Epidemiology
and Control Policy
of Tuberculosis in Taiwan

Third Division, Taiwan CDC
2011.02
Natural history of pulmonary TB

Most exposed persons will not become infected.

Approximately 30% of contacts will become infected.

Infection ≠ Disease, and we couldn’t know who will.

Age < 4 y/o or Age > 65 y/o
Immunity ↓ Disease ↑

Figure 3. Transmission of Tuberculosis and Progression from Latent Infection to Reactivated Disease.
Among persons who are seronegative for the human immunodeficiency virus (HIV), approximately 30 percent of heavily exposed persons will become infected. In 5 percent of persons with latent infection, active disease will develop within two years, and in an additional 5 percent, progression to active disease will occur later. The rate of progression to active disease is dramatically increased among persons who are coinfected with HIV.
TB incidence rate, 2009

Data from: WHO, Global TB Control -2010 report (per 100 thousand persons)
In 2010, there were 13,200 newly confirmed TB cases and the estimated incidence rate was 57/10^5 persons.

The official report would be presented in Taiwan TB control report (TCDC).
TB related death number and death proportion of outcome, 2005-2009

<table>
<thead>
<tr>
<th>Year</th>
<th>TB related death</th>
<th>% of death at 12 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>970</td>
<td>19.6%</td>
</tr>
<tr>
<td>2006</td>
<td>832</td>
<td>18.6%</td>
</tr>
<tr>
<td>2007</td>
<td>783</td>
<td>18.4%</td>
</tr>
<tr>
<td>2008</td>
<td>762</td>
<td>19.2%</td>
</tr>
<tr>
<td>2009</td>
<td>748</td>
<td>19.9%</td>
</tr>
</tbody>
</table>
Incidence Rate by Age of Newly Confirmed Cases

<table>
<thead>
<tr>
<th>年齡</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>2.2</td>
<td>3.0</td>
<td>3.3</td>
<td>1.9</td>
<td>2.5</td>
</tr>
<tr>
<td>5-9</td>
<td>2.3</td>
<td>1.6</td>
<td>1.9</td>
<td>2.2</td>
<td>2.0</td>
</tr>
<tr>
<td>10-14</td>
<td>3.5</td>
<td>3.5</td>
<td>3.3</td>
<td>4.0</td>
<td>3.2</td>
</tr>
<tr>
<td>15-19</td>
<td>22.7</td>
<td>21.7</td>
<td>19.9</td>
<td>17.5</td>
<td>20.2</td>
</tr>
<tr>
<td>20-24</td>
<td>31.0</td>
<td>27.9</td>
<td>26.5</td>
<td>28.4</td>
<td>22.0</td>
</tr>
<tr>
<td>25-29</td>
<td>33.2</td>
<td>26.9</td>
<td>26.4</td>
<td>27.3</td>
<td>23.3</td>
</tr>
</tbody>
</table>

Taiwan CDC
http://www.cdc.gov.tw
Age Distribution of Newly Confirmed Cases, 2009

- 0~14: 53%
- 15~24: 14%
- 25~34: 8%
- 35~44: 7%
- 45~54: 1%
- 55~64: 1%
- 65+: 5%
TB Mortality Trends in Taiwan, 1947-2009

TB deaths in Taiwan in 2009: 748 (15th leading cause of death)
TB Death Cases by Age Groups in Taiwan

<table>
<thead>
<tr>
<th>Year</th>
<th>0-14</th>
<th>15-24</th>
<th>25-34</th>
<th>35-44</th>
<th>45-54</th>
<th>55-64</th>
<th>65+</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>78.0%</td>
</tr>
<tr>
<td>2001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>77.5%</td>
</tr>
<tr>
<td>2002</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>80.3%</td>
</tr>
<tr>
<td>2003</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>78.8%</td>
</tr>
<tr>
<td>2004</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>79.0%</td>
</tr>
<tr>
<td>2005</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>81.2%</td>
</tr>
<tr>
<td>2006</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>81.4%</td>
</tr>
<tr>
<td>2007</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>81.4%</td>
</tr>
<tr>
<td>2008</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>82.9%</td>
</tr>
<tr>
<td>2009</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>81.4%</td>
</tr>
</tbody>
</table>
Trend of Prevalence of HIV in new diagnosed TB cases in Taiwan

People living with HIV
HIV(+) TB cases
new diagnosed TB cases
Treatment Outcomes for New Cases, 2005-2008

- Smear positive
- All forms
## Treatment Outcomes for New Cases, 2005-2008

<table>
<thead>
<tr>
<th>Age younger than 50 y/o</th>
<th>2005 cohort</th>
<th>2006 cohort</th>
<th>2007 cohort</th>
<th>2008 cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successfully treated</td>
<td>80.5</td>
<td>82.5</td>
<td>84.5</td>
<td>85.1</td>
</tr>
<tr>
<td>Died</td>
<td>3.9</td>
<td>3.5</td>
<td>3.4</td>
<td>3.7</td>
</tr>
<tr>
<td>Failed</td>
<td>1.1</td>
<td>1.9</td>
<td>3</td>
<td>2.9</td>
</tr>
<tr>
<td>Defaulted</td>
<td>3.9</td>
<td>4.8</td>
<td>3.2</td>
<td>2.5</td>
</tr>
<tr>
<td>Transferred treated</td>
<td>0.2</td>
<td>0.1</td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td>not evaluated</td>
<td>10.4</td>
<td>7.2</td>
<td>5.7</td>
<td>5.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age elder than 50 y/o</th>
<th>2005 cohort</th>
<th>2006 cohort</th>
<th>2007 cohort</th>
<th>2008 cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successfully treated</td>
<td>64.3</td>
<td>65.3</td>
<td>65.6</td>
<td>64.3</td>
</tr>
<tr>
<td>Died</td>
<td>26.4</td>
<td>24.9</td>
<td>24.4</td>
<td>25.6</td>
</tr>
<tr>
<td>Failed</td>
<td>0.9</td>
<td>1.5</td>
<td>2.9</td>
<td>3.3</td>
</tr>
<tr>
<td>Defaulted</td>
<td>2.1</td>
<td>3.1</td>
<td>2.6</td>
<td>2.1</td>
</tr>
<tr>
<td>Transferred treated</td>
<td>0.1</td>
<td>0</td>
<td>0.1</td>
<td>0</td>
</tr>
<tr>
<td>not evaluated</td>
<td>6.1</td>
<td>5.1</td>
<td>4.4</td>
<td>4.6</td>
</tr>
</tbody>
</table>
Surveillance of Drug Resistance

Drug Resistance Pattern

Period of data: 2009/7/1-2010/3/31
Proportion of MDR-TB among new TB cases in Taiwan

- 2007: 149 MDRTB cases, 1.0% MDRTB/TB
- 2008: 159 MDRTB cases, 1.1% MDRTB/TB
- 2009: 176 MDRTB cases, 1.3% MDRTB/TB
- 2010: 164 MDRTB cases, 1.2% MDRTB/TB
Mobilization Plan to Halve Tuberculosis Incidence in Ten Years

Halve the incidence rate (72 per 10^5 population → 36 per 10^5 population)
Action Plans

● Plan 1 — Case finding campaign
● Plan 2 — Laboratory capacity improvement
● Plan 3 — Direct Observe Treatment (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
Large-scale Implementation of DOTS Program

- Launched on 1 April 2006
- Budget: NT$ 300 millions/ US$ 9.4 millions
- Target groups: Every TB case
- DOTS implementation rate among bacteriology proof patients reached 92%
- Over 680 observers have been hired by Oct. 2010
Procedure of Enrollment

DOT observer accompanies PHN to visit patients in the hospital

Meet patient at a designated site

Observation by pharmacist

TB education and DOT program introduction

Home visit
DOT Tasks

- Deliver medication
- Check for side effects
- Verify medication
- Watch patients take pills
- Document the visit
- Assist patients with keeping appointments and connecting them with social services
- Reporting to the case management team
Expanding DOT Target Groups

1. Smear(-) and culture (-) with relapse, homeless, uncooperative, aboriginal group, mountainous area
2. LTBI

Confirmed cases which were under treatment
Evaluation of Effect of DOT Program

- After adjusted for factors associated with TB treatment outcome, the proportion of “DOT/treatment days” the patients received is dose response related to treatment outcome.

- Compared to TB cases received zero day of DOT, those who received DOT 0~60%, DOT reduced 80% bad treatment outcome (failed, default and death); those who received DOT >60%, DOT reduced 98% bad treatment outcome (failed, default and death).

- MDRTB in new TB cases was consistently around 1%, and the proportion in re-registered cases (6%) would be followed-up longer (2009/7~2010/3).
DOTS implementation quality in bacteriology confirmed cases, 2010
Treatment for TB is not only a matter of individual health; it is also a matter of public health.

All providers, public and private, who undertake to treat a patient with TB, must have the responsibility.

~ International Standards for Tuberculosis Care ~
To Implement Standard Treatment

- Standard operating procedures
- 2nd Line Drug Management
- DOT-Plus for MDRTB cases

Taiwan Association of Family Medicine
Taiwan Pediatric Association
Infectious Disease Society of Taiwan
Taiwan Society of Pulmonary and Critical Care Medicine
Taiwan Society of Internal Medicine
Taiwan Society of Tuberculosis
The Impact of Endorsement of Standardized Regimens on TB care

**Table**
The Comparison of Regimen before and after The Endorsement of Standardized Regimens for TB Care at National Level, 2007 vs. 2008.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total evaluated 108</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total evaluated 104</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>non-standardized regimen</td>
<td>16 (14.8%)</td>
<td>5 (4.8%)</td>
<td>0.02*</td>
</tr>
<tr>
<td>non-standardized dosage</td>
<td>31 (28.7%)</td>
<td>23 (22.1%)</td>
<td>0.345</td>
</tr>
<tr>
<td>Rifampin undr-dosage</td>
<td>16 (14.8%)</td>
<td>6 (5.8%)</td>
<td>0.04*</td>
</tr>
<tr>
<td>Weight recorded in case management card</td>
<td>12 (11.1%)</td>
<td>0 (0%)</td>
<td>0.0003*</td>
</tr>
<tr>
<td>Lacked proper documentation of medication</td>
<td>30 (27.8%)</td>
<td>0 (0%)</td>
<td>&lt;0.0001*</td>
</tr>
</tbody>
</table>

* Fisher's Exact Test was performed
Collaboration with NHI

Inadequate Regimen

- The physicians with inadequate TB regimens are listed by TCDC gathering from public health.
- Purposive sampling of treatment records for patients taken care by the above physicians is arranged.
- Experts review TB treatment records provided by NHI to decide the amount of reimbursement fee.
- NHI assists to guide the physicians who provide inadequate regimen through discounting the reimbursement and education.
The Introduction of Reducing of Reimbursement from NHI to Improve the Inadequate Regimen for TB Care

Duration:
March to December, 2008

Total:
199 charts
-- 50.3% (100) were appropriate
-- 49.7% (99) were inappropriate

<table>
<thead>
<tr>
<th>Result of Review</th>
<th>Number</th>
<th>percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inappropriate</td>
<td>99</td>
<td></td>
</tr>
<tr>
<td>Non-standardized regimen in combination</td>
<td>28</td>
<td>28.3</td>
</tr>
<tr>
<td>Inadequate/over dosage</td>
<td>32</td>
<td>32.3</td>
</tr>
<tr>
<td>Inappropriate frequency</td>
<td>19</td>
<td>19.2</td>
</tr>
<tr>
<td>Others</td>
<td>9</td>
<td>9.1</td>
</tr>
<tr>
<td>Inadequate dosage combined with inappropriate frequency</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Inappropriate frequency combined with non-standardized regimen</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Inadequate dosage combined with non-standardized regimen</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Inappropriate frequency, inadequate dosage, combined with non-standardized regimen</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
Medical care system for MDR-TB

- **Set**: May 2007
- **Goal**
  - To provide and promote medical care services to MDR-TB
  - Expanded to cases with RMP mono-resistance or resistance to 3 first line anti-TB drugs or more since 2011
- **Requirement**
  - Qualified staff & facilities
  - Taiwan MDR-TB Consortium (TMTC)
    - 724 MDR-TB cases were enrolled in DOTS-plus program up to 2011/1/31.
    - provide DOTs-plus services.
    - culture conversion rate (enrolled 6M) : 76.6%
    - Treatment success rate (enrolled 24M) : 75.3%
Hospital Care Enhancement

- Continue Implement NHI specific project, encourage case management enrollment and improve treatment successful rate
- TB related medical expenditure pay by governmental fiscal budgets
  - TB medical expenditure co-payment (include LTBI treatment and contact exam)
  - Medical expenditure of compulsive isolation
  - C2:  \(\leq 14\) days hospitalized medical expenditure of S(+) cases
  - C3:  \(\leq 30\) days hospitalized medical expenditure of TB cases within side effect by taking anti-TB drugs
  - C4: medical expenditure of TB cases without NHI (include LTBI treatment and contact exam)
  - Diagnosis and ward fee of chronic TB cases
Laboratory Diagnosis

- **Mycobacteria Contract Lab**
  - Around 37% of samples were processed by contract labs in 2009
  - External quality control of the laboratory’s proficiency was handled by Taiwan CDC and CAP
  - Incentives: Taiwan CDC picked up part of the contract lab’s maintenance fee, plus provided a specimen-based subsidy in the name of examination fee

- **Authorized Diagnostic Organization for TB**
  - Department of Health issued a 4-year license to each of them to carry on confirmation tests of TB
  - Up to Feb. 1, 2011, 33 such organizations had been authorized and these organizations were under constant monitoring and tests
MDR Confirmation

- All strains with INH and RMP resistance are required to be confirmed by National Reference Lab since May, 2008.
  - Molecular diagnosis → Traditional DST
  - At least two sets of sputum sent for molecular diagnosis positive for MDRTB

- Molecular diagnosis of MDRTB is available since 2010 for patients who are
  - relapse, default, failure, or
  - those who have been contacts with MDRTB or
  - TB cases in aboriginal area within high incidence rate of MDRTB (花蓮縣卓溪鄉、萬榮鄉、秀林鄉)
Strategies for TB Contact Tracing

- **Strengthening and monitoring contact tracing tasks**
  - Since Jul. 2007, medical expenditure co-payment of contact examinations was paid by governmental fiscal budgets from TCDC

- **Target population**
  - Household
  - Over 8 hrs/day or accumulative over 40hrs (contact with index cases during their infectious period)
  - Other special indications

- **Examination method**
  - Contacts elder than 13 y/o should receive CXR
  - Contacts younger than 13 y/o should receive both CXR and TST

Average contact number of per index increase from 2.6 persons (2006) to 6.4 persons (2010)
Average Contact Numbers per TB cases

Average contact numbers / index is 4.9 persons, 2006-2010
The Proportion of Cases Found through Active Case Finding Process vs. Total TB cases

- TB cases found by contact tracing or CXR survey / new cases (%)
- TB cases diagnosed due to symptom / new cases (%)

<table>
<thead>
<tr>
<th>Year</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>1%</td>
<td>2%</td>
<td>2%</td>
<td>3%</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td>50%</td>
<td>55%</td>
<td>60%</td>
<td>65%</td>
<td>70%</td>
<td>75%</td>
</tr>
<tr>
<td></td>
<td>80%</td>
<td>85%</td>
<td>90%</td>
<td>95%</td>
<td>100%</td>
<td></td>
</tr>
</tbody>
</table>
Regulating Air Travel by Infectious TB Cases on Flights Exceeding 8 Hours

- Based on the second edition of WHO publication “Tuberculosis and Air Travel”
  - Based on Article 42 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
Observed and Targeted Values of Tuberculosis cases in Taiwan

What can we do to achieve sustainable reducing of TB case except expand DOTS?

The official report would be presented in Taiwan TB control report (TCDC).
DOT Implement Rate for Smear Positive TB
Control Policy of Tuberculosis

Source: Interventions for Tuberculosis Control and Elimination, IUATLD 2002
In contact populations, the average incidence of TB was 8-240 times higher than the general ones in Taiwan, especially in <12 y/o age group.

Lin DL et al. The 2 year follow-up report for contact of tuberculosis. (Oral presentation - 2009 Annual Meeting of Taiwan Society of Pulmonary and Critical Care Medicine)

Yang CH et al. Clinical features of TB associated with HIV infection in Taiwan. (17th IAC poster)
Latent TB Infection Treatment

- Prophylaxis/ LTBI treatment was endorsed since Apr. 2008
  - Target group
    - Children contacts <13 y/o with highly transmitted index (smear+ or culture+ or CXR cavity), accessed by LTBI physician
  - Strategy
    - DOPT of 9 month INH regimen (prophylaxis or treatment)
  - Other
    - If contact match the above criteria but age elder than 13 y/o, could enroll in this program
Trend of LTBI Treatment, 2008/4-2010/12

- Apr.~Dec., 2008: 1440 cases, DOPT(%) 85%
- 2009: 2650 cases, DOPT(%) 91%
- 2010: 3874 cases, DOPT(%) 92%
The Efficacy of LTBI Treatment in children <13 y/o

7,899 TB contacts < 13 y/o
(contact with contagious pulmonary TB)

2,160 (28%) first TST (+)

1,421 (66%) started LTBI treatment
(DOPT 91%)
(Completion of treatment 90%)

739 (34%) did not start LTBI treatment

None of them became case
(RR: 0.04 [95% CI: 0.002-0.71])
(provided 96% protection)

6 of them became cases
(Incidence 812/100,000)

Excluded 13 TB cases detected at contact tracing
TB Contact Tracing Plus Project

Timeframe

- **Since Jan. 2010 to Dec. 2012 (3 years)**
  - 1st stage: choose 2 pilot sites (Taipei Wanhua, Kaohsiung Zuoying) and MDR-TB Medicare system to involve
  - 2nd stage: add 3 pilot sites (Taoyuan Longtan, Tainan Yongkang, Kaohsiung Sinsing)
  - 3rd stage: extend to all administrative districts in Taiwan

Future goals

- **Establish standard contact tracing model**
  - Standard questionnaire
  - Design a access system
  - Determining infectious period
  - Standardized hours of exposure
  - Standard priority classifications

- **Usage of effective diagnostic test for LTBI**
  - Use QFT for contacts born before 1986 (who have been boosted BCG at least twice)

- **Extend LTBI treatment to all population** (no age limitation)
### Performance evaluation of TB control in Taiwan

<table>
<thead>
<tr>
<th>Period</th>
<th>Confirmed No.</th>
<th>Incidence rate (ID) ((1/10^5))</th>
<th>The decrease in ID (%)</th>
<th>Dead No.</th>
<th>Mortality ((1/10^5))</th>
<th>The decrease in Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>16,472</td>
<td>72.5</td>
<td></td>
<td>970</td>
<td>4.3</td>
<td></td>
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<tr>
<td>2006</td>
<td>15,378</td>
<td>67.4</td>
<td>7.0</td>
<td>832</td>
<td>3.6</td>
<td>16.3</td>
</tr>
<tr>
<td>2007</td>
<td>14,480</td>
<td>63.2</td>
<td>6.2</td>
<td>783</td>
<td>3.4</td>
<td>5.6</td>
</tr>
<tr>
<td>2008</td>
<td>14,265</td>
<td>62.0</td>
<td>1.9</td>
<td>762</td>
<td>3.3</td>
<td>2.9</td>
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<tr>
<td>2009</td>
<td>13,400</td>
<td>58.0</td>
<td>6.5</td>
<td>748</td>
<td>3.2</td>
<td>3.0</td>
</tr>
<tr>
<td>2010</td>
<td>13,200</td>
<td>57.0</td>
<td>0.9</td>
<td>700</td>
<td>3.0</td>
<td>6.9</td>
</tr>
</tbody>
</table>
Thanks for your attention!

ON THE MOVE AGAINST TB