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Taiwan Epidemiology Bulletin

Evaluation of a Directly Observed Therapy Short-Course Project for Treating Tuberculosis on Offshore Island Kinmen County

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Abstract

Tuberculosis (TB) came first in both the incidence and death rates amongst all notifiable infectious diseases in Taiwan. In order to improve the situation, Taiwan CDC implemented a Directly Observed Therapy Short-course (DOTS) project in Kinmen County for the first time from July 2004 to December 2005, which will later serve as a reference in establishment of a full-scale DOTS program covering the entire Taiwan area in 2006.

Patients who either had a positive sputum smear or poor compliance to medications were enrolled in the DOTS project after counseling. Original information of the target cases was obtained from the TB database of the CDC, and all treatment outcomes in the project were classified into three categories: cured, dropped outs, and died.

Between July 2004 and December 2005, there were 23 TB cases reported in Kinmen County and filed into the CDC TB database, of which 20 cases (12 cases being sputum smear positive) were male and 3 cases (all sputum smear-positive) female. Their average age was 63.2 years old. After counseling, 12 cases agreed to participate in the project, which represented a coverage rate of 52.2%. Out of the 12 cases, 11 were males (10 smear positive) and one female (one smear positive), and the average age of the group was 61.7 years old. Among the individuals who were enrolled in this DOTS project, it was 83.3% in the cured category at the end of the project with no dropped outs. In comparison, the rate of the cured category was only 45.5% for those individuals who did not sign up in the project, and the dropped out rate was 9.1%.

The outcomes from this pilot project indicated that the implementation of DOTS has significant beneficial effects on the case management of TB. According to the strategy formulated and recommended by the World Health

Organization, active promotion of DOTS strategy is so far the most effective way to fight against TB. Therefore, it is very encouraging for us to continue our efforts in implementing the DOTS into the management of TB cases in Taiwan.

Introduction

Tuberculosis (TB) is the current leader among all notifiable infectious diseases in Taiwan both in its incidence and death rates. In order to effectively improve this situation, Centers for Disease Control of Taiwan (Taiwan CDC) put forward a policy on 23rd of March 2005 aiming at "cutting Taiwan's TB population down to half of its current level in ten years time". To reach such goal, the CDC formulated the following four strategies: 1. Revise the national TB prevention and control program, 2. Increase the rate of finding new TB cases, 3. Improving the cure rate of TB, and 4. Collaborating with international agencies [1].

How to prevent and control TB is a very important global issue. According to an estimation made by the World Health Organization (WHO), there is approximately one third of the world population infected with *Mycobacterium tuberculosis*, and among those, about 9 millions each year suffer from clinical symptoms and 2 millions eventually die from TB [2]. In recent years, the already controlled TB infection seems to be fighting its way back throughout the world [2-5] due to reasons such as (1) co-infection with HIV/AIDS, (2) failure to recognize and diagnose TB by general physicians, (3) booming of the homeless, (4) problem with drug abuse or overdose, and (5) failure of therapy due to multi-drug resistant TB strains. In aware of this, WHO called out an emergency conference in 1993 to announce TB as a "global emergency" [2] and strongly promoted the so-called Directly Observed Therapy Short-Course (DOTS), which

emphasizes the buildup of a mutual trust relationship between the physician and the patient, and through close direct supervision to make sure that the patient has duly followed the treatment procedures or taken each and every dose of medication the physician prescribed, so the case can have the best chance to be cured. This in term will effectively cut off the infection source, and prevent the occurrence of multi-drug resistant bacterial strains [6, 7]. According to some published studies conducted in Malawi, Tanzania, Mozambique, and ten provinces in Mainland China, DOTS has repeatedly been proven to be cost effective in the control and prevention of TB [8-10].

One study from the United States revealed that the implementation of DOTS could increase the cure rate to over 90% in newly diagnosed cases whose sputum smear were positive with non-drug resistant strains [11]. Furthermore, another report suggested that under the condition of no HIV infection involved, if the detection rate could reach 70% together with a cure rate of 85%, and then the prevalence of TB would be brought down. In such case, the incidence of TB can then drop by 5 to 10 percent each year [12]. As a result, over the past few years, many nations throughout the world have been using DOTS as their primary TB control strategies in order to achieve a higher cure rate and reduce the incidence rate, death rate and drop outs [7, 9].

In Taiwan, we have limited experience in the past with DOTS, and hence there were a lack of relevant reports. In July 2004, for the very first time, Taiwan CDC implemented a TB DOTS pilot project on one of its geographically isolated offshore islands, Kinmen County, in the hope that through the clinical experiences from this trial, it can be a useful reference national wise. And of course the utmost goal will be to reach a target set by the WHO: reducing the prevalence and death rate of TB by 50% before year 2015 (compared to 1990).

Materials and methods

A. Subjects

Subjects were collected from the current Kinmen County TB case file in the TB database of Taiwan CDC. Variable items included: age, sex, diagnosis and treatments results.

B. Duration

From January 1, 1996 to December 31, 2005

C. TB DOTS project

In this project, we adopted the three-level, four-role management model originally proposed by Osler [7, 13]. The four roles consisted of nursing manager, case manager, clinical nursing personnel and community carer. Each role had its own unique job description. The local county health bureau was responsible for the DOTS project carried out at all health stations and medical institutions (i.e. hospitals, and clinics) and it had a role as the nursing manager at Level 1 model. Whereas those public health nurses working at all health stations in the county were responsible for close supervision of each DOTS TB case's therapeutic treatment plan, providing relevant health education, tracking the treatment progress and keeping things in order, and assisting the clinical nurses or community carers in the DOTS project. Hence the public health nurses at health stations played act as case managers at second level of the model. Finally, those clinical nursing personnel or the community carers belonged to a role of the third level where they were responsible for direct supervision of each individual case to ensure that prescribed medication was taken regularly. Treatment diary or logbook was required to be filled out afterwards.

Criteria for patients enrolled in DOTS project were as followed: positive

sputum smear, poor drug compliance, and voluntarily agreed to join the project after counseling. Therefore, we started our study by looking into the CDC TB database files to search for TB cases with positive sputum smear and poor drug compliance in Kinmen County notified between January 1, 2004 and December 31, 2005. The cases with "poor drug compliance" referred to those TB cases with negative sputum smear and were found out by the house-visiting nurse (scheduled one week after the notification and once a month thereafter) that they did not follow the exact treatment instructions by either failing to take medication on a regular basis or take the wrong dosage each time. The approach of implementation we adopted was as follows:

Case manager explained the entire DOTS treatment plan to the newly notified case within one week after the notification. The case would then only be enrolled into the DOTS project after giving consent.

After a carer (either a clinical nurse or a community member) was appointed, the case manager then met up with both the case and carer to agree upon what time on each day the case should take the medication. In the meantime, the case manager would also inform the carer assignment and things needing extra attention.

The case manager would inspect how the case took medication the first time to ensure the method was correct. Timing for the medication could be varied, which meant that the case could choose anytime during the day as long as the entire daily dosage was taken at once every day.

Thereafter, the carer would visit the case in person everyday to witness the case taking medication, and then make detailed record on a diary or logbook afterwards.

Should the case appear to suffer from any side effects during treatment, the

carer would notify the case manager right away. The case manager would then decide whether referral to a doctor for further assessment was required.

Twice a month an inspector from Kinmen County Health Bureau would visit the case without notice to assess medication compliance and the logbook record was checked.

D. Treatment results

In this study we used the Taiwan CDC TB database for our DOTS project. According to the WHO classification on TB treatment results, it included (1) *cured*: which means the patient has shown to have at least one negative sputum smear during the treatment period and also the smear is negative at the final month of the treatment period; (2) *failed*: which means the newly diagnosed patient remains to be sputum smear positive at the end of the fifth months of treatment, or a recurring patient shows smear positive at the end of the repeated treatment, or a smear negative patient when entering the treatment procedure turns into sputum smear positive or culture positive after two months of treatment; (3) *completed treatment*: which means likewise the patient has gone through the treatment procedure but the post sputum examination can not be sure whether it's cured or failed; (4) *defaulted*: which means the patient has interruption of the treatment for at least 2 months (5) *transferred*: which means the patient has moved to another healthcare institution or location and is no longer under the care of the former care manager; (6) *died*: which means the case passes away for any cause during the course of the treatment [14]. However, in this study, due to limitation of our resources, we classified the treatment results into only five categories i.e. cured, defaulted, died, altered diagnosis, and transferred out, instead of WHO's seven. The result of our each case was able to be classified into one of these five

categories which were distinctive and unique [15]. At the final stage of this study for the purpose of statistical analysis, we then further simplified the 5 categories into three i.e. cured, defaulted, and died

Cured: patients showed improvements in the clinical symptoms and signs, chest X-ray, and bacteriological results. Patients had also completed the registration in the TB database within 12 months after being notified,

Defaulted: patients were still alive, but failed to register into the TB database within12 months after notification.

Died: patients died of various causes during the course of treatment.

E. Statistical analysis

The information for each subject of this study was downloaded from Taiwan CDC TB notification registration database and Microsoft Excel 97 software was used for data entering, error correction, and diagrammatic drawings. The incidence rate of TB was calculated by the number of newly notified TB cases filed in the CDC database each year divided by the total population of all ages in Kinmen County.

Results

A. TB incidence rate

The total population in Kinmen County was 17,924 in 1996 and has increased to 64,456 by year 2005. Within that decade, the total number of confirmed TB cases (including both male and female) in a year was somewhere between 13 to 24 cases. Generally speaking, the incidence rate of Kinmen County male TB cases was on a decline in those years, i.e. from 35.9 cases per one hundred thousand capita per year in 1996 gradually dropped to 23.5 cases per one hundred thousand capita per year in 2005. The rate of Kinmen County female

TB cases was also on a decreasing trend, from 13.1 cases per one hundred thousand capita per year in 1996 gradually dropped to 6.6 cases per one hundred thousand capita per year in 2005. The interesting point noted was that the male incidence rate of Kinmen County was somewhat 1 to 8-folds higher than female (see Figure 1). We also noticed that from the data of incidence rates versus various age groups over the decade clearly showed a trend of higher incidence rate with increasing age. The highest incidence rate occurs with those ages older than 65, then those between 55-64 and the lowest incidence rate among those aged 0-14 (see Figure 2)

B. Treatment results

From 1996 to 2005 there were 1778 Kinmen County people reported as TB cases and filed in the CDC TB database which was then used in this analytical study. An analysis on their treatment outcomes showed that 117 cases (66.1%) were cured, with 29 cases (16.4%) being defaulted and 31 cases (17.5%) died during the TB management course. Under the definitions of various treatment results adopted in this study, we compared the trends of treatment results between different generations and found that the "cured" rate was in the range between 50% and 80% in the years studied. The "defaulted" rate was on a slowly decline trend: from 25% in 1996 to 0.0% in 2005 and the fraction of the total cases each year that ended up dead during the TB management course was between 4.8% and 30.0% (see Table 1).

C. Introducing DOTS

When the DOTS project was implemented in Kinmen County during July 2004 to December 2005, there were 23 confirmed new TB cases filed into the CDC TB database, and subsequently chosen to be the subjects of our analytical study. Among those 23 cases, 20 were males (12 of them were sputum smear

positive) and 3 were females (all sputum smear positive), and the age distribution ranged from 23.1 to 89.0 years old (the average age and standard deviation were 63.2 and 17.5, respectively). After counseling, 12 patients agreed to enroll in the project with a covering rate of 52.2% (12 out of possible 23). 11 of them were males (9 of them were sputum smear positive) and 1 female (sputum smear positive), and age distribution ranged from 43.1 to 80.3 (the average age and standard deviation were 61.7 and 11.6, respectively). Two cases were found to have poor compliance, which means they did not take medications regularly as instructed. This accounted for 17% of the participating group. According to the case manager, there were various reasons expressed by those cases refusing to take part in the project, which included feeling bothered by the daily visits, worrying about other people knowing he or she was sick, or unable to fit the project into their own schedule etc. From the project results, apart from the 2 participating cases (16.7%) died at the end of the project, 10 other participants were classified as cured (83.3%), with no defaulted cases. In comparison, the other 11 notified cases that were not included in the DOTS project had somewhat different outcomes, i.e. only 45.5% were cured and 9.1% defaulted (see the details in Table 2). Therefore, we could conclude that with the intervene of this project, Kinmen County TB cases had no defaulted situation in 2005.

Discussion

As far as Taiwan region is concerned, TB has the highest incidence rate among all notifiable infectious diseases. According to the report by Taiwan DOH in 2004 and 2005, the domestic TB incidence rate was 76.7 and 52.1 new cases per one hundred thousand capita respectively [16]. On the other hand, TB

incidence rate of Kinmen County at the same period was 36.7 (male: 53.0; female: 19.7) and 15.5 (male: 23.6; female: 6.6), respectively. This indicated that regardless in male or female cases, the TB incidence rate in Kinmen County was obviously much lower than Taiwan Main Island. Above figures certainly proved that in the past Kinmen County has done a good job in TB prevention and control. However, more TB related prevention and control policies are still needed due to situations below: (1) Taiwan now has more and more foreign labors and brides coming from Southeast Asian countries with high prevalence of TB incidence rate; (2) the open policy of "mini-three links" involving Kinmen and Matsu giving our residents more chances to be infected by TB; and (3) there are more and more active TB cases with partial treatment walking around in our society to make new case prevention harder than ever. All of the above reasons required immediate attention with more effective control strategy.

As we mentioned earlier in this article, WHO categorized "TB treatment results" into cured, completed treatment (no laboratory confirmation of cure), died, failed, defaulted, transferred, and not evaluated [14]. However, in our study, the subjects were chosen from Taiwan CDC TB database with limited resources, we were unable to match our cured, failed and defaulted results with the WHO definitions. Therefore, the researchers suggested to the CDC to file up each cases' complete medical records and sputum tests results (the case's preliminary three sets of sputum smear microscopic results as well as the last one taken in the fifth month of the treatment process) and classify them into cured, failed or defaulted according to the WHO definitions, and then keep all files in the "TB tracking and managing system" of the CDC TB database system in a hope that this modification would make our database and managing system fit in better with the global standard and make it easier for comparison in the future.

In our continuous efforts to promote TB prevention and control program, one that needs immediate attention is to effectively research and formulate a standard protocol to enhance DOTS coverage rate. This ideal protocol will be a management plan designed centered around the case to match his needs, including adjusting ways of taking medications (e.g. appropriate place to take the medication, frequency of the medication) to suit the case's life style; proper social and financial supports e.g. food, clothing, books supply, treatment allowance, subsidies for travel expanses for the case to see a doctor, etc.; overcome the community's cultural discrimination against TB e.g. house visiting health workers could dress casual clothes to minimize the emotional frustration of the case, or carry out daily house visits or supervision by non hospital medical staff or community volunteers. If we put together all these small points into practice, we can then improve the DOTS coverage rate more effectively [17]. During the period of our study for the project, we only provided the human resources to for medication supervision, and the DOTS coverage rate was 52.2% at the time. In order to improve the coverage rate more effectively so that we could extend DOTS program across all regions in Taiwan, the Taiwan CDC spend a budget of NT$ 180 million (about US$ 5.5 million) launching a nationwide campaign using the WHO recommended DOTS strategy. In this campaign, it not only provide funding to all cities and counties to cover the manpower costs for direct case caring program, but also allocates part of the funding for social and financial supports to the enrolled individual in an attempt to increase the DOTS coverage rates.

Defaulted cases are found to be a very important variable affecting TB prevention and control. In general, the main reasons resulting in for defaulted cases are poor compliance during treatment, interruption of the treatment, and not

having full understanding about the nature of TB by the individual case [18]. Although the duration of this study was only one year and a half, it demonstrated that those who joined the DOTS project clearly had a much better outcome when compared to previous years (without DOTS strategy). There was no defaulted case in this study, which again proved that the implementation of DOTS project obviously had a positive impact on the case management, especially on the aspect of case holding. However, the cured category did not show a clear improvement compared to the pre-DOTS project years. We assumed that the main reason for such outcome would be due to the fact that the "died" category accounted for 30% of the total in this particular project, which would have relatively pulled down the cured ratio.

In this study, selection bias could occur since the selection of the subjects was not by random allocation. As a result, those cases that died would have no way to join DOTS in the first place and hence the non-DOTS patients would have a higher death rate (five out of seven). However, the main limitation in our study was the fact that random allocation was not possible during the study due to limited case number (there were only 13 sputum smear positive cases) and timing. Nevertheless, there seemed to be no clear differences in the aspect of age and sex between the DOTS and the non-DOTS group, we believed that the outcomes from these two groups should still be compatible. Due to our small study size, we are afraid to draw any conclusions based on this study. However, DOTS has no doubt been proven to be the best method to stop TB and it is therefore necessary for us to continue our efforts to include it into our TB prevention and control policy.

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References

1. Dept. of Health, the Executive Yuan. An all-out mobilization campaign for cutting Taiwan TB population down in half in the next decade. 2006. (in Chinese)
2. World Health Organization. The global plan to stop TB, 2006-2015. 2006.
3. Hopewell PC. Impact of human immunodeficiency virus infection on the epidemiology, clinical features, management, and control of tuberculosis. Clinical Infectious Diseases 1992; 15: 540-547.
4. Selik RM, Chu SY, Buehler JW. HIV infection as leading cause of death among young adults in US cities and states. JAMA 1993; 269: 2991-2994.
5. Brudney K, Dobkin J. Resurgent tuberculosis in New York City. Human immunodeficiency virus, homelessness, and the decline of tuberculosis control programs. American Review of Respiratory Disease 1991; 144: 745-749.
6. World Health Organization. What is DOTS? A guide to understanding the WHO-recommended TB control strategy known as DOTS. In Geneva, World Health Organization 1999; 13p.
7. Chaulk CP, Pope DS. The Baltimore City Health Department program of directly observed therapy for tuberculosis. Clinics in Chest Medicine 1997; 18: 149-154.
8. Murray CJ, DeJonghe E, Chum HJ, et al. Cost effectiveness of chemotherapy for pulmonary tuberculosis in three sub-Saharan African countries. Lancet 1991; 338: 1305-1308.

9. Anonymous. Results of directly observed short-course chemotherapy in 112,842 Chinese patients with smear-positive tuberculosis. China Tuberculosis Control Collaboration. Lancet 1996; 347: 358-362.
10. World Health Organization tuberculosis handbook. Geneva, World Health Organization. 1998.
11. Dye C, Watt CJ, Bleed DM, et al: Evolution of tuberculosis control and prospects for reducing tuberculosis incidence, prevalence, and deaths globally. JAMA 2005; 293: 2767-2775.
12. Borgdorff MW, Floyd K, Broekmans JF. Interventions to reduce tuberculosis mortality and transmission in low- and middle-income countries. Bulletin of the World Health Organization 2002; 80 :217-227.
13. Chaulk CP, Moore-Rice K, Rizzo R, et al. Eleven years of community-based directly observed therapy for tuberculosis. JAMA 1995; 274: 945-951.
14. World Health Organization Global tuberculosis control: surveillance, planning, financing, WHO report 2006. Geneva, World Health Organization. 2006.
15. Promulgated definitions of TB database of Taiwan CDC (in Chinese): http://203.65.72.83/ch/dt/upload/QC/QC_index.htm.
16. Department of Health, the Executive Yuan, ROC. Public health in Taiwan area, Republic of China. Taipei. Department of Health, the Executive Yuan, ROC. 2005.
17. Chaulk CP, Kazandjian VA. Directly observed therapy for treatment completion of pulmonary tuberculosis: Consensus Statement of the Public Health Tuberculosis Guidelines Panel. JAMA 1998; 279: 943-948.
18. Hu HY, Tsai WC, Kung PC. A study on reasons why TB cases could not complete their therapeutic treatments. Taiwan Journal of Public Health 1995; 24: 345-356. (in Chinese)

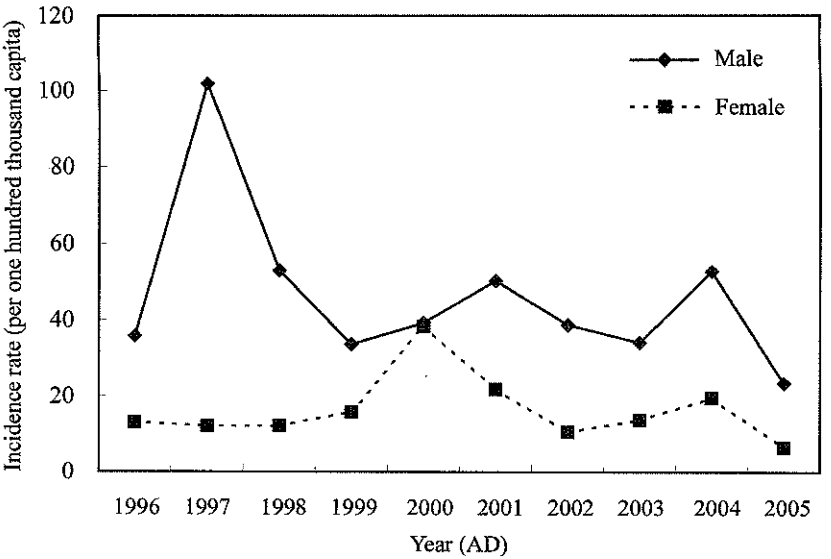

Figure 1. Variation of TB incidence rates of different sexes in Kinmen County between 1996 and 2005.

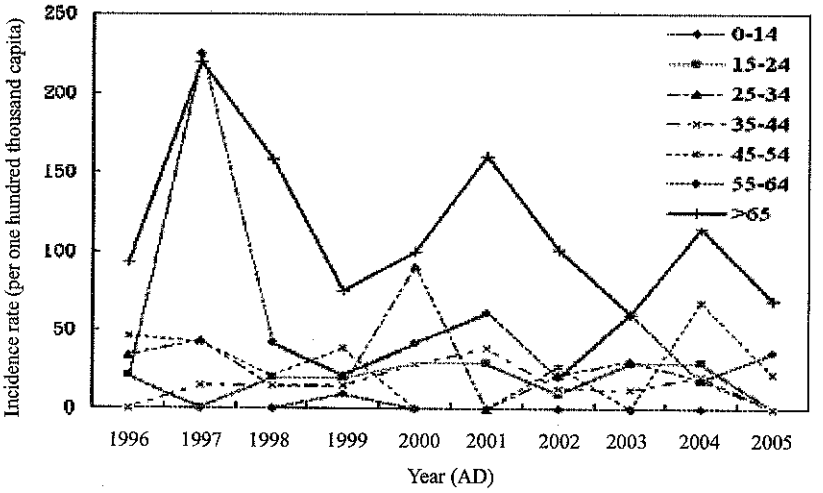

Figure 2. Variation of TB incidence rates of different age groups in Kinmen County between 1996 and 2005.

Table 1. Treatment result analysis of TB cases in Kinmen County between 1996 and 2005

Year reported	No. of cases (%)			
	Defaulted	Cured	Died	Total
1996	3 (25.0)	6 (50.0)	3 (25.0)	12 (100.0)
1997	5 (17.2)	15 (51.7)	9 (31.0)	29 (100.0)
1998	4 (23.5)	12 (70.6)	1 (5.9)	17 (100.0)
1999	3 (23.1)	7 (53.8)	3 (23.1)	13 (100.0)
2000	4 (19.0)	16 (76.2)	1 (4.8)	21 (100.0)
2001	4 (19.0)	14 (66.7)	3 (14.3)	21 (100.0)
2002	2 (13.3)	11 (73.3)	2 (13.3)	15 (100.0)
2003	1 (6.7)	12 (80.0)	2 (13.3)	15 (100.0)
2004	3 (12.5)	17 (70.8)	4 (16.7)	24 (100.0)
2005	0 (0.0)	7 (70.0)	3 (30.0)	10 (100.0)
Total	29 (16.3)	117 (66.1)	31 (17.5)	177 (100.0)

Table 2. Demographic information analysis of TB cases taking part in the Kinmen County DOTS project between July 2004 and December 2005 versus those left out of the project

	DOTS		Non-DOTS		Total
Sex	Female	Male	Female	Male	
	1	11	2	9	23
Age	50.4	62.4±11.9	86.0±4.1	60.2±22.5	63.2±17.5
DOTS duration (months)	5.8	6.3±3.4	—	—	—
Starting with smear positive	1	9	1	2	13
Treatment result No. of cases (%)					
Defaulted	0 (0.0)	0 (0.0)	0 (0.0)	1 (11.0)	1 (4.3)
Cured	1 (100.0)	9 (81.8)	0 (0.0)	5 (55.6)	15 (65.2)
Died	0 (0.0)	2 (14.3)	2 (100.0)	3 (33.3)	7 (30.5)
Total	1 (100.0)	11 (100.0)	2 (100.0)	9 (100.0)	23 (100.0)