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Original Article

Enhanced directly-observed treatment short-course for tuberculosis control program in mountain areas of Taiwan

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Abstract

Introduction: Directly Observed Treatment Short course (DOTS) is one of the most cost-effective approaches for TB treatment. However, TB incidence rates remain high in the mountain areas of Taiwan. A lay health advisor (LHA) strategy is integrated into DOTS as an Enhanced-DOTS (E-DOTS) to provide trustworthy, culturally-specific services in mountain areas that consider the characteristics of local ethnic groups.
Methodology: We recruited two Taiwanese indigenes as LHAs (one for each county) to screen close contacts in five townships of Hualien and Nantou counties from January 1, 2011 to December 31, 2013. Incidence and active finding rates of TB during the E-DOTS periods (2011-2013 for Hualien and 2012-2013 for Nantou) were compared with data when traditional DOTS was implemented (2006-2010 for Hualien and 2006-2011 for Nantou) to evaluate the effectiveness of E-DOTS using the before-and-after study design.
Results: Incidence rate in Hualien decreased from 393.3 in 2011 to 235.7 in 2013 per 100,000 population and from 338 in 2012 to 235.5 in 2013 in Nantou mountain area. Furthermore, the active case finding rate increased from 15.42% in 2012 to 27.38% in 2013 as compared to an average of 6.5% for CDC, Taiwan, for the specified years. TB treatment success rates were significantly improved from an average of less than 80% to an average of higher than 90% after E-DOTS was implemented.
Conclusions: Our findings highlighted that the use of LHAs in E-DOTS is an effective and applicable strategy for controlling tuberculosis in the mountain areas of Taiwan.

Key words: tuberculosis; enhanced-DOTS; lay health advisors; active case finding; close contact.

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Introduction

Tuberculosis (TB) is one of the most important infectious diseases around the world. In 2014, there were about 9.6 million new TB cases globally, leading to 1.5 million deaths annually [1]. In Taiwan, there were 11,326 TB cases (48.4 cases per 100,000 population) and 591 TB related deaths (2.5 cases per 100,000 population) in 2014 [2]. Although the incidence rate and death rate were reduced by 24.1% and 1.8%, respectively, compared to 2005, TB is still one of the most important public health issues in Taiwan.

Directly Observed Treatment Short course (DOTS) is one of the most cost-effective approaches to TB treatment [3,4]. The cure rate of TB was 82% among patients participating in the DOTS strategy worldwide, significantly higher than among those who did not take part in tDOTS (68%), in 2002 [5]. In Taiwan, the DOTS implementation rate among smear-positive patients reached 92.6% in December 2007 [6]. Furthermore, the incidence rate of TB has decreased from 72.5/100,000 in 2005 to 48.4/100,000 in 2014, ever since the implementation of DOTS at 2006 in Taiwan [2]. However, TB incidence rates remain even higher in the mountain areas [7]. This result may be related to the unique geographic environment in Taiwan: the central mountains mainly run north and south and the mostly rugged forest-covered mountains and hills account for two-thirds of the area of Taiwan. Human activities normally surround fertile soil and water, thus a special mountain village tribal lifestyle has tended to develop in the mountains. For instance, people living in the mountain areas have less medical resources and less access to medical services due to the vastness of their territory. Besides, residents living in the mountain areas

are mostly indigenes who frequently join social events such as religious activities, harvest festivals, wedding ceremonies and family gatherings. These activities increase the chance of transmission of TB [8].

The incidence of TB in Taiwan is known to be high in mountain areas [7,9]. According to the "Taiwan Tuberculosis Control Report 2014" [2], the TB incidence rate was 164.4/100,000 in mountain counties, three times higher than the national average (48.4/100,000) in 2014. This trend appears to be stable, as one study indicated that the TB incidence rate in indigenous population was 3.6-5.2 times higher than people not living in indigenous areas, between the years 1997-2001 [10]. This result is in line with the situation among American Indian/Alaska Native (AIAN) populations, where the indigenous group had a TB incidence rate seven times higher than non-Hispanic Whites [11]. Moreover, among Taiwanese indigenes, 32.7% of TB cases occurred at age 24-45 years, , which is different to their same-age counterparts living in non-indigenous areas, among whom the TB incidence rate is only 20.1% [10].

Not only the TB incidence rate but also the death rate was higher in mountain areas than in other regions. The most recent estimated mortality rate of TB in mountain areas was 8.0/100,000, higher than the national average of 2.7/100,000 in 2014.[2] Similar results were found in a survey during 1997 to 2001, when the mortality rate of TB in indigenous regions was 5.5-6.5 times higher than in other regions [10]. From the results of previous studies, the TB incidence rate and the death rate in mountain areas were still higher than the national averages [7]. This result implies that the TB case management protocol needs to be improved [12], and that the DOTS strategy had a limited effect on TB prevention in mountain areas.

Ineffective DOTS in mountain areas of Taiwan could be explained by three aspects: (1) from the patient side: poor access to medical resources/services due to living in the remote mountain area; (2) from the public health side: unable to obtain up-to-date epidemiological information and to perform effective contact investigations due to the vast territory; difficulty to apply DOTS strategies due to cultural differences; (3) from the medical side: delayed diagnosis and treatment, unable to retrieve first-hand information about treatment responses and side effects from patients immediately, resulting in treatment failure or loss. Therefore, visual supervision of drug administration was not applied to DOTS [6]. A modified DOTS strategy is needed solve the problems in the mountain areas, a new approach that would fit with the characteristics of local ethnic groups, especially indigenous ones. Lay health advisors (LHAs) have emerged as a potential strategy to reduce or eliminate health disparities [13]. For example, the LHA strategy has been validated to be effective among Latinos, increasing their ability to achieve health behavior or health status changes [14]. We hypothesized that LHA may be an effective approach for improving access to care, and to better health outcomes and health behaviors among people living in the mountain areas. Although the use of LHAs is widely advocated among many "underserved" populations [15-18], the empirical evidence to support their use with people living in mountain areas, particularly those with special ethnic or cultural background, is still lacking. This study reinforced the original DOTS framework by taking account of the geographical distribution of ethnic groups in Taiwan and their lifestyle to become the Enhanced-DOTS (E-DOTS) strategy. The aim of this study was to compare the TB incidence rate and clinical efficacy of the treatment under two different strategies: DOTS and Enhanced-DOTS, in mountain areas of Taiwan.

Methodology

Study design and population

The national TB registry database of Taiwan CDC contains data collected on TB cases; it was established in 1996 and recorded treatment outcomes during the DOTS and E-DOTS study period in Hualien county (Shlin, Wanrung and Zhuoxi townships) and Nantou county (Renai and Shini townships) mountain areas of Taiwan from January 1, 2011 up to December 31, 2013 and from January 1, 2012 up to December 31, 2013, respectively. Patients' databases were reviewed and data collected on sex, age, AFB and TBC, as well as status of participating in the E-DOTS strategy during treatment. We also collected data from January 1, 2006 to December 31, 2010 in Hualien and January 1, 2006 to December 31, 2011 in Nantou as control groups, when traditional DOTS was implemented. Therefore, patients were classified as DOTS and E-DOTS and were compared in a before-and-after study design. The final number of patients recruited for analysis was 1712, comprising 1239 subjects participating in DOTS and 473 in E-DOTS. The E-DOTS strategy employed indigenous case managers to screen close contacts by inquiring into TB cases' circle of friends and family life, as well as ensuring patients' adherence to TB treatment. Unlike the DOTS strategy, E-DOTS improved treatment adherence rate by strengthening case managers' language ability, knowledge of local

Table 1. Comparison of the DOTS and Enhanced-DOTS strategies.

DOTS	Enhanced-DOTS
Case manager - Ensure patients' compliance to treatment	**Indigene case manager** - Speaking the same language, knowing local habits and customs for effective case finding -Ensure patients' compliance to treatment
Active case finding - Screening the close contacts	**Active case finding** - Help with screening frequent visitors of index case and household contacts using chest x-ray

customs and life styles (see detailed comparison in Table 1). In the active case finding, sputum samples were collected for acid fast bacilli (AFB) smears and culture (TBC) test from TB contacts for definite diagnosis, if they had an abnormal chest x-ray result. Chest x-ray examination was performed for close contacts as well as for frequent visitors of index case and household contacts.

Recruitment and training of LHAs

The research team recruited case managers (LHAs) through the local public health office, based on four criteria: (1) being trusted community leaders who had been local residents for a period of time; (2) being aborigine with understanding of the local ethnic, cultural, linguistic, and topographic characteristics, so that it is easier to communicate with patients; (3) having an undergraduate or higher degree; (4) being willing and able to be trained as LHAs and to implement DOTS. In the present study, we recruited two Taiwanese indigenes as LHAs. One screened close contacts in three townships of Hualien County (a total of 28,162 residents with 97 TB cases in 2011) during 2011 to 2013, and the other did the same in two townships of Nantou County (a total of 32,654 residents with 109 TB cases in 2012) during 2012 to 2013.

The LHA training consisted of classroom instruction by doctors specialized in chest medicine, and field practice with public health nurses. Within a 1-week period the doctors provided a 2-3-hour course every morning on signs and symptoms of TB, DOTS, prescription for TB, and how to promote patient compliance to treatment. In the afternoons, local public health nurses accompanied by the case managers visited communities where patients lived to become acquainted with community leaders, patients and their families.

Data analysis

Demographic characteristics and laboratory findings were expressed as actual numbers and the corresponding percentages. The significant differences between groups of DOTS and E-DOTS were

Table 2. Demographic characteristics and laboratory findings of subjects during DOTS and E-DOTS periods in Nantou and Hualien counties.

	DOTS			Enhance-DOTS			
	Nantou 2006-2011 (n = 668)	Hualien 2006-2010 (n = 571)	total (n = 1239)	Nantou 2012-2013 (n = 184)	Hualien 2011-2013 (n = 289)	total (n = 473)	P value
Sex							
Male	457 (68.4)	372 (65.1)	829 (66.9)	131 (71.2)	194 (67.1)	325 (68.7)	0.477
female	211 (31.6)	199 (34.9)	410 (33.1)	53 (28.8)	95 (32.9)	148 (31.3)	
Age (years)							**0.089**
0-20	36 (5.4)	84 (14.7)	120 (9.7)	7 (3.8)	33 (11.4)	40 (8.5)	
21-30	53 (7.9)	54 (9.5)	107 (8.6)	17 (9.2)	20 (6.9)	37 (7.8)	
31-40	112 (16.8)	101 (17.7)	213 (17.2)	27 (14.7)	41 (14.2)	68 (14.4)	
41-50	149 (22.3)	117 (20.5)	266 (21.5)	38 (20.7)	62 (21.5)	100 (21.1)	
51-60	99 (14.8)	100 (17.5)	199 (16.1)	39 (21.2)	63 (21.8)	102 (21.6)	
61-70	75 (11.2)	48 (8.4)	123 (9.9)	24 (13.0)	37 (12.8)	61 (12.9)	
71-80	96 (14.4)	51 (8.9)	147 (11.9)	21 (11.4)	22 (7.6)	43 (9.1)	
81-90	45 (6.7)	16 (2.8)	61 (4.9)	11 (6.0)	10 (3.5)	21 (4.4)	
91-100	3 (0.4)	0 (0)	3 (0.2)	0 (0)	1 (0.3)	1 (0.2)	
Sputum							**0.145**
AFB (+) TBC (+)	313 (46.9)	304 (53.2)	617 (49.8)	97 (52.7)	140 (48.4)	237 (50.1)	
AFB (-) TBC (+)	258 (38.6)	160 (28.0)	418 (33.7)	48 (26.1)	96 (33.2)	144 (30.4)	
AFB (+) TBC (-)	14 (2.1)	15 (2.6)	29 (2.3)	2 (1.1)	4 (1.4)	6 (1.3)	
AFB (-) TBC (-)	81 (12.1)	78 (13.7)	159 (12.8)	34 (18.5)	45 (15.6)	79 (16.7)	
Not done/unknown	2 (0.3)	14 (2.5)	16 (1.3)	3 (1.6)	4 (1.4)	7 (1.5)	

Table 3. Active case finding of TB case in two mountain areas of Taiwan, 2011-2013.

Area	2011			2012			2013		
	Index patients	New case	Active case finding (%)	Index patients	New case	Active case finding (%)	Index patients	New case	Active case finding (%)
Nantou									
Renai	–	–	–	69	13	18.8	40	8	20.0
Shini	–	–	–	39	6	15.4	32	5	15.6
Hualien									
Shlin	71	12	16.9	73	11	15.1	47	10	21.3
Zhuoxi	22	5	22.7	12	2	16.7	15	9	60.0
Wanrung	16	2	12.5	18	2	11.1	10	2	20.0

determined using the Chi-square test. A *P* value less than 0.05 was considered to be significant. Data were analyzed and interpreted using SPSS version 21.0.

Results

DOTS relapse

A total of 1239 cases were registered with all forms of TB in the Nantou and Hualien mountain areas of Taiwan from 2006 up to 2011. Examinations done were similar between DOTS and E-DOTS in terms of gender, age and sputum results. The cases were mostly male(DOTS: 66.9%; E-DOTS: 68.7%) and the predominant age group was 41-60 years (DOTS: 37.6%; E-DOTS: 42.7%). Sputum examination results for AFB and TBC were alike between two groups. There were no significant statistically differences between DOTS and E-DOTS in terms of the basic demographic characteristics and sputum detection (Table 2).

The number of TB cases detected by active case screening were increasing annually in both Nantou and Hualien area.. The year with the highest number of TB cases detected by active case screening was in 2013 in Zhuoxi Township of Hualien (60.0%) (Table 3).

The TB incidence rate in Renai Township was higher than in Shini Township in Nantou County, whether DOTS or E-DOTS was implemented. Overall, the incidence rate remained stable when DOTS was applied throughout Nantou County, however, there was a trend to decline in the incidence rate when E-DOTS was applied in the same area (Figure 1A). Similarly, in Hualien County, Shilin Township continued to have the highest TB incidence rate whether under DOTS or E-DOTS; the incidence rate increased slightly when E-DOTS was first applied then declined afterwards (Figure 1B).

In line with the TB incidence rates, TB treatment success rates in Nantou and Hualien counties improved significantly after E-DOTS was implemented (Table 4). During DOTS periods (2006-2011 in Nantou and 2006-2010 in Hualien), TB treatment success rates were always less than 85% (ranging from 51.4% to 84.6%) in the five townships. However, in 2013, when E-DOTS had been implemented for one or two years, the rates were dramatically improved. to a satisfactory range from 82.5% to 100%.

Figure 1. Change of TB incidence rates (per 100,000) before and after the implementation of E-DOTS in two mountain areas of Taiwan, 2006-2013. (A) Natou county and (B) Hualien county. The E-DOTS was applied in Nantou county since 2012 and in Hualien since 2011. Before the implementation of E-DOTS, the DOTS was applied in both areas.

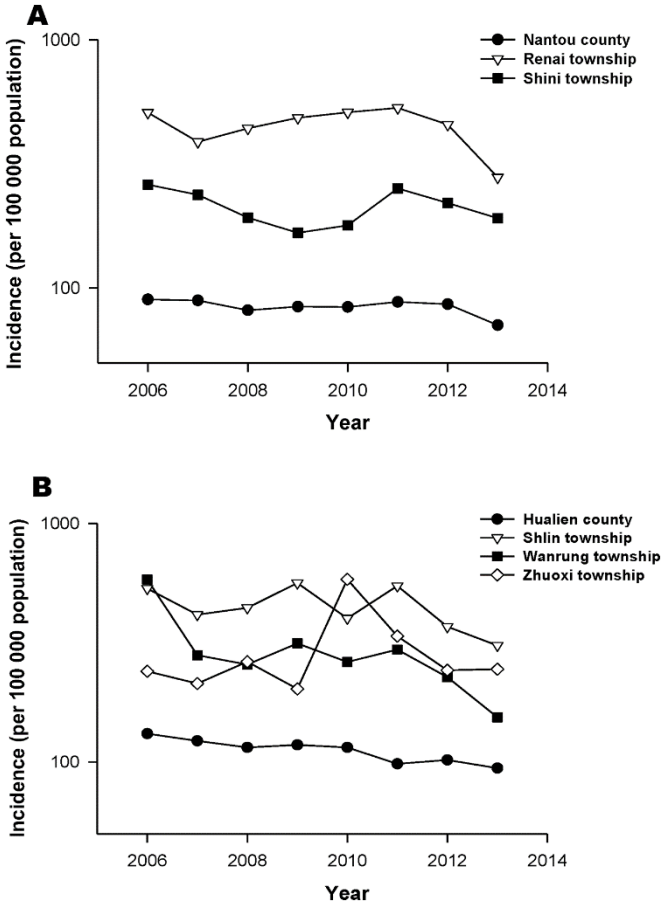

Table 4. TB treatment success rate during DOTS and E-DOTS periods in two mountain areas of Taiwan.

Area	Year							
	2006	2007	2008	2009	2010	2011	2012	2013
Nantou (DOTS was implemented during 2006-2011 and E-DOTS was implemented since 2012)								
Renai	72.7	74.0	80.0	82.4	73.8	82.1	81.4	84.6
Shini	61.9	56.3	62.1	61.5	60.7	73.2	60.6	96.7
Hualien (DOTS was implemented during 2006-2010 and E-DOTS was implemented since 2011)								
Shlin	79.2	78.7	77.4	81.3	82.0	87.5	76.8	82.5
Zhuoxi	81.8	58.8	62.5	71.4	74.2	87.5	57.1	92.3
Wanrung	51.4	72.7	84.6	72.2	58.8	68.8	53.8	100.0

Discussion

The main findings of this study highlight that the use of LHAs in DOTS, i.e., E-DOTS, can be an effective strategy to curb the incidence of TB and increase the case finding rate in mountain areas. After implementing E-DOTS, TB incidence rates significantly decreased both in Nantou and Hualien counties. These results may not arise from demographic characteristics as there were no statistically differences between DOTS and E-DOTS in terms of the basic demographic characteristics and screening results. The distributions of gender, age, and sputum test results were comparable between DOTS and E-. Moreover, the demographic characteristics and biologic screening results in this study were consistent with the data from the Ministry of Health and Welfare CDC TB survey [2]. Therefore, the decreased incidence rates of TB in the two mountain areas can most likely be attributed to the implementation of E-DOTS. The significant improvement in TB treatment success rates during 2011-2013 in both areas also supports the effectiveness of E-DOTS. The characteristics of TB cases in mountain areas are typified by males of a certain age group. Therefore, cases with the characteristics of elderly, male, AFB(+) and TBC(+) need more attention for TB prevention in Taiwan mountain areas in the future.

Findings from the index patients with active screening also demonstrated that E-DOTS is an appropriate strategy in mountain areas. During the study period, new case rates increased annually both in Nantou and Hualien Counties, and new contacts exceeded 10% each year. This finding is likely to be a result of the high risk of infection among close contacts of TB patients. According to a WHO database, TB subjects can transmit infection to 10-15 people via close contact within a year, and 2/3 of TB subjects will die without proper treatment [19]. To achieve effective TB control and prevention, besides treatment for TB subjects, control strategies that are designed and implemented by and for indigenous communities are needed. Also needed are effective partnerships between patients and health care professionals, and consideration for the socioeconomic conditions and cultural characteristics of the indigenous people, especially their languages [20-22]. Further, how to monitor close contacts needs to be addressed; these may include not only family members, as previous studies suggested, but should be broadened to include others with frequent contact with index cases, like colleagues, friends, church members and drinking buddies. Active case screening, early detection, and monitoring of contacts' pathogenesis can not only improve early diagnosis and treatment of TB, but also block the spread of TB [12].

E-DOTS as implemented in this study is modified from DOTS based on characteristics of indigenous groups from two Taiwan mountain areas. E-DOTS is different from DOTS in that indigenes were employed as case managers or lay health advisors, who sharelanguage, similary living habits and life patterns with the TB cases, enabling them to build better relationships with indigene TB cases. In addition, indigene LHAs can discuss and contact the health center immediately regarding regimen changes, once they have discovered any TB cases experiencing discomfort during treatment or an unsatisfactory treatment outcome. This an help to avoid defaulting and increase the DOTS adherence rate.. One previous study in Taiwan has supported this approachusing indigenous case managers, showing that they can significantly increase completion rate, efficiently follow up TB cases and contacts, and carry out active screening to provide early diagnosis and treatments, resulting in a decrease in the close contact incidence rate [12]. In summary, the success of E-DOTS in TB prevention is mainly due having LHAs who are community members with the same ethnicity and life experiences, linking TB cases or high risk groups in mountain areas to health providers and health service systems [13,23]. By being part of the care team, LHAs provide education, conduct outreach,

or serve as a navigators for TB cases and close contacts [17].

An effective case finding strategy can result in an improvement of treatment success rate. Our data showed that during 2006-2010 when DOTS was implemented in the two mountain areas, the TB treatment success rates among five townships were all less than 85% which is the world average value across the same period [24]. However, after the E-DOTS was implemented for 1-2 years, the TB treatment success rate for the five townships reached an average of 91%, much higher than the world average of 86%. This finding partly supports the effectiveness of implementig E-DOTS in mountain areas and incorporating the LHAs strategy.

A few limitations need to be considered in interpreting our findings. (1) The results were derived from secondary data analyses, therefore the effect of E-DOTS may be underestimated. (2) This study did not take into account potential confounders such as meteorological or socioeconomic changes therefore we cannot exclude the possibility that the changes in incidence and active case finding rates might be due to other confounding factors. (3) Only two counties were studied, which limits the generalization of our findings to other mountain areas in Taiwan or elsewhere.

Conclusion

E-DOTS is an effective strategy to decrease TB incidence rates and to increase TB active case finding rates and TB treatment success rates in two mountain areas,. The use of local lay health advisors is promoted as a strategy to address health disparities experienced by mountain communities in Taiwan. This success of E-DOTS in Taiwan provides a solution for the limited effects of DOTS in mountain areas, addressing problems on both the patient side and the public health side. As a result, a more acceptable, friendly, and comprehensive service can be provided for indigenous people living in mountain areas.

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