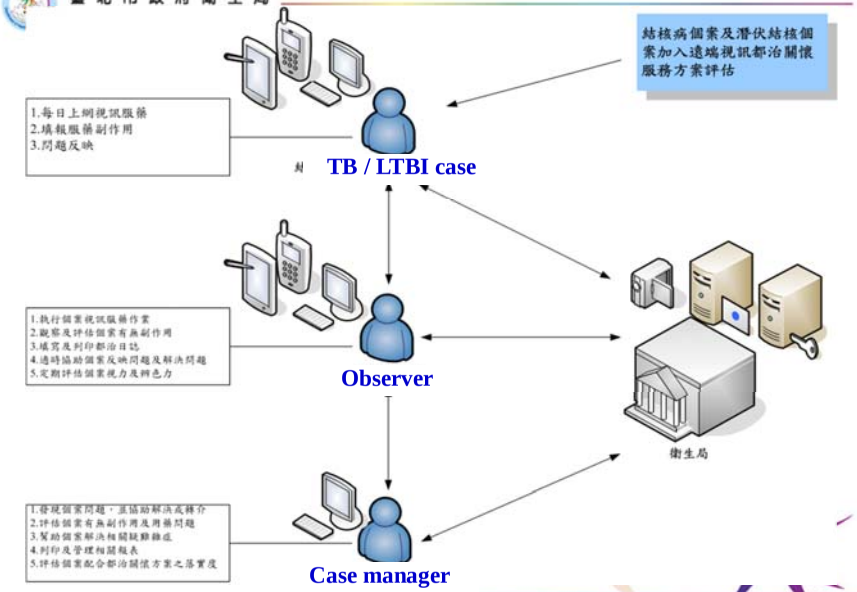
The eCloud Video DOTS Care Program

- Redesign DOTS care process thought eCloud video technology to protect patient's privacy and improve convenience
- For improving the DOTS coverage rate
- To eliminate TB patient exposure and stigma

The eCloud Video DOTS Care Diagram



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The Further Goals during the next five years

- To promote the DOTS coverage rate up to 95%
- To increase the TB cases successful treatment rate up to 75%
- To reduce TB incidence rate under 33.7 per 100,000 population and mortality rate lower than 1.3 per 100,000 population
- To approach the goal of “Halving TB in 10 Years”

體驗一座健康美麗的城市

THANKS FOR YOUR ATTENTION